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1. Risk of Tuberculosis Infection in Young Children Exposed to Multidrug-resistant Tuberculosis in the TB-CHAMP Multi-site Randomized Controlled Trial.

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BACKGROUND: Young children have a high risk of developing tuberculosis (TB) disease following infection with Mycobacterium tuberculosis in the absence of preventive treatment. Infection prevalence and risk factors for infection impact delivery of prevention strategies. We aimed to determine the prevalence of infection in child household contacts aged <5 years exposed to adults with confirmed pulmonary multidrug-resistant (MDR)-TB and to determine risk factors for infection.
METHODS: TB-CHAMP was a trial of MDR-TB prevention that recruited children younger than age 5 years, regardless of M. tuberculosis infection status. All children enrolled had an interferon-gamma release assay (IGRA) at baseline. We described M. tuberculosis infection prevalence, developed directed acyclic graphs to clarify causal relationships, and used modified Poisson regression models to assess the relationship between risk factors and IGRA positivity.
RESULTS: Of 785 included children, 160 (20.4%) had a positive IGRA. Duration of cough and drug misuse in the index patient, age of the child, relationship between the child and the index patient, and study site were significantly associated with risk of infection.
CONCLUSIONS: The prevalence of infection was lower than observed in previous studies. This may be related to improved diagnosis and treatment of MDR-TB in the study setting and/or test limitations and has implications for TB preventive treatment. When considering TB preventive treatment for child contacts, healthcare providers should be especially concerned about any young child exposed to an adult index patient who is his/her parent/primary caregiver, has a

chronic cough, and/or a history of drug misuse.

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2. A Phase 2a Study of the Early Bactericidal Activity of Rifampicin in Combination With Meropenem Plus Amoxicillin/Clavulanate Among Adults With Rifampicin-Resistant Pulmonary Tuberculosis.

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BACKGROUND: In vitro, meropenem is shown to restore the activity of rifampicin in rifampicin-resistant Mycobacterium tuberculosis strains. This phase 2a trial aimed to determine if addition of rifampicin increases the early bactericidal activity (EBA) of meropenem plus amoxicillin/clavulanate in patients with rifampicin-resistant tuberculosis (RR-TB).
METHODS: Individuals with RR-TB were randomized to either 2 g meropenem infusion 3 times daily plus amoxicillin/clavulanate 500 mg/125 mg orally 3 times daily with 20 mg/kg rifampicin orally once daily (M-AC-R arm) or the same treatment without rifampicin (M-AC). Sputum samples were collected at baseline and throughout the 14-day treatment. Colony-forming unit (CFU) and time-to-positivity (TTP) data were analyzed using nonlinear mixed-effects modeling. Plasma samples at day 13 were used to derive rifampicin and meropenem

pharmacokinetic parameters using noncompartmental analysis. Rifampicin minimum inhibitory concentrations (MICs) were determined from baseline sputum isolates with and without meropenem.
RESULTS: Of the 52 participants enrolled, 38 participants completed the trial. The majority (67%) were male, and the median age was 37 years. The median (95% prediction interval) predicted 14-day EBA in CFU was 1.33 (-0.15 to 3.64) and 1.20 (0.05-2.66) log10 CFU/mL, and TTP increased by 0.220 (0.098-0.551) and 0.216 (0.126-0.505) log10 hours for the M-AC-R and M-AC arms, respectively. No statistically significant difference was found between the 2 arms. Meropenem pharmacokinetics were similar in both arms, and rifampicin MICs were not meaningfully reduced by meropenem.
CONCLUSIONS: Adding rifampicin to meropenem plus amoxicillin/clavulanate did not enhance short-term antibacterial activity in patients with RR-TB.

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3. Mycobacterium tuberculosis manipulates LINC02528 in macrophages to modulate anti-tuberculosis metabolic immunity.

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Host defenses are crucial in deciding the fate of Mycobacterium tuberculosis (Mtb) infections, as less than 10% of infected individuals develop tuberculosis. Oxidative stress plays a critical role in the host defense against Mtb. However, the mechanisms by which Mtb modulates redox homeostasis to evade immune responses remain poorly understood. In this study, we primarily identified a pathogen-responsive long noncoding RNA, LINC02528, which was selectively upregulated in peripheral blood mononuclear cells (PBMCs) from tuberculosis (TB) patients. In Mtb-infected macrophages, LINC02528 dynamically relocalizes from the nucleus to the cytoplasm. Functionally, CRISPR-Cas9-mediated knockout (KO) of LINC02528 in macrophages resulted in reduced Mtb survival concurrent with an elevated IL-1β expression. Importantly, these antimicrobial effects were abrogated by IL-1 receptor antagonist (IL-RA) treatment. Interestingly, LINC02528 was found to directly bind to TOMM22, a mitochondrial outer membrane translocase, as validated by co-localization analysis using in situ hybridization of lung tissue sections from a TB patient. The ECAR results revealed that LINC02528 deficiency significantly increased glycolysis and elevated Mtb-induced mitochondrial ROS (mtROS) production. Notably, TOMM22 knockdown phenocopied LINC02528 deletion effects, suggesting functional interdependence in modulating mitochondrial dynamics and the host's anti-TB immunity. Collectively, our findings reveal a novel strategy wherein Mtb hijacks the lncRNA-mitochondrial axis to rewire redox-metabolic checkpoints to favor immune evasion. Targeting LINC02528 could dually disrupt the pathogen-permissive redox balance and activate mtROS-IL-1β-mediated antimicrobial defense, offering novel therapeutic avenues for TB.

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4. Adverse Drug Reaction to Linezolid in Drug-Resistant Tuberculosis: A Systematic Review.

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Background/Objectives: The use of linezolid in drug-resistant tuberculosis has shown good effectiveness but has a high risk of adverse drug reactions (ADRs). Linezolid-related ADRs have been widely reported and may affect their therapeutic effect. This systematic review aimed to describe linezolid-related ADRs in drug-resistant tuberculosis. Methods: This literature review was conducted on PubMed, Scopus, ProQuest, and Sage without year limitation, up to June 2023. Study quality was assessed using the JBI checklist to evaluate method quality and risk of bias in the included articles. Inclusion criteria included studies assessing linezolid-correlated ADRs in drug-resistant tuberculosis patients with individual regimens, having access to the full text, and using the English or Indonesian language. Potential reporting bias was minimized by comprehensive database search and duplicate screening. Results: Initially, we identified 650 potential studies. Upon further assessment for relevance and eligibility, seven articles were selected for analysis. From seven articles, it was shown that all articles were reporting about linezolid-correlated ADRs. The three main ADRs are hematologic toxicity, peripheral neuropathy, and optic neuritis. In addition, gastrointestinal disorder and hyperlactatemia are reported as ADRs too. Varied doses of linezolid were used in the seven articles; they range from 300 mg to 1200 mg, with 600 mg/twice daily and 1200 mg/day being dominant. Conclusions: Linezolid-associated ADRs are dose- and duration-dependent. Hematological toxicity most commonly occurs at the beginning of treatment, while peripheral neuropathy and optic neuritis appear after long-term use. Therefore, intensive monitoring and therapeutic drug monitoring are essential to ensure the safety of linezolid therapy.

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5. Tre-DST: A Drug Susceptibility Test for Mycobacterium tuberculosis Using Solvatochromic Trehalose Probes.

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Update of
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In 2024, an estimated 10 million people developed Tuberculosis (TB), nearly half a million of whom were infected with drug-resistant tuberculosis (DR-TB). Early detection of infection and drug resistance enables rapid engagement in effective care. Bacterial culture and nucleic acid testing remain the primary diagnostic methods, with smear microscopy being phased out. However, these methods present significant limitations for diagnosing drug resistance, such as lengthy time-to-result for phenotypic tests, as well as the need for prior knowledge of resistance mutations and prohibitive cost for molecular tests. To address this, we developed a rapid phenotypic TB drug susceptibility test, termed Tre-DST, based on novel metabolically incorporated trehalose probes, which specifically detect live mycobacteria. We used the nonpathogenic Mycobacterium smegmatis and the virulence-attenuated Mycobacterium tuberculosis (Mtb) H37Ra or auxotrophic Mtb to demonstrate a strong correlation between cost-effective plate reader results and flow cytometry data, suggesting that the plate reader is a suitable fluorescence detector for Tre-DST. We determined that adding a 1-week incubation step allowed Mtb samples originally seeded at 104 CFU/mL to become detectable, over 2 weeks earlier than colony-forming unit analysis. We found that Tre-DST reports on drug susceptibility in a drug-agnostic manner, demonstrating loss of fluorescence with frontline TB drugs as well as the newer drug bedaquiline. Tre-DST distinguished RIF- and INH-resistant auxotrophs from susceptible controls and accurately reported the resistance activity. Ultimately, because Tre-DST is agnostic to mechanisms of drug resistance, this assay is likely compatible with all WHO-recommended and future DR-TB drugs as a diagnostic in reference laboratories.

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6. Multidrug-resistant tuberculosis (MDR-TB): an evolving threat to the Nigerian health system - a review.

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Multidrug-resistant tuberculosis (MDR-TB) is an increasing public health issue that threatens the efforts in the treatment and control of tuberculosis (TB) worldwide, including in Nigeria. According to the World Health Organization, there were 558 000 MDR-TB cases globally in 2019. Nigeria, being the most populous country in Africa, is said to carry a larger proportion of MDR-TB in the world. If not addressed promptly, many Nigerian populations will continue to suffer from MDR-TB, which could result in increased morbidity and mortality rates. Eliminating the threat of MDR-TB in Nigeria requires a multifaceted approach that combines national and international efforts. These approaches should be centered on the molecular testing of MDR-TB using line probe assays and GeneXpert MTB/RIF technology, which enables early and efficient diagnosis of Mycobacterium tuberculosis and TB drug resistance among patients in high-risk populations. Improvements can occur through the development and implementation of new treatment therapies and investment in research to discover additional treatment options for TB. Public awareness and education about the disease are also important. If these recommendations are implemented, they can significantly decrease the burden of MDR-TB in Nigeria.

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7. Analysis of the drug target of the anti-tuberculosis compound OCT313: phosphotransacetylase is a potential drug target for anti-mycobacterial agents.

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Tuberculosis (TB) is one of the most common infectious diseases caused by bacteria worldwide. The increasing prevalence of multidrug-resistant TB (MDR-TB)

and latent TB infection (LTBI) has intensified the global TB burden. Therefore, the development of new drugs for MDR-TB and LTBI is urgently required. We have reported that the derivative of dithiocarbamate sugar derivative, 2-acetamido-2-deoxy-β-D-glucopyranosyl N,N-dimethyldithiocarbamate (OCT313), exhibits anti-mycobacterial activity against MDR-MTB. Here, we identified the target of OCT313. In experimentally generated OCT313-resistant bacteria, adenine at position 1,092 in the metabolic enzyme phosphotransacetylase (PTA) gene was replaced with cytosine. This mutation is a nonsynonymous mutation that converts methionine to leucine at position 365 in the PTA protein. OCT313 inhibited the enzymatic activity of recombinant wild-type PTA, but not of the mutant PTA (M365L). PTA is an enzyme that produces acetyl-coenzyme A (acetyl-CoA) from acetyl phosphate and CoA and is involved in metabolic pathways; therefore, it was expected to also be active against dormant Mycobacterium tuberculosis bacilli. OCT313 exhibits antibacterial activity in the Wayne model of dormancy using Mycobacterium bovis BCG, and overexpression of PTA in OCT313-resistant bacilli restored sensitivity to OCT313. Collectively, the target of OCT313 is PTA, and OCT313 is a promising antimicrobial candidate for MDR-TB and LTBI.IMPORTANCEThrough this study, we propose a new target for the development of medicines to treat multidrug-resistant tuberculosis and latent tuberculosis infection. The target enzyme phosphotransacetylase (PTA) is a key enzyme that functions in major metabolic pathways, and the homologous structures of PTA enzymes vary greatly among bacterial species. Since the treatment of mycobacterial disease is long term, the development of antibiotics targeting PTA is useful for species-specific therapy.

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8. Diagnostic accuracy of the BD MAX MDR-TB assay on sputum and tongue swabs for Mycobacterium tuberculosis complex detection in adults under investigation for TB in South Africa.

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Despite the availability of molecular diagnostics, only 48% of newly diagnosed tuberculosis (TB) cases were confirmed using nucleic acid amplification tests in

2023. The MAX Multi Drug Resistant Tuberculosis (MAX MDR-TB) assay detects Mycobacterium tuberculosis complex (MTBC) and resistance to rifampicin (RIF) and isoniazid (INH), but data on clinical performance are limited. This study assessed the assay's performance on sputum and tongue swabs (TSs). The assay was evaluated for MTBC detection and RIF and INH resistance profiling on sputum using liquid culture as the reference and Xpert MTB/RIF Ultra (Ultra) as a comparator. Diagnostic accuracy for MTBC detection on TS was also assessed. Among 335 participants (56% HIV prevalence), MAX MDR-TB on raw sputum showed an overall sensitivity and specificity of 88.7% (95% confidence interval [CI]: 78.1-95.3) and 98.2% (95% CI: 95.8-99.4) compared with culture and strong agreement with Ultra (Cohen's kappa = 0.853). A total of 15/55 (27%) sputum samples were classified as "MTB low POS." Two false RIF-resistant results were observed. INH resistance was missed in two cases. Although specimen numbers were small, TS demonstrated better diagnostic accuracy when using a diluted sample treatment reagent (STR) (66%) buffer. Although the MAX MDR-TB assay demonstrated good agreement with Ultra, Ultra identified more TB cases. Preliminary findings suggest that TS, particularly with a diluted STR buffer, may be a feasible specimen type, but larger studies are required. The high frequency of MTB low POS results highlights the importance of technology assessment by TB programs prior to implementation to minimize repeat testing and enhance diagnostic reliability.
IMPORTANCE: This study evaluates the accuracy of the BD MAXTM MDR-TB assay in detecting Mycobacterium tuberculosis complex using sputum and tongue swabs from individuals being assessed for tuberculosis (TB) in South Africa. Rapid and reliable TB diagnosis is crucial for early treatment and preventing transmission. The MAX Multi Drug Resistant Tuberculosis (MAX MDR-TB) assay is a fully automated molecular test that can simultaneously detect TB and drug resistance, offering a potentially faster and more efficient alternative for TB diagnosis. By assessing its performance on different specimen types, this study provides valuable insights into its reliability in clinical settings. Although the MAX MDR-TB assay demonstrated strong agreement with the Xpert MTB/RIF Ultra assay, it identified fewer TB cases. Tongue swabs were also shown to be a feasible specimen type for testing. This research contributes to global TB control efforts by evaluating advanced diagnostics that could streamline testing, reduce delays, and ultimately improve patient outcomes.

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9. The Peak Plasma Concentration (Cmax)/Minimum Inhibitory Concentration (MIC) of bedaquiline and levofloxacin with special attention to the sputum conversion in

the treatment of multidrug-resistant tuberculosis in Indonesia.

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BACKGROUND: Tuberculosis in Indonesia remains a serious public health concern, as the country has the third-largest number of multidrug-resistant tuberculosis (MDR-TB) patients in the world. Bedaquiline and levofloxacin are the primary drug regimen for MDR-TB treatment in Indonesia. This study aimed to investigate whether the Cmax/MIC of bedaquiline and levofloxacin differs between patients with sputum conversion and those without sputum conversion during the first four months of MDR-TB treatment in Indonesia.
METHODS: A cohort study was performed in adult patients (18-65 years old) treated with the 18-24-month oral regimen. Patients were excluded if they were pregnant or HIV positive, with uncontrolled diabetes, or had any of the following severe conditions: cancer, digestive, cardiovascular system disorders, hepatic, or renal problems. Two blood samples were collected to measure the plasma concentrations of bedaquiline and levofloxacin using liquid chromatography-tandem mass spectrometry (LC-MS/MS). Mycobacterium tuberculosis (Mtb) isolates from patients' sputum were used to determine the MIC of individual drugs using liquid growth media (MGIT).
RESULTS: Among the 74 patients enrolled, 16 dropped out during the four-month follow-up period. Blood samples were successfully obtained 1-2 hours after drug

administration from 48 patients and 4-6 hours after drug administration from 32 patients, which were used for pharmacokinetic analysis. Sputum conversion was detected in 84.5% of patients during four months of the MDR-TB treatment. The mean Cmax/MIC ratio of bedaquiline was higher in the sputum conversion group compared with the non-conversion group (9.10 vs. 1.65, respectively). Meanwhile, a small difference in the Cmax/MIC ratio of levofloxacin was observed between the sputum conversion group and the non-conversion group; it was not significant (45.64 vs. 41.72, respectively; p = 0.941).
CONCLUSIONS: Cmax/MIC of bedaquiline was higher in MDR-TB patients with sputum conversion compared to those without conversion within the first four months of treatment, suggesting a potential relationship between Cmax/MIC of bedaquiline and sputum conversion, which was not seen in the levofloxacin cases. However, the application of clinical practice should be carefully considered and supported by further study in various settings.

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10. Effect of smoking on drug-resistant tuberculosis treatment outcomes and potential mechanistic pathways: a multicountry cohort study.

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Update of
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BACKGROUND: People who smoke are at increased risk of unfavourable tuberculosis treatment outcomes compared with those who do not, but the pathways that explain this disparity are unclear.
OBJECTIVE: To estimate the difference in a successful end-of-treatment outcome by smoking status among people with multidrug- or rifampicin-resistant tuberculosis (MDR/RR-TB) and to examine if this difference changes if people who smoked had the same retention in treatment as those who did not smoke.
DESIGN AND METHODS: Using data from the prospective endTB Observational Study, we estimated the difference in treatment success by cigarette smoking status, adjusting for baseline confounders including demographics, social history and comorbidities. To examine how this difference changed if everyone was retained in treatment, we censored participants who were lost to follow-up and applied inverse probability of censoring weights to simulate this scenario.
RESULTS: Among 1786 participants in 12 countries, 539 (30.2%) reported smoking at least one cigarette daily. People who smoked were more frequently found in post-Soviet countries and had a complex social history (eg, incarceration and substance use) and infectious comorbidities (eg, hepatitis C). At the end of treatment, 73.5% of people who smoked and 80.3% of people who did not smoke had treatment success (risk difference in percentage points: -6.8, 95% CI -11.1 to -2.6). After adjusting for baseline confounders, the risk difference was similar (-5.2 percentage points), but the 95% CI was less precise (-14.1 to 3.2). When simulating a scenario in which everyone was retained in treatment, the risk difference was attenuated (-1.9 percentage points; 95% CI -11.1 to 4.7).
CONCLUSION: People who smoked had a lower frequency of MDR/RR-TB treatment success than those who did not smoke. Eliminating loss to follow-up reduced this difference by smoking status, suggesting that pathways related to retention in treatment were a major driver of this disparity.

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11. Saturation mutagenesis identifies activating and resistance-inducing FGFR kinase domain mutations.

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Variants of uncertain significance represent the biggest challenge for genomics-based precision oncology. Activated fibroblast growth factor receptors (FGFRs) frequently drive tumorigenesis by different genetic aberrations. However, it remains unknown which of the many point mutations affecting FGFR1, FGFR2, FGFR3 or FGFR4 in cancer are druggable, that is, activating signaling while not mediating FGFR inhibitor resistance. Here we implemented a saturation mutational scanning platform to screen all 11,520 possible point mutations covering the kinase domains of FGFR1-4. Pooled positive selection screens identified 474 activating and 738 mutations mediating resistance to the FGFR inhibitors pemigatinib and futibatinib, together revealing 301 druggable FGFR mutations analogous to a strong PS3/BS3 evidence level. The screens also identified loss-of-function mutations and an association of gain-of-function mutations with hydrophobic changes. The functional screens identified 97% of acquired resistance mutations in clinical trials. Our comprehensive catalog of every druggable mutation in the FGFR kinase domains is readily available for clinical decision support.

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12. Development of machine learning models to identify potentially active compounds against tuberculosis.

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Tuberculosis (TB) is a contagious bacterial disease affecting millions of people globally and is one of the major causes of morbidity and mortality, particularly in the developing world. The spread of multi-drug-resistant (MDR) and extensively drug-resistant (XDR) tuberculosis has emerged as a major challenge to TB treatment, demanding the discovery of novel drug candidates. The process requires fast and efficient lead identification methodologies. This research content embarks on a comprehensive exploration of machine learning algorithms applied to identify potential compounds active against TB. Leveraging a comprehensive dataset encompassing 23,791 molecules from 5 targets with unique SMILES and ChEMBL IDs obtained from the ChEMBL database, a total of 103 classification models were developed based on six different types of molecular representations, namely RDKit descriptors (RDKitDes), MACCS fingerprints (MACCSFP), Morgan fingerprints (MorganFP), Atom-pair fingerprints (PairsFP), PubChem fingerprints (PubChemFP), and RDKit fingerprints (RDKitFP). In this

regard, seven machine learning algorithms, e.g., Random Forest (RF), XGBoost, Decision Tree (DT), k-Nearest Neighbors (KNN), Gaussian Naive Bayes (GNB), Logistic Regression (LR), and ANN, were employed to build these models using different combinations of dataset. Further, the performance of the models was assessed using a tenfold cross-validation, with the area under the receiver operating characteristic curve (AUC) as the evaluation metric. In addition to that, the contribution of the important descriptors in the molecule's bioactivities was interpreted using the SHapley Additive exPlanations (SHAP) method.

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13. Different MicroRNAs expression in Mycobacterium tuberculosis and correlation with prognosis of the disease.

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Tuberculosis, caused by Mycobacterium tuberculosis, is an infectious disease linked to high mortality and can stay in the host cell longer when inactive. Multiple factors are linked to disease prognosis, including microRNAs. It is a diminutive single-stranded RNA that regulates the expression of its target mRNAs. It consists of a brief nucleotide sequence, often 19-25 nucleotides in length, of non-coding RNA. It is also essential for early embryonic development, invasion, cell migration, apoptosis, and cell death. The review aims to analyse the transcriptome characteristics of various miRNAs in the tuberculosis prognosis. However, miR-155, miR-29, circ-miRNA, and lncRNAs regulate gene expression. In TB patients' serum exosomes, miRNA-146 expression was noticeably higher than in healthy individuals. Drug-resistant tuberculosis was related to miR-548 m, miR-631, miR-328-3p, and miR-let-7e-5p, as well as let-7b-5p, miR-30a-3p, IL-27, and CXCL9/10/11 in TB patients' lesion tissue and peripheral blood. Therefore, further miRNA research will focus on TB progression.

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14. Diagnostic performance of the Sanity 2.0 assay to detect resistance to rifampicin, isoniazid, and fluoroquinolones in tuberculosis.

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Effective tuberculosis (TB) management relies on prompt diagnosis of Mycobacterium tuberculosis complex (MTBC) and associated drug resistance. The Sanity 2.0 assay is a high-resolution melting assay designed for direct respiratory sample testing, enabling simultaneous detection of MTBC and resistance to rifampicin (RIF), isoniazid (INH), and fluoroquinolones (FQ) in a single step. This study evaluated its diagnostic performance in two registered multicenter trials among bacteriologically confirmed TB patients. Diagnostic performance was evaluated for MTBC detection, as well as for the identification of resistance to RIF, INH, and FQ, using phenotypic drug susceptibility testing, whole-genome sequencing, and a composite reference standard. Agreement analyses were conducted between the Sanity 2.0 assay and Xpert MTB/RIF and Xpert MTB/XDR. Among 611 patients, the Sanity 2.0 assay detected MTBC in 563 patients, exhibiting a sensitivity of 92.1% (95% CI: 89.7-94.0). For detecting resistance to RIF, INH, and FQ, sensitivities exceeded 90%, with specificities of 95.8% (95% CI: 88.5-98.6), 100.0% (95% CI: 96.4-100.0), and 97.8% (95% CI: 93.8-99.3) against the composite reference standard, respectively. The agreement with Xpert MTB/RIF for RIF detection was 98.6% (95% CI: 96.9-99.3). For INH and FQ resistance, the agreement with Xpert MTB/XDR was 92.0% (95% CI: 88.5-94.5) and 94.3% (95% CI: 91.2-96.3), respectively. The Sanity 2.0 assay is a rapid and user-friendly platform capable of detecting both MTBC and key drug resistance. It demonstrated good diagnostic performance and could potentially be an

effective alternative to guide individualized anti-TB treatment, especially in resource-limited settings.
IMPORTANCE: Rapid and accurate detection of both Mycobacterium tuberculosis complex (MTBC) and key drug resistance is critical to improving tuberculosis treatment outcomes and reducing transmission. However, current molecular diagnostic workflows often require sequential testing, which can delay the initiation of effective and individualized therapy. We evaluated the Sanity 2.0 assay, an integrated high-resolution melting test that simultaneously detects MTBC and resistance to rifampicin, isoniazid, and fluoroquinolone resistance directly from respiratory samples in about 2-3 hours. The assay demonstrated excellent performance, with MTBC detection sensitivity of 92.1% and drug resistance sensitivities exceeding 90% and specificities over 95% against a composite reference standard, as well as strong concordance with World Health Organization-endorsed molecular assays. Implementation of the Sanity 2.0 assay could streamline TB diagnostic workflows; enable rapid, single-step resistance profiling; and facilitate timely, individualized treatment-particularly in resource-limited settings where rapid and comprehensive resistance testing remains a critical unmet need.

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15. Insights from aquaporin structures into drug-resistant sleeping sickness.

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Update of
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Trypanosoma brucei is the causal agent of African trypanosomiasis in humans and animals, the latter resulting in significant negative economic impacts in afflicted areas of the world. Resistance has arisen to the trypanocidal drugs pentamidine and melarsoprol through mutations in the aquaglyceroporin TbAQP2 that prevent their uptake. Here, we use cryogenic electron microscopy to determine the structure of TbAQP2 from T. brucei, bound to either the substrate glycerol or to the sleeping sickness drugs, pentamidine or melarsoprol. The drugs bind within the AQP2 channel at a site completely overlapping that of glycerol. Mutations leading to a drug-resistant phenotype were found in the channel lining. Molecular dynamics (MD) simulations showed the channel can be traversed by pentamidine, with a low energy binding site at the centre of the channel, flanked by regions of high energy association at the extracellular and intracellular ends. Drug-resistant TbAQP2 mutants are still predicted to bind pentamidine, but the much weaker binding in the centre of the channel observed in the MD simulations would be insufficient to compensate for the high energy processes of ingress and egress, hence impairing transport at pharmacologically relevant concentrations. The structures of drug-bound TbAQP2 represent a novel paradigm for drug-transporter interactions and are a new mechanism for targeting drugs in pathogens and human cells.

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16. Multidrug-resistant tuberculosis involving breast and adnexa uteri: a case report and literature review.

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BACKGROUND: Multidrug-resistant tuberculosis (MDR-TB) remains a major global public health challenge, whereas extrapulmonary involvement is relatively uncommon. Here, we report a rare case of disseminated MDR-TB presenting with simultaneous involvement of multiple organs. A review of the literature identified a single previously reported case of MDR-TB of the breast and six cases involving the female reproductive system, and none exhibited a pattern of organ involvement or microbiological characteristics comparable to those observed in the present case.
CASE PRESENTATION: A 33-year-old woman presented with a five-month history of breast swelling and pain, accompanied by fever for three days. Microbiological testing confirmed disseminated MDR-TB with simultaneous involvement of the lungs, breast, and adnexa uteri. The patient showed marked clinical improvement following individualised, guideline-based anti-tuberculosis therapy.
CONCLUSION: This case highlights the exceptional rarity of MDR-TB with atypical multi-organ involvement and underscores the importance of maintaining high clinical suspicion for tuberculosis in uncommon sites. Early implementation of comprehensive microbiological and drug resistance assessments, followed by appropriate standardised therapy, is essential to prevent diagnostic delay and improve clinical outcomes.

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authors declare no competing interests.

17. Application of FreezeTB, a targeted nanopore sequencing assay, for identification of drug resistance and lineages among pulmonary tuberculosis cases in Alaska.

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Alaska has the highest incidence of tuberculosis (TB) in the United States, with 8% mortality while undergoing TB treatment. With a quarter of TB cases lacking sputum culture to enable drug resistance testing, FreezeTB aimed to develop tools tailored to meet the challenges in Alaska while being translatable to other settings. We designed a rapid and cost-effective laboratory workflow and software to identify drug-resistant mutations in Mycobacterium tuberculosis using targeted next-generation sequencing (tNGS). FreezeTB, a Fast, Reliable, Economical Evaluation tool to Zap Endemic Tuberculosis, amplifies 22 gene loci associated with resistance to 16 anti-tuberculosis drugs. M. tuberculosis isolates from Alaska (2011-2024) were blinded and underwent analysis with FreezeTB, then compared with phenotypic drug susceptibility testing (pDST) and whole genome sequencing (WGS). Compared with WGS (n = 79), FreezeTB provided the same mutations in 96% (n = 76/79) of samples with 100% lineage agreement (n = 79/79). Compared with pDST using Cohen's kappa, FreezeTB had almost perfect agreement for rifampin (RIF, 0.90; n = 97/98) and ethambutol (EMB, 1.00; n = 98/98), strong agreement for isoniazid (INH, 0.80; n = 88/98), moderate

agreement for ethionamide (ETO, 0.78; n = 95/98), weak agreement for streptomycin (STR, 0.56; n = 95/98), and no agreement for pyrazinamide (PZA, 0.20; n = 91/98). Using a portable nanopore sequencer, each sample cost under $30 for sequencing, which included a flow cell, a barcoding kit, a flow cell wash kit, a polymerase, and primers. FreezeTB provides a portable, 1-day laboratory and bioinformatic workflow for sequencing M. tuberculosis. Freeze TB can accurately determine mycobacterial lineage and resistance for RIF, INH, ETH, and ETO at a low cost.IMPORTANCEGlobally, tuberculosis is the leading infectious cause of mortality with 10.8 million new cases and 1.25 million deaths occurring in 2024. Targeted next-generation sequencing (tNGS) is a rapid, cost-effective method for identifying mutations in the Mycobacterium tuberculosis genome associated with drug resistance. FreezeTB was created to provide low-cost, portable sequencing and tNGS analysis for drug resistance. FreezeTB selectively amplifies and sequences 24 targets of the M. tuberculosis genome that cover regions the WHO has designated as containing mutations conferring drug resistance, as well as provides species confirmation and rapid lineage determination. Freeze TB is a laboratory workflow and free, open-source (OS) low dependency bioinformatic software that can be downloaded onto a computer with no further need for internet access. Using M. tuberculosis isolates from Alaska, FreezeTB provided the same mutations in 96% (n = 76/79) of samples with 100% lineage agreement (n = 79/79) compared with whole genome sequencing.

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18. The Structure, Properties, and Clinical Utility of Contezolid for Antituberculosis: A Narrative Review.

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Tuberculosis (TB) continues to represent a significant global public health concern, with China being a country that bears the burden of a high incidence of TB cases on a global scale. Although linezolid (LZD) has been recommended for treating drug-resistant tuberculosis (DR-TB), its intolerability and adverse events, such as myelosuppression, neurotoxicity, etc., have limited its long-term usage in anti-TB treatment. Contezolid (CZD), a new generation of oxazolidinone drug, shows comparable or superior antibacterial activity to LZD, with lower risks of myelosuppressive toxicity, neurotoxicity, and lactic acidosis. Its unique metabolic pathway and favorable pharmacokinetic profile render it a promising alternative to LZD for TB treatment. Recent years have seen mounting evidence of the potential of CZD in treating TB. In this paper, the development history, the mode of action, resistance mechanisms, and research progress on CZD for TB treatment are reviewed, aiming to enhance understanding of its role in anti-TB therapy and to provide valuable references for clinical use and future research.

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19. Transforming pulmonary care with applications of endobronchial valves beyond emphysema: a narrative review.

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BACKGROUND AND OBJECTIVE: Endobronchial one-way valves (EBVs) were originally developed for lung volume reduction in severe emphysema. Because EBVs allow unidirectional airflow, they have been used off-label to manage persistent air leaks (PALs)/bronchopleural fistulas (BPFs), haemoptysis, cavitary tuberculosis (TB), and other complex pulmonary conditions. This review summarises the evidence of endobronchial valve applications beyond emphysema.
METHODS: We conducted a narrative review of English-language literature from January 1, 2000 to August 1, 2025, searching PubMed, Embase, Scopus, and Google

Scholar for clinical trials, observational studies, case series, and case reports describing EBV use beyond emphysema. The selection of articles was based on relevance to the topic, with emphasis on clinical outcomes. No formal quantitative synthesis was performed given the narrative scope.
KEY CONTENT AND FINDINGS: Across case series, EBV placement achieves cessation or substantial reduction of air leaks in roughly half to 80% of patients with postoperative or spontaneous BPFs, often allowing chest tube removal within days and avoiding reoperation. Reported complications are uncommon and include valve migration, expectoration, transient hypoxaemia, and localized infection. Case reports indicate EBVs can serve as emergency bronchoscopic plugs to control massive haemoptysis when conventional therapy fails. Emerging evidence in multidrug-resistant TB shows that collapse therapy using EBVs alongside appropriate chemotherapy accelerates sputum culture conversion and cavity closure; in a randomized trial, EBV treatment markedly improved culture conversion and long-term cure rates compared with chemotherapy alone. EBVs have also been used in critical care settings to isolate injured lungs and facilitate weaning from mechanical ventilation or extracorporeal membrane oxygenation (ECMO).
CONCLUSIONS: EBVs have evolved into a versatile tool in pulmonary medicine, extending well beyond emphysema treatment. The literature to date indicates that EBVs can effectively seal PALs, control focal pulmonary haemorrhage, and induce therapeutic lung collapse in cavitary disease-all with a minimally invasive approach. EBVs hold significant promise for improving patient care in challenging scenarios, and further research is warranted.

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20. Pharmacokinetics and Safety of Clofazimine in Women With Rifampicin-resistant Tuberculosis During Pregnancy and the Postpartum Period: Results From IMPAACT P1026s.

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BACKGROUND: There are no published data on clofazimine pharmacokinetics during pregnancy, and safety data are limited. We present data from pregnant and postpartum women receiving clofazimine for treatment of rifampicin-resistant tuberculosis (RR-TB).

METHODS: IMPAACT P1026s was an observational study to assess the pharmacokinetics of tuberculosis and/or antiretroviral drugs during pregnancy. Between 2017 and 2019, pregnant women receiving ≥2 second-line antituberculosis drugs in routine care were enrolled in the second or third trimester and had intensive pharmacokinetic sampling at least once during pregnancy, and 2-8 weeks postpartum. Pharmacokinetic parameters were estimated using noncompartmental methods and compared between the antepartum and postpartum periods using geometric mean ratios (GMR) with 90% confidence intervals (CIs) and the Wilcoxon signed rank test for paired data.
RESULTS: Eleven pregnant women from South Africa, 7 (64%) with HIV, were receiving clofazimine (100 mg daily) at enrollment, of which 82% received clofazimine for more than 8 weeks prior to pharmacokinetic evaluation. Nine (82%) women continued treatment postpartum. Peak plasma concentrations and area-under-the-concentration-time-curve over 12 hours were comparable to historical clofazimine pharmacokinetic data in nonpregnant women with RR-TB but were approximately 30% higher in the third trimester of pregnancy compared to the postpartum period. Eight women and 8 infants experienced at least one severe adverse event while on study but direct relatedness to clofazimine was considered unlikely.
CONCLUSIONS: Overall, antepartum and postpartum clofazimine exposures were comparable to those reported in nonpregnant women with RR-TB. Exposures were lower than expected in the postpartum period, particularly compared with the third trimester of pregnancy.

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21. The genetic diversity of drug resistance in Mycobacterium tuberculosis strains from the Tibetan Plateau.

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OBJECTIVE: This study aimed to characterize the genetic diversity of drug resistance in Mycobacterium tuberculosis (MTB) isolates from the Tibetan Plateau, elucidate the molecular epidemiological profile of tuberculosis (TB) in this high-altitude region, and offer a molecular basis to guide improved diagnostic, therapeutic, and preventive strategies.
METHODS: A total of 169 clinical MTB isolates were collected from the General Hospital of Xizang Military Command between January 2024 and April 2025. Drug resistance-associated mutations were identified via targeted gene sequencing.
RESULTS: Among the 169 isolates, the overall rate of genotypic resistance was 20.71 %, comprising mono-resistance (14.79 %), poly-resistance (1.78 %), and multidrug-resistance (MDR, 4.14 %). Retreated patients exhibited a higher resistance rate than newly treated cases (26.09 % vs. 14.29 %), with MDR exclusively identified in the retreatment group. Resistance to streptomycin was most prevalent (8.28 %), followed by isoniazid (7.69 %) and rifampicin (7.10 %). The predominant mutations observed were rpsL K43R and katG S315T. No mutations conferring resistance to second-line drugs were detected.
CONCLUSION: The substantial burden of drug-resistant TB on the Tibetan Plateau-particularly streptomycin resistance-underscores the critical need for implementing precision diagnostics and optimizing therapeutic regimens.

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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.

22. Relapse and Emergent Resistance With Novel Short-Course Regimens for Multidrug-Resistant Tuberculosis, United States, 2022-2024.

Open Forum Infect Dis. 2026 Jan 14;13(1):ofaf786. doi: 10.1093/ofid/ofaf786. eCollection 2026 Jan.

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BACKGROUND: Bedaquiline, pretomanid, and linezolid with or without moxifloxacin (BPaL/M) are recommended oral 6-month treatment regimens for multidrug- or

rifampin-resistant (MDR/RR) tuberculosis (TB). Since the US rollout of these regimens in 2019, the US Centers for Disease Control and Prevention (CDC) and partners have identified patients who failed or relapsed on these regimens.
METHODS: Here, we report a case series of US patients with TB treated with BPaL/M-containing regimens, who experienced adverse outcomes during the period 2022–2024, including drug resistance, relapse, and treatment failure.
RESULTS: Clinical and public health outcomes were significant for US patients reported. There were 8 patients identified (n = 8). 5 (62.5%) were male, with a median age 57 years, 2 (25%) were previously treated for TB, and 8 (100%) presented with cavitary disease. This included a patient who died from infectious TB with acquired resistance after exposing over 100 healthcare workers, a waitress who was found to have highly infectious TB at the time of her relapse, and a son who contracted Mycobacterium tuberculosis (Mtb) with reduced activity to bedaquiline from his mother in a household transmission event.
CONCLUSIONS: These patients highlight consequences, both for the individual and public health, of relapse and treatment failure in real-life operational settings that may not be readily evident in well-controlled and well-resourced clinical trials. Despite the advent of shorter and better tolerated bedaquiline-based regimens, US clinicians continue to face challenges in managing drug-resistant TB. These data support the need for expert management of these patients beyond routine TB care, as well as the need for close monitoring and follow-up months after treatment completion.

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23. Evaluation of tuberculosis education effects on healthcare workers' knowledge attitudes and practices in Jiangsu China 2019 to 2023.

Sci Rep. 2025 Dec 24;15(1):44437. doi: 10.1038/s41598-025-28031-4.

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Tuberculosis (TB) remains a global health concern, and healthcare workers (HCWs) face a relatively high risk of TB infection because of their frequent exposure. This study evaluated the effectiveness of a TB infection control education program implemented in Jiangsu Province, China, by assessing changes in HCWs' knowledge, attitudes, and practices (KAP). This study, carried out from December 2019 to October 2023, included pre- and post-intervention surveys administered to HCWs in selected drug-resistant hospitals. The Wilcoxon rank-sum test was used to assess the changes in KAP scores before and after the implementation. Additionally, multivariate regression and Spearman correlation tests were conducted to explore potential relationships between KAP scores and factors such as gender, age, duration of employment, department, and program participation. The mean score for knowledge and attitudes increased after the implementation (7.40 vs. 9.96, p = 2.769e-15; 35.29 vs. 36.05, p = 0.008652). In contrast, the practice score slightly decreased (39.22 vs. 37.14, p = 0.003767), which may be due to many "not applicable" answers. Moreover, a positive, weak but significant relationship was observed between attitudes and practices. This study revealed significant improvements in knowledge and attitude and a slight decrease in the practice scores, indicating that education led to enhanced knowledge and attitude, but greater efficacy in translating knowledge into practice is needed. The correlation between attitude and practice indicates further efforts to improve HCWs' attitudes to potentially enhance their practice, thereby diminishing the risk of TB infection.

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24. Drug-resistant TB treatment outcomes and factors associated with discontinuation and LTFU in Germany: No1Lost study protocol.

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Treatment discontinuation, including loss to follow-up (LTFU), is an important challenge for TB treatment, particularly for multidrug- or rifampicin-resistant TB (MDR/RR-TB). Evidence from low-incidence countries evaluating risk factors for unsuccessful outcomes is scarce. Our study aims to examine treatment outcomes and factors associated with treatment discontinuation for MDR/RR-TB patients in the German health care setting. This observational prospective, multi-centre cohort study will enrol 150 MDR/RR-TB patients in treatment centres between 2025 and 2027. Primary outcome is the description of treatment results. Exploratory analyses will be performed, including logistic regression to assess demographic, clinical, and important factors like social determinants possibly associated with treatment discontinuation. Secondary outcomes will include the descriptive analysis of outcomes and safety of the recently recommended 6-9 months and longer MDR/RR-TB regimens, barriers for adherence to TB guidelines and the clinical structures for MDR/RR-TB management. The prospective No1Lost MDR/RR-TB cohort study will improve the understanding of risk factors and barriers for treatment discontinuation and LTFU in a low-incidence setting to address high rates of treatment discontinuation in this vulnerable population with targeted interventions.

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25. Construction of a diagnostic model for tuberculosis based on long non-coding RNA.

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BACKGROUND: The World Health Organization encourages the development of novel diagnostic tools based on 'non-sputum' samples to meet global goals for tuberculosis (TB) control. We aimed to develop a machine learning-driven model for TB diagnosis, using long non-coding RNAs (lncRNAs) as biomarkers.
METHODS: Peripheral blood mononuclear cells (PBMCs) from 10 TB patients, 10 latent TB infection individuals (LTBI), and 10 healthy controls (HCs) underwent microarray analysis, and the TB-related lncRNA modules were identified by weighted gene co-expression network analysis (WGCNA). Key lncRNAs were validated by qPCR and selected using LASSO regression. Five machine learning algorithms were employed to construct a diagnostic model, with the ROC analysis assessing its performance.
RESULTS: Based on the differential lncRNA profile, WGCNA identified 12 key modules associated with TB. From the most significant modules, 45 candidate lncRNAs were validated by qPCR, with 14 showing differential expression among TB (n = 192), LTBI (n = 55), HC (n = 66), and NTB (n = 78) groups. Five lncRNAs demonstrating the greatest contribution to TB diagnosis were further selected by LASSO analysis. AdaBoost algorithm incorporating these five lncRNAs achieved optimal diagnostic performance, with an area under the curve (AUC) of 0.97 (95%CI: 0.95-0.98) in the training cohort (n = 272) and 0.91 (95%CI: 0.86-0.96) in the validation cohort (n = 119). Independent validation of the model in another cohort (n = 206) showed an AUC of 0.92 (95%CI: 0.88-0.95).
CONCLUSIONS: This study established a novel, blood-based diagnostic model incorporating five host-derived lncRNAs with an AdaBoost algorithm, offering a non-sputum approach to enhance TB diagnosis.

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26. Diet and nutrition status of adult multidrug-resistant tuberculosis cases, household controls, and community controls in Mumbai, India.

PLOS Glob Public Health. 2026 Jan 13;6(1):e0005778. doi: 10.1371/journal.pgph.0005778. eCollection 2026.

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India accounts for the largest national proportion of global multi-drug resistant (MDR-TB) cases and TB mortality. However, evidence on the role of diet and nutrition in MDR-TB infection remains limited. This study aimed to multifacetedly evaluate and compare diet and nutrition status of MDR-TB cases and controls in high TB-burden slum areas of Mumbai. We recruited 352 pulmonary MDR-TB cases receiving domiciliary treatment, household controls, and age-, sex-, and area-matched community controls 18-60 years of age. Participants were assessed for habitual food and nutrient intake using a validated semi-quantitative food-frequency questionnaire, other food consumption-related habits, diet quality metrics, anthropometry, biochemical measurements, and diet-related non-communicable diseases. Measures of diet and nutrition status were compared within and between study arms using hypothesis tests and multiple regression. The prevalence of dietary adequacy was < 50% for 18 of 24 assessed nutrients among cases and 12/24 nutrients among controls. Compared to both household and community controls, cases had significantly ($p < 0.05$) higher prevalence of underweight (66% vs. 23% and 15%, respectively), anemia (22% vs. 9% and 10%), and diabetes (18% vs. 4% and 5%); lower consumption of major healthy food groups including non-tuberous vegetables, deep orange vegetables, legumes, whole grains, and nuts and seeds; lower Global Diet Quality Score (GDQS); and higher prevalence of nutrient inadequacies including protein, thiamine, folate, and vitamins A, C, and E. Women had significantly poorer adequacy of most nutrients than men in all three study arms, and intake of most nutrients declined with asset index and age in models adjusted for age, sex, study arm, and asset index. Results indicate an urgent need to improve diet and nutrition in Mumbai slum dwellers - particularly among the MDR-TB-infected population, women, the elderly, and the poorest households - and highlights the potentially key role of nutrition interventions in reducing MDR-TB burden in urban India.

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Conflict of interest statement: The authors have declared that no competing interests exist.

27. Diagnostic algorithms for tuberculosis in Europe: insights from the European Reference Laboratory Network for Tuberculosis (ERLTB-Net).

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The reported poor treatment outcomes for extensively drug-resistant tuberculosis (TB) in the European region highlight the urgent need for effective and context-appropriate diagnostic strategies. While the World Health Organisation (WHO) provides model algorithms, these require adaptation to the European Union/European Economic Area (EU/EEA) context, a setting with low TB incidence but high resources. This viewpoint from the European Reference Laboratory Network for TB (ERLTB-Net) proposes a tailored diagnostic algorithm that prioritises the universal use of WHO-recommended molecular rapid diagnostic

tests, systematic culture, and whole genome sequencing (WGS). This approach integrates phenotypic drug susceptibility testing strategically and outlines the possible role of targeted next-generation sequencing (tNGS) in the EU/EEA setting. The algorithm also addresses the importance of diagnostic harmonisation, cross-border collaboration, and sustained investment in sequencing capacity. By aligning diagnostic practices with the regional epidemiology and laboratory infrastructure, this stepwise, resource-sensitive approach aims to strengthen TB control, improve treatment outcomes, and guide public health action in the EU/EEA.

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28. Evaluation of the Simple One-Step (SOS) stool method for Truenat MTB plus and Xpert MTB/XDR assay.

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Comment in
doi: 10.1128/jcm.01041-25.

Stool is a recommended sample for the diagnosis of Mycobacterium tuberculosis (MTB) using Xpert MTB/RIF (Ultra) (GXU) in children, and the Simple One-Step (SOS) stool method is one of the recommended processing methods. We investigated modifications to the protocol of the SOS stool method to make it fit for testing

stool with Truenat MTB Plus and MTB-RIF Dx (Truenat) and Xpert MTB/XDR (GXX). Experiments were conducted using stool spiked with different MTB concentrations and using modified versions of the SOS stool processing method. The established protocol was then validated on routine clinical stool samples from presumptive TB patients, comparing the performance of Truenat and GXX against GXU. The concordance for MTB detection between GXU and Truenat using 50, 100, and 150 mg of stool was 100%. Truenat did not provide valid results at 300 mg. In routine stools, concordance for MTB detection was 89.3% and 90.6% when comparing Truenat-100 mg to GXU-100 and 600 mg, respectively. For rifampicin detection, 44.8% of results were indeterminate on Truenat, but none on GXU (except Trace calls). GXX stool testing gave valid results, although for low bacterial loads, GXX less often detected MTB. We conclude that stool can be tested on Truenat to detect MTB using the SOS stool Xpert method adapted to the test composition of Truenat. In addition, the SOS protocol, as originally developed for GXU, can be used for GXX. This provides opportunities to expand access to rapid molecular testing to detect TB and resistance to first- and second-line anti-TB drugs for children and adults who cannot produce sputum.IMPORTANCEFollowing World Health Organization recommendations, countries commenced stool testing on GeneXpert as the primary test to improve tuberculosis (TB) case finding among children who cannot produce sputum. To further expand access to rapid molecular testing, we adapted the Simple One-Step (SOS) stool method for GeneXpert to the test kit composition of the Truenat platform through a series of laboratory experiments. Truenat is being introduced on a large scale by countries for near point-of-care testing as it can operate better in more remote settings. As part of our experiments, we also concluded that stool can be tested with the Xpert MTB/XDR cartridge using the original SOS protocol. Our findings further expand access to rapid molecular testing to detect TB and resistance to diverse anti-TB drugs for children and adults who cannot produce sputum. Increased access to TB testing in these vulnerable populations will support TB case finding efforts and timely and appropriate treatment.

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29. Uncovering the structural impact of KatG Ser315 mutations in Mycobacterium tuberculosis via cryo-EM.

Protein Sci. 2026 Jan;35(1):e70409. doi: 10.1002/pro.70409.

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Mycobacterium tuberculosis (Mtb), the causative agent of tuberculosis (TB), is

responsible for a global health burden affecting over a quarter of the world's population. The increasing prevalence of drug-resistant TB poses a significant threat to current treatment strategies. Isoniazid (INH) is a first-line prodrug used in TB therapy, which requires activation by the catalase-peroxidase enzyme KatG. Upon activation, INH inhibits InhA, thereby disrupting mycolic acid biosynthesis, a crucial process for maintaining Mtb's distinctive, lipid-rich cell wall. The most common naturally occurring resistance-associated mutation in KatG is S315T, though other variants at this position, such as S315G, S315N, S315I, and S315R, have also been reported. In this study, we employ cryo-electron microscopy (cryo-EM) to investigate the structural basis of INH resistance conferred by these KatG variants. We present high-resolution cryo-EM structures that reveal heterogeneity in heme loading among the mutants. Detailed structural analysis highlights alterations in the hydrogen-bonding network and substrate access channel unique to each variant, offering direct comparisons with the wild-type (WT) KatG protein. Our findings provide a molecular explanation for clinical INH resistance and lay the groundwork for the rational design of next-generation anti-TB therapeutics.

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30. Evaluation of stool-based testing to diagnose tuberculosis in children using the Truenat platform in routine settings in Nigeria.

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The World Health Organization (WHO) recommends testing stool with Xpert MTB/RIF Ultra (Xpert-Ultra) as an initial diagnostic test for detection of tuberculosis (TB) and rifampicin resistance in children. The option of testing stool on the Truenat platform could benefit children and their caregivers in remote areas where GeneXpert is not available. We report the results of research to validate a protocol for processing and testing stool on Truenat using an adapted Simple One Step (SOS) stool method in routine settings in Nigeria. Stool specimens from children with presumptive TB were tested with Truenat MTB Plus (Truenat) and Xpert-Ultra using a comparative cross-sectional study design. A total of 510 children were enrolled and submitted a stool specimen. Of these, 482 (94.5%) had valid results on both platforms, 28 (5.8%) with MTB detected and 454 MTB not detected. Of the 28 with MTB detected, eight were detected on both platforms, seven on Truenat only, and 13 on Xpert-Ultra only. The concordance rate between Truenat and Xpert-Ultra was high at 95.8%. Significantly more non-determinate (error/invalid) results were observed with Truenat compared to Xpert-Ultra (4.7% versus 1.2% respectively; $P < 0.001$). Truenat can accurately detect MTB using 100 mg of stool with an adapted SOS stool protocol. Further optimizing extraction methods could reduce the frequency of non-determinate results. These results hold promise for expansion of childhood TB diagnosis services to hard-to-reach areas with limited infrastructure that are suitable for Truenat placement. Global scale-up of these alternative testing approaches will be necessary to close the gap in childhood TB case finding.IMPORTANCEFollowing WHO recommendations, high TB burden countries have commenced testing stool on GeneXpert to improve TB case finding among children and others who may not easily produce sputum. In previous work, we adapted the Simple One Step (SOS) stool method for GeneXpert for the Truenat platform. In the present study, we validated the revised processing method under routine conditions in health care facilities in Nigeria. We tested stool from 510 children with presumptive TB on both the GeneXpert and Truenat platforms across a variety of health care settings. Concordance between Truenat and Xpert MTB detection was high at 95.8%, confirming stool can be tested on Truenat in routine services. Our study demonstrates that TB diagnostic testing for children can be provided in peripheral health facilities located in remote geographic areas with limited infrastructure where Truenat can be placed. Global scale-up will help further close the gap in childhood TB case finding.

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31. Distinct mechanisms drive post-antibiotic Tuberculosis relapse post-cure versus Post-treatment-failure.

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Tuberculosis (TB) remains a global health concern, as Mycobacterium tuberculosis (Mtb) infects a quarter of the world's population. Though many TB patients sterilize infection with treatment regimens including the current standard, incomplete sterilization leads to post-treatment relapse and development of drug resistance. Two mechanisms have been hypothesized as driving relapse: persistence, where treatment kills all replicating Mtb, and relapse follows once non-replicating Mtb return to a replicative niche; and threshold, where replicating Mtb remain alive, yet below detectable levels. Relapse is often detected through a combination of clinical and bacteriological testing, often clinically described as recurrence of TB <2 years after a "cure" diagnosis, while many experimental studies examine relapse ~2-months after treatment completion. Our capacity to untangle these considerations and identify mechanisms driving relapse in vivo are limited. Here, we examine the impact of both threshold and persistence mechanisms on relapse post-treatment completion and post-cure diagnosis using our computational model capturing whole-host Mtb infection dynamics. Simulations show that erroneous TB-negative diagnosis post-treatment (false cure) rates are regimen-specific, specifically, the historic standard HRZE is more likely to result in false cure than the contemporary regimens RMZE or BPaL. We also identify how threshold-driven or persistence-driven relapse correlates with both pre-treatment bacterial burden and diagnostic tests used at treatment completion. Simulations show that post-cure relapse is almost exclusively persistence driven, while threshold-driven relapse is most common without a "cured" inclusion criterion. Thus, for patients with negative bacteriological diagnostic results at treatment completion, subsequent relapse may best be personalized by targeting non-replicating Mtb.

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PMID: 41542609

32. Extensive Lymphadenopathy in an HIV-Negative Patient With Multidrug-Resistant Tuberculosis.

Respirol Case Rep. 2026 Jan 20;14(1):e70480. doi: 10.1002/rcr2.70480.

eCollection 2026 Jan.

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Tuberculous lymphadenitis is generally more severe in patients with HIV infection. We present an HIV-negative patient with multidrug-resistant tuberculosis who developed severe, extensive lymphadenitis involving multiple extrapulmonary regions. This clinical image highlights that marked lymph node involvement may occur in HIV-negative patients presenting with pronounced systemic symptoms.

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PMID: 41567593

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33. 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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34. Overview of Tuberculosis Cases Reported in 2024 in the Capital Region: Seoul Metropolitan City, Incheon Metropolitan City, Gyeonggi-do, and Gangwon State.

Jugan Geongang Gwa Jilbyeong. 2026 Jan 15;19(2):31-60. doi: 10.56786/PHWR.2026.19.2.1. Epub 2025 Dec 8.

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OBJECTIVES: Following up on 2023 analyses, this study re-evaluated tuberculosis incidence patterns in the Capital Region (Seoul Metropolitan City, Incheon Metropolitan City, Gyeonggi-do, and Gangwon State) using the latest 2024 data. These findings serve as foundational data to guide effective tuberculosis management strategies centered on high-risk groups.
METHODS: This study obtained and analyzed data from the National Tuberculosis Integrated Information System (2015-2024). These analyses focused on high-risk groups: the elderly (≥65 years), foreign nationals, Medical Aid beneficiaries, and drug-resistant tuberculosis patients. Incidence rates per 100,000 population were calculated using population data from Korean Statistical Information Service.
RESULTS: In 2024, 8,035 tuberculosis cases were reported in the Capital Region (a 7.7% decrease from 2023), continuing a steady quantitative decline. Within this trend, pronounced structural changes were identified: the proportions of the elderly (51.8% to 52.2%) and foreign nationals (7.8% to 8.4%) increased. Incidence among Medical Aid recipients (141.7 per 100,000) was 5.3-fold higher than that among Health Insurance beneficiaries (26.5). The proportion of multidrug/rifampicin-resistant tuberculosis was 2.8% (national: 2.6%), which was 3.3-fold higher among retreatment cases (6.2%) than among new cases (1.9%). Notably, the incidence among the elderly in Gangwon State (137.6) was markedly higher than that in the Seoul metropolitan area (94.1).
CONCLUSIONS: Although tuberculosis case notifications in the Capital Region continued a 10-year decreasing trend, the proportions of the elderly (≥65 years) and foreign nationals continued to rise. This trend, driven by population aging and an influx of foreign workers from high-tuberculosis -burden countries, combined with group-specific vulnerabilities, justifies the targeted programs

implemented since 2024 (e.g., "Tuberculosis Awareness for Foreign Workers" and "Tuberculosis Prevention for Seniors [Gangwon State]"). Future efforts must expand these tailored management systems to other vulnerable groups, such as the homeless, Jjokbang residents, and undocumented migrants, to establish a comprehensive and integrated care network.

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PMID: 41555914

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35. Novel pyrimido[1,2-a]imidazole derivatives as potent Pks13-TE inhibitors: structure-based virtual screening and rational design.

RSC Med Chem. 2026 Jan 8. doi: 10.1039/d5md00942a. Online ahead of print.

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Tuberculosis (TB) remains a major global health threat, exacerbated by the emergence of drug-resistant strains. The mycobacterial enzyme Pks13 has emerged as a promising drug target for novel anti-TB agents. We herein report the design, synthesis, and biological evaluation of a series of pyrimido[1,2-a]imidazole derivatives as potent Pks13-TE inhibitors. An integrated virtual and biological screening of 10.5 million commercially available compounds identified TJA-31 as a hit compound, which showed moderate Pks13-TE inhibitory activity (IC50 = 1.34 μM). The systematic optimization of TJA-31 based on its physicochemical properties, docking scores, and MM/GBSA binding free energy estimates led to the synthesis of 50 analogues, among which 20 compounds exhibited submicromolar inhibition. The most promising derivative,

compound 34, demonstrated significantly enhanced potency with an IC50 value of 0.23 μM, representing a sixfold improvement over the hit. Molecular docking studies indicated that the high activity of compound 34 could be attributed to a halogen bond between its bromine substituent and the nitrogen atom of residue His1664, a water-mediated hydrogen bond between the Ala1564 nitrogen and the 3-methoxy oxygen, and π-π stacking interactions with residues within the Pks13-TE binding pocket. These results underscore the pyrimido[1,2-a]imidazole scaffold as a promising lead series for the development of Pks13-TE inhibitors.

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PMID: 41522623

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36. HIV-1 drug resistance among pregnant and breastfeeding mothers and its association with paediatric HIV infections in the Dolutegravir era in Uganda.

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OBJECTIVES: To determine the prevalence and patterns of HIV drug resistance

mutations among pregnant and breastfeeding women in Uganda following the rollout of dolutegravir, characterize circulating HIV-1 subtypes and their association with resistance, and identify factors associated with vertical HIV transmission.
MATERIALS AND METHODS: This study involved 46 pregnant and 154 breastfeeding mothers in Uganda with viral loads (VLs) >1000 copies/mL. Residual plasma underwent genotypic resistance testing on the Illumina MiSeq platform, and HIVDRMs and subtypes were interpreted using the Stanford HIVdb algorithm. Participant characteristics were summarized descriptively, and associations between subtypes, HIVDRMs, and vertical transmission were assessed using chi-square tests, t-tests, and logistic regression.
RESULTS: Among 200 participants, 53.0% (95% CI: 46.0-59.9) had resistance to at least one antiretroviral therapy (ART) class. HIVDRM prevalence was 41.5% (CI: 34.8-48.5) for NNRTIs, 20.5% (CI: 15.4-26.7) for NRTIs, 4.0% (CI: 2.0-7.8) for PIs and 3.5% (CI: 1.7-7.2) for INSTIs. Notably, 13.5% had accessory mutations, including T97A, which can contribute to DTG resistance. HIV-1 subtypes A (57.0%) and D (30.5%) were most common, with few subtype C (6.5%) and recombinant forms (6.0%). Subtype D and routine/repeat VL monitoring following intensive adherence counselling were associated with HIVDRMs (P=0.01 and P=0.04 respectively). Seven infants tested HIV-1 positive, with poor maternal adherence and repeat VL significantly associated with seropositivity (P=0.004 and P=0.027, respectively).
CONCLUSION: This high HIVDRM burden highlights the urgent need for routine resistance testing, subtype-specific treatment strategies and improved ART adherence support to reduce mother-to-child-transmission, particularly in women with subtype D infections.

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PMCID: PMC12802964
PMID: 41221803 [Indexed for MEDLINE]

37. Spectrochemical, medicinal, and toxicological studies of moxifloxacin and its novel analogs: a quantum chemistry and drug discovery approach.

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Moxifloxacin (MOX) is regarded as a fourth-generation fluoroquinolone, demonstrating effectiveness against multidrug-resistant tuberculosis (TB) by inhibiting bacterial DNA gyrase. The therapeutic effectiveness of MOX is negatively influenced by side effects that are dependent on dosage, including heart rate-corrected QT interval prolongation and hepatotoxicity. This study explored the physicochemical, spectral, biological, and pharmacokinetic properties of MOX and its analogues. We incorporated various functional groups such as CH3, NH2, OCF3, NHCONH2, and Cl into the core MOX framework. The geometry was optimized utilizing density functional theory with the B3LYP/6-31g basis set. We conducted geometrical, thermodynamic, molecular orbital, and electrostatic potential analyses to deepen our understanding of their physical and chemical properties. We have obtained the FT-IR and UV-vis spectra and have established correlations with the observed experimental data. The determination of the HOMO-LUMO gap is essential for assessing the chemical reactivity of MOX and its analogs. The methodology of molecular docking was executed, incorporating MOX and its analogs in connection with the targeted protein (PDB ID 5BS8). ADMET prediction was performed to assess absorption, distribution, metabolism, and toxicity, whereas PASS predictions were carried out to examine biological and toxicological properties. MOX13 exhibited a notable HOMO-LUMO gap (3.61 eV), alongside the highest binding affinity (-8.5 kcal mol-1) when compared to all examined analogues. MOX13 exhibits a notably pronounced dipole moment (14.88 debye), alongside an exceptional degree of reactivity. Investigations utilizing molecular dynamics were conducted to assess the stability of receptor-ligand complexes by analyzing RMSD, RMSF, H-bonds, and SASA, suggesting that the ligand would remain bound to its original site.

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PMID: 41523743

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38. Novel risk scoring system for predicting intravenous immunoglobulin resistance and coronary artery aneurysm in Thai children with Kawasaki disease.

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BACKGROUND: This study aimed to develop an alternative risk scoring system for intravenous immunoglobulin (IVIG) resistance and coronary artery aneurysm (CAA) development in patients with Kawasaki disease (KD) in Thai population.
METHODS: This study is a retrospective and prospective study from January 2012 to September 2024. Data on demographics, clinical features, laboratory parameters, echocardiographic results, and outcomes were analyzed. Multivariable logistic regression was used to identify predictors for IVIG resistance and CAA.
RESULTS: A total of 150 patients diagnosed with KD were enrolled. IVIG resistance occurred in 12.9% of cases. Independent predictors were neutrophil-to-lymphocyte ratio (NLR) ≥ 3.5 (aOR 25.0, 95%CI 2.92-214.3), neutrophil-to-lymphocyte platelet ratio (NLPR) ≥ 1.8 (aOR 11.83, 95%CI 2.24-62.28), and total bilirubin (TB) ≥ 0.9 mg/dL (aOR 3.51, 95%CI 1.21-10.23). A new risk scoring system for IVIG resistance demonstrated an AUC of 0.84 (95% CI 0.74-0.95). CAA developed in 31.6% of KD cases. Independent predictors included age ≤ 6 months (aOR 2.77, 95%CI 1.02-7.50), illness duration before IVIG ≥ 10 days (aOR 5.31, 95%CI 2.09-13.49), and C-reactive protein (CRP) ≥ 10 mg/dL (aOR 2.54, 95%CI 1.08-5.97). A new CAA risk scoring system was developed with an AUC of 0.74 (95% CI 0.64-0.83).
CONCLUSIONS: This study provided practical tools to identify high risk patients and optimize KD management. NLR, NLPR and TB are strong predictors of IVIG resistance, while younger age, delayed IVIG treatment, and high CRP are key predictors of CAA.

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Conflict of interest statement: Declarations. Ethical approval and consent to participate: Written informed consent for publication was obtained from the guardian of each patient. Research procedures were performed in accordance with the international guidelines for the protection of human subjects under the Declaration of Helsinki. Ethical approval for the study was obtained from the Institutional Review (COA No. 0097/2024, IRB No. 0587/66), Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand. Consent for publication: Written informed consent for publication was obtained. Competing interests: The authors declare no competing interests.

39. Effects of zinc carnosine on bone loss in mice with diabetic osteoporosis.

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Diabetic osteoporosis (DOP) is on the rise globally, presenting a notable healthcare challenge due to its complex pathogenesis and high fracture risk. Currently, available treatments have limitations, highlighting an urgent need for novel therapeutic approaches. Zinc carnosine (ZnC), a compound formed by the chelation of carnosine with trace-element zinc ions, has shown potential in inhibiting the accumulation of advanced glycation end products in the bone microenvironment, yet its effects on DOP remain under-explored. The present study aimed to examine the effects of ZnC on bone loss in a mouse model of DOP. A total of 24 male mice, aged 6 weeks, were assigned to control, type 2 diabetes mellitus (T2DM) and ZnC intervention groups. DOP was induced using a high-fat diet combined with streptozotocin (STZ). Following 8 weeks of treatment with ZnC at a dosage of 100 mg/kg/day, bone parameters were evaluated using micro-computed tomography (micro-CT), histological staining and molecular analyses. The micro-CT analysis revealed that bone mineral density (BMD), bone volume/tissue volume (BV/TV), number of bone trabeculae (Tb.N), thickness of cortical bone (Ct.Th) and area of cortical bone (Ct.Ar) were significantly lower in the T2DM model group compared with that in the control group ($P<0.05$). Conversely, bone trabecular separation (Tb.Sp) structural model index (SMI) and porosity of cortical bone (Ct.Po) were significantly higher in the T2DM model

group compared with those in the control group (P<0.05). The ZnC intervention group showed significant increases in BMD, BV/TV, Tb.N, Ct.Th and Ct.Ar, and significant decreases in Tb.Sp compared with the T2DM model group. Tartrate-resistant acid phosphatase staining demonstrated a notable reduction in osteoclast numbers in the ZnC intervention group relative to the T2DM model group. Furthermore, immunohistochemical staining and reverse transcription-quantitative PCR indicated an upregulation of osteoblastic markers, including type Ⅰ collagen, osteocalcin and osteoprotegerin, alongside a downregulation of the osteoclastic marker receptor activator of nuclear factor-κB ligand in the ZnC group. In conclusion, ZnC supplementation was shown to mitigate bone loss in DOP by promoting bone formation and reducing bone resorption. This was evidenced by enhancements in bone microstructure, a reduction in osteoclast activity and favorable changes in bone metabolism markers. These findings underscore the potential of ZnC as a therapeutic option for bone diseases associated with diabetes.

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40. Viral failure and associated factors in adults on second line antiretroviral therapy in public hospitals of Harari Region and Dire Dawa administration, Eastern Ethiopia.

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BACKGROUND: Virological failure in second-line antiretroviral therapy (ART) occurs when HIV patients have a viral load exceeding 1000 copies/ml, presenting significant public health challenges, including increased risk of transmission of HIV, heightened morbidity and mortality rates, and the risk of developing drug resistance. The extent of virological failure among second-line ART patients in the Harari region and Dire Dawa city of Eastern Ethiopia has not been thoroughly investigated. This study aimed to determine the prevalence of virological failure and its influencing factors from January 1 to December 31, 2023.

DESIGN AND METHODS: A cross-sectional study was conducted among 478 adult second-line antiretroviral therapy users at an institution-based setting. A census was employed to recruit the study participants. Data was collected using a semi-structured data extraction checklist entered into EpiData version 4.6 and exported to SPSS version 26 for analysis. Descriptive statistics, along with bivariable and multivariable logistic regression analyses, were performed to determine the associations between virological failure and independent variables, using adjusted odds ratios with 95% confidence intervals. A p-value less than 0.05 was used to declare the statistical significance.
RESULTS: The overall prevalence of virological failure among adult second-line ART users was 12.76% (95% CI = 10.05-16.07). Smoking (AOR = 2.81), BMI status (AOR = 6.97), TB-HIV co-infection (AOR = 0.20), history of INH prophylaxis (AOR = 4.25), and enhanced ART adherence counseling (AOR = 7.02) were found to be significantly associated with virological failure among second-line ART users.
CONCLUSION: Nearly 1 in 10 adults on second-line ART experienced virological failure. Factors such as smoking, nutritional status, TB-HIV co-infection, and adherence counseling significantly influenced outcomes. Continuous monitoring and clinical interventions are crucial to reduce virological failures in this population.

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41. Experimental and computational analyses for elucidation of structural, electronic, thermal, and vibrational properties of ethionamide crystal.

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Ethionamide (ETH) is a second-line drug widely used to treat multidrug-resistant tuberculosis (MDR-TB), but its low aqueous solubility compromises bioavailability and limits its therapeutic efficacy. To understand the ways to improve these properties, we combined experimental and computational approaches to elucidate the structural, electronic, thermal, and vibrational properties of ETH crystals. Powder X-ray diffraction analysis revealed a monoclinic crystal system (C1c1-space group), stabilized by intermolecular interactions, primarily H···H (49.3%) and H···S/S···H (22.1%) contacts. Energy framework analysis revealed the anisotropic nature of intermolecular interactions, with dispersion forces accounting for approximately 60% of the total stabilization energy, while Coulombic interactions showed significant directionality along the crystallographic a-axis and within the bc-plane. The total energy framework indicated that the strongest stabilization propagates along the b-axis, suggesting the formation of highly stable molecular chains, which directly influence crystal morphology and dissolution behavior. Thermal analysis confirmed ETH stability up to 162.2 °C, with melting and decomposition events characterized by endothermic peaks. Density functional theory (DFT) calculations confirmed ETH high electronic gap (7.84–8.09 eV), indicating low reactivity, while solvation studies highlighted its greater stability in polar solvents like water and methanol. Theoretical nuclear magnetic resonance studies (1H and13C) showed minimal solvent influence on chemical shifts, reinforcing the structural stability of ETH across environments. Vibrational spectroscopy, supported by DFT, identified key modes associated with the pyridine ring, NH2, and C=S groups. Hirshfeld surface analysis further revealed the dominance of hydrogen bonds and van der Waals interactions, with minimal void space (5.3%) in the crystal lattice. Electrostatic potential maps identified electron-rich regions around nitrogen atoms as potential sites for hydrogen bonding and protonation, which are relevant for pharmacological interactions. These findings offer critical insights for optimizing ETH's solid-state properties to enhance its solubility and bioavailability, paving the way for improved formulations against MDR-TB.
SUPPLEMENTARY INFORMATION: The online version contains supplementary material available at 10.1038/s41598-025-29051-w.

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42. Preclinical evaluation of long-acting cabotegravir and rilpivirine for HIV post-exposure prophylaxis in a macaque model.

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BACKGROUND: Current guidelines for post-exposure prophylaxis (PEP) recommend 28 days of daily oral antiretroviral drugs. However, low adherence and inadequate regimen completion represent important challenges. We investigated in macaques whether a single injection of the combination of long-acting cabotegravir and rilpivirine (CAB LA/RPV LA) could serve as an effective PEP regimen.
METHODS: Six macaques received a clinically relevant dose of CAB LA/RPV LA 24 h after a single rectal exposure to a high dose of reverse transcriptase simian-human immunodeficiency virus (RT-SHIV). Infection outcome was compared with seven untreated controls.
FINDINGS: CAB LA/RPV LA conferred protection against infection, with two of the six treated macaques becoming infected with RT-SHIV compared with all untreated controls ($p = 0.021$, Fisher's, exact test). The two breakthrough infections were characterized by early detection of proviral DNA, delayed detection of plasma viral RNA and seroconversion within 3-10 months, and emergence of RPV resistance. The remaining four treated macaques tested negative by multiple serological and molecular assays through 16 months of follow-up. The calculated efficacy of CAB LA/RPV LA was 66.7% (95% CI = -3.4%, 89.3%; $p = 0.0571$) although the large confidence interval adds uncertainty to the point estimate.
INTERPRETATION: We document protection in macaques by one-time CAB LA/RPV LA PEP under highly stringent modeling conditions. Delayed breakthrough infections highlight potential diagnostic challenges associated with this PEP modality and underscore the need for prolonged follow-up.
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43. In vitro efficacy of sulbactam/durlobactam combined with β-lactam antibiotics in Australian Mycobacterium abscessus isolates.

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BACKGROUND AND OBJECTIVES: Mycobacterium abscessus has extensive innate and acquired antibiotic resistance resulting in limited antibiotic treatment options and poor clinical outcomes. Currently, the only β-lactam antibiotics with efficacy against M. abscessus are imipenem and cefoxitin. Durlobactam is a β-lactamase inhibitor that may overcome intrinsic resistance mechanisms and enable the use of alternative oral β-lactam antibiotics. The objective of this study was to determine whether sulbactam/durlobactam increases the susceptibility of M. abscessus to alternative β-lactam antibiotics.
MATERIAL AND METHODS: Antibiotic susceptibility testing was performed for durlobactam, meropenem, cefuroxime/amoxicillin alone, and sulbactam/durlobactam alone and in combination with meropenem and cefuroxime/amoxicillin according to

Clinical Laboratory Standards Institute (CLSI) standards. These results were then compared with imipenem susceptibility with and without relebactam. RESULTS: Sulbactam/durlobactam significantly lowered the MICs of M. abscessus to meropenem, cefuroxime and cefuroxime/amoxicillin to MICs comparable to those of imipenem and imipenem/relebactam. The culture medium used had a significant impact on MIC, with Middlebrook 7H9 having significantly lower MICs for all combinations containing durlobactam compared with CLSI standard CAMHB media. CONCLUSION: Sulbactam/durlobactam significantly increased susceptibility to oral and intravenous β-lactam antibiotics in the form of cefuroxime, cefuroxime/amoxicillin and meropenem against clinical isolates of M. abscessus. This study also found significant differences in susceptibility to β-lactam antibiotics dependent on the culture media used, highlighting that the optimal culture methods for determining MIC in M. abscessus remains uncertain. Future in vivo studies are required to determine whether the in vitro efficacy of the β-lactam combinations studied could result in clinical efficacy for M. abscessus disease.

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Recent TB News

Tuberculosis screening gaps possible in the evolving immunotherapy landscape
https://www.infectiousdiseaseadvisor.com/news/tuberculosis-screening-immunotherapy-recommendations/
A large literature review was completed by investigators at the University of California, San Francisco to review the recommendations for TB screening among immunotherapy recipients dating from 2000 to January 2025. While all guidelines recommended screening for tumor necrosis factor inhibitor use, there were mixed findings regarding recommended screenings among different classes of immunotherapy. Inconsistencies need to be addressed to reduce screening gaps for immunotherapies with the highest risk of developing TB.

AI detects tuberculosis on photos of chest x-rays
https://www.auntminnie.com/clinical-news/digital-x-ray/article/15815476/ai-detects-tuberculosis-on-photos-of-chest-xrays
A new strategy to diagnose TB has been developed by researchers in Ethiopia. Health professionals can now use photographing film x-rays to create digital files and then give those files to Artificial Intelligence (AI). This new diagnosis tool can improve the detection and diagnosis of TB on chest x-rays in areas of the world where resources and radiologists may be scarce.