1. Immunotherapy targeting drug-tolerant Mycobacterium tuberculosis persisters accelerates tuberculosis cure in preclinical models.

J Clin Invest. 2026 Feb 3;136(7):e196648. doi: 10.1172/JCI196648. eCollection 2026 Apr 1.

Karanika S(1), Wang T(1)(2), Yilma A(1), Ruelas Castillo J(1), Gordy JT(2), Bailey H(1), Quijada D(1), Fessler K(2), Tasneen R(1), Rouse Salcido EM(1), Shamma F(1), Harris HT(1), Chen F(2), Bates RE(2), Ton H(2), Meza J(2), Li Y(2), Taylor AD(2), Zheng JJ(2), Zhang J(2), Karantanos T(3), Maxwell AR(4), Nuermberger E(1), Peske JD(5), Markham RB(2), Karakousis PC(1).

Author information:
(1)Center for Tuberculosis Research, Division of Infectious Diseases, Department of Medicine, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA.
(2)W. Harry Feinstone Department of Molecular Microbiology and Immunology, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland, USA.
(3)Division of Hematological Malignancies, Department of Oncology, Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins University Hospital, Baltimore, Maryland, USA.
(4)Department of Molecular and Comparative Pathobiology, Research Animal Resources, Johns Hopkins University, Baltimore, Maryland, USA.
(5)Department of Pathology, Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins University Hospital, Baltimore, Maryland, USA.

Mycobacterium tuberculosis remains a global health crisis, ranking among the deadliest infectious diseases worldwide. In response to the WHO's call for therapeutic vaccines to complement antibiotic regimens and reduce tuberculosis (TB) treatment duration, we developed an intranasal DNA vaccine fusing the M. tuberculosis stringent response gene relMtb with the gene encoding the DC-targeting chemokine Mip3a (also known as CCL20). Administered alongside the first-line regimen, this vaccine accelerated a stable cure in immunocompetent murine TB models, reducing lung inflammation and eliciting robust and sustained RelMtb-stimulated T cell responses systemically and locally. The Mip3a/relMtb vaccine enhanced DC recruitment, activation, and spatial coordination with T cells, suggesting improved innate-adaptive immune synergy. Notably, it augmented the efficacy of a novel drug-resistant TB regimen as well. Critically, the vaccine induced analogous antigen-stimulated T cell immunity in nonhuman primates, the gold standard for preclinical TB vaccine evaluation, with responses detected in blood and bronchoalveolar lavage mirroring those observed in the murine models. These findings underscore the potential of this strategy to advance therapeutic TB vaccine development targeting M. tuberculosis persisters while providing a framework to define correlates of vaccine-mediated protection.

DOI: 10.1172/JCI196648
PMCID: PMC13038216
PMID: 41632540 [Indexed for MEDLINE]

2. Photodynamic therapy: A paradigm shift in overcoming drug-resistant tuberculosis (Review).

Mol Med Rep. 2026 May;33(5):145. doi: 10.3892/mmr.2026.13855. Epub 2026 Mar 27.

Cheng S(1), Wang Y(2), Yao J(2), Cheng G(2), Ye G(2), Shi F(2), Ma X(2).

Author information:
(1)Clinical Medical College, Qinghai University, Xining, Qinghai 810016, P.R. China.
(2)Department of Respiratory Medicine I, The Fourth People's Hospital of Qinghai Province, Xining, Qinghai 810000, P.R. China.

Tuberculosis (TB) poses a notable threat to global public health. Conventional antibiotic treatments are hampered by long treatment courses, notable toxicity and rising levels of drug resistance. By contrast, photodynamic therapy (PDT) offers a promising alternative to antibiotics. This approach employs photosensitizers (PSs), light and oxygen to generate reactive oxygen species, which induce oxidative stress to eliminate Mycobacterium tuberculosis. The present review explores the mechanisms, benefits and primary challenges of PDT in the context of TB treatment. The present review also discusses advanced strategies that address hurdles, such as the robust mycobacterial cell wall, hypoxic environments and biofilm formation. These strategies include rational PS design, innovative nanodelivery systems and synergistic combination therapies. The present review also explores pathways for future clinical translation, highlighting the potential of PDT as a viable supplement or alternative to traditional TB chemotherapy through interdisciplinary innovation.

DOI: 10.3892/mmr.2026.13855
PMCID: PMC13051530
PMID: 41891964 [Indexed for MEDLINE]

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

3. Membrane-associated effluxosomes coordinate multi-metal resistance in Mycobacterium tuberculosis.

EMBO J. 2026 Apr;45(7):2306-2337. doi: 10.1038/s44318-026-00715-1. Epub 2026 Feb 13.

Dupuy P(1), Boudehen YM(2)(3), Faucher M(2)(4), Buglino JA(5), Fay A(5), Cantaloube S(6), Grimoire Y(2), Marcoux J(2)(7), Levet F(8)(9), Bettarel L(8), Voisin B(2), Rech J(6), Bouet JY(6), Saurel O(2), Sibarita JB(8), Glickman M(5), Gutierrez C(2), Neyrolles O(10).

Author information:
(1)Institut de Pharmacologie et de Biologie Structurale, IPBS, Université de

Toulouse, CNRS, UPS, Toulouse, France. Pierre.Dupuy@ipbs.fr.
(2)Institut de Pharmacologie et de Biologie Structurale, IPBS, Université de Toulouse, CNRS, UPS, Toulouse, France.
(3)Institut Pasteur, CNRS UMR 3528, Université Paris Cité, Bacterial Cell Cycle Mechanisms Unit, F-75015, Paris, France.
(4)G.CLIPS BIOTECH, Labège, France.
(5)Immunology Program, Sloan Kettering Institute, New-York, NY, 10065, USA.
(6)Centre de Biologie Intégrative (CBI), Université de Toulouse, CNRS, UPS, 31000, Toulouse, France.
(7)Infrastructure Nationale de Protéomique, ProFI, UAR 2048, Toulouse, France.
(8)Interdisciplinary Institute for Neuroscience, University of Bordeaux, CNRS, Bordeaux, France.
(9)Univ. Bordeaux, CNRS, INSERM, Bordeaux Imaging Center, BIC, UAR3420, US 4, F-33000, Bordeaux, France.
(10)Institut de Pharmacologie et de Biologie Structurale, IPBS, Université de Toulouse, CNRS, UPS, Toulouse, France. Olivier.Neyrolles@ipbs.fr.

Update of
bioRxiv. 2025 Mar 26:2025.03.25.645379. doi: 10.1101/2025.03.25.645379.

Bacterial pathogens must withstand metal-induced stress during infection, yet the mechanisms by which they sense and respond to toxic metal ions remain incompletely understood. Here, we uncover a previously unrecognized mechanism in Mycobacterium tuberculosis, the causative agent of tuberculosis, which assembles dynamic, membrane-associated platforms organized by PacL proteins to mediate resistance to multiple metals. The small membrane-associated proteins PacL1, PacL2, and PacL3 coordinate the clustering of P-type ATPase pumps, namely CtpC, CtpG, and CtpV, into functional complexes that we term effluxosomes. Using single-particle tracking, we reveal distinct dynamic populations, with highly mobile PacL proteins integrating into more slowly mobile effluxosomes. PacL proteins stabilize CtpC and CtpG within these assemblies, promoting cross-resistance to zinc and cadmium, with PacL1 acting as a multi-substrate metallochaperone that binds zinc, cadmium, and copper via a conserved C-terminal motif. Single-molecule-based super-resolution microscopy shows that conserved residues within the PacL transmembrane domain are essential for effluxosome assembly. Strikingly, proximity labeling reveals a broad PacL1 interaction network, suggesting that effluxosomes contribute to a wider stress adaptation program. These findings establish effluxosomes as dynamic membrane machineries that orchestrate coordinated multi-metal resistance in M. tuberculosis, opening new avenues for antimicrobial targeting.

DOI: 10.1038/s44318-026-00715-1
PMCID: PMC13043812
PMID: 41688792 [Indexed for MEDLINE]

Conflict of interest statement: Disclosure and competing interests statement. MSG has received consulting fees from Vedanta Biosciences, PRL NYC and has equity in Vedanta Biosciences. The remaining authors declare no competing

interests.

4. Redefining Therapies for Drug-Resistant Tuberculosis: Synergistic Effects of Antimicrobial Peptides, Nanotechnology, and Computational Design.

Adv Healthc Mater. 2026 Apr;15(14):e03964. doi: 10.1002/adhm.202503964. Epub 2026 Jan 19.

Carnero Canales CS(1), Marquez Cazorla JI(2), Marquez Cazorla RM(2)(3), Santos AMD(4), Lobato Duarte J(4), Oliveira Catarin Nunes L(4)(5), Reis TC(4), Cerazi Salvador L(5), Santos-Filho NA(4)(5), Sábio RM(6), Santos HA(7), Pavan FR(6).

Author information:
(1)Vicerrectorado de Investigación, Universidad Autónoma del Perú (UA), Lima, Perú.
(2)School of Pharmacy, Biochemistry and Biotechnology, Universidad Católica Santa María (UCSM), Arequipa, Perú.
(3)Nanovida Research Center, Arequipa, Perú.
(4)School of Pharmaceutical Sciences, São Paulo State University, Araraquara, Brazil.
(5)Institute of Chemistry, São Paulo State University, Araraquara, Brazil.
(6)Tuberculosis Research Laboratory, School of Pharmaceutical Sciences, São Paulo State University, Araraquara, Brazil.
(7)Department of Biomaterials and Biomedical Technology, The Personalized Medicine Research Institute (PRECISION), University Medical Center Groningen, University of Groningen, Groningen, The Netherlands.

Tuberculosis (TB), caused by Mycobacterium tuberculosis (Mtb), remains a major global health concern, particularly due to the emergence of multidrug-resistant and extensively drug-resistant strains. The persistence and propagation of TB are favored by the pathogen's sophisticated virulence mechanisms, its ability to evade immune responses, and the formation of latent infections within granulomas. Current therapeutic regimens are limited by long treatment durations, drug resistance, and significant socioeconomic burdens. Antimicrobial peptides (AMPs) have emerged as promising alternatives because of their broad-spectrum activity and reduced likelihood of resistance development. Nevertheless, their clinical application is hindered by rapid proteolytic degradation, low specificity and limited bioavailability. Recent advances in nanotechnology have facilitated the encapsulation and targeted delivery of AMPs, improving their therapeutic potential against TB. Furthermore, the integration of computational approaches-such as molecular docking and molecular dynamics (MD) simulations-has enabled the rational design and optimization of AMPs, expediting the discovery of novel anti-TB agents. This review summarizes the pathogenesis and resistance mechanisms of Mtb, highlights the current landscape and limitations of AMP-based therapies, and discusses the role of nanotechnology and in silico tools in the development of new treatment strategies for TB.

DOI: 10.1002/adhm.202503964
PMCID: PMC13068362
PMID: 41549858 [Indexed for MEDLINE]

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

5. Factors Influencing Early Sputum Culture Conversion in Pulmonary Drug-resistant Tuberculosis.

J Glob Infect Dis. 2026 Mar 27;18(1):27-34. doi: 10.4103/jgid.jgid_116_25. eCollection 2026 Jan-Mar.

Kotokey UK(1), Kumari S(2).

Author information:
(1)Department of Respiratory Medicine, National Institute of Tuberculosis and Respiratory Diseases (NITRD), New Delhi, India.
(2)Department of Biotechnology, All India Institute of Medical Sciences, New Delhi, India.

INTRODUCTION: India bears the highest global burden of tuberculosis (TB), with multidrug-resistant TB (MDR-TB) posing substantial treatment challenges. Sputum culture conversion is a vital indicator of treatment response and an early predictor of success in drug-resistant TB (DR-TB). This study aimed to evaluate the time to early sputum culture conversion (within 6 months) in DR-TB patients and identify factors influencing this outcome across different resistance patterns: MDR, MDR with fluoroquinolone resistance, MDR with second-line injectable resistance, and extensively DR-TB (XDR-TB).
METHODS: This prospective cross-sectional observational study was conducted in India. Seventy-four DR-TB patients enrolled between January and October 2019 were assessed. Demographic data, comorbidities, and culture conversion times were analyzed using Chi-square tests and univariate logistic regression. $P < 0.05$ was considered statistically significant.
RESULTS: Among the 74 patients (62.2% male; mean age 30 years), most MDR-TB patients (52%) achieved culture conversion within 3 months, while pre-XDR and XDR cases mostly converted within 2 months. Smoking ($P = 0.03$), low body mass index (BMI) ($P = 0.025$), cavitary lesions on chest X-ray ($P = 0.01$), and lower socioeconomic status ($P = 0.02$) were significantly associated with delayed conversion.
CONCLUSION: Early sputum culture conversion is a key milestone in DR-TB treatment. Addressing modifiable risk factors such as smoking, undernutrition, and cavitary disease may improve outcomes. Further studies are needed to identify interventions to accelerate culture conversion and enhance treatment success.

DOI: 10.4103/jgid.jgid_116_25
PMCID: PMC13061139

PMID: 41958492

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

6. Implementing shorter all-oral treatment durations for multidrug-resistant tuberculosis in the UK: from concept to application.

BMJ Open Respir Res. 2026 Apr 2;13(1):e003861. doi: 10.1136/bmjresp-2025-003861.

Chavda A(1), Gilchrist M(2)(3), Capstick T(4), Chen C(5), Kon OM(6)(7).

Author information:
(1)Department of Pharmacy, Imperial College Healthcare NHS Trust, London, UK aneeka.chavda1@nhs.net.
(2)Department of Infectious Disease, Imperial College London, London, UK.
(3)Department of Infectious Diseases and Microbiology, Imperial College London, London, UK.
(4)Medicines Management and Pharmacy Services, Leeds Teaching Hospitals NHS Trust, Leeds, UK.
(5)Department of Pharmacy, Barts Health NHS Trust, London, UK.
(6)Chest and Allergy Clinic, Imperial College Healthcare NHS Trust, London, UK.
(7)Imperial College London, London, UK.

Multidrug-resistant tuberculosis (MDR-TB) is a global public health threat associated with high mortality and challenging treatment regimens. The UK, like many countries, faces a growing incidence of MDR-TB, with 105 (1.9% of all notified cases) treated as MDR-resistant or rifampicin-resistant TB in 2024. Recent clinical trials have demonstrated the efficacy and safety of shorter, all-oral regimens such as BPaLM (bedaquiline, pretomanid, linezolid, moxifloxacin), yet their implementation in the UK presents unique challenges, particularly around the antimicrobial stewardship (AMS) agenda, such as the lack of licensed drugs, pharmacokinetic/dynamic concerns, fragile supply chains and high cost of second-line antituberculosis drugs. This narrative review outlines how the UK has addressed implementation hurdles through coordinated efforts by the British Thoracic Society MDR-TB Clinical Advice Service and National Health Service England. This collaboration has facilitated the adoption of new regimens, with 54 out of 60 requests for using pretomanid-containing regimens approved in the UK up to January 2026. Furthermore, resources like the TB Drug Monographs and the shift to video-observed therapy have streamlined care delivery. The UK has effectively navigated the transition to shorter, all-oral MDR-TB regimens, significantly enhancing patient care and operational efficiency. The integration of clinical guidance, AMS principles, policy reform and specialised monitoring tools provides a robust framework for managing evolving treatment landscapes and delivering patient-centred care.

DOI: 10.1136/bmjresp-2025-003861

PMCID: PMC13052542
PMID: 41927314 [Indexed for MEDLINE]

Conflict of interest statement: Competing interests: AC is a Clinical Service Adviser at the BTS MDR-TB Clinical Advice Service. MG reports consultancy fees from Pfizer, Menarini, Mundipharma, Napp and Advanz. CC is a Clinical Service Adviser at the BTS MDR-TB Clinical Advice Service, and reports speaker and consultancy fees from AstraZeneca, Chiesi, GSK, Insmed outside of the current work. TC is co-author of the TB Drug Monographs website and a Steering Group Member of the BTS MDR-TB Clinical Advice Service, and reports speaker and consultancy fees from AstraZeneca, Chiesi, GSK, Insmed and a project grant from Chiesi outside of the current work, and his employer has received payment for teaching and consultancy from AstraZeneca, Boehringer Ingelheim, Chiesi, GSK, and Insmed. OMK is co-author of the TB Drug Monographs website and a Steering Group Member of the BTS MDR-TB Clinical Advice Service, chairs an annual Qiagen sponsored global summit and has received speaker fees from Revvity.

7. Safety of treatment regimens for drug-resistant TB over a 15-year period: a scoping review.

IJTLD Open. 2026 Apr 13;3(4):208-217. doi: 10.5588/ijtldopen.25.0728. eCollection 2026 Apr.

Amiri M(1), Cheraghi M(1), Nasiri MJ(1), Silva DR(2), Sotgiu G(3), D'Ambrosio L(4), Centis R(5), Kontsevaya I(6), Gandhi HK(7), Oberdhan D(7), Girbinger V(6), Dara M(6).

Author information:
(1)Department of Microbiology, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran.
(2)Faculdade de Medicina, Universidade Federal do Rio Grande do Sul (UFRGS), Porto Alegre, Brazil.
(3)Clinical Epidemiology and Medical Statistics Unit, Department of Medicine, Surgery and Pharmacy, University of Sassari, Sassari, Italy.
(4)Public Health Consulting Group, Lugano, Switzerland.
(5)Servizio di Epidemiologia Clinica delle Malattie Respiratorie, Istituti Clinici Scientifici Maugeri, IRCCS, Tradate, Italy.
(6)Otsuka Novel Products GmbH, Munich, Germany.
(7)Otsuka Pharmaceutical Development & Commercialization, Inc., Princeton, NJ, USA.

BACKGROUND: A previous review summarised the evolution and efficacy of the regimens to treat rifampicin-resistant/multidrug-resistant TB (RR/MDR-TB), underscoring the persistent need for efficacious shorter treatments. The aim of this scoping review was to explore safety, quality of life (QoL), and unmet needs associated with RR/MDR-TB in studies published between 2009 and 2024.
METHODS: We searched PubMed/MEDLINE, Embase, Cochrane CENTRAL, Scopus, and Web
of Science for studies reporting safety, QoL, and unmet needs in the last 15

years.
RESULTS: Fifty-seven studies including 9,874 patients were identified, with significant variation in geographic distribution, sample size, and other core variables. The overall proportion of serious adverse events (AEs) ranged between 0.2% and 10.1% in retrospective studies, 1.0%-72.4% in prospective cohorts, and 20.0%-25.0% in experimental studies, with no data on QoL. Almost all studies containing linezolid (LZD) reported gastrointestinal and haematological AEs. In studies based on individual patient data, AEs associated with bedaquiline (1.7%-2.4%) and fluoroquinolones (3%-4%) were less frequent than those associated with LZD (14.1%-17.2%). The World Health Organization 95% credible interval range was 10.1%-27.0%.
CONCLUSION: While efficacious RR/MDR-TB regimens are recommended, individual drugs still cause AEs potentially leading to decreased adherence. New efficacious treatments with improved safety/tolerability profiles are needed.

DOI: 10.5588/ijtldopen.25.0728
PMCID: PMC13080302
PMID: 41994187

8. Risk factors for treatment failure of drug-resistant pulmonary tuberculosis: results from a two-decade data analysis.

J Thorac Dis. 2026 Mar 31;18(3):201. doi: 10.21037/jtd-2025-1-2548. Epub 2026 Mar 24.

Kėvelaitienė K(1)(2), Puronaitė R(3), Davidavičienė VE(4), Nakčerienė B(4), Danila E(1)(2).

Author information:
(1)Institute of Clinical Medicine, Clinic of Chest Diseases, Immunology and Allergology, Vilnius University Faculty of Medicine, Vilnius, Lithuania.
(2)Centre of Pulmonology and Allergology, Vilnius University Hospital Santaros Klinikos, Vilnius, Lithuania.
(3)Center of Informatics and Development, Vilnius University Hospital Santaros Klinikos, Vilnius, Lithuania.
(4)Programs and Tuberculosis State Information System Department, Vilnius University Hospital Santaros Klinikos, Vilnius, Lithuania.

BACKGROUND: Drug-resistant tuberculosis (DR-TB) remains a major public health challenge worldwide, particularly in Eastern Europe, where high disease burden and complex treatment regimens contribute to suboptimal outcomes. Lithuania has historically reported high rates of pulmonary DR-TB; however, data on long-term treatment outcomes and their determinants over extended periods are limited. This study evaluated long-term treatment outcomes among adults with pulmonary DR-TB in Lithuania over a 22-year period and assessed associations between treatment outcomes, individual risk factors, and temporal trends.

METHODS: A retrospective cohort analysis was conducted using data from the National Tuberculosis Information System for 2000-2021. The study included 5,761 adults with DR-TB, categorized into three periods: Period I (2000-2007), Period II (2008-2015), and Period III (2016-2021). Treatment outcomes were classified as successful (treatment completion with recovery) or unsuccessful [treatment failure, progression to chronic TB, death before completion, or transition from multidrug-resistant tuberculosis (MDR-TB) to extensively drug-resistant tuberculosis (XDR-TB)]. Associations between outcomes and risk factors such as smoking, alcohol and substance use, comorbidities, and sociodemographic variables were examined using multivariate analysis.
RESULTS: Treatment success rates increased steadily across periods (66.2%, 68.5%, and 79.5%), while mortality rates declined (30.7%, 29.5%, and 20.1%). Non-lethal treatment failure rates decreased markedly (3.0%, 2.0%, and 0.3%). Treatment failure was significantly associated with low body mass index, male gender, unemployment, homelessness, tobacco and alcohol use, substance abuse, and comorbidities including cancer, cardiovascular and chronic lung disease, diabetes mellitus, human immunodeficiency virus (HIV) infection, and renal failure.
CONCLUSIONS: Treatment outcomes of DR-TB in Lithuania have shown improvement over a 22-year period. Successful treatment outcomes were strongly influenced by a combination of clinical, behavioral, and socioeconomic factors, underscoring the complexity of DR-TB management. The relative importance of these components may vary for each individual patient. Incorporating multifaceted strategies, such as psychological support, social assistance (including access to food and shelter), and employment opportunities, into the national DR-TB control framework could enhance health system responsiveness and reduce inequities in care.

DOI: 10.21037/jtd-2025-1-2548
PMCID: PMC13077367
PMID: 41988260

Conflict of interest statement: Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jtd.amegroups.com/article/view/10.21037/jtd-2025-1-2548/coif). The authors have no conflicts of interest to declare.

9. Single Saliva Sample Model-Informed Precision Dosing of Levofloxacin for Multidrug-Resistant Tuberculosis.

Clin Pharmacokinet. 2026 Apr;65(4):583-594. doi: 10.1007/s40262-026-01619-3. Epub 2026 Feb 10.

Nguyen TA(1)(2)(3), Nguyen TP(4), Nguyen AT(5)(6)(7), Dinh LV(8), Nguyen HB(8), Vu HD(9), Nguyen TNB(7), Vu D(7), Fox GJ(5)(6), Alffenaar JC(1)(2)(3), Stocker SL(10)(11)(12)(13)(14).

Author information:
(1)Faculty of Medicine and Health, Sydney Pharmacy School, The University of Sydney, Pharmacy Building (A15), Sydney, NSW, 2006, Australia.
(2)Department of Pharmacy, Westmead Hospital, Sydney, NSW, Australia.
(3)Sydney Institute for Infectious Diseases, The University of Sydney, Sydney, NSW, Australia.
(4)Ho Chi Minh City University of Technology, Ho Chi Minh City, Vietnam.
(5)Faculty of Medicine and Health, The University of Sydney, Sydney, NSW, Australia.
(6)Woolcock Institute of Medical Research, Hanoi, Vietnam.
(7)The University of Sydney Vietnam Institute, Ho Chi Minh City, Vietnam.
(8)National Lung Hospital, Hanoi, Vietnam.
(9)National Drug Information and Adverse Drug Reactions Monitoring Centre, Hanoi University of Pharmacy, Hanoi, Vietnam.
(10)Faculty of Medicine and Health, Sydney Pharmacy School, The University of Sydney, Pharmacy Building (A15), Sydney, NSW, 2006, Australia. sophie.stocker@sydney.edu.au.
(11)Department of Pharmacy, Westmead Hospital, Sydney, NSW, Australia. sophie.stocker@sydney.edu.au.
(12)Sydney Institute for Infectious Diseases, The University of Sydney, Sydney, NSW, Australia. sophie.stocker@sydney.edu.au.
(13)St Vincent's Clinical Campus, School of Clinical Medicine, The University of New South Wales, Darlinghurst, NSW, Australia. sophie.stocker@sydney.edu.au.
(14)Department of Clinical Pharmacology and Toxicology, St Vincent's Hospital, Darlinghurst, NSW, Australia. sophie.stocker@sydney.edu.au.

BACKGROUND AND OBJECTIVES: Levofloxacin is an essential drug in multidrug-resistant tuberculosis (MDR-TB) treatment, but high pharmacokinetic variability necessitates therapeutic drug monitoring (TDM) to optimise exposure and improve outcomes. Traditional TDM requires invasive blood sampling, limiting feasibility. Saliva sampling, a non-invasive matrix may simplify implementation. We aimed to develop a levofloxacin population pharmacokinetic (popPK) model integrating plasma and saliva data, and to evaluate saliva-based limited sampling strategies to support model-informed TDM for levofloxacin in practice.
METHODS: Adults receiving oral levofloxacin for ≥ 7 days had plasma and saliva samples collected at 0, 2, and 5 h post-dose. A plasma-and-saliva popPK model was developed using NONMEM, including covariate evaluation. Predictive performance of saliva-based limited sampling strategies for estimating plasma AUC24 was assessed using Bayesian estimation and Monte Carlo simulations.
RESULTS: A total of 57 patients with 342 paired plasma-saliva samples were evaluated. One-compartment model incorporating saliva bio-compartment with first-order absorption (with a lag time) and elimination best described the data. No significant covariates were identified. Simulations showed that the three-point saliva strategy (0, 2, 5 h) predicted plasma AUC24 within clinically acceptable limit (< 15% prediction error). A single 2-h sample yielded comparable accuracy. Two- and three-sample saliva strategies up to 16 h post-dose also showed clinically acceptable accuracy.
CONCLUSIONS: The developed popPK model enables reliable estimation of levofloxacin exposure from limited saliva samples. A single 2-h post-dose saliva concentration may support model-informed levofloxacin TDM in routine MDR-TB

care. This approach may be beneficial in settings where plasma-based TDM is logistically or ethically challenging.

DOI: 10.1007/s40262-026-01619-3
PMCID: PMC13038660
PMID: 41665863 [Indexed for MEDLINE]

Conflict of interest statement: Declarations. Consent to Participate: Written informed consent was obtained from all participants prior to study enrolment, in accordance with the approved protocol. Consent for Publication: Not applicable. Code Available: The model codes that support the findings of this study can be accessible in Table S4, Supplementary Material. Data Availability: The data supporting this study's findings may be available on request from the principal investigator of the study (J.W. Alffenaar). Ethics Approval: Ethical approval was granted by the University of Sydney, Australia (Protocol No. 2021/082, dated 21.10.2021) and the National Lung Hospital, Vietnam (Approval No. 25/21/CN-HDDD, dated 27/04/2021). Author Contributions: T.A. Nguyen conceptualised the study, performed drug concentration analysis, performed the pharmacometrics data analyses and wrote the manuscript. T.P. Nguyen performed the pharmacometrics data analyses and revised the manuscript. A.T. Nguyen revised the manuscript. L.V. Dinh revised the manuscript. B.H. Nguyen revised the manuscript. D.H. Vu revised the manuscript. T.N.B. Nguyen revised the manuscript. D. Vu revised the manuscript. G.J. Fox conceptualised the study and revised the manuscript. J.W. Alffenaar conceptualised the study, supervised the analysis and revised the manuscript. S.L. Stocker conceptualised the study, supervised the analysis and revised the manuscript. All authors revised the manuscript and accepted submission to the journal. Conflict of Interest: Jan-Willem C. Alffenaar and Sophie L. Stocker are Editorial Board members of Clinical Pharmacokinetics. They were not involved in the selection of peer reviewers for the manuscript nor any of the subsequent editorial decisions. The others declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

10. Non-invasive environmental DNA sampling reveals tuberculosis risks at the human - Great Ape Interface in Africa.

Emerg Microbes Infect. 2026 Dec;15(1):2645874. doi: 10.1080/22221751.2026.2645874. Epub 2026 Mar 23.

Kalalizi E(1)(2), Flores L(3)(4)(5), Pérez-Sancho M(6)(7), Perelló A(1), Herranz C(6)(7), Herrera L(8), Romero B(6), Kaleme P(4)(9), García-Seco T(6), Kujirakwinja D(10), Kalonji A(11), Kashongwe Z(12)(13), Birembano-Machara F(13), Baganda D(4), Nkonzi P(4), Del Burgo IV(3), Gal FL(14), De La Fuente J(1)(15), Domínguez L(6)(7), Gortázar C(1).

Author information:
(1)SaBio Instituto de Investigación en Recursos Cinegéticos (IREC)

CSIC-UCLM-JCCM, Ciudad Real, Spain.
(2)L'Université Cinquantenaire de Lwiro, South Kivu, Democratic Republic of Congo.
(3)Lwiro Primate Rehabilitation Center (LPRC), South Kivu, Democratic Republic of Congo.
(4)Centre de Recherche en Sciences Naturelles de Lwiro (CRSN Lwiro), South Kivu, Democratic Republic of Congo.
(5)One Health Conservation Initiative (OHCI), Lwiro, Democratic Republic of Congo.
(6)Faculty of Veterinary, Department of Animal Health, VISAVET Health Surveillance Center, Complutense University of Madrid, Madrid, Spain.
(7)Faculty of Veterinary, Department of Animal Health, Complutense University of Madrid, Madrid, Spain.
(8)Department of Bacteriology, National Centre of Microbiology, Instituto de Salud Carlos III, Majadahonda, Spain.
(9)Institut Supérieur des Techniques Médicales de Bukavu, South Kivu, Democratic Republic of Congo.
(10)Institut Supérieur de Tourisme, North Kivu, Democratic Republic of Congo.
(11)Kahuzi-Biega National Park, South Kivu, Democratic Republic of Congo.
(12)University of Kinshasa (Unikin), Kinshasa, Democratic Republic of Congo.
(13)Le Programme National de Lutte Contre la Tuberculose (PNLT), Kinsasa, Democratic Republic of Congo.
(14)Laboratoires de Microbiologie Clinique, Bobigny, France.
(15)Department of Veterinary Pathobiology, Center for Veterinary Health Sciences, Oklahoma State University, Stillwater, OK, USA.

The current range of African great apes includes countries with some of the world's highest incidence rates of human tuberculosis (TB). Non-human primates (NHPs) living in their natural habitats are expected to be free of TB. However, TB represents a known threat to captive NHP communities. We applied a non-invasive sponge-based environmental DNA (eDNA) sampling to run a cross-sectional survey at the human-animal interface in a challenging setting: the East of the Democratic Republic of Congo (DRC). The study sites included a primate rehabilitation centre, the local health area, and a nearby national park with critically endangered Eastern Lowland Gorillas (Gorilla beringei graueri). Sponge samples were tested for two PCR targets, IS6110 and mpb70. Positive samples were further characterized by spoligotyping, species identification and detection of molecular resistance against rifampicin and isoniazid. We detected Mycobacterium tuberculosis eDNA in 26% of the samples from all three sites including samples linked to humans, wild gorillas and captive NHPs. The spoligotype could be identified in 18 cases. Spoligotype SIT130 was detected in all sites including human and gorilla environment samples. These findings are strongly suggestive of epidemiological links between human and NHP TB in equatorial Africa.

DOI: 10.1080/22221751.2026.2645874
PMCID: PMC13011094
PMID: 41869690 [Indexed for MEDLINE]

Conflict of interest statement: No potential conflict of interest was reported

by the author(s).

11. Impact of Drug-Resistant Tuberculosis Prevention and Control Strategies in Southeast China: Evidence from a Longitudinal Study on Disease Epidemic Trends and Predictions Across 15 Years.

Infect Drug Resist. 2026 Apr 17;19:597234. doi: 10.2147/IDR.S597234. eCollection 2026.

Wu Y(1), Li M(1), Zhu Y(2), Peng Y(2)(3), Wang F(2), Chen X(2)(3), Zu Z(2), Chen B(2)(3), Zhou L(2)(3), Chen D(1).

Author information:
(1)School of Public Health, Hangzhou Medical College, Hangzhou, Zhejiang, People's Republic of China.
(2)Department of Tuberculosis Control and Prevention, Zhejiang Provincial Center for Disease Control and Prevention, Hangzhou, Zhejiang, People's Republic of China.
(3)Zhejiang Key Laboratory of Vaccine, Infectious Disease Prevention and Control, Hangzhou, Zhejiang, People's Republic of China.

PURPOSE: Despite intensified efforts in drug-resistant tuberculosis control, the true burden and long-term trends of multidrug-resistant and rifampicin-resistant tuberculosis (MDR/RR-TB) remain unclear in many Asian settings. In China, where MDR/RR-TB accounts for a substantial share of global cases, regional variations in detection and reporting are pronounced. We aimed to examine changes in the burden and temporal trends of MDR/RR-TB in Zhejiang Province (2015-2023) and assess the impact of existing prevention and control measures. In addition, future incidence trends were projected to 2030 using an ARIMA model.
PATIENTS AND METHODS: Individual-level MDR/RR-TB data from the Tuberculosis Information Management System were analyzed. Cases were estimated using the World Health Organization model. Temporal trends were assessed with Joinpoint regression, and future incidence was projected to 2030 using an autoregressive integrated moving average model.
RESULTS: Among 4,950 patients included, the detection rate increased from 24·55% in 2015 to 81·29% in 2023. Over the same period, the estimated MDR/RR-TB burden declined substantially (average annual percentage change: -17·20; 95% CI -20·89 to -14·36, p<0·0010), whereas notified cases increased initially and declined after 2018. The gap between estimated and notification cases narrowed markedly, indicating improved surveillance sensitivity. Substantial heterogeneity was observed across regions subgroups. Projections suggest a continued decline in incidence through 2030, although uncertainty increases over time.
CONCLUSION: Strengthened surveillance and treatment strategies in Zhejiang Province have substantially reduced MDR/RR-TB burden and improved case detection, providing regionally relevant evidence for optimizing MDR/RR-TB control strategies in similar Asian settings.

DOI: 10.2147/IDR.S597234
PMCID: PMC13100827
PMID: 42028456

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

12. Prevalence and resistance spectrum of ahpC mutations in isoniazid-resistant Mycobacterium tuberculosis isolates.

Microbiol Spectr. 2026 Apr 7;14(4):e0249625. doi: 10.1128/spectrum.02496-25. Epub 2026 Mar 19.

Wu X(#)(1), Zheng H(#)(1), Chen Y(1), Zhao B(2), Li F(1), Xia H(2), Xiao J(1), Qi H(1), Jiao W(1), Mi K(3), Ou X(2), Zhao Y(2), Sun L(1).

Author information:
(1)Laboratory of Respiratory Diseases, Beijing Pediatric Research Institute, Beijing Children's Hospital, Capital Medical University, Beijing Key Laboratory of Core Technologies for the Prevention and Treatment of Emerging Infectious Diseases in Children, Key Laboratory of Major Diseases in Children, Ministry of Education, National Clinical Research Center for Respiratory Diseases, National Center for Children's Health, Beijing, China.
(2)National Key Laboratory of Intelligent Tracking and Forecasting for Infectious Diseases, National Center for Tuberculosis Control and Prevention, Chinese Centre for Disease Control and Prevention, Beijing, China.
(3)Laboratory of Pathogen Microbiology and Immunology, Institute of Microbiology, Chinese Academy of Sciences, Medical School, University of Chinese Academy of Sciences, Beijing, China.
(#)Contributed equally

To characterize the mutation profile of the ahpC gene in isoniazid resistance (INHr) Mycobacterium tuberculosis (MTB) isolates and to evaluate the correlation between specific mutations and resistance levels, a total of 1,337 INHr MTB isolates were collected through the Chinese Drug Resistance Surveillance Program (2013-2020). The minimum inhibitory concentrations (MICs) for INH, rifampicin (RIF), and ethionamide were determined by broth microdilution, followed by whole-genome sequencing analysis. Among 1,337 INHr-MTB isolates, 45.5% (608/1,337) were multidrug-resistant (MDR), and 54.5% (729/1,337) were RIF-sensitive cases, with lineage 2 predominating (1,013/1,337, 75.8%). Resistance mutations were identified in 79.1% (1,058/1,337) of strains, primarily katG Ser315Thr (65.5%, 695/1,058) and inhA C-777T (19.7%, 208/1,058). Notably, 5.3% (56/1,058) isolates harbored standalone ahpC mutations, with 83.3% (5/6) C-81T, 60.0% (9/15) G-48A, 57.1% (4/7) C-54T, 50.0% (3/6) C-57T, and 42.1% (8/19) C-52T mutations showing high-level INH resistance. Accordingly, 91.7% (11/12) dual katG315+inhA mutations conferred high-level INH resistance, while ahpC C-57T mutants universally exhibited MDR. The ahpC mutations are associated with high-level INH resistance in variants without concurrent katG or inhA mutations. This finding significantly advances our understanding of tuberculosis

resistance profiling, enabling more comprehensive detection of INHr-MTB and optimizing therapeutic strategies.IMPORTANCEAmong INH-resistant MTB clinical isolates, mutations in the ahpC promoter region have been considered to occur in combination with other mutations, such as katG and inhA, in a compensatory role. While the ahpC mutations have been incorporated into the World Health Organization (WHO)-recommended rapid diagnostic test, Xpert MTB/extensively drug-resistant tuberculosis (XDR), it has been still ambiguous about the standalone effects on INH resistance spectrum. Our findings demonstrate that the ahpC mutations are associated with high-level INH resistance in variants without concurrent katG or inhA mutations. This finding significantly advances our understanding of TB resistance profiling, enabling a more comprehensive detection of INHr-MTB and optimizing therapeutic strategies.

DOI: 10.1128/spectrum.02496-25
PMCID: PMC13055390
PMID: 41856489 [Indexed for MEDLINE]

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

13.Pattern and prevalence of rifampicin and isoniazid-resistant tuberculosis using genotype MTBDRplus assay in Ethiopia.

Microbiol Spectr. 2026 Apr 7;14(4):e0145425. doi: 10.1128/spectrum.01454-25. Epub 2026 Feb 20.

Getahun M(1), Ameni G(2)(3), Mollalign H(1), Diriba G(1), Beyene D(4).

Author information:
(1)Ethiopian Public Health Institute, Addis Ababa, Ethiopia.
(2)Aklilu Lemma Institute of Pathobiology, Addis Ababa University, Addis Ababa, Ethiopia.
(3)Department of Veterinary Medicine, College of Agriculture and Veterinary Medicine, United Arab Emirates University, Al Ain, UAE.
(4)Department of Microbial, Cellular and Molecular Biology, Addis Ababa University, Addis Ababa, Ethiopia.

Resistance-conferring mutations in Mycobacterium tuberculosis (Mtb) are primary drivers of therapeutic challenges. However, comprehensive resistance mutation profiles are lacking in low- and middle-income countries. This study assesses the patterns and prevalence of isoniazid (INH) or multidrug/rifampicin-resistant (MDR/RR) tuberculosis (TB) mutations. We used stored Mtb isolates obtained from smear-positive TB patients recruited from 32 health facilities as part of the drug resistance survey (DRS). Line probe assay (LPA) testing was conducted on phenotypically confirmed INH-resistant and MDR/RR Mtb isolates. A total of 65 MDR/RR and 62 mono-INH-resistant Mtb isolates were analyzed. LPA detects 93.8% of rifampicin-conferred mutations in phenotypically confirmed MDR/RR Mtb isolates. The most frequent mutations were found at rpoB codons 530-533 (63.9%), and the S531L mutation comprised 59% of the MDR/RR TB isolates. The katG315

mutations were observed in the majority of MDR/RR (98%) and mono-INH-resistant (91.6%) Mtb isolates. The proportion of katG315 mutations was higher in newly diagnosed INH-resistant TB patients (72.7%) than those who had had prior treatment (27.3%). In 29.5% of MDR/RR and 2.5% of mono-INH resistant Mtb isolates, resistance was inferred. This study reports the proportion of mutations conferring resistance to rifampicin and INH using isolates collected from the national DRS.
IMPORTANCE: Drug resistance mutations vary by location, effectiveness of the national control programs, and the diagnostic methods employed. Rapid molecular diagnostic tests are the primary methods used to detect drug-resistant tuberculosis. Comprehensive resistance mutation profiles are often lacking in low- and middle-income countries. The goal of this study was to assess the patterns and frequencies of mutations conferring first-line drug resistance in Ethiopia using isolates collected from the drug resistance survey. The isolates were obtained before the implementation of rapid molecular tests. The findings will enhance our understanding of the patterns and frequencies of mutations that confer resistance, which is crucial for developing a comprehensive catalog of mutations.

DOI: 10.1128/spectrum.01454-25
PMCID: PMC13055254
PMID: 41718507 [Indexed for MEDLINE]

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

14. Genetic diversity and drug resistance profiles of Mycobacterium tuberculosis among Ethiopian children as determined by whole-genome sequencing.

Microbiol Spectr. 2026 Apr 7;14(4):e0273625. doi: 10.1128/spectrum.02736-25. Epub 2026 Feb 27.

Abebaw Y(1)(2), Ayele A(3), Alemayehu DH(3), Gebremicael G(2), Diriba G(2), Weldemariam AG(2), Zerihun B(2), Moga S(2), Adnew B(3), Melaku K(3), Getahun M(2), Argaw R(4), Sheth A(5), Abebe M(3), Abegaz WE(1).

Author information:
(1)Department of Microbiology, Immunology and Parasitology, College of Health Sciences, Addis Ababa University, Addis Ababa, Ethiopia.
(2)Ethiopian Public Health Institute, Addis Ababa, Ethiopia.
(3)Armauer Hansen Research Institute, Addis Ababa, Ethiopia.
(4)Department of Pediatrics and Child Health, College of Health Sciences, Addis Ababa University, Addis Ababa, Ethiopia.
(5)Department of Medicine, School of Medicine, Emory University, Atlanta, Georgia, USA.

Ethiopia ranks 30th among the tuberculosis (TB) burden countries, with children representing a significant yet understudied population group. This study aims to investigate the genetic diversity and drug-resistant profile among Ethiopian children. We included children under 15 years of age diagnosed with

culture-confirmed pulmonary TB/drug-resistant TB between January 2017 and June 2023. Phenotypic drug susceptibility testing and whole-genome sequencing were conducted for 85 Mycobacterium tuberculosis (MTB) isolates. Demographic data were combined with genomic information. Lineage 4 was the most dominant (77.6%), while lineage 2 was less common (1%). Within lineage 4, several sub-lineages were identified, with lineage 4.2.2.2 being notably the most predominant (48%). Most of these cases were from Oromia (58%), including the hotspot areas for lineage 4 that were identified at a 99% confidence level. Among 17 MDR/pre-XDR-TB isolates, lineages 3 and 4.2.2.2 were the dominantly observed lineages/sub-lineages, with proportions of 29% and 65%, respectively. Of the 85 cases, 30.5% were drug-resistant TB to at least one of the five first-line anti-TB drugs tested by phenotypic drug susceptibility testing. Of these 26 drug-resistant TB cases, 23 were concordant with whole-genome sequencing characterization. The most frequent resistance mutations to rifampicin were found in the rpoB gene, specifically p.Ser450Leu (88%), followed by isoniazid in the katG gene, p.Ser315Thr (86%). Multidrug-resistant TB was strongly associated with MTB lineages (P = 0.007). This study identified high genetic diversity of M. tuberculosis and related drug-resistance mutations, with a strong concordance between whole-genome sequencing-based predictions and phenotypic drug susceptibility testing.
IMPORTANCE: Our findings revealed a high genetic diversity of Mycobacterium tuberculosis among Ethiopian children, with the most common lineage being lineage 4, specifically lineage 4.2.2.2, in which a higher frequency of multidrug-resistant tuberculosis (TB) was observed. Additionally, we identified regional hotspots, suggesting ongoing community transmission. Moreover, whole-genome sequencing demonstrated high concordance with phenotypic drug susceptibility testing and identified mutation genes associated with first- and second-line anti-TB drugs, highlighting its usefulness in providing comprehensive results for resistance detection in children. Thus, it is essential for integrating genomic surveillance into childhood TB and drug resistance control.

DOI: 10.1128/spectrum.02736-25
PMCID: PMC13055266
PMID: 41757911 [Indexed for MEDLINE]

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

15. Exposure-QTc modeling of bedaquiline, pretomanid, and clofazimine in adults with Tuberculosis.

Antimicrob Agents Chemother. 2026 Apr;70(4):e0139925. doi: 10.1128/aac.01399-25. Epub 2026 Mar 9.

Abdelwahab MT(1), Svensson EM(2)(3), Diacon AH(4), Conradie A(5), Olugbosi M(5), Dawson R(6), Maartens G(1), Denti P(1).

Author information:

(1)Division of Clinical Pharmacology, Department of Medicine, University of Cape Town, Cape Town, South Africa.
(2)Department of Pharmacy, Pharmacology and Toxicology, Radboud University Medical Center, Nijmegen, the Netherlands.
(3)Department of Pharmacy, Uppsala University, Uppsala, Sweden.
(4)Task, Bellville, South Africa.
(5)Global Alliance for TB Drug Development, New York, New York, USA.
(6)Division of Pulmonology and Department of Medicine, University of Cape Town Lung Institute, Cape Town, South Africa.

Drug resistance (DR) poses a critical challenge to global efforts to manage tuberculosis (TB). Limited information is available on the combined cardiotoxicity of bedaquiline (BDQ), pretomanid (Pa), and clofazimine (CFZ), key drugs in current DR-TB treatment regimens. All of those prolong the QT interval. We aimed to describe this interaction to predict possible toxicities with established and novel dosing regimens to identify patients at higher risk of QT prolongation. The data for this analysis were obtained from an early-bactericidal activity study in drug-susceptible-TB of several TB drugs. We developed a competitive interaction model to evaluate combined concentration-QTc effect of all three drugs. The model was developed using ECG-matched PK measurements (105 patients, 2,062 observations). The model identified a maximum QT increase by all three drugs of 44.5 ms with respective EC50 values for BDQ, Pa, and CFZ of 0.57, 0.903, and 26.9 mg/L. For patients aged 70 years with non-black ancestry, at risk of increased BDQ exposure, simulations showed that 39.1% had a drug-induced QT change >30 ms after the loading period; this was 29.4% for following BDQ 400 mg daily regimen (part of UNITE4TB program). Reassuringly, no simulations resulted in a QTcF >500 ms, and less than 1% exceeded 480 ms or a change from baseline of >60 ms. We present a joint concentration-QT model of BDQ, Pa, and CFZ. The competitive interaction model serves as a tool to predict possible combined exposure-induced QT prolongation of these drugs in different dosing regimen and identify patients at high risk of significant QT-prolongation.

DOI: 10.1128/aac.01399-25
PMCID: PMC13041299
PMID: 41801043 [Indexed for MEDLINE]

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

16. Predicting isoniazid resistance in Mycobacterium tuberculosis complex in New York State using whole-genome sequencing.

J Clin Microbiol. 2026 Apr 8;64(4):e0160925. doi: 10.1128/jcm.01609-25. Epub 2026 Mar 18.

Patel K(#)(1), Shea J(#)(1), Lapierre P(1), Halse TA(1), Kohlerschmidt D(1), Dickinson M(1), Escuyer V(1), Musser KA(1).

Author information:
(1)Wadsworth Center, New York State Department of Health, Albany, New York, USA.
(#)Contributed equally

Isoniazid (INH) is a critical antibiotic used worldwide for the treatment and prophylaxis of tuberculosis. Drug resistance (DR) to INH is the single most common type of DR, mediated by multiple genes/loci, including katG, inhA, mabA, mabA-inhA, and the oxyR-ahpC intergenic region. Over the course of 6 years, we performed a two-phase study of 3,696 Mycobacterium tuberculosis complex (MTBC) strains, aiming to determine the molecular basis of INH resistance and assess whole-genome sequencing (WGS) for predicting resistance. In phase 1, we performed a side-by-side study, including 1,767 strains with paired phenotypic drug susceptibility testing (DST) and genotypic DST. We found WGS capable of accurately predicting INH resistance with a sensitivity of 90.3% and a specificity of 99.8%. The negative predictive value of WGS for INH susceptibility was 98.8%. Based on these findings, we developed a molecular testing algorithm where phenotypic DST (pDST) was reduced and applied this new testing algorithm in phase 2 to 1,929 MTBC strains, resulting in streamlined testing, reduced cost, and decreased turnaround time (TAT). The prevalence of INH resistance among MTBC strains in New York was found to be 10.2%. Of the 3,696 isolates tested, 337 were predicted INH-resistant by WGS. Of 41 additional strains exhibiting phenotypic INH resistance, 38 were found to have mutations in genes known to be associated with INH resistance. This study demonstrates the utility of WGS as a molecular tool for predicting INH DR and shows that the vast majority of INH resistance in MTBC has a molecular basis in known resistance loci.
IMPORTANCE: Isoniazid (INH) is one of the two most critical antibiotics used as part of standard treatment of tuberculosis and is also used as preventative therapy for contacts of tuberculosis patients, despite having a higher rate of drug resistance than all other antibiotics used in standard therapy. Furthermore, isoniazid resistance typically precedes rifampin resistance in the development of multidrug-resistant TB. As such, the reliable detection of INH resistance is crucial for case management and to limit the acquisition of additional drug resistance. The present study describes a whole-genome sequencing approach to predicting INH resistance from clinical isolates and models how this technology can be used within a reduced phenotypic drug susceptibility testing algorithm to limit duplicate testing, saving resources and time while maintaining the sensitivity of resistance detection.

DOI: 10.1128/jcm.01609-25
PMCID: PMC13059772
PMID: 41848297 [Indexed for MEDLINE]

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

17. Safety and Effectiveness of Contezolid versus Linezolid in Drug-Resistant Tuberculosis: A 12-Month Retrospective Study from China.

Infect Drug Resist. 2026 Mar 25;19:573058. doi: 10.2147/IDR.S573058. eCollection

2026.

Xiao Y(#)(1), Huang PF(#)(1), Xie L(1), Gao L(1), Han Y(1), Liu S(1), Liang YX(1), Xiong YJ(1), Wang H(1).

Author information:
(1)Department of Tuberculosis, Anhui Provincial Chest Hospital (Anhui Institute of Tuberculosis Control), Hefei, Anhui, 230022, People's Republic of China.
(#)Contributed equally

BACKGROUND: Contezolid (CZD), a novel oxazolidinone, is a promising therapeutic option for the treatment of Mycobacterium tuberculosis. However, clinical evidence of its safety and efficacy in managing drug-resistant tuberculosis (DR-TB) remains limited.
METHODS: A retrospective analysis was performed on 135 patients with DR-TB treated at Anhui Chest Hospital between January 2022 and September 2024, including 27 on CZD-based regimens and 108 on linezolid (LZD)-based regimens. Drug-related adverse events (AEs), including bone marrow suppression, peripheral neuropathy, optic neuritis, and gastrointestinal reactions, were systematically recorded. Therapeutic efficacy was comprehensively evaluated based on clinical symptoms, radiological findings, and microbiological results. The 12-month safety and efficacy of the two regimens in DR-TB were assessed.
RESULTS: The incidence of AEs in the LZD group reached 54.63%, significantly higher than the 3.7% observed in the CZD group ($\chi 2 = 22.69$, $P < 0.001$). Notably, the rates of bone marrow suppression and peripheral neuropathy in the LZD group were 22.22% and 27.78%, respectively, whereas no such AEs were reported in the CZD group ($P = 0.004$; $P < 0.001$, respectively). Regarding efficacy, CZD and LZD showed comparable outcomes in patients with DR-TB ($P = 0.491$).
CONCLUSION: CZD may have clinical efficacy comparable to LZD in treating DR-TB, while appearing to offer an improved safety profile, notably in reducing bone marrow suppression and peripheral neuropathy.

DOI: 10.2147/IDR.S573058
PMCID: PMC13033251
PMID: 41913743

Conflict of interest statement: The authors report no conflicts of interest in this work.

18. Limited contribution of compensatory mutations to MDR/RR-TB clustering in Hunan Province, China: a population-based whole-genome sequencing study.

Microbiol Spectr. 2026 Apr 7;14(4):e0259725. doi: 10.1128/spectrum.02597-25. Epub 2026 Mar 3.

He W(1), Tan Y(2), Song Z(3), Bai H(2), Hu P(2), Ou X(4), Zhao B(4), Liu X(1), Zhao Y(4).

Author information:
(1)Department of Clinical Laboratory, Capital Medical University, Beijing Tongren Hospital, Beijing, China.
(2)Hunan Provincial Chest Hospital, Tuberculosis Control Institution of Hunan Province, Changsha, Hunan, China.
(3)Department of Clinical Laboratory, Capital Medical University, Capital Institute of Pediatrics, Beijing, China.
(4)National Key Laboratory of Intelligent Tracking and Forecasting for Infectious Diseases, Chinese Center for Disease Control and Prevention, National Center for Tuberculosis Control and Prevention, Beijing, China.

Transmission of rifampicin-resistant and multidrug-resistant tuberculosis (MDR/RR-TB) is a major driver of the global drug-resistant TB epidemic, yet the contribution of compensatory mutations to its spread remains uncertain. We analyzed 206 non-duplicate MDR/RR-TB isolates collected from five surveillance sites in Hunan Province, China, between 2013 and 2020 using whole-genome sequencing. Transmission clusters were defined by ≤12 single-nucleotide polymorphism (SNP) differences, and compensatory mutations in rpoA, rpoB, and rpoC were identified through a curated mutation catalog and phylogenetic evidence. Clusters were further classified based on whether compensatory mutations predated transmission (C-type), arose after transmission (M-type), or were absent (N-type), with M-type clusters excluded to reduce confounding. Among the 206 isolates, 63 (30.6%) carried at least one compensatory mutation, predominantly in rpoC, and 27 clusters (32.5%) were identified, ranging from 2 to 6 isolates. No significant difference was observed in clustering frequency between compensated and non-compensated strains (21.7% vs 32.8%, P = 0.113), nor in cluster size between C-type and N-type clusters (P = 0.961). These findings demonstrate that compe nsatory mutations do not significantly affect transmission clustering at the population level; instead, prolonged infectious periods associated with diagnostic delays and treatment challenges are more likely to sustain MDR/RR-TB spread, underscoring the importance of rapid detection, timely effective therapy, and robust patient management to curb transmission.IMPORTANCEUnderstanding the drivers of multidrug-resistant and rifampicin-resistant tuberculosis (MDR/RR-TB) transmission is critical for global TB control. Compensatory mutations in RNA polymerase subunits have been proposed as key contributors to the success of drug-resistant strains, yet population-level evidence has been limited. In this population-based genomic study of 206 MDR/RR-TB isolates collected over 8 years in Hunan Province, China, we systematically examined the association between compensatory mutations and transmission clustering. Our results show that compensatory mutations did not significantly increase clustering frequency or cluster size, indicating a limited impact on the spread of MDR/RR-TB in the community. These findings challenge the prevailing assumption that compensatory evolution is a major determinant of transmission success and provide robust genomic evidence to refine our understanding of drug-resistant TB epidemiology.

DOI: 10.1128/spectrum.02597-25

PMCID: PMC13055236
PMID: 41773868 [Indexed for MEDLINE]

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

19. Inequalities in financial burden of tuberculosis among affected families across 19 low- and middle-income countries.

PLOS Glob Public Health. 2026 Apr 3;6(4):e0006172. doi: 10.1371/journal.pgph.0006172. eCollection 2026.

Eshun G(1)(2), Sesay U(3)(4), Osborne A(5).

Author information:
(1)Seventh-Day Adventist Hospital, Agona-Asamang, Ghana.
(2)The Royal (Dick) School of Veterinary Studies, University of Edinburgh, Midlothian, United Kingdom.
(3)Africa Field Epidemiology Network, Freetown, Sierra Leone.
(4)Africa Center for Disease Control and Prevention, Addis Ababa, Ethiopia.
(5)Institute for Development, Western area, Freetown, Sierra Leone.

Tuberculosis (TB) remains a major global public health problem, with majority of the cases occurring in low- and middle-income countries (LMICs). Despite its growing burden, cross-country evidence on inequalities in financial burden among affected families is limited. This study aims to assess catastrophic costs and related inequalities across 19 LMICs. The study employed a cross-country analysis of 19 national TB Patient Cost Surveys data extracted from the WHO Health Equity Assessment Toolkit (HEAT) online software. The main outcome was the percentage of families affected by TB facing catastrophic costs due to TB. Inequalities were assessed by drug resistance status, comparing drug-susceptible TB (DS-TB) and drug-resistant TB (DR-TB), using four summary measures: Difference (D), Ratio (R), Population Attributable Risk (PAR), and Population Attributable Fraction (PAF). No inferential statistics were done beyond the descriptive phase. The average percentage of TB-affected families experiencing catastrophic costs due to TB ranged from 19.2% in Lesotho to 80% in Zimbabwe. In 10 of the 19 countries, over half of TB-affected families faced catastrophic costs. When disaggregated, all countries reported higher catastrophic costs among DR-TB-affected families, except Burkina Faso. The absolute difference (D) between DR-TB and DS-TB ranged from -4% in Burkina Faso to 74.8% in Lesotho. The highest disparities were in Lesotho (D = 74.8%), Kenya (D = 60%), and Papua New Guinea (D = 51%). Ratio showed DR-TB families were up to 5.3 times more likely to experience catastrophic costs in Lesotho, with high ratios also in Kenya (3.3) and Thailand (2.6). All PAR and PAF values were negative, indicating that reducing the financial burden on DR-TB families to the level of DS-TB families could significantly lower the overall rate of catastrophic costs. The greatest potential gains were observed in Mongolia (PAR = 6%), DRC (PAR = 5%), and Brazil (PAR = 3.7%). The study showed substantial inequalities in the financial burden of TB on families across 19 LMICs, with DR-TB-affected families facing higher

risks of catastrophic health cost than DS-TB families. There is an urgent need for targeted financial protection interventions, integrated within broader UHC strategies, to ensure that no TB-affected family is left behind.

DOI: 10.1371/journal.pgph.0006172
PMCID: PMC13048425
PMID: 41931476

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

20. Factors Predicting successful treatment outcome with novel BPaLM/BPaL regimen in individuals with drug-resistant tuberculosis: Experience From Indonesia.

PLoS One. 2026 Apr 1;21(4):e0345702. doi: 10.1371/journal.pone.0345702. eCollection 2026.

Soeroto AY(1)(2), Purwiga A(1), Suryadinata H(1)(2), Alisjahbana B(1)(3), Makmun A(1)(4), Supriatna YA(1)(2), Pranggono EH(1)(2), Lestari BW(5)(6).

Author information:
(1)Department of Internal Medicine, Faculty of Medicine Universitas Padjadjaran, Dr. Hasan Sadikin General Hospital, Bandung, West Java, Indonesia.
(2)Division of Respirology and Critical Care Medicine, Faculty of Medicine Universitas Padjadjaran, Dr. Hasan Sadikin General Hospital, Bandung, West Java, Indonesia.
(3)Division of Tropical and Infectious Disease, Faculty of Medicine Universitas Padjadjaran, Dr. Hasan Sadikin Bandung General Hospital, West Java, Indonesia.
(4)Division of Nephrology and Hypertension, Faculty of Medicine, Universitas Padjadjaran, Dr. Hasan Sadikin Bandung General Hospital, West Java, Indonesia.
(5)Department of Public Health, Faculty of Medicine Universitas Padjadjaran, Bandung, West Java, Indonesia.
(6)Research Center for Care and Control of Infectious Disease, Universitas Padjadjaran, Bandung, Indonesia.

BACKGROUND AND AIMS: Drug-resistant tuberculosis (DR-TB) poses a serious challenge in Indonesia, with treatment success rates of only 50%. The BPaLM/BPaL regimen represents the latest therapeutic approach, offering shorter duration, minimal side effects, and treatment success rates of 84-90%. An operational research study conducted in Indonesia from July 2022 to March 2023 demonstrated a highly promising treatment success rate of 97.6% with the BPaLM/BPaL regimen. This study aimed to evaluate the effectiveness of the BPaLM/BPaL regimen through real-world implementation among individuals with DR-TB and identify key factors

associated with successful treatment outcomes.
METHODS: This retrospective cohort study analyzed 170 DR-TB individuals treated with BPaLM/BPaL regimens at Hasan Sadikin General Hospital, a tertiary hospital in West Java, Indonesia from January 2024 to January 2025. Data were collected from the Indonesian National DR-TB registers. A successful treatment outcome was defined as completion of treatment with bacteriological response and no evidence of treatment failure. Multivariate logistic regression was used to identify factors most associated with successful treatment outcomes and presented as adjusted odds ratios (aOR) with 95% confidence intervals.
RESULTS: The study achieved an 88.8% successful treatment rate with BPaLM/BPaL regimens. Multivariate analysis revealed treatment with no missed dose events as the most important predictor for successful treatment outcome with aOR=6.42 (95%CI 1.44-28.45, p = 0.01), followed by nutritional status improvement during treatment with aOR=3.31 (95%CI 1.06-10.37, p = 0.03). A total of 132 patients (77.6%) experienced adverse effects, predominantly gastrointestinal symptoms (93.1%) and peripheral neuropathy (30.3%). Culture conversion occurred within 2 months in 95.2% of patients, with a median time to conversion of 111 days.
CONCLUSION: No missed dose events and nutritional status improvement are key predictors of successful treatment outcome. These findings support the implementation of BPaLM/BPaL regimens in Indonesia's national TB program, with emphasis on ensuring treatment adherence and nutritional status monitoring for optimal outcomes.

DOI: 10.1371/journal.pone.0345702
PMCID: PMC13042743
PMID: 41920826 [Indexed for MEDLINE]

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

21. Treatment outcomes and long-term relapse-free survival after multidrug-resistant tuberculosis treatment in Latvia: a retrospective national cohort study.

Lancet Reg Health Eur. 2026 Apr 9;65:101676. doi: 10.1016/j.lanepe.2026.101676. eCollection 2026 Jun.

Meier SC(1)(2)(3), Kukša L(3), Ķauķe S(3), Riekstina V(3), Biraua E(3), Jain N(1)(3)(4), Lange C(2)(5)(6)(7)(8), Brehm TT(2)(8)(9).

Author information:
(1)Faculty of Medicine, Riga Stradiņš University, 16 Dzirciema Street, Riga, Latvia.
(2)Department of Clinical Infectious Diseases, Research Center Borstel, Leibniz

Lung Center, Borstel, Germany.
(3)Riga East University Hospital Centre of TB and Lung Diseases, Riga, Latvia.
(4)Statistics Unit, Riga Stradiņš University, 16 Dzirciema Street, Riga, Latvia.
(5)Respiratory Medicine and International Health, University of Lübeck, Germany.
(6)Baylor College of Medicine and Texas Children's Hospital, Global TB Program, Houston, TX, USA.
(7)Institute for Infection Research and Vaccine Development (IIRVD), University Medical Center Hamburg-Eppendorf, Hamburg, Germany.
(8)German Centre for Infection Research (DZIF), Partner Site Hamburg-Lübeck-Borstel-Riems, Germany.
(9)Division of Infectious Diseases, I. Department of Internal Medicine, University Medical Center Hamburg-Eppendorf, Hamburg, Germany.

BACKGROUND: Treatment success rates of multidrug-resistant and rifampicin-resistant tuberculosis (MDR/RR-TB) lag behind those for drug-susceptible TB. However, outcome definitions censoring follow-up at treatment completion may underestimate effectiveness and fail to capture relapse-free survival.
METHODS: We conducted a retrospective national cohort study including all adults initiating individualized MDR/RR-TB treatment in the Republic of Latvia between 2005 and 2021. Demographic, clinical, and microbiological data were linked to long-term follow-up on relapse and vital status. Treatment outcomes were classified according to World Health Organization (WHO), TBnet (Tuberculosis Network European Trials Group), expert consilium, and long-term outcome definitions. Predictors of cure were assessed using Firth logistic regression. A landmark analysis at 18 months evaluated the association between treatment duration (≤9 months, 10-17 months, and ≥18 months) and relapse-free survival.
FINDINGS: Among 1299 patients (median age 44 years; 74.9% male), cure rates were 4.8% (n = 62) under WHO definitions, 53.1% (n = 690) under TBnet definitions, and 60.8% (n = 790) under the consilium-based classification. Under long-term follow-up outcome definitions, 56.5% (n = 734) achieved cure and 76.9% (n = 999) achieved relapse-free survival. Receiving ≥3 susceptible drugs independently predicted WHO-defined treatment success (adjusted OR 6.53, 95% CI 2.22-31.69; p < 0.001). In the landmark analysis, treatment duration ≤9 months was associated with higher hazard of relapse or death compared with ≥18 months (HR 1.76, 95% CI 1.03-3.00; p = 0.038), whereas outcomes were similar for 10-17 months vs. ≥18 months (HR 0.71, 95% CI 0.42-1.22; p = 0.22).
INTERPRETATION: In this national cohort treated with individualized MDR/RR-TB regimens, long-term relapse-free outcomes substantially exceeded treatment success defined at treatment completion. These findings support relapse-free survival as complement to end-of-treatment metrics.
FUNDING: This study received no external funding.

DOI: 10.1016/j.lanepe.2026.101676
PMCID: PMC13091304
PMID: 42006570

Conflict of interest statement: C.L. reports personal fees from Astra Zeneca,

Gilead, GSK, INSMED, MedUpdate, MedUpdateEurope and Pfizer for lecturing at sponsored symposia outside of the presented work. S.C.M., L.K., S.K., V.R., E.B., N.J. and T.T.B have no interests to declare.

22. Targeted next-generation sequencing for comprehensive diagnosis and drug resistance detection in pulmonary and extrapulmonary tuberculosis: a single-center retrospective study.

Microbiol Spectr. 2026 Apr 7;14(4):e0169825. doi: 10.1128/spectrum.01698-25. Epub 2026 Feb 27.

Dai J(#)(1)(2), Li Q(#)(1), Wan J(1), Sun F(3)(4), Zhou G(3), Yang M(1), Dong C(1), Fang Y(1), Li L(3), Wang L(5), Liu G(1).

Author information:
(1)Department of Public Laboratory, The Third People's Hospital of Kunming City/Infectious Disease Clinical Medical Center of Yunnan Province, Kunming, Yunnan, People's Republic of China.
(2)International Research Fellow, Prince of Songkla University, Hat Yai, Songkhla, Thailand.
(3)Genskey Medical Technology Co., Ltd, Beijing, People's Republic of China.
(4)College of Life Sciences, Peking University, Beijing, People's Republic of China.
(5)Department of Medical Laboratory, The Third People's Hospital of Kunming City/Infectious Disease Clinical Medical Center of Yunnan Province, Kunming, Yunnan, People's Republic of China.
(#)Contributed equally

Tuberculosis (TB), including drug-resistant forms, is a significant global health issue requiring accurate and rapid diagnostic tools. Traditional diagnostic methods suffer from low sensitivity and slow results, while nucleic acid amplification tests (NAATs) like Xpert MTB/RIF provide faster but incomplete solutions. Targeted next-generation sequencing (tNGS) has the potential to simultaneously detect Mycobacterium tuberculosis, drug resistance mutations, and co-infecting pathogens. This study evaluates the effectiveness of tNGS for TB detection across various pulmonary and extrapulmonary TB samples. We retrospectively enrolled 159 patients with suspected TB at Kunming Third People's Hospital. Specimens included 126 pulmonary and 33 extrapulmonary samples. All samples underwent tNGS, and results were compared against conventional microbiological tests and NAATs. tNGS demonstrated high diagnostic sensitivity for both pulmonary TB and extrapulmonary TB, achieving 83.9% sensitivity in bronchoalveolar lavage fluid, 89.5% in sputum, and 100% in extrapulmonary samples. tNGS showed an 83.3% agreement with Xpert in detecting rifampicin resistance. Additionally, tNGS also identified 22 drug resistance mutations, which are critical for predicting multidrug-resistant TB and pre-extensively drug-resistant TB. Additionally, tNGS effectively detected co-infecting respiratory pathogens, enhancing the understanding of complex TB cases. tNGS offers a highly sensitive and comprehensive approach for detecting TB and drug resistance, outperforming traditional methods in both pulmonary and

extrapulmonary samples. It effectively identifies co-infections, providing a holistic view that enhances patient management, particularly in cases involving multidrug-resistant strains. These findings underscore tNGS's potential to improve TB diagnostics and patient management through faster and more precise detection methods.IMPORTANCETuberculosis (TB) continues to be a leading cause of morbidity and mortality worldwide, particularly among marginalized populations. Timely and accurate diagnosis of TB, particularly extrapulmonary TB, remains challenging in low-resource settings, primarily due to non-specific clinical presentations that hinder early suspicion, along with limitations in both diagnosis and drug resistance detection. Additionally, targeted next-generation sequencing can identify co-infections with other clinically relevant pathogens, providing a more comprehensive understanding of each patient's infectious profile. By leveraging advanced sequencing technologies, our findings highlight a powerful diagnostic approach that can improve TB diagnosis, support appropriate treatment strategies, and may increasingly benefit patients in underserved settings as sequencing platforms become more accessible and costs continue to decrease.

DOI: 10.1128/spectrum.01698-25
PMCID: PMC13055381
PMID: 41757961 [Indexed for MEDLINE]

Conflict of interest statement: L.L., G.Z., and F.S. are employed by Genskey Inc., Beijing, China. The other authors declare that they have no conflict of interest to report.

23. Factors Influencing Adherence to All-Oral Short-Course Treatment for DR-TB and Establishment of a Predictive Model.

Infect Drug Resist. 2026 Apr 9;19:590929. doi: 10.2147/IDR.S590929. eCollection 2026.

Huang J(#)(1)(2), Zhu QD(#)(2), Li ZF(2), Xie K(2), Deng JN(2), Ma QY(2), Su HZ(2), Lu TT(2), Lu XF(2), Hu YL(1), Xie ZH(2).

Author information:
(1)Faculty of Data Science, City University of Macau, Macau, 999878, People's Republic of China.
(2)HIV/AIDS Clinical Treatment Center of Guangxi (Nanning) and The Fourth People's Hospital of Nanning, Nanning, 530000, People's Republic of China.
(#)Contributed equally

OBJECTIVE: To explore factors influencing adherence to all-oral short-course treatment for drug-resistant tuberculosis (DR-TB) and establish a predictive model.
METHODS: The study is retrospective and single-center. 241 TB patients treated at our hospital from January 2022 to December 2024 were retrospectively selected. Using a random number table method in a 7:3 ratio, patients were divided into a modeling group (n=169) and a validation group (n=72). The

modeling group patients were categorized into groups of good adherence (n=89) and poor adherence (n=80). Univariate and binary Logistics regression analyses were used to identify influencing factors. A predictive model was constructed using SPSS, and R language was utilized to assess the model's application value through receiver operating characteristic (ROC) curves, calibration curves, and decision curve analysis (DCA).
RESULTS: Binary logistic regression analysis showed that family monthly income, level of education, history of previous confirmed TB, and family-supervised drug administration were influencing factors for adherence to short-course treatment for DR-TB (P<0.05). The combined predictive model expression was Logit(P) = -1.394 + (0.421*family monthly income) + (0.344*level of education) + (0.310*history of previous confirmed TB) + (0.452*family-supervised drug administration). The model demonstrated good consistency between predicted risks and actual risks, with calibration curves showing a slope close to 1 in both the modeling group and validation group. ROC analysis indicated an area under the curve of 0.88 in the modeling group. For the validation group, the AUC was 0.85. The DCA curve illustrated a clear net benefit, indicating good clinical utility of the model.
CONCLUSION: Family monthly income, level of education, history of previous confirmed TB, and family-supervised drug administration are factors influencing adherence to short-course treatment for DR-TB. The model established based on these factors holds significant value in predictive applications.

DOI: 10.2147/IDR.S590929
PMCID: PMC13075505
PMID: 41983105

Conflict of interest statement: Jie Huang and Qing-Dong Zhu are co-first authors for this study. The authors declare no conflicts of interest in this work.

24. Unequal patterns of tuberculosis in women of reproductive age: Insights from the Global burden of disease study 2021.

Infect Med (Beijing). 2026 Mar 26;5(2):100250. doi: 10.1016/j.imj.2026.100250. eCollection 2026 Jun.

Liu T(1)(2), Zhang L(2), Liu J(2)(3), Liu Y(2)(4), Xiong A(2)(3), Ran Q(2), He X(2), Jiang L(1)(5), Li G(2)(3), Wang J(1)(2)(3).

Author information:
(1)Clinical Medicine Department, North Sichuan Medical College, Nanchong 637000, China.
(2)Laboratory of Allergy and Precision Medicine, Department of Respiratory Medicine, Chengdu Institute of Respiratory Health, The Third People's Hospital of Chengdu, Chengdu 610041, China.
(3)College of Medicine, Southwest Jiaotong University, Chengdu 611756, China.

(4)State Key Laboratory of Quality Research in Chinese Medicine, Macao University of Science and Technology, Macao Special Administrative Region 999078, China.
(5)Department of Respiratory and Critical Care Medicine, The Affiliated Hospital of North Sichuan Medical College, Nanchong 637000, China.

BACKGROUND: Tuberculosis (TB) remains a major global cause of mortality and is a leading cause of death among women of reproductive age (WRA). Untreated TB in this population endangers both maternal and neonatal health, yet the age-stratified burden and the shifting distribution of drug-resistant tuberculosis remain poorly defined in global health agendas. This study aims to employ data from the 2021 Global Burden of Disease Study to systematically evaluate the global, regional, and age-specific burden of TB among WRA, to delineate temporal trends in drug-resistant TB, and to assess associated risk factors using standardized estimation methods.
METHODS: Leveraging data from the Global Burden of Disease Study 2021 covering 204 countries and territories, we systematically assessed TB burden in WRA aged 15-49 years from 1990 to 2021. We analyzed age-standardized incidence, prevalence, mortality, and disability-adjusted life years across socio-demographic index (SDI) regions, TB subtypes, and risk factors. Projections to 2030 were generated using autoregressive integrated moving average models.
RESULTS: Between 1990 and 2021, the global prevalence and incidence of TB among WRA declined significantly. However, this decline was uneven across age groups, disease types, and regions. TB incidence peaked in women aged 15-24 years, while mortality and disease burden were highest among those aged 45-49 years. Drug-resistant tuberculosis was most prominent in the 25-29 age group. Geographically, sub-Saharan Africa remained the core of the global TB burden, with BRICS (Brazil, Russia, India, China, South Africa) countries carrying significantly higher burdens than G7 countries. Risk attribution patterns revealed a shift from behavioral to metabolic drivers, with high body mass index emerging as the leading risk factor in high-SDI regions. Middle-SDI regions showed a combination of metabolic and behavioral risks, while metabolic factors remained dominant in low-SDI settings. Drug-susceptible tuberculosis was primarily linked to smoking and malnutrition, whereas drug-resistant tuberculosis was increasingly associated with metabolic dysfunction.
CONCLUSIONS: Despite global declines in TB prevalence and incidence among WRA, stark disparities persist. The age-stratified rise in drug-resistant TB, particularly in resource-constrained regions, underscores the need for targeted, gender-responsive interventions that integrate infectious disease control with metabolic health strategies.

DOI: 10.1016/j.imj.2026.100250
PMCID: PMC13090512
PMID: 42004739

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.

25. Accuracy of nanopore-based targeted next-generation sequencing assay for detection of Mycobacterium tuberculosis and drug resistance from non-sputum specimens: a multicenter prospective study in China.

J Clin Microbiol. 2026 Apr 8;64(4):e0143325. doi: 10.1128/jcm.01433-25. Epub 2026 Feb 24.

Yang Z(#)(1), Ma Z(#)(1), Liu Z(#)(2)(3), Li P(#)(4), Liu Y(#)(5), Cai L(#)(6), Su B(#)(7), Li D(#)(2), Wang L(4), Cui L(4), Shao R(5), Fan D(6), Tan Y(7), Shen D(2), Shi H(2), Li L(1), Pang Y(1).

Author information:
(1)Beijing Key Laboratory for Key Technologies in Tuberculosis Prevention and Control, Department of Bacteriology and Immunology, Beijing Chest Hospital, Capital Medical University/Beijing Tuberculosis and Thoracic Tumor Research Institute, Beijing, China.
(2)Zhejiang Key Laboratory of Digital Technology in Medical Diagnostics, Dian Diagnostics Group Co., Ltd., Hangzhou, Zhejiang, China.
(3)Department of Infectious Diseases, Sir Run Run Shaw Hospital of Zhejiang University School of Medicine, Hangzhou, China.
(4)Department of the Fifth Tuberculosis, Chongqing Public Health Medical Center, Chongqing, China.
(5)Infectious Disease Hospital of Heilongjiang Province, Harbin, Heilongjiang, China.
(6)Department of Clinical Laboratory, Hangzhou Red Cross Hospital, Hangzhou, China.
(7)Department of Clinical Laboratory, Guangzhou Chest Hospital, Guangzhou, China.
(#)Contributed equally

Tuberculosis (TB) remains the leading cause of mortality caused by a single infectious agent. Targeted next-generation sequencing (tNGS) has become a promising molecular method for TB diagnosis, but its accuracy and application for non-sputum specimens still remain unexplored. In this multicenter prospective lab-developed assay, 701 participants from five designated TB hospitals from different provinces in China were recruited. Non-sputum specimens were collected for tNGS, Xpert Mycobacterium tuberculosis (MTB)/RIF (Xpert), and culture tests. The diagnostic accuracy of tNGS for TB patients was evaluated compared with the microbiological reference standard (MRS). Phenotypic drug susceptibility tests (DSTs) were conducted using culture-positive isolates and employed to assess the accuracy of tNGS for detecting drug resistance. We found that the tNGS assay exhibited high diagnostic accuracy with sensitivity and specificity of 93.4% (95% CI, 91.5%-95.2%) and 93.2% (95% CI, 91.3%-95.0%) when utilizing MRS as the gold standard. The diagnostic performance of tNGS was robust regardless of specimen types and clinical symptoms. tNGS also showed a detection potential for other coinfecting respiratory pathogens. More than 90%

of tNGS-positive individuals gained drug susceptibility results, which were mainly dependent on bacterial loads. Compared with phenotypical DSTs, tNGS had high sensitivities and specificities for the detection of rifampicin, isoniazid, streptomycin, ethambutol, and levofloxacin resistance. Our findings illustrated that tNGS assay is a rapid and highly sensitive test for TB diagnosis and simultaneous detection of drug resistance in non-sputum specimens. Its accuracy gain compared with conventional methods is most remarkable in TB patients with low bacterial loads.IMPORTANCETuberculosis (TB) diagnosis still remains challenging, especially in non-sputum patients. Nanopore-based targeted next-generation sequencing (tNGS) is a promising technology for the detection of TB cases and drug resistance, which has capacities to provide a panel of drug resistance profiles. The purpose of this study is to explore the diagnostic performance of tNGS for non-sputum specimens from five designated TB hospitals from different regions in China. Compared with the microbiological reference standard (MRS), tNGS exhibited high sensitivity and specificity, which are associated with bacterial loads in samples. Meanwhile, tNGS has capacities to detect coinfecting respiratory pathogens and produce drug-resistant profiles. Therefore, our findings suggested that tNGS is an alternative method for the diagnosis of non-sputum TB patients.CLINICAL TRIALSThis study is registered with Chinese Clinical Trial Registry as ChiCTR2400088518.

DOI: 10.1128/jcm.01433-25
PMCID: PMC13059801
PMID: 41733380 [Indexed for MEDLINE]

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

26. Philadelphus tenuifolius Leaf Extract Exhibits Anti-Tuberculosis Activity by Enhancing Host Autophagy and Immunity: A Promising Host-Directed Therapeutic Candidate.

J Microbiol Biotechnol. 2026 Mar 26;36:e2601032. doi: 10.4014/jmb.2601.01032.

Nguyen TD(1)(2), Choi JA(1)(2), Son D(1)(2)(3), Yuk HJ(4), Lee J(1)(2)(3), Son S(1)(2), Kim J(1)(2), Jo S(1)(2)(3), Kim DS(4), Song CH(1)(2)(3).

Author information:
(1)Department of Microbiology, College of Medicine, Chungnam National University, Daejeon 35015, Republic of Korea.
(2)Department of Medical Science, College of Medicine, Chungnam National University, Daejeon 35015, Republic of Korea.
(3)Translational Immunology Institute, Chungnam National University, Daejeon 34134, Republic of Korea.
(4)Herbal Medicine Research Division, Korea Institute of Oriental Medicine, Daejeon 34054, Republic of Korea.

The global emergence of drug-resistant Mycobacterium tuberculosis (Mtb) necessitates the urgent discovery of novel anti-tuberculosis agents.

Philadelphus tenuifolius Rupr., a Korean aromatic herb, has been historically recognized for its traditional medicinal uses. This study aimed to scientifically investigate the anti-tuberculosis (TB) potential of the P. tenuifolius leaf extract (PT-LE) and elucidate its underlying mechanism of action. PT-LE was prepared by 50% ethanolic extraction. Its anti-TB activity was evaluated against intracellular Mtb in BMDMs. Mechanistic studies focused on the activation of the MAPK pathway and autophagy flux. Synergistic effects with conventional anti-TB drugs were also assessed. For the in vivo evaluation, Mtb-infected mice were orally treated daily with PT-LE (100 mg/kg), followed by the determination of the lung bacterial burden. PT-LE exhibits negligible host cell cytotoxicity and effectively reduced the bacterial load of intracellular Mtb within macrophages. Mechanistically, PT-LE was shown to significantly activate the MAPK signaling pathway, which subsequently enhanced autophagy flux - a critical host defense mechanism against Mtb. Furthermore, PT-LE demonstrated potent synergistic activity with existing anti-TB drugs and modulated the host immune response by increasing the production of the chemokine MCP-1. Critically, the in vivo experiments showed that oral administration of PT-LE significantly reduced the Mtb bacterial burden in the lungs of infected mice. These findings reveal a novel anti-TB function of PT-LE, which operates by enhancing host autophagy and immunity. PT-LE represents a promising and effective host-directed therapeutic candidate for both drug-sensitive and drug-resistant tuberculosis.

DOI: 10.4014/jmb.2601.01032
PMCID: PMC13036502
PMID: 41889020 [Indexed for MEDLINE]

Conflict of interest statement: Conflict of Interest The authors have no financial conflicts of interest to declare.

27. Amikacin exposure in MDR-TB patients in Uganda: Revisiting old drugs in a new era of resistance - A pharmacokinetic assessment.

New Microbes New Infect. 2026 Feb 27;70:101734. doi: 10.1016/j.nmni.2026.101734. eCollection 2026 Apr.

Hongler J(1)(2), Haller S(1)(2)(3), Adakun AS(4), Lutz N(2)(5), Buzibye A(2), Kälin M(2)(5), Castelnuovo B(2), Sekaggya-Wiltshire C(2), Abongomera G(1)(6), Jetter A(7), Fehr J(1).

Author information:
(1)Department of Public and Global Health, Epidemiology, Biostatistics and Prevention Institute, University of Zurich, Zurich, Switzerland.
(2)Infectious Diseases Institute, College of Health Sciences, Makerere University, Uganda.
(3)Division of Infectious Diseases, Infection Prevention and Travel Medicine, HOCH Cantonal Hospital St. Gallen, St. Gallen, Switzerland.
(4)National Tuberculosis Treatment Centre, Mulago National Referral and Teaching Hospital, Kampala, Uganda.
(5)Department of Infectious Diseases and Hospital Epidemiology, University

Hospital Zurich, Zurich, Switzerland.
(6)Swiss Centre for International Health, Swiss Tropical and Public Health Institute, Basel, Switzerland.
(7)Tox Info Suisse, Swiss National Poison Centre, Associated Institute of the University of Zurich, and Department of Clinical Pharmacology and Toxicology, University Hospital Zurich and University of Zurich, Zurich, Switzerland.

BACKGROUND: Amid rising resistance to bedaquiline, aminoglycosides remain an important fallback option for multidrug-resistant tuberculosis (MDR-TB) treatment, particularly in high-burden settings. Their use is limited by nephro- and ototoxicity, which is associated with cumulative drug exposure. In this study we investigated amikacin exposure in Ugandan MDR-TB patients using a validated limited sampling strategy and compared the results to previously published data from a Western European cohort.
METHODS: In this single-centre prospective observational study, 29 MDR-TB patients received amikacin at a dose of 10-15 mg/kg. Serum levels were measured on day 30 at 1, 4 and 5 h post-administration using liquid chromatography/mass spectrometry. Individual concentration-time curves were modelled using a one-compartment model and compared to a Dutch population-pharmacokinetic (PK) model.
RESULTS: Twenty patients had complete PK data. Patients received a median amikacin dose of 10.9 (IQR 10 - 14.9) mg/kg; clearance was 4.79 L/h (IQR 4.03 - 5.75), volume of distribution (Vd) 16.3 L (IQR 14.07 - 21.49), AUC0-24h 125.15 h x mg/l (IQR 106.73 - 174.46), maximum serum concentration (Cmax) 27.8 mg/l (IQR 22.9 - 48.7).
CONCLUSIONS: This population-PK study shows that major differences in PK between Ugandan MDR-TB patients and those in the Global North are unlikely. Our findings reinforce the suitability of a one-compartment model for therapeutic drug monitoring in both high- and low-resource settings. Readily obtained aminoglycoside PK parameters in a limited resource setting facilitate future efforts in optimizing drug exposure with minimal toxicities, in the population most affected by the pandemic of TB.

DOI: 10.1016/j.nmni.2026.101734
PMCID: PMC12991953
PMID: 41852916

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. A periplasmic protein complex mediates arabinofuranosyltransferase activity and intrinsic drug resistance in Mycobacterium tuberculosis.

Sci Adv. 2026 Apr 3;12(14):eaec5100. doi: 10.1126/sciadv.aec5100. Epub 2026 Apr 1.

Klevorn T(1)(2), Brown C(3), Hardy CD(4), Cuthbert BJ(4), Spencer A(5), Jinich A(5), Chan L(1), Angala SK(6), Manzer J(6), Mendoza J(4), de Miranda R(4), Kim H(1), Schnappinger D(1), Jackson M(6), Rhee K(2)(3), Goulding CW(4)(7), Ehrt S(1)(2).

Author information:
(1)Department of Microbiology and Immunology, Weill Cornell Medical College, New York, NY, USA.
(2)Immunology and Microbial Pathogenesis Graduate Program, Weill Cornell Graduate School of Medical Sciences, Cornell University, New York, NY, USA.
(3)Department of Medicine, Weill Cornell Medical College, New York, NY, USA.
(4)Department of Molecular Biology & Biochemistry, University of California, Irvine, Irvine, CA, USA.
(5)Department of Chemistry & Biochemistry, Skaggs School of Pharmacy & Pharmaceutical Sciences, University of California, San Diego, San Diego, CA, USA.
(6)Mycobacteria Research Laboratories, Department of Microbiology, Immunology and Pathology, Colorado State University, Fort Collins, CO, USA.
(7)Department of Pharmaceutical Sciences, University of California, Irvine, Irvine, CA, USA.

The intrinsic drug resistance of Mycobacterium tuberculosis (Mtb) is a major barrier to effective tuberculosis (TB) treatment and is largely due to its complex, impermeable cell envelope. We identified a periplasmic protein complex comprising FecB and Rv3035 that is essential for maintaining envelope integrity and mediating intrinsic multidrug resistance in Mtb. FecB interacts with Rv3035, forming a stable heterodimer that associates with the cell envelope biosynthesis protein AftB. We report the structures of Rv3035 alone and in complex with FecB and identify critical residues for complex formation and function. Coessentiality and genetic interaction analyses support a functional link between FecB, Rv3035, and AftB, an arabinofuranosyltransferase that synthesizes arabinogalactan and lipoarabinomannan. Loss of FecB or Rv3035 disrupted AftB-mediated arabinan synthesis, suggesting that these proteins support AftB's enzymatic activity. FecB is required for Mtb virulence in mice, underscoring its physiological relevance. These findings highlight FecB, Rv3035, and AftB as promising therapeutic targets.

DOI: 10.1126/sciadv.aec5100
PMCID: PMC13041763
PMID: 41920993 [Indexed for MEDLINE]

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

29. Persistent Hyperglycaemia and Transient Dysglycaemia in Tuberculosis: Evaluating the Bidirectional Interaction With Type-2 Diabetes Mellitus and Clinical Outcomes.

Trop Med Int Health. 2026 Apr;31(4):523-531. doi: 10.1111/tmi.70102. Epub 2026

Feb 24.

Boadu AA(1)(2), Asare P(1), Yeboah-Manu M(3), Osei-Wusu S(1), Konadu ED(1), Asante-Poku A(1), Klinogo Y(4), Adjei A(4), Acheampong DO(2), Afriyie-Mensah JS(4)(5), Yeboah-Manu D(1), Atiase Y(5)(6).

Author information:
(1)Department of Bacteriology, Noguchi Memorial Institute for Medical Research, University of Ghana, Accra, Ghana.
(2)Department of Biomedical Sciences, School of Allied Health Sciences, University of Cape Coast, Cape Coast, Ghana.
(3)University of Ghana Medical Center, University of Ghana, Legon, Ghana.
(4)Department of Chest Diseases, Korle-Bu Teaching Hospital, Accra, Ghana.
(5)University of Ghana Medical School, Accra, Ghana.
(6)National Diabetes Management and Research Center, Korle-Bu Teaching Hospital, Accra, Ghana.

INTRODUCTION: Poor glycaemic control, indicated by a haemoglobin A1c (HbA1c) level of 7% or higher, increases the risk of active tuberculosis (TB) in patients with diabetes, while active TB can worsen glucose tolerance and insulin resistance, contributing to type-2 diabetes mellitus (DM) progression. The bidirectional relationship between TB and DM is well recognised, but the evolution of glycaemic status during TB treatment, particularly the distinction between transient and persistent dysglycaemia, is not well understood in high-burden settings.
METHODS: We conducted a prospective cohort study of 120 newly diagnosed pulmonary TB patients in Ghana, categorised as TB-Only (n = 66), TB with established DM on metformin (TB-DMt, n = 39), and TB with dysglycaemia not requiring pharmacological therapy (TB-DMnt, n = 15). HbA1c was measured at baseline, 3, 6 and 9 months.
RESULTS: TB-DMt patients were older, had higher BMI and persistently elevated HbA1c ($p < 0.001$). In contrast, TB-DMnt patients showed significant HbA1c decline during and after TB treatment, normalising by 6 months ($p < 0.016$). Most TB-Only patients maintained stable euglycaemia. Transient dysglycaemia resolved in TB-DMnt, while persistent hyperglycaemia was confined to those with pre-existing DM (TB-DMt).
CONCLUSION: Routine HbA1c monitoring during TB therapy can distinguish transient dysglycaemia from true diabetes, supporting more precise risk stratification and tailored management of TB patients.

DOI: 10.1111/tmi.70102
PMCID: PMC13050612
PMID: 41734898 [Indexed for MEDLINE]

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

30. Comparative evaluation of sputum microscopy and Xpert MTB/RIF assay for tuberculosis detection and rifampicin resistance surveillance in Biratnagar, Nepal.

Microbiol Spectr. 2026 Apr 7;14(4):e0246025. doi: 10.1128/spectrum.02460-25. Epub 2026 Mar 11.

Ojha S(1), Adhikari A(2), Adhikari S(3), Khanal S(3), Kalwar CS(4), Panta OP(1).

Author information:
(1)Department of Microbiology, Central Campus of Technology, Dharan, Nepal.
(2)Institute of Agriculture and Animal Science, Paklihawa Campus, Bhairahawa, Nepal.
(3)Faculty of Animal Science, Veterinary Science and Fisheries, Agriculture and Forestry University, Chitwan, Nepal.
(4)Sam Higginbottom University of Agriculture, Technology and Sciences, Prayagraj, India.

Tuberculosis (TB) control in Nepal faces persistent challenges due to underdiagnosis and increasing drug resistance. This study assessed the diagnostic performance of the Xpert MTB/RIF assay compared with conventional smear microscopy and estimated the prevalence of rifampicin-resistant TB (RR-TB) in Biratnagar, a high-burden urban center. Between March and September 2023, 509 clinical specimens from TB suspects were analyzed by Ziehl-Neelsen (ZN) staining, fluorescence microscopy (FM), and Xpert MTB/RIF. Using Xpert as the operational reference, ZN and FM exhibited overall sensitivities of 55.9% (89/159) and 68.5% (109/159), respectively. In paired sputum-only analyses (n = 446; sputum Xpert positives = 145), ZN and FM sensitivities were 60.0% (87/145) and 70.3% (102/145), respectively; sputum specificity was 100% for both methods. Xpert detected 31.2% (159/509) positive cases-78.7% more than ZN and 45.9% more than FM. Rifampicin resistance was identified in 5.03% (8/159) of Xpert-positive samples and was strongly associated with prior treatment ($P < 0.001$); RR-TB occurred in 66.7% (6/9) of retreatment cases vs 1.3% (2/150) of new cases. Xpert increased detection in paucibacillary and extrapulmonary specimens. These findings support expanded use of rapid molecular testing, but results should be interpreted cautiously because culture/speciation was not performed.IMPORTANCEThe spread of drug-resistant tuberculosis (TB) is a growing public health threat in Nepal. Using a rapid molecular test in Biratnagar, we simultaneously diagnosed TB and identified rifampicin resistance. We found rifampicin-resistant TB in >5% of Xpert-positive patients, higher than national averages for new cases, and a markedly elevated risk among previously treated patients. Rapid detection of resistance permits earlier initiation of appropriate therapy and can reduce onward transmission.

DOI: 10.1128/spectrum.02460-25
PMCID: PMC13055257
PMID: 41811027 [Indexed for MEDLINE]

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

31. High efficacy of BPaL among patients infected with Mycobacterium tuberculosis lineage 1 in the Philippines.

IJTLD Open. 2026 Apr 13;3(4):226-231. doi: 10.5588/ijtldopen.25.0677.
eCollection 2026 Apr.

High efficacy of BPaL among patients infected with Mycobacterium tuberculosis lineage 1 in the Philippines.

Flores I(1)(2), Tujan MAA(3), Basilio R(3), Dizon TJR(3), Lim DR(3), Reyes LT(3), Reyes RVAG(3), Rojas S(3), Valencia AK(3), Capin JB(3), Mirtskhulava V(4)(5), Palparan AG(3), Cabalitan C(6), Carpin PJ(6), Malbacias C(7), Lee JS(8), Gebhard A(4), Quelapio M(1)(4)(9), Timm J(9).

Author information:
(1)Tropical Disease Foundation, Makati City, Philippines.
(2)Jose B. Lingad Memorial General Hospital, San Fernando City, Philippines.
(3)Department of Health, Research Institute for Tropical Medicine, Muntinlupa, Philippines.
(4)KNCV Tuberculosis Foundation, The Hague, the Netherlands.
(5)Faculty of Natural Sciences and Medicine, Ilia State University, Tbilisi, Georgia.
(6)Philippine Business for Social Progress, Mandaluyong City, Philippines.
(7)Department of Health, National TB Program, Disease Prevention and Control Bureau, City of Manila, Philippines.
(8)International Tuberculosis Research Center, Changwon, Republic of Korea.
(9)TB Alliance, New York, NY, USA.

BACKGROUND: WHO recommends the bedaquiline-pretomanid-linezolid regimen with/without moxifloxacin (M) (BPaL/M) for the treatment of multidrug- or rifampicin-resistant TB. However, Mycobacterium tuberculosis (MTB) lineage 1 (L1) is less susceptible to pretomanid than other lineages, and there are limited BPaL/M efficacy data from regions where L1 is prevalent.
METHODS: We performed whole genome sequencing (WGS) on baseline MTB isolates from a subgroup (34/103) of patients from the highly successful Philippine BPaL Operational Research Study to characterise their lineage and genotypic drug susceptibility testing (DST) profile. Phenotypic DST for BPaL drugs was also conducted.
RESULTS: WGS analysis showed that L1 (68%) predominated, followed by L4 (26%) and L2 (6%). Out of the 22 L1 isolates tested, 20 exhibited higher pretomanid minimum inhibitory concentrations than isolates from other lineages, including one with borderline resistance. Two patients had confirmed bedaquiline resistance; no linezolid resistance was detected. All 34 patients with characterised isolates had culture converted by end of treatment. At month 12 follow-up, 30/31 patients who provided sputum remained culture negative; the single culture-positive participant harboured MTB L4.
CONCLUSION: In this study, patients infected with MTB L1 responded to BPaL as well as those infected with other lineages. Baseline bedaquiline resistance was linked to the unique recurrence in the study.

DOI: 10.5588/ijtldopen.25.0677
PMCID: PMC13080305
PMID: 41994186

Conflict of interest statement: Conflicts of interest: none declared.

32. A new multiplex molecular assay based on padlock probes and rolling circle amplification for MDR-TB detection in clinical specimens: a prospective diagnostic accuracy study.

Ther Adv Infect Dis. 2026 Apr 18;13:20499361261436542. doi: 10.1177/20499361261436542. eCollection 2026 Jan-Dec.

Dudnyk A(1)(2)(3), Tytarenko N(4)(5), Lytvyniuk O(2), Tolstova O(6), Millet JP(7)(8), Molina I(7), Antuori A(1)(9), Ciobanu N(10)(11), Crudu V(10)(11), Domínguez J(4)(12)(13).

Author information:
(1)Germans Trias i Pujol Research Institute (IGTP), Badalona, Barcelona, Spain.
(2)Department of Tuberculosis, Clinical Immunology and Allergy, National Pirogov Memorial Medical University, Vinnytsia, Ukraine.
(3)Serveis Clínics, Carrer de García Mariño, 4, Sarrià-Sant Gervasi, 08022 Barcelona, Spain.
(4)Germans Trias i Pujol Research Institute (IGTP); Badalona, Barcelona, Spain.
(5)Odesa I. I. Mechnikov National University, Odesa, Ukraine.
(6)Microbiology Laboratory, Regional Phthisiopulmonology Center, Vinnytsia, Ukraine.
(7)Serveis Clinics, Barcelona, Spain.
(8)CIBER de Epidemiología y Salud Pública, CIBEREESP, Instituto de Salud Carlos III, Madrid, Spain.
(9)Microbiology Department, Laboratori Clínic Metropolitana Nord (LCMN), Hospital Universitari Germans Trias i Pujol, Badalona, Barcelona, Spain.
(10)PMSI Institute of Pneumology "Chiril Draganiuc," Chișinău, Moldova.
(11)Department of Pneumology & Allergology, Nicolae Testemitanu State University of Medicine and Pharmacy, Chisinau, Moldova.
(12)Department of Genetics and Microbiology, Universitat Autònoma de Barcelona, Badalona, Barcelona, Spain.
(13)CIBER Enfermedades Respiratorias, CIBERES, Instituto de Salud Carlos III, Madrid, Spain.

BACKGROUND: Patients with multidrug-resistant tuberculosis (MDR-TB) receive treatment that is at least 20% less effective than drug-susceptible cases globally.
OBJECTIVES: The study evaluated the diagnostic accuracy of mfloDx MDR-TB assay (EMPE Diagnostics AB, Solna, Sweden) for simultaneous detection of resistance to isoniazid (INH) and rifampicin (RIF) compared to culture-based drug susceptibility test (DST).

DESIGN: A prospective diagnostic accuracy study.
METHODS: Clinical samples from 287 patients (mean age 45.3 (95% CI 43.3-47.2) years; 50 (17.0%) were female) from TB facilities in Ukraine (n = 82, 28.6%), Moldova (n = 37, 12.9%) and Spain (168, 58.5%) with bacteriologically confirmed TB and persons evaluated for non-tuberculous mycobacteria (NTM) were consecutively tested. The results of the mfloDx MDR-TB assay were compared with culture-based DST.
RESULTS: A total of 186 out of 287 sputum specimens (64.8%) yielded conclusive results that allowed a definitive interpretation of resistance to at least one drug. The mfloDx MDR-TB assay demonstrated sensitivity at 86.9 (95% CI 80.6-91.7) and specificity at 100 (95% CI 79.4-100) correctly differentiating mycobacterium tuberculosis complex from NTM in smear positive sputum samples. Considering only conclusive results in sputum samples, the mfloDx MDR-TB assay simultaneously predicted resistance to INH and RIF in TB patients showing high sensitivity 100 (95% CI 93.0-100) and specificity 98.7 (95% CI 92.8-100) compared to MDR-TB detection by culture-based DST.
CONCLUSION: While approximately one-third of tests yielded inconclusive results, the mfloDx™ MDR-TB assay demonstrated potential as a rapid screening tool for INH and RIF resistance, offering a time advantage over conventional culture-based DST.

Plain Language Summary: A new molecular test to quickly detect multidrug-resistant tuberculosis in patient samples Why was the study done: Tuberculosis (TB) is an infectious disease that mainly affects the lungs. Some forms of TB no longer respond well to standard medicines. These cases are called multidrug-resistant tuberculosis (MDR-TB) when resistance to the most effective drugs, such as isoniazid (INH) and rifampicin (RIF), is documented. There are only a limited number of technologies that are able to identify this resistance in a single test. People with MDR-TB have a much lower chance of being cured than those with drug-sensitive TB. How we did it: This study tested a new laboratory method, called the mfloDx MDR-TB assay, developed by EMPE Diagnostics (Sweden). The goal was to see how accurately this test could detect whether TB bacteria are resistant to INH and RIF. The results were compared with the standard, slower culture-based drug susceptibility test (DST). Clinical samples from 287 individuals were tested from February to August 2024. What we found: The mfloDx test produced clear results in about two-thirds (65%) of the samples. Among these, the test correctly identified resistance to INH and RIF with high accuracy: Sensitivity: 100% — how often the test detected MDR-TB resistance when it was truly present. Specificity: 98.7% — how often the test correctly showed no MDR-TB resistance when the bacteria were sensitive to both medicines. The test also accurately distinguished TB bacteria from other similar organisms, known as non-tuberculous mycobacteria (NTM). What do the findings mean: Although one-third of the samples did not produce clear results, the mfloDx MDR-TB test performed well in identifying TB drug resistance quickly and accurately. This rapid testing method could help doctors begin the correct treatment much sooner than with traditional culture-based methods, which can take several weeks.

DOI: 10.1177/20499361261436542

PMCID: PMC13100431
PMID: 42028411

Conflict of interest statement: The authors declare that there is no conflict of interest.

33. Hemoptysis in a patient with MDR-tuberculosis: successful diagnosis with photon counting CT and embolization of a Rasmussen aneurysm.

Infection. 2026 Apr;54(2):983-989. doi: 10.1007/s15010-025-02660-3. Epub 2025 Oct 9.

van de Sand L(1), Schaarschmidt BM(2), Wienker J(3), Witzke O(1), Zettler M(4).

Author information:
(1)Department of Infectious Diseases, University Hospital Essen, University Duisburg-Essen, Hufelandstraße 55, Essen, 45147, Germany.
(2)Institute of Diagnostic and Interventional Radiology and Neuroradiology, University Hospital Essen, University Duisburg- Essen, Essen, Germany.
(3)Department of Pulmonary Medicine, University Hospital Essen- Ruhrlandklinik, University Duisburg-Essen, Essen, Germany.
(4)Department of Infectious Diseases, University Hospital Essen, University Duisburg-Essen, Hufelandstraße 55, Essen, 45147, Germany.
markus.zettler@uk-essen.de.

BACKGROUND: Multidrug-resistant tuberculosis (MDR-TB) remains a significant clinical challenge and may be complicated by life-threatening hemoptysis. One rare but serious cause of hemoptysis in TB patients is the development of pulmonary artery pseudoaneurysms, known as Rasmussen aneurysms, which typically arise within or adjacent to tuberculous cavitary lesions.
CASE PRESENTATION: We report the case of a 57-year-old male patient who was diagnosed with MDR-TB in July 2024, confirmed by phenotypic resistance against rifampicin and isoniazid. According to WHO recommendations treatment with the BPaLM regimen (bedaquiline, pretomanid, linezolid, and moxifloxacin) was initiated in early August 2024 and was administered according to an extended 9-month schedule due to clinical considerations. After approximately seven months of therapy, the patient was re-hospitalized in March 2025 due to hemoptysis. A thoracic photon counting CT scan revealed regressing bilateral cavitary lesions. During the same month, a pseudoaneurysm arising from a subsegmental pulmonary artery within a cavity-consistent with a Rasmussen aneurysm-was identified. Successful embolization of the feeding vessel was performed under angiographic guidance. Post-interventional bronchoscopy showed minimal residual bloody secretions at the embolization site but no evidence of active bleeding after thorough irrigation. At that time, pending cultures for M. tuberculosis finally converted negative. The patient recovered well, and no further hemoptysis occurred.
CONCLUSIONS: This case highlights the importance of considering Rasmussen aneurysms as a potential cause of hemoptysis in patients with cavitary MDR-TB, even several months after starting antibiotic therapy. Prompt imaging-based

diagnosis and endovascular intervention are critical to avoid life-threatening complications.

DOI: 10.1007/s15010-025-02660-3
PMCID: PMC13021701
PMID: 41065995 [Indexed for MEDLINE]

Conflict of interest statement: Declarations. Ethics approval and consent to participate: Ethical approval from our hospital’s review committee is not required for case reports, and written informed consent was obtained from the patient. Consent for publication: The patient reported in this case has given us his explicit consent for publication and the use of his health data. There are no name tags or identity reveals throughout this case report. Competing interests: The authors declare no competing interests.

34. Artificial Intelligence in the Diagnosis and Management of Pulmonary Tuberculosis: A Review of Current Applications and Future Perspectives.

Ther Clin Risk Manag. 2026 Mar 31;22:596651. doi: 10.2147/TCRM.S596651. eCollection 2026.

Ou Y(1), Zhang Q(2), Meng C(3), Zhou X(4), Na M(1), Yu Z(4), Ma W(4), Huang C(4).

Author information:
(1)Department of Infectious, No. 926 Hospital, Joint Logistics Support Force of PLA, Kaiyuan, Yunnan, 661699, People's Republic of China.
(2)Department of Cardiothoracic Surgery, No. 926 Hospital, Joint Logistics Support Force of PLA, Kaiyuan, Yunnan, 661699, People's Republic of China.
(3)Department of Laboratory, No. 926 Hospital, Joint Logistics Support Force of PLA, Kaiyuan, Yunnan, 661699, People's Republic of China.
(4)Department of Radiology, No. 926 Hospital, Joint Logistics Support Force of PLA, Kaiyuan, Yunnan, 661699, People's Republic of China.

Pulmonary tuberculosis (PTB) remains a major global public health challenge, with traditional diagnostic and management approaches plagued by diagnostic delays, time-consuming drug resistance testing, and subjective efficacy assessment. Artificial intelligence (AI) has emerged as a revolutionary solution for these bottlenecks. This review comprehensively summarizes AI's current applications in PTB care: deep learning models enable automated detection, segmentation and activity differentiation of PTB lesions on chest X-ray/CT with performance comparable to or exceeding human experts (sensitivity >90% for X-ray detection); AI-driven whole-genome sequence analysis rapidly predicts anti-TB drug resistance, shortening testing time from weeks to days; multimodal AI models also show potential in dynamic treatment response monitoring and individualized outcome prediction. However, AI's clinical translation is hindered by data quality/bias, poor model generalizability, low algorithm

interpretability, and regulatory/ethical issues. Future priorities include multimodal data fusion, federated learning, prospective clinical validation, and developing lightweight AI models for resource-limited settings. Interdisciplinary collaboration is critical to transform AI from a research tool into a safe, reliable and equitable clinical assistant for PTB care.

DOI: 10.2147/TCRM.S596651
PMCID: PMC13050177
PMID: 41937887

Conflict of interest statement: The authors declare that they have no conflicts of interest in this work.

35. Missed PrEP opportunities and vulnerability to HIV during rifampicin-resistant tuberculosis treatment in South Africa.

Front Public Health. 2026 Mar 23;14:1797716. doi: 10.3389/fpubh.2026.1797716. eCollection 2026.

Leonard A(1), Lowensen K(1)(2), Di Giacomo E(1), Duroseau B(1), Mlandu N(2), Kadernani Y(2), Arcêncio R(3), Budhathoki C(1)(2), Evans D(2)(4), Ndjeka N(2)(5), Farley JE(1)(2).

Author information:
(1)Center for Infectious Disease and Nursing Innovation (CIDNI), Johns Hopkins School of Nursing, Baltimore, MD, United States.
(2)BringBPaL2Me (BB2) Trial, Gqeberha, South Africa.
(3)College of Nursing at Ribeirão Preto, University of São Paulo, Ribeirão Preto, Brazil.
(4)Health Economics and Epidemiology Research Office, Wits Health Consortium, University of the Witwatersrand, Johannesburg, South Africa.
(5)Tuberculosis Control and Management, National Department of Health, Pretoria, South Africa.

BACKGROUND: Adults receiving rifampicin-resistant TB (RR-TB) treatment have prolonged engagement with the health system, yet healthcare professionals frequently miss opportunities to promote HIV prevention-particularly pre-exposure prophylaxis (PrEP)-in high-burden settings. We examined HIV vulnerability, PrEP awareness and uptake, and HIV and sexually transmitted infection (STI) incidence among HIV-negative adults receiving RR-TB treatment.
METHODS: We conducted an exploratory analysis within the BringBPaL2Me (BB2) Trial across two South African provinces. HIV-negative adults who had a BB2 study outcome within the first 24 months of the trial were included. Sexual risk indicators, HIV testing, and PrEP outcomes were assessed longitudinally. HIV and STI incidence rates were calculated per 100 person-years with exact Poisson 95% confidence intervals.
RESULTS: Among 288 participants (mean age 38.0 years; 72.9% male), HIV

vulnerability was prevalent, with 45.8% reporting condomless sex and 5.9% empirically treated for an STI at enrollment. Forty-two percent were aware of PrEP; 60.8% were offered PrEP, yet only 10.1% initiated PrEP. Over 110.7 person-years of follow-up, six incident HIV infections occurred (5.42 per 100 person-years; 95% CI: 1.99-11.80) and empiric treatment for an STI resulted in an STI incidence of 9.66 per 100 person-years (95% CI: 4.99-16.88). CONCLUSION: HIV-negative adults receiving RR-TB care experience substantial and ongoing HIV risk, yet uptake of biomedical prevention remains limited. Strengthening integration of HIV prevention within TB services represents a critical opportunity to advance sexual health and reduce HIV incidence in high-risk, underserved populations.

DOI: 10.3389/fpubh.2026.1797716
PMCID: PMC13050846
PMID: 41948027 [Indexed for MEDLINE]

Conflict of interest statement: The author(s) declared that this work was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

36. Impact and Economic Evaluation of the Patient-Provider Support Agency Model Under India's National Tuberculosis Elimination Program: Protocol for a Cohort Study.

JMIR Res Protoc. 2026 Apr 6;15:e76302. doi: 10.2196/76302.

Raula N(1), van der Putten IM(1), Dukers-Muijrers NHTM(2)(3), Dapkekar S(4), Nayak P(5), Evers SMAA(1)(6).

Author information:
(1)Department of Health Services Research, CAPHRI Care and Public Health Research Institute, Maastricht University, Minderbroedersberg 4-6, 6211 LH, Maastricht, P.O. Box 616 6200 MD, The Netherlands, 91 7008978561.
(2)Department of Health Promotion, Care and Public Health Research Institute (CAPHRI), Maastricht University, Maastricht, The Netherlands.
(3)Department of Sexual Health, Infectious Diseases and Environmental Health, Public Health Service South Limburg, Heerlen, The Netherlands.
(4)Public Health Department, Disha Foundation, Nashik, India.
(5)World Health Organisation Health Emergency Programme (WHE), WHO Country Office, Ankara, Turkey.
(6)Centre of Economic Evaluation, Trimbos, Netherlands Institute of Mental Health and Addiction, Utrecht, The Netherlands.

BACKGROUND: India is set to eliminate tuberculosis (TB) from the country by 2025, 5 years ahead of the global target. Optimizing TB care pathways is challenged by the predominance of private sector care-seeking among symptomatic

patients (60%-70%), a setting associated with significant under-notification. To improve the notification of TB among private providers and improve patient management in the private sector, the National Tuberculosis Elimination Program (NTEP), India, has implemented the Patient-Provider Support Agency (PPSA). The PPSA model enables state and district TB units to engage third-party agencies to involve private providers in TB care, providing comprehensive services including diagnosis, notification, and treatment support.
OBJECTIVE: The objective of this study is to assess the cost-effectiveness and feasibility of introducing the PPSA in the National TB elimination program to improve patient management by improving TB case notification, drug-resistant TB case notification, and treatment outcome and reducing loss to follow-up compared to baseline ongoing programs.
METHODS: A cohort study will be conducted in 2 parallel groups in the private sector to assess the impact of the PPSA intervention on the primary and secondary outcomes of the NTEP. Eligible patients with TB from the intervention and control district, notified within a defined time frame, will be included. The intervention group will receive all the facilities and benefits under the PPSA model under the NTEP. The control group will receive care under usual conditions. The study will consist of three parts: (1) impact assessment study, (2) cost-effectiveness study, and (3) feasibility and accessibility study. The primary outcomes shall be TB case notification, drug-resistant TB case notification, universal drug susceptibility testing coverage, and treatment outcome. Secondary outcomes shall include the time between the onset of symptoms and treatment initiation, treatment adherence, adverse drug reaction management, improvement in quality of life, and societal costs. Outcome assessments will be done using questionnaires at baseline, after 3 months, at the completion of treatment, and 6 months after the completion of treatment.
RESULTS: The study received Institutional ethical approval from Jodhpur School of Public Health Institutional Review Board, India, in accordance with the compliance of Section 4, National Ethical Guidelines for Biomedical and Health Research Involving Human Participants, ICMR (2017), with IRB Number: 10032/IRB/20-21. Data collection is underway.
CONCLUSIONS: Our work will add to other implementation studies capturing the role of the private sector in TB care in India. A key strength of this work is its use of detailed patient pathway data from the study site, suggesting that private sector engagement can support TB elimination while improving the quality and coordination of TB services across India's fragmented health care system.

DOI: 10.2196/76302
PMCID: PMC13053004
PMID: 41941727 [Indexed for MEDLINE]

Conflict of interest statement: Conflicts of Interest: None declared.

37. Exposure to the Four First-Line Anti-Tuberculosis Drugs and Treatment Outcomes:

A Target Trial Emulation Study in Ghana.

Res Sq [Preprint]. 2026 Apr 10:rs.3.rs-9255541. doi: 10.21203/rs.3.rs-9255541/v1.

Opoku-Mireku M, Kwara A, Lartey MYM, Peloquin CA, Amenuke DYA, Twum KA, Nortey PA, Manu AA, Koram KA.

Background Tuberculosis (TB) treatment outcomes in sub-Saharan Africa remain suboptimal despite high adherence to first-line therapy. Variability in drug pharmacokinetics, resulting in subtherapeutic plasma concentrations, may contribute to treatment failure and the development of resistance. This study estimated the causal effect of subtherapeutic plasma concentrations of first-line anti-TB drugs on treatment failure or death among individuals with drug-susceptible pulmonary TB in Ghana. Methods We conducted a prospective cohort study of 164 adults receiving standard WHO weight-band dosing at five Ghanaian hospitals. Peak plasma concentrations (C max) of rifampicin, isoniazid, pyrazinamide, and ethambutol were measured at months 1-2 using validated LC-MS/MS. We emulated a target trial comparing two static strategies: (1) therapeutic C max of at least one first-line drug versus (2) subtherapeutic C max of all four drugs. Using the clone-censor-weight approach, we estimated the per-protocol analogue risk difference (RD) and risk ratio (RR) for treatment failure (smear positive at months 5 or 6) or death by month 6. Models were adjusted for baseline covariates using inverse probability of censoring weighting. Sensitivity analyses included inverse probability weighting with regression adjustment, plain inverse probability weighting, and E-values. Results Of 164 participants, 120 had complete pharmacokinetic and outcome data; 20.0% (24/120) had subtherapeutic concentrations of all four drugs. The 6-month risk of treatment failure or death was 33.3% under the low-exposure strategy versus 4.2% under the adequate-exposure strategy (crude RD: 29.1 percentage points). In weighted analyses, low drug exposure was associated with a 25.6 percentage-point increase in absolute risk of treatment failure or death (95% CI: 5.7-45.6; p = 0.012) and an 8.6-fold higher relative risk (95% CI: 2.34-31.92; p = 0.001), corresponding to approximately one additional poor outcome for every four patients with subtherapeutic levels. Sensitivity analyses were consistent (ATE: 19.9%, 95% CI: 2.3-37.5). The E-value was 15.5 (lower bound 5.0). Conclusions Subtherapeutic exposure to all four first-line drugs was strongly associated with increased risk of treatment failure or death. Preventing multidrug subtherapeutic exposure through therapeutic drug monitoring or optimized dosing warrants randomized evaluation in high-burden settings. Trial registration Clinical trial number: not applicable.

DOI: 10.21203/rs.3.rs-9255541/v1
PMCID: PMC13082148
PMID: 41994124

38. Glucose driven bacterial persistence in extensively drug-resistant tuberculosis with diabetes.

Front Public Health. 2026 Mar 26;14:1746879. doi: 10.3389/fpubh.2026.1746879. eCollection 2026.

Yao X(#)(1)(2), Shi Y(#)(1)(2), Kong M(1)(2), Zhang Y(1)(2), Chen J(2), Wang W(1), Liu Z(1)(2).

Author information:
(1)The Key Laboratory of Environmental Pollution Monitoring and Disease Control, Ministry of Education, School of Public Health, Guizhou Medical University, Guiyang, China.
(2)Shanghai Key Laboratory of Tuberculosis, Shanghai Pulmonary Hospital, Tongji University School of Medicine, Shanghai, China.
(#)Contributed equally

BACKGROUND: Diabetes mellitus (DM) disrupts the metabolic environment of extensively drug-resistant tuberculosis (XDR) patients, promoting mycobacterial persistence. Key factors influencing bacterial clearance remain unclear. This study aimed to identify critical host factors and assess the therapeutic value of intensive glucose control.
METHOD: A 48-month single-center retrospective cohort study compared sputum smear conversion (bacterial clearance) between 57 XDR-only (XDR) and 84 XDR with DM (XDR + DM) patients (similar treatment, consistent in vitro MIC resistance profiles). Kaplan-Meier analysis, Cox regression, generalized linear models, and mediation analysis were used to explore associations between diabetic status, blood glucose (GLU) levels, and bacterial clearance, as well as the impact of glucose control on treatment progression.
RESULTS: Compared with XDR patients, the XDR + DM group exhibited a significantly lower bacterial clearance rate (80.7% vs. 45.2%) and longer median clearance time (6 vs. 12 months), despite comparable baseline smear grades. Crucially, XDR + DM patients displayed distinct immunometabolic dysregulation, characterized by elevated inflammatory markers (CRP) and a disrupted CD4+ /CD8+ T-cell balance (increased CD4+, decreased CD8+ counts). Multivariable analysis identified hyperglycemia as the primary driver of delayed clearance (aHR = 1.48, 95% CI: 1.23-1.77, $p < 0.001$), serving as a significant mediator between DM and impaired outcomes (mediation effect: -0.82, $p = 0.006$). A glucose "dose-response" relationship was observed: severe hyperglycemia (GLU ≥ 11.1 mmol/L) markedly increased clearance delay risk (aHR = 5.29, $p < 0.001$), whereas optimal control (GLU < 7 mmol/L) mitigated these disadvantages.
CONCLUSION: Dysregulated glucose metabolism and subsequent immune imbalance in diabetes are key drivers of delayed bacterial clearance in XDR patients, independent of the anti-tuberculosis regimen. Precise glucose control should be regarded as a core strategy, on a par with anti-XDR treatment.

DOI: 10.3389/fpubh.2026.1746879
PMCID: PMC13062200
PMID: 41971300 [Indexed for MEDLINE]

Conflict of interest statement: The author(s) declared that this work was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

39. Multidrug-resistant tuberculosis (MDR-TB) in people living with HIV: Clinical issues, therapeutic challenges and perspectives in sub-Saharan Africa. A narrative review.

J Clin Tuberc Other Mycobact Dis. 2026 Apr 13;43:100602. doi: 10.1016/j.jctube.2026.100602. eCollection 2026 May.

Tague C(1)(2).

Author information:
(1)Department of Research, Medical Research Circle (MedReC), Goma, DR, Congo.
(2)Faculté de Médecine, Université libre des pays des grands lacs, Goma, DR, Congo.

HIV coinfection and multidrug-resistant tuberculosis (MDR-TB) pose a major public health challenge in sub-Saharan Africa, where high HIV prevalence promotes tuberculosis progression and complicates its management. In people living with HIV (PLHIV), profound immunosuppression leads to atypical clinical presentations, low bacillary load, and increased diagnostic difficulty. Despite advances such as the introduction of the GeneXpert test and all-oral treatments such as the BPaL regimen, access to these tools remains uneven, exacerbating diagnostic delays and mortality. Drug interactions between antiretrovirals and second-line antituberculosis drugs, as well as the toxicity of prolonged regimens, further complicate clinical management. Mortality among coinfected patients remains high, sometimes exceeding 40%, particularly in the absence of early diagnosis and adequate treatment. Improved early detection, integration of HIV/MDR-TB care and accessibility to innovative treatments are essential to change the trajectory of this dual epidemic in the region.

DOI: 10.1016/j.jctube.2026.100602
PMCID: PMC13101606
PMID: 42027875

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

40. Visible Photosensitizing Disinfectant Spray for Combating Multidrug-Resistant Candidozyma Auris in Healthcare Settings.

Exploration (Beijing). 2026 Mar 10;6(2):20250276. doi: 10.1002/EXP.20250276. eCollection 2026 Apr.

Xu X(1), Wu MY(2)(3), Li B(1), Li J(1)(4)(5), Chen S(1), Chen L(1), Yu D(1)(5), Yang L(1), Hong Z(1), Pan H(6)(7), Xiang W(4), Feng S(3), Kim JS(8), Wang L(1)(9), Li Z(1)(5), Chen S(1)(10), Gu M(1)(5).

Author information:
(1)Department of Neurosurgery, Zhongnan Hospital of Wuhan University Ministry of Education Key Laboratory of Combinatorial Biosynthesis and Drug Discovery School of Pharmaceutical Sciences Wuhan University Wuhan Hubei China.
(2)College of Biomedical Engineering Sichuan University Chengdu China.
(3)Sichuan Engineering Research Center for Biomimetic Synthesis of Natural Drugs School of Life Science and Engineering Southwest Jiaotong University Chengdu Sichuan China.
(4)Department of Medical Intensive Care Unit Maternal and Child Health Hospital of Hubei Province Tongji Medical College Huazhong University of Science and Technology Wuhan Hubei China.
(5)Hubei International Science and Technology Cooperation Base for Research and Clinical Techniques for Brain Glioma Diagnosis and Treatment Wuhan University Wuhan Hubei China.
(6)Institute of Hepatobiliary Diseases of Wuhan University Transplant Center of Wuhan University Hubei Key Laboratory of Medical Technology on Transplantation Wuhan China.
(7)Department of Critical Care Medicine Zhongnan Hospital of Wuhan University Clinical Research Center of Hubei Critical Care Medicine Wuhan China.
(8)Department of Chemistry Korea University Seoul South Korea.
(9)Institute of Pediatrics, Shenzhen Children's Hospital Department of Respiratory Diseases Shenzhen China.
(10)Department of Critical Care Medicine, Intensive Care Unit, Shenzhen Key Laboratory of Microbiology in Genomic Modification & Editing and Application, Shenzhen Institute of Translational Medicine, Shenzhen University Medical School, Shenzhen Second People's Hospital The First Affiliated Hospital of Shenzhen University Shenzhen China.

Developing simple and convenient strategies to eliminate drug-resistant pathogen-transmission routes efficiently is extremely urgent for hospital healthcare. Candidozyma auris (C. auris) is an emerging nosocomial pathogen with multidrug resistance that easily forms biofilms, aggravating the risk of spreading in public places. Herein, a novel visible light-induced disinfectant spray with a boric-acid-functionalized lipophilic cation, TB, was developed. The boronic acid groups enable simultaneous targeting of polysaccharide-rich cell walls and extracellular polymeric substances within biofilms. TB spray achieved a > 99.9% reduction in C. auris with light and reduced biofilm biomass by approximately 85.2%. TB's polysaccharide targeting, pH-enhanced properties, positive charge, and particle size enable it to effectively bind to C. auris in acidic biofilm microenvironments, boosting photodynamic inactivation, collapsing biofilms, and preventing recurrence. It produces reactive oxygen species through Type I and II pathways, ensuring high efficacy even in hypoxic conditions, making it ideal for disinfecting high-touch surfaces. In a rat model of ventilator-associated pneumonia, TB markedly reduced pulmonary C. auris loads by over 100-fold and significantly attenuated lung injury. Furthermore, the

breakdown of polysaccharides enhanced the hydrophobicity of both abiotic and biological surfaces, as well as the increased contact angle, inhibiting biofilm adhesion. Multiomics analysis revealed that TB suppressed C. auris by disrupting genes associated with oxidative stress response, ergosterol biosynthesis, and biofilm maintenance. This visible light-induced disinfectant spray holds great potential to combat outbreaks of high-risk pathogens and could revolutionize disinfection practices in healthcare settings.

DOI: 10.1002/EXP.20250276
PMCID: PMC13094532
PMID: 42016766

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

41.Global, regional, and national economic value of reducing amenable tuberculosis Mortality.

Infect Dis Model. 2026 Apr 3;11(3):1234-1247. doi: 10.1016/j.idm.2026.04.003. eCollection 2026 Sep.

Liu Y(1), Zhu N(2), Shen M(1)(3)(4)(5).

Author information:
(1)China-Australia Joint Research Center for Infectious Diseases, School of Public Health, Xi'an Jiaotong University Health Science Center, Xi'an, Shaanxi, 710061, PR China.
(2)Shaanxi Provincial Center for Disease Control and Prevention, Xi'an, Shaanxi, 710054, PR China.
(3)Key Laboratory for Disease Prevention and Control and Health Promotion of Shaanxi Province, Xi'an, Shaanxi, 710061, PR China.
(4)The Interdisciplinary Center for Mathematics and Life Sciences, School of Mathematics and Statistics, Xi'an Jiaotong University, Xi'an, Shaanxi, 710049, PR China.
(5)Key Laboratory of Environment and Genes Related to Diseases (Xi'an Jiaotong University), Ministry of Education, Xi'an, 710061, PR China.

BACKGROUND: Progress in reducing Tuberculosis (TB) mortality falls short of one-third of the End TB Strategy target, partly due to a high proportion of amenable deaths, most of which occur among individuals aged 15-64 years. The loss of this working-age population has a deterrent effect on human capital and economic growth. Our objective was to estimate the global, regional, and national economic value of reducing amenable TB mortality at the macroeconomic level.
METHODS: We utilized TB burden data from the 2021 Global Burden of Disease (GBD) to estimate amenable TB mortality across countries and regions, stratified by sex, age, and drug-resistance type. Economic data were obtained from the World

Bank. We estimated the economic losses due to amenable TB mortality using the Value of Lost Welfare (VLW) approach, which integrates the Value of Statistical Life (VSL), Years of Life Lost (YLL) and Gross Domestic Product (GDP). The age-specific percentage of economic losses relative to GDP was calculated. RESULTS: The global number of amenable TB deaths in 2021 was 616,736, accounting for 53.04% of total TB mortality. The global economic losses due to amenable TB mortality in 2021 were estimated at $480.75 billion, accounting for 0.31% of global GDP. Losses among individuals aged 15-49 and 50-64 accounted for 48.73% and 34.12%, respectively., respectively. Lower-middle-income countries had the largest economic losses at $376.77 billion, corresponding to 1.30% of their GDP, while the percentage of economic losses relative to GDP was highest in low-income countries at 1.73%, with losses of $24.79 billion. CONCLUSION: Amenable TB mortality can lead to disproportionate economic losses, especially among deaths in people aged 15-49 years and in lower-middle-income countries. As these deaths and economic losses can be avoidable, investments in improving healthcare services will bring huge economic value.

DOI: 10.1016/j.idm.2026.04.003
PMCID: PMC13091826
PMID: 42011321

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.

42. Drug Exposure Dictates Evolutionary Dynamics of Drug-Resistant Tuberculosis: A Longitudinal Cohort Study in Beijing, China.

Infect Drug Resist. 2026 Mar 23;19:580421. doi: 10.2147/IDR.S580421. eCollection 2026.

Wen S(#)(1), Li H(#)(2), Shi Y(3), Wei R(1), Ge F(1), Pang Y(2), Liu Y(1).

Author information:
(1)Department of Biobank, Beijing Chest Hospital, Capital Medical University / Beijing Tuberculosis and Thoracic Tumor Research Institute, Beijing, People's Republic of China.
(2)Department of Bacteriology and Immunology, Beijing Key Laboratory for Key Technologies in Tuberculosis Prevention and Control, Beijing Chest Hospital, Capital Medical University/Beijing Tuberculosis and Thoracic Tumor Research Institute, Beijing, People's Republic of China.
(3)Department of Clinical Laboratory, Beijing Chest Hospital, Capital Medical University/Beijing Tuberculosis and Thoracic Tumor Research Institute, Beijing, People's Republic of China.
(#)Contributed equally

BACKGROUND: Despite global efforts to combat drug-resistant tuberculosis

(DR-TB), key gaps remain in understanding how resistance amplifies during treatment and the role of collateral drug effects in this process. Resistance amplification complicates management and undermines outcomes. This study aimed to identify the risk factors and collateral drug effects contributing to resistance amplification.
METHODS: We conducted a retrospective, longitudinal cohort study of 133 DR-TB patients with paired phenotypic drug susceptibility tests (pDSTs) at Beijing Chest Hospital in Beijing, China, from January 2018 to January 2023. Patients were classified into "progression" and "non-progression" groups based on acquisition of new drug resistance. Multivariable logistic regression identified risk factors, and a restrictive cohort analysis assessed collateral drug effects.
RESULTS: The median number of resistances per isolate increased significantly from 7.0 (IQR 5-9) to 8.0 (IQR 6-10) ($P < 0.05$), with 76 patients (57.1%) exhibiting resistance progression. A dominant trajectory was identified from isoniazid monoresistance (INH-Mono) to multidrug-/rifampicin-resistant TB (MDR/RR-TB) (9/14, 64.3%). In univariate analysis, bedaquiline (BDQ) use was associated with reduced progression ($P=0.032$), while pyrazinamide (PZA) use correlated with increased progression ($P=0.035$), though neither remained significant in multivariable models. Importantly, collateral effect analysis revealed that PZA exposure was strongly associated with acquired rifabutin (Rfb) resistance (OR, 5.94; 95% CI, 1.90-18.53; $P=0.001$).
CONCLUSION: Resistance amplification during DR-TB treatment is frequent, with INH-Mono representing a high-risk transitional state. While BDQ may offer a protective effect, the strong collateral association between PZA and Rfb resistance highlights the need for careful regimen design. These findings underscore the importance of individualized, resistance-informed therapy to mitigate further resistance amplification in DR-TB patients.

DOI: 10.2147/IDR.S580421
PMCID: PMC13032138
PMID: 41908598

Conflict of interest statement: All authors declare no competing interests.

43. Prevalence of Latent Tuberculosis Infection in Vulnerable Groups in the State of Santa Catarina, Brazil.

Rev Soc Bras Med Trop. 2026 Mar 30;59:e03292025. doi: 10.1590/0037-8682-0329-2025. eCollection 2026.

Carvalho EDR(1)(2), Kupek E(2)(3).

Author information:
(1)Universidade Federal de Santa Catarina, Departamento de Pediatria, Florianópolis, SC, Brasil.
(2)Universidade Federal de Santa Catarina, Programa de Pós-Graduação em Ciências Médicas, Florianópolis, SC, Brasil.
(3)Universidade Federal de Santa Catarina, Faculdade de Saúde Pública, Florianópolis, SC, Brasil.

BACKGROUND: Tuberculosis remains a major public health challenge that exerts substantial pressure on healthcare systems worldwide. Despite advances in diagnosis and treatment, the proper management of latent tuberculosis infection (LTBI) remains inefficient, especially among vulnerable populations. In the State of Santa Catarina, Brazil, the absence of comprehensive and specific records on LTBI prevalence in these at-risk groups limits effective public health planning and interventions.
METHODS: Interferon-gamma release assay (IGRA) test records in the State of Santa Catarina, Brazil, contained partial information on risk factors for LTBI. Multiple imputations were used to estimate the likely risk groups among individuals without such information. The study was approved by the Human Research Ethics Committee under protocol number CAAE 79499224.4.0000.5361.
RESULTS: The estimated LTBI prevalence among individuals with available IGRA results was 6.89%, with higher rates among people living with human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (18.25%) and immigrants (3.65%). Underreporting was notable among individuals deprived of liberty, those experiencing homelessness, those who use illicit drugs, and those with diabetes mellitus. Missing data were frequent among individuals living with HIV; people of African, Indigenous, or Asian descent; and those exposed to drug-resistant TB. More than 10% of LTBI cases occurred in children and adolescents aged <15 years.
CONCLUSION: HIV was the most prevalent risk factor among IGRA-positive individuals and was substantially underestimated. An urgent expansion of LTBI identification efforts is needed for all vulnerable populations, with special attention paid to children and adolescents who present a high risk of progressing to active TB.

DOI: 10.1590/0037-8682-0329-2025
PMCID: PMC13037719
PMID: 41983896 [Indexed for MEDLINE]

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

44.Interferon-gamma release assay positivity in populations at high risk of TB infection.

IJTLD Open. 2026 Apr 13;3(4):232-240. doi: 10.5588/ijtldopen.25.0684. eCollection 2026 Apr.

Dagnew AF(1), Han LL(1), Cinar A(1), Gaikwad D(2), Garcia-Basteiro AL(3)(4)(5), Gler MT(6), Hadinegoro SR(7), Hanekom WA(8), Lama JR(9), Muyoyeta M(10), Musala S(11), Nduba V(12), Rolla VC(13), Roy T(14), Sutherland JS(15), Viegas S(16), Wajja A(17)(18), Walker TM(19)(20), Noble R(1), Schlehuber L(1), Sunshine J(1), Schmidt AC(1); TBV02-E01 Study Group.

Author information:
(1)Gates Medical Research Institute, Clinical Development, Cambridge, MA, USA.
(2)Department of Pulmonary Medicine, PCMC'S PGI YCM Hospital, Pune, India.
(3)Centro de Investigação em Saúde de Manhiça (CISM), Maputo, Mozambique.
(4)Barcelona Institute for Global Health, ISGlobal, Barcelona, Spain.
(5)Centro de Investigación Biomédica en Red de Enfermedades Infecciosas (CIBERINFEC), Barcelona, Spain.
(6)TB HIV Innovations and Clinical Research Foundation, Cavite, Philippines.
(7)Department of Child Health, Faculty of Medicine, University of Indonesia, Jakarta, Indonesia.
(8)Africa Health Research Institute, KwaZulu-Natal, South Africa.
(9)Asociación Civil Impacta Salud y Educación, Lima, Peru.
(10)Centre for Infectious Disease Research in Zambia (CIDRZ), Lusaka, Zambia.
(11)National Tuberculosis Program/National TB Reference Laboratory, Kinshasa City, Democratic Republic of the Congo.
(12)Kenya Medical Research Institute, Centre for Respiratory Diseases Research (CRDR), Nairobi, Kenya.
(13)National Institute of Infectious Diseases Evandro Chagas - Fiocruz, Rio de Janeiro, Brazil.
(14)IRD Global, Bangladesh Country Office, Dhaka, Bangladesh.
(15)Vaccines and Immunity Theme, Medical Research Council Unit the Gambia at the London School of Hygiene and Tropical Medicine, Fajara, the Gambia.
(16)Instituto Nacional de Saúde, Marracuene, Mozambique.
(17)Medical Research Council/Uganda Virus Research Institute and London School of Hygiene and Tropical Medicine Uganda Research Unit, Entebbe, Uganda.
(18)Department of Clinical Research, London School of Hygiene and Tropical Medicine, London, UK.
(19)Oxford University Clinical Research Unit, Ho Chi Minh City, Vietnam.
(20)Centre for Tropical Medicine and Global Health, Nuffield Department of Medicine, University of Oxford, Oxford, UK.

BACKGROUND: Phase 3 TB vaccine trials are challenging in low-incidence settings due to the need for large sample sizes and extended follow-up. This global, observational study evaluated population-based interferon-gamma release assay (IGRA) status - a measure of TB infection (TBI), as a proxy for TB incidence to identify trial sites in high-incidence areas.
METHODS: Participants (15-34 years) were recruited from 45 sites in 14 countries. IGRA status at Day 1 and Month 12, association of IGRA status with age, and IGRA conversion (TBI) were assessed.
RESULTS: Among 7,164 enrolled participants, Day 1 IGRA positivity varied across sites and within countries, with the highest prevalence observed in South Africa (58.7%, site 1006; 53.1%, site 1010; 51.9%, site 1007) and the Democratic Republic of Congo (50.0%, site 2303). IGRA positivity was generally higher among

older participants. At Month 12, sites with highest IGRA conversion were observed in the Philippines (32.3%, site 1507) and Zambia (30.6%, site 1303). CONCLUSION: In TB vaccine efficacy trials with clinical endpoints, selecting sites with the highest TB incidence is critical to optimise sample size and follow-up duration. Site-level IGRA status could inform site selection by identifying communities at increased risk of Mycobacterium tuberculosis infection.

DOI: 10.5588/ijtldopen.25.0684
PMCID: PMC13080303
PMID: 41994179

Conflict of interest statement: Conflicts of Interests: AFD, LLH, AC, DG, SRH, WAH, JRL, MM, SM, VN, TR, JSS, SV, AW, TMW, RN, LS, JS, and ACS declare no competing interests. ALG-B reports research grants from European & Developing Countries Clinical Trials Partnership, National Institutes of Health (NIH), European Research Council, and Gates Medical Research Institute (Gates MRI); honoraria for lectures at the annual conference of the Spanish Association of Nursing and Vaccines; remuneration for time invested in BioNTech advisory board meetings; travel support from the Gates Foundation for meetings related to TB vaccines. ALG-B has also participated in advisory roles in malaria vaccine trials sponsored by Sanaria, BioNTech, and the Innovative Medicines Initiative – European Union, and is associate editor for BMJ Global Health journal, associate editor for International Journal of Tuberculosis and Lung Disease, and has chaired the TB Group at the European Respiratory Society from 2000 to 2023. MTG reports funds from Gates MRI and PPD for implementing study activities. VCR reports support for TBV02-E01 study activities from Brazil's Departamento de Ciência e Tecnologia (Secretaria de Ciência e Tecnologia, Ministério da Saúde) and NIH/NIAID grants, research funds from TB Alliance for Drug Development, Impacto da COVID-19 Nas Manifestações Clínicas, Diagnóstico, Desfecho Do Tratamento e Resposta Imune para Tuberculose Pulmonar, Associative BRICS Research in COVID-19 and Tuberculosis (ABRICOT), RePORT International Data Harmonization, Transcriptional Signature of TB in advanced HIV, Predictors of Resistance Emergence Evaluation in Multidrug-resistant Tuberculosis Patients on Treatment – PREEMPT, Caribbean, Central, and South America network for HIV Epidemiology (CCASAnet), Immunogenetic predictors of active and incipient TB in HIV-negative and HIV-positive close TB contacts, consulting fees from ONU-OMS for an HIV response review in Myanmar, honoraria for lectures from GlaxoSmithKline Brasil Ltda, Qiagen, and Virology education events, travel support from ViiV 18 European AIDS conference.

45. Experiences from Ukraine in expanding TB infection diagnosis and treatment, including for drug-resistant TB.

IJTLD Open. 2026 Apr 13;3(4):247-254. doi: 10.5588/ijtldopen.25.0670.
eCollection 2026 Apr.

Shukatka V(1), Skoklyuk L(1), Germanovych M(1), Bogdanov A(1), Ivanenko T(1), Zherebko N(1), Klinkenberg E(2), Dravniece G(1).

Author information:
(1)PATH, Kyiv, Ukraine.
(2)ConnectTB, The Hague, the Netherlands.

BACKGROUND: Ukraine faces intersecting epidemics of HIV and drug-resistant TB (DR-TB), with high risk of progression from TB infection to active disease. The Support TB Control Efforts in Ukraine project supported the National TB Program's efforts to operationalise World Health Organization recommendations on TB infection testing and TB preventive treatment (TPT) across 17 regions of Ukraine.
DESIGN: In September 2021, QuantiFERON-TB Gold Plus (QFT-Plus) testing was introduced through a public-private laboratory model. Eligible populations included TB contacts and other high-risk groups. Data on referrals, test outcomes, and TPT initiation were collected electronically and analysed descriptively.
RESULTS: Out of 11,495 individuals referred for testing, 9,788 (85.2%) completed QFT-Plus testing, with adult TB contacts showing the highest positivity rate at 28.1%. Among 1,717 eligible for TPT, 1,512 (88.1%) started TPT, and this was 93.3% for drug-susceptible TB (DS-TB) contacts and 82.8% for DR-TB contacts. DS-TB contacts were offered shorter rifapentine-based regimens, while DR-TB contacts received levofloxacin. Implementation challenges were addressed through training and mentorship.
CONCLUSION: Ukraine's implementation of QFT-Plus testing and shorter TPT regimens marks progress in broadening TB prevention efforts, particularly for DR-TB contacts. These initial results highlight that such approaches are feasible even in challenging, high-burden environments, offering insights for future expansion.

DOI: 10.5588/ijtldopen.25.0670
PMCID: PMC13080308
PMID: 41994180

46. Hematological Profiles of Pulmonary Tuberculosis and Multi-Drug-Resistant Tuberculosis Patients at Debre Tabor Comprehensive Specialized Hospital, North-Central Ethiopia: A Comparative Cross-Sectional Study.

Health Sci Rep. 2026 Apr 2;9(4):e72223. doi: 10.1002/hsr2.72223. eCollection 2026 Apr.

Berhan A(1), Sharew B(1), Almaw A(1), Damtie S(1), Legese B(1), Erkihun M(1), Assefa A(1), Malkamu B(1), Abeje G(1), Getie B(1), Solomon Y(1).

Author information:

(1)Department of Medical Laboratory Science, College of Health Sciences Debre Tabor University Debre Tabor Ethiopia.

BACKGROUND AND AIMS: Tuberculosis is a major infectious disease that affects hematological profiles. However, limited data assess changes in hematological profiles among patients with pulmonary and multidrug-resistant tuberculosis. Therefore, this study aimed to compare the hematological profiles of pulmonary and multidrug-resistant tuberculosis patients at Debre Tabor Comprehensive Specialized Hospital from January 1 to May 30, 2023.
METHODS: An institution-based cross-sectional study was conducted on 159 study participants selected by the consecutive sampling technique. Sociodemographic and clinical data were collected through a structured questionnaire and checklist, respectively. A complete blood count was performed using an automated hematology analyzer, and a sputum sample was analyzed using the Gene Xpert MTB/RIF. The data were entered into Epi-Data software and analyzed using SPSS version 20 software. The median values of hematological parameters were compared using the Kruskal-Wallis H test. A p-value less than 0.05 was considered statistically significant.
RESULTS: The median and interquartile ranges of red blood cell parameters (red blood cell, hemoglobin, hematocrit, mean cell volume, and mean cell hemoglobin concentration) were significantly lower in pulmonary tuberculosis patients compared to those with multidrug-resistant tuberculosis and healthy controls. In pulmonary tuberculosis patients, the magnitude of anemia and neutrophilia was 18.2% (29/159) and 9.4% (15/159), respectively. Meanwhile, eosinophilia 8.2% (13/159) and neutropenia 6.3% (10/159) were high among multidrug-resistant tuberculosis patients.
CONCLUSION: Patients with pulmonary tuberculosis show lower red blood cell parameters, higher counts of white blood cells and neutrophils compared to multi-drug-resistant tuberculosis and healthy controls. Multi-drug-resistant tuberculosis patients also exhibit reduced red blood cells, hemoglobin, and hematocrit levels versus healthy individuals. Both pulmonary tuberculosis and multidrug-resistant tuberculosis patients displayed various hematological abnormalities like anemia, leucopenia, neutropenia, eosinophilia, and thrombocytopenia. Therefore, assessing these hematological profiles can aid in diagnosing and monitoring tuberculosis patients.

DOI: 10.1002/hsr2.72223
PMCID: PMC13051925
PMID: 41948654

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

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

Front Cell Infect Microbiol. 2026 Mar 26;16:1826950. doi: 10.3389/fcimb.2026.1826950. eCollection 2026.

Zhang H(1), Zhang L(1), Yang B(2), Gao C(1), Liu H(1), Zhang Y(3), Chen X(4).

Author information:
(1)Department of Tuberculosis, Xuzhou Hospital, Beijing Ditan Hospital Affiliated to Capital Medical University, Xuzhou, Jiangsu, China.
(2)Center for Infectious Diseases, Vision Medicals Co., Ltd, Guangzhou, Guangdong, China.
(3)Department of Science and Education, Xuzhou Hospital, Beijing Ditan Hospital Affiliated to Capital Medical University, Xuzhou, Jiangsu, China.
(4)Xuzhou Hospital, Beijing Ditan Hospital Affiliated to Capital Medical University, Xuzhou, Jiangsu, China.

Erratum for
Front Cell Infect Microbiol. 2026 Jan 29;15:1726935. doi: 10.3389/fcimb.2025.1726935.

[This corrects the article DOI: 10.3389/fcimb.2025.1726935.].

DOI: 10.3389/fcimb.2026.1826950
PMCID: PMC13064540
PMID: 41969652

48. Simultaneous measurement of 16S-rRNA and pre-16S-rRNA as a strategy to monitor clinical tuberculosis.

Front Antibiot. 2026 Apr 8;5:1760862. doi: 10.3389/frabi.2026.1760862. eCollection 2026.

Dombay E(1), Sabiiti W(1), Alferes de Lima Headley D(1), Légrády MB(2), van Campen N(3), Zweijpfennig S(3), Boeree MJ(3), Sloan DJ(1), Gillespie SH(1).

Author information:
(1)School of Medicine, University of St Andrews, St Andrews, United Kingdom.
(2)School of Chemistry, University of St Andrews, St Andrews, United Kingdom.
(3)Department of Pulmonary Diseases, TB Expert Centre, Research Institute for Medical Innovation, Radboud University Medical Center, Radboudumc Center for Infectious Diseases, Nijmegen, Netherlands.

BACKGROUND: Culture-based biomarkers of TB treatment response monitoring, e.g., Mycobacterial Growth Indicatory Tube (MGIT), are compromised when bacteria enter a non-replicating persister phase limiting the measurement of antibiotic efficacy and resistance. Understanding how antibiotic exposure to antibiotics alters bacterial physiology could help develop more effective TB therapies. We developed a novel assay with simultaneous measurement of 16S rRNA (bacterial

burden) and its precursor, pre-16S rRNA (metabolic activity), and tested it on samples from patients in a trial of optimised-dose rifampicin.
METHODS: We developed a multiplex reverse transcriptase quantitative PCR assay (RT-qPCR) to measure relative gene expression of pre-16S rRNA and 16S rRNA in pre-treatment (control) and sequential samples from patients in the Phase II HIGHRIF2 (NCT00760149) clinical trial. We constructed a mathematical model to assess changes in pre-16S gene expression relative to 16S rRNA over time, facilitating the comparison of rifampicin doses' efficacy.
FINDINGS: In a retrospective study of 19 patients, pre-16S rRNA and 16S rRNA decreased steadily during the initial 36 days of treatment. This was evidenced by the rising cycle threshold (Cq) values slope 0.404 and 0.212, respectively, however, pre-16S rRNA decreased significantly quicker ($P<0.0001$). The changes in the relative gene expression of pre-16S rRNA during treatment fitted a double exponential decay curve ($R2 = 0.996$). According to this model, 1200 mg RIF-containing therapy exerted the most potent and rapid impact on pre-16S rRNA expression (Maximum suppression (Rmin)=1.694, T (time) =9.78 days), and also resulted in the swiftest daily reduction in bacterial load (-0.072 log10 CFU ml-1/day).
INTERPRETATION: The pre-16S rRNA and 16S rRNA gene expression multiplex PCR reported here provides an easy to use and rapid marker of drug efficacy and has potential to assess the efficacy of existing or novel drug combinations.

DOI: 10.3389/frabi.2026.1760862
PMCID: PMC13101433
PMID: 42028555

Conflict of interest statement: The author(s) declared that this work was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

49. Evaluation of contezolid's cerebrospinal fluid concentration and safety in tuberculous meningitis patients.

Microbiol Spectr. 2026 Apr 7;14(4):e0239925. doi: 10.1128/spectrum.02399-25. Epub 2026 Mar 13.

Huang M(#)(1)(2), Wang Y(#)(1)(2), Chen T(3), Lu Y(2)(4), Chu N(1)(2), Nie W(1)(2).

Author information:
(1)Department of Tuberculosis, Beijing Chest Hospital, Capital Medical University, Beijing, China.
(2)Beijing Tuberculosis and Thoracic Tumor Institute, Beijing, China.
(3)Shanghai Institute of Infectious Disease and Biosecurity, Fudan University, Shanghai, China.
(4)Drug Research Laboratory, Beijing Chest Hospital, Capital Medical University,

Beijing, China.
(#)Contributed equally

Tuberculous meningitis (TBM) is the most severe form of tuberculosis (TB) with high mortality. This study evaluated the cerebrospinal fluid (CSF) concentration and safety of the novel oxazolidinone contezolid compared to linezolid in TBM patients. In this randomized prospective study, 10 TBM patients received either a linezolid-containing (n = 5) or contezolid-containing (n = 5) anti-TB regimen. CSF and blood concentrations were measured at 2 and 6 h post-dose. Peak (2 h) and trough (6 h) concentrations, area under the concentration-time curve (AUC), and safety were assessed. Contezolid CSF concentrations exceeded the Mycobacterium tuberculosis (Mtb) MIC (0.5 µg/mL) at 2 h (median: 1.0806 µg/mL, range: 0.9295-1.3165 µg/mL) but declined by 6 h (median: 0.7920 µg/mL, range: 0.1867-1.0194 µg/mL). Linezolid CSF concentrations were significantly higher than contezolid at both 2 h (median: 3.251 µg/mL, range: 1.9545-4.9636 µg/mL; P = 0.008) and 6 h (median: 1.623 µg/mL, range: 0.941-1.765 µg/mL; P = 0.016), remaining above MIC in all samples at 6 h. The mean CSF AUC for contezolid (4.637 µg·h/mL, 95% CI: 3.599-5.675) was significantly lower than that for linezolid (12.537 µg·h/mL, 95% CI: 7.8797-17.277; P = 0.008). Blood concentrations were higher than CSF for both drugs at all time points. No serious drug-related adverse events occurred. Contezolid effectively penetrates the blood-CSF barrier in TBM patients, achieving CSF concentrations above the MIC for Mtb. Although its CSF exposure was significantly lower than linezolid, its demonstrated penetration and safety profile suggest contezolid warrants further investigation as a potential treatment option for drug-resistant TBM.IMPORTANCETuberculous meningitis (TBM) is the deadliest form of tuberculosis, especially difficult-to-treat drug-resistant TBM. Finding new, effective, and safe medicines is critical. This study provides evidence in TBM patients that a newer antibiotic, contezolid, successfully reaches the infection site in cerebrospinal fluid (CSF) at levels expected to kill Mycobacterium tuberculosis. While linezolid achieved higher levels in CSF, contezolid still reached concentrations predicted to be effective and caused no serious side effects in our study. This is important because contezolid might offer a safer alternative to linezolid, which can have significant long-term toxicity. These promising results suggest contezolid could become a valuable new weapon against refractory drug-resistant TBM, potentially saving lives where current options are limited or too toxic.

DOI: 10.1128/spectrum.02399-25
PMCID: PMC13055287
PMID: 41823550 [Indexed for MEDLINE]

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

50. Key impact of Beijing strains including new resistant clusters on spread of multidrug-resistant tuberculosis in northern Russia.

Microbiol Spectr. 2026 Apr 7;14(4):e0343125. doi: 10.1128/spectrum.03431-25. Epub 2026 Mar 19.

Popova Y(1), Vyazovaya A(2), Eliseev P(1)(3), Miteneva E(1), Polev D(2), Mokrousov I(#)(2), Mariandyshev A(#)(1)(4).

Author information:
(1)Northern State Medical University, Arkhangelsk, Russia.
(2)St. Petersburg Pasteur Institute, St. Petersburg, Russia.
(3)National Medical Research Center for Phthisiopulmonology and Infectious Diseases, Moscow, Russia.
(4)Northern Arctic Federal University, Arkhangelsk, Russia.
(#)Contributed equally

Northern Russia is characterized by socio-environmental conditions contributing to the spread of tuberculosis (TB) and a high ~30% rate of primary multidrug-resistant (MDR) TB. We applied high-resolution molecular methods to study the Mycobacterium tuberculosis population in the Arkhangelsk region of Northern Russia. All available M. tuberculosis isolates recovered from newly diagnosed patients from January to December 2018 (n = 88) were genotyped using 24-loci MIRU-VNTR, spoligotyping, and, partly, by whole-genome sequencing (WGS). The population structure revealed a predominance of the Beijing genotype and Euro-American lineage, with significant drug resistance burden associated with Beijing and its B0/W148 strain. Beijing strains showed a significantly higher association with MDR and pre-extensively drug-resistant (pre-XDR) TB compared to non-Beijing strains (P = 0.0013). All Beijing B0/W148 isolates were MDR, whereas the majority (71.4%) of Beijing Central Asian/Russian subtype strains were drug-sensitive. WGS analysis of newly discovered Beijing clusters 3828-32 and 10167-32 in this area indicated a historical transmission over several decades, reflecting long-term endemic circulation. The presence of compensatory mutations in rpoC among MDR strains suggests enhanced fitness facilitating their ongoing transmission. An intriguing cluster of recent transmission of a non-Beijing strain (spoligotype SIT53, L4.8 sublineage) was identified through combined epidemiological and genomic investigation. To conclude, the prevalence of Beijing strains rose from 39.3% in 1998 to 67.0% (P < 0.001), and Russian epidemic MDR strain B0/W148 increased its rate from 11.2% in 1998 to 20.5% (P = 0.097). This highlights the key role of MDR Beijing strains, including new resistant clusters, in disseminating MDR-TB in the region and the importance of continuous surveillance using high-resolution genotyping.IMPORTANCEThe Arkhangelsk region is the largest province of northern European Russia. One-third of newly diagnosed tuberculosis patients are infected with multidrug-resistant (MDR) Mycobacterium tuberculosis strains. We assessed the molecular population structure of M. tuberculosis in the Arkhangelsk region in the COVID-19 pre-pandemic year 2018. We identified important MDR clusters and elucidated tuberculosis transmission patterns. An intriguing cluster of recent transmission was identified through the combined use of epidemiological investigation and whole-genome sequencing. The prevalence of Beijing genotype strains increased from 39.3% in 1998 to 67.0%, and the Russian epidemic MDR strain B0/W148 doubled from 11.2% in 1998 to 20.5%. Furthermore, we described new MDR clusters emerging within the Beijing genotype. This highlights the key

impact of the MDR Beijing strains and the importance of continuous surveillance using high-resolution genotyping. This study of the pre-pandemic strain collection provides an indispensable intermediate time point between earlier studies carried out 25 years ago and ongoing surveillance.

DOI: 10.1128/spectrum.03431-25
PMCID: PMC13055271
PMID: 41854248 [Indexed for MEDLINE]

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

51. Effect of Drug Cost-Exemption Policy on Treatment Outcomes in Multidrug-Resistant Tuberculosis Patients in Guangxi Zhuang Autonomous Region, China: A Nested Case-Control Study.

Clinicoecon Outcomes Res. 2026 Mar 27;18:577874. doi: 10.2147/CEOR.S577874. eCollection 2026.

Liu A(#)(1), Liao Y(#)(2), Ye J(#)(3), Wang Q(4), Huang J(5), Tang Y(5), Feng L(4).

Author information:
(1)Department of Infectious Diseases, Guangxi Zhuang Autonomous Region Chest Hospital, Liuzhou, People's Republic of China.
(2)Department of Tuberculosis, Guangxi Zhuang Autonomous Region Chest Hospital, Liuzhou, People's Republic of China.
(3)GCP Institutional Office, Guangxi Zhuang Autonomous Region Chest Hospital, Liuzhou, People's Republic of China.
(4)Guangxi Center for Tuberculosis Control and Medical Quality, Liuzhou, People's Republic of China.
(5)Public Health Department, Guangxi Zhuang Autonomous Region Chest Hospital, Liuzhou, People's Republic of China.
(#)Contributed equally

BACKGROUND: The most effective patient support interventions in low- and middle-income countries remain a research gap in World Health Organization consolidated guidelines on tuberculosis. We explored the impact of a partial drug cost-exemption policy (including cycloserine, moxifloxacin, linezolid, and clofazimine) implemented in Guangxi Zhuang Autonomous Region, China, on treatment outcomes among local multidrug-resistant tuberculosis (MDR-TB) patients.
METHODS: This case-control study enrolled 424 MDR-TB patients receiving anti-TB treatment between 2020 and 2022 in Guangxi Zhuang Autonomous Region. Data on demographics, treatment regimen, drug cost-exemption status, and adverse reactions were extracted from electronic medical records. Multivariable logistic regression analysis was used to identify factors associated with successful treatment outcomes.
RESULTS: Among the 424 enrolled MDR-TB patients, 212 (50.0%) had successful treatment outcomes, including 79 cured (18.6%) and 133 treatment completed

(31.4%). Unfavorable outcomes were observed in 212 patients (50.0%), comprising 190 lost to follow-up (44.8%), 19 deaths (4.5%), and 3 treatment failures (0.7%). Multivariable analysis revealed that female sex (aOR = 2.99, 95% CI: 1.55-5.78), absence of adverse drug reactions (aOR = 11.58, 95% CI: 3.81-35.18), and receiving drug cost-exemption (aOR = 37.47, 95% CI: 10.97-127.96) were associated with favorable treatment outcomes. Furthermore, receiving an increasing number of exempted drugs was progressively associated with higher treatment success. Compared to one drug exemption, the aOR for successful outcomes was 3.24 (95% CI: 2.16-4.87) for two-drug cost-exemption and 5.13 (95% CI: 2.73-9.65) for three-drug cost-exemption.
CONCLUSION: This nested case-control study demonstrates that implementing drug cost-exemption support policy is associated with significantly improved MDR-TB treatment success rates in resource-limited, high-burden settings in China.

DOI: 10.2147/CEOR.S577874
PMCID: PMC13037532
PMID: 41923896

Conflict of interest statement: The authors report no conflicts of interest in this work.

52. 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.

RSC Med Chem. 2026 Feb 4;17(3):1672-1686. doi: 10.1039/d5md00738k. eCollection 2026 Mar 25.

Alshabani LA(1), Abdali JM(1), Brown AK(2), de Sousa DP(1)(3), Willcocks S(4)(5), Kumar A(6), Alhejaili AYG(2), Estrada DF(6), Simons C(1).

Author information:
(1)School of Pharmacy & Pharmaceutical Sciences, Cardiff University Cardiff CF10 3NB UK simonsc@cardiff.ac.uk.
(2)Bioscience Institute, Newcastle University Newcastle upon Tyne NE2 4HH UK.
(3)Department of Pharmaceutical Sciences, Federal University of Paraiba João Pessoa Brazil.
(4)London School of Hygiene & Tropical Medicine London WC1E 7HT UK.
(5)Brunel University London Uxbridge UB83PH UK.
(6)Department of Biochemistry, Jacobs School of Medicine and Biomedical Science, University at Buffalo Buffalo New York-14203 USA.

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.

DOI: 10.1039/d5md00738k
PMCID: PMC12895674
PMID: 41695589

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

53. Improving Tuberculosis Treatment Outcomes in Somalia: A Narrative Review of Strategies, Challenges, and Policy Recommendations.

Risk Manag Healthc Policy. 2026 Apr 17;19:595510. doi: 10.2147/RMHP.S595510. eCollection 2026.

Mohamoud JH(1)(2).

Author information:
(1)Department of Public Health, Faculty of Medicine and Health Sciences, SIMAD University, Mogadishu, Somalia.
(2)SIMAD Institute for Global Health, SIMAD University, Mogadishu, Somalia.

Tuberculosis (TB) remains a major public health concern in Somalia, driven by prolonged conflict, population displacement, fragile health systems, and adverse social determinants of health. Although Somalia has made progress in expanding TB services and achieving favourable treatment outcomes for drug-susceptible TB, the country continues to experience a high TB burden and emerging drug-resistant tuberculosis (DR-TB). Persistent challenges include delayed diagnosis, treatment

interruption, catastrophic patient costs, paediatric TB care gaps, and reliance on external donor funding. This narrative review synthesizes evidence from peer-reviewed articles, programmatic reports, and international guidelines to examine TB treatment outcomes, key challenges, and current strategies in Somalia. Literature was searched in PubMed, Google Scholar, and Scopus databases, as well as relevant grey literature from the World Health Organization and humanitarian organizations. Publications between 2010 and 2024 were considered, and 35 studies were identified, of which 15 met the inclusion criteria and were included in the final synthesis. The findings highlight the importance of decentralized and community-based care, rapid molecular diagnostics, multimodal adherence support, shorter all-oral DR-TB regimens, and integration of TB services with nutrition and humanitarian support. Strengthening health system resilience and prioritizing vulnerable populations are essential for sustaining improvements in TB treatment outcomes in Somalia and other fragile settings.

DOI: 10.2147/RMHP.S595510
PMCID: PMC13098548
PMID: 42022926

Conflict of interest statement: The author declares that there are no competing interests in this work.

54. Combined computational and classical medicinal chemistry procedure to disclose novel pyrrole-based compounds as potential antituberculosis agents.

J Comput Aided Mol Des. 2026 Apr 6;40(1):92. doi: 10.1007/s10822-026-00794-6.

Ragno R(1), Zwergel C(2), Valente S(2), Astolfi R(3), Lambona C(2), Proia E(2), Giuliani L(2), Franzblau SG(4), Fioravanti R(5), Mai A(2).

Author information:
(1)Rome Center for Molecular Design, Department of Drug Chemistry and Technologies, Sapienza University of Rome, Piazzale Aldo Moro 5, 00185, Rome, Italy. rino.ragno@uniroma1.it.
(2)Department of Drug Chemistry and Technologies, Sapienza University of Rome, Piazzale Aldo Moro 5, Rome, 00185, Italy.
(3)Rome Center for Molecular Design, Department of Drug Chemistry and Technologies, Sapienza University of Rome, Piazzale Aldo Moro 5, 00185, Rome, Italy.
(4)Institute for Tuberculosis Research, Department of Pharmaceutical Sciences, University of Illinois Chicago, 833 South Wood Street, Chicago, IL, 60612, USA.
(5)Department of Drug Chemistry and Technologies, Sapienza University of Rome, Piazzale Aldo Moro 5, Rome, 00185, Italy. rossella.fioravanti@uniroma1.it.

Tuberculosis (TB) remains a major global health challenge, worsened by the rise of multidrug-resistant (MDR) and extensively drug-resistant (XDR) strains. In this study, we employed a combined computational and medicinal chemistry approach to design, synthesize, and evaluate new pyrrole-based analogues of Sudoterb (1, LL-3858) as potential anti-TB agents. Ligand-based quantitative structure-activity relationships (QSAR) and 3-D QSAR models, as well as structure-based docking and COMBINE analyses, were developed and used to analyze the anti-TB structural determinants and investigate the putative targeting to the MmpL3 transporter. Nineteen new analogues, belonging to amide (2a-j) and carbamate (3a-i) series, were synthesized and tested against Mycobacterium tuberculosis H37Rv resistant strain using the microplate Alamar Blue assay. Most of the synthesized analogues showed enhanced potency compared to Sudoterb (MIC = 20.7 μM), with 2i (MIC = 2.8 μM) and 3 h (MIC = 2.4 μM) emerging as the most potent and selective derivatives (IC50 > 80 μM in Vero cells). Computational predictions aligned well with experimental results, validating the modeling workflow. These findings identify 2i and 3 h as promising lead compounds and highlight the utility of integrating computational modeling with rational synthesis to accelerate anti-TB drug discovery.

DOI: 10.1007/s10822-026-00794-6
PMCID: PMC13053371
PMID: 41940996 [Indexed for MEDLINE]

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

55. Breakthrough Tuberculosis in a Large Cohort of People Living With HIV on Preventive Treatment.

Trop Med Int Health. 2026 Apr;31(4):560-566. doi: 10.1111/tmi.70107. Epub 2026 Feb 19.

Ruswa N(1)(2), Günther G(1)(3), Claassens M(1).

Author information:
(1)School of Medicine, Faculty of Health Sciences and Veterinary Medicine, University of Namibia, Windhoek, Namibia.
(2)National TB and Leprosy Programme, Directorate of Special Programmes, Ministry of Health and Social Services, Windhoek, Namibia.
(3)Department of Pulmonology, Allergology and Clinical Immunology, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland.

BACKGROUND: Tuberculosis is a leading infectious cause of death globally and the main cause among those with HIV. TB preventive treatment (TPT) is key for preventing TB in people with HIV (PWH). Healthcare workers often worry about adverse effects of TPT regimens, including breakthrough TB-active TB during treatment. The burden of breakthrough TB remains largely unknown. This study

aimed to determine the incidence and factors associated with breakthrough TB in PWH receiving HIV care.
METHODS: We analysed the nationwide electronic patient management system (EPMS) for HIV care and TB registers in Namibia, following PWH registered for HIV care to determine TB incidence before, during and after TPT and applying logistic regression to determine factors associated with breakthrough TB.
RESULTS: Of 334,606 PWH reviewed, 46,199 developed TB before, during, or after receiving TPT while being followed up for HIV care. PWH were followed for 114,667 patient-years (PYs) while receiving TPT, with breakthrough TB incidence of 1.40 per 100 PYs (95% CI: 1.33-1.47). The 1790 true breakthrough cases had a median age of 37 (IQR 30-45). Median time to breakthrough TB was 2.5 months. Only 43 (2.4%) cases were drug-resistant TB. In a logistic regression model comparing breakthrough versus non-breakthrough TB cases, receiving ART increased breakthrough TB risk (aOR = 2.88; 95% CI: 1.07-7.78). The 3 month isoniazid-rifapentine TPT regimen showed lower risk (aOR = 0.46; 95% CI: 0.36-0.63) than the 6 month isoniazid regimen, while 9H increased risk (aOR = 1.44; 95% CI: 1.18-2.52) but incidence rates were comparable between the regimens.
CONCLUSION: The incidence of breakthrough TB was low at 1.4 per 100 PYs of TPT provision but indicating a need for improved screening of PWH before TPT. The incidence rate of TB among PWH during and after the shorter TPT regimen (3HP) is comparable to that of the 6H and 9H regimens.

DOI: 10.1111/tmi.70107
PMCID: PMC13050615
PMID: 41711404 [Indexed for MEDLINE]

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

56.Time to sputum culture conversion, treatment outcomes, and associated factors among rifampicin-resistant or multidrug-resistant tuberculosis patients in the Sidama region, Ethiopia: A retrospective follow-up study.

PLoS One. 2026 Apr 13;21(4):e0327705. doi: 10.1371/journal.pone.0327705. eCollection 2026.

Geda WA(1), Betru KT(2), Solomon T(2), Daniel S(2).

Author information:
(1)Sidama Regional Public Health Institute, Hawassa, Sidama, Ethiopia.
(2)School of Public Health, College of Medicine and Health Sciences, Hawassa University, Hawassa, Sidama, Ethiopia.

BACKGROUND: Time to sputum culture conversion is critical for follow-up treatment effectiveness in multidrug-resistant tuberculosis patients. However, the evidence regarding time to culture conversion, treatment outcomes, and the

associated factors was sparse and inconsistent.
OBJECTIVE: This study aimed to determine the time to culture conversion, treatment outcomes, and associated factors among rifampicin-resistant and multidrug-resistant tuberculosis cases in the Sidama region from April 1 to December 31, 2024.
METHODS: We conducted a retrospective follow-up study of 346 patients who enrolled between January 2013 and June 2024. We collected data from patients' medical records using a standardized form, entered the data, and analyzed it using Stata 16.1 software. We performed the analysis using the Kaplan-Meier model for time to culture conversion, Weibull distribution gamma frailty, and logistic regression models to assess factors associated with time to culture conversion and treatment outcomes, respectively. We considered an adjusted hazard or odds ratio with a 95% CI and a p-value < 0.05 to determine significance.
RESULTS: Among the participants, 302 (87.3%) achieved culture conversion in a median time of 76 days (95% CI: 71-79 days). Patients with a history of previous loss to follow-up experienced an approximately fivefold delay in culture conversion (AHR = 0.2; 95% CI: 0.1-0.6; p = 0.001), while relapse cases had a twofold delay (AHR = 0.5; 95% CI: 0.2-0.9; p = 0.02) compared with new patients. The treatment success rate was 234/346 (67.6%). Female patients had higher odds of achieving a favorable treatment outcome (AOR = 1.8; 95% CI: 1.0-3.3; p = 0.04), whereas patients who experienced culture reversion had significantly lower odds of a favorable outcome (AOR = 0.05; 95% CI: 0-0.4; p = 0.001).
CONCLUSIONS: The majority of patients experienced culture conversion within three months. However, patients with a history of loss to follow-up and relapse experienced delayed culture conversion. These findings highlight the urgent need to improve patient adherence.

DOI: 10.1371/journal.pone.0327705
PMCID: PMC13075698
PMID: 41973720 [Indexed for MEDLINE]

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

57. Fc gamma receptor binding modulates IgG clearance in cancer cachexia.

Front Immunol. 2026 Mar 31;17:1676732. doi: 10.3389/fimmu.2026.1676732. eCollection 2026.

Remaily BC(1), Kim K(1), Thomas J(1), Adeluola A(1), Young G(1), Hai M(1), Fukuda M(1), Mulcahy G(1), Stanton C(1), Granchie L(1), Kumar P(1), Vu T(1), Jeffrey F(2), Palozzi N(2), Mo X(3), Kulp SK(1), Owen DH(4)(5)(6), Mace

TA(5)(6)(7), Coss CC(#)(1)(5)(6), Phelps MA(#)(1)(5)(6), Ganesan LP(#)(2).

Author information:
(1)Division of Pharmaceutics and Pharmacology, College of Pharmacy, The Ohio State University, Columbus, OH, United States.
(2)Department of Internal Medicine, The Ohio State University, Columbus, OH, United States.
(3)Department of Biomedical Informatics, The Ohio State University, Columbus, OH, United States.
(4)Division of Medical Oncology, The Ohio State University James Comprehensive Cancer Center, Columbus, OH, United States.
(5)The Ohio State University - James Comprehensive Cancer Center, Columbus, OH, United States.
(6)The Pelotonia Institute for Immuno-Oncology, The Ohio State University, Columbus, OH, United States.
(7)Division of Gastroenterology, Hepatology & Nutrition, Department of Medicine, The Ohio State University, Columbus, OH, United States.
(#)Contributed equally

BACKGROUND: Patients with cancer-cachexia display a general resistance to Immune Checkpoint Inhibitor (ICI) therapy, as well as an elevated baseline catabolic clearance (CL) of ICIs, which serves as a prognostic indicator of overall survival independent of dose and drug exposure. Increased rate of ICI CL is present in the Lewis Lung Carcinoma (LLC) murine model of cachexia, but absent in the non-cachectic MC38 model. Fc-Gamma Receptors (FcγRs) bind the Fc portion of antibodies and can impact ICI anti-tumor efficacy.
METHODS: A pharmacokinetic study of human IgG1 (hIgG1) and hIgG1 with D265A (D265A) mutation, to abrogate all FcγR binding, was performed in mice that were either LLC tumor bearing (TB) or tumor free (TF). Immunofluorescence studies using fluorescence conjugated anti-human IgG were conducted to detect and localize infused hIgG1 in the mouse liver. To further investigate, FcγRIIb knockout mice were utilized in pharmacokinetic studies with hIgG.
RESULTS: CL of both IgG1 and D265A significantly increased in LLC TB mice compared to TF controls, however the CL of D265A was significantly lower compared to hIgG1 in LLC TB mice. Immunofluorescence image of mouse livers portrays colocalization of the administered hIgG1 and FcγRIIb in liver sinusoidal endothelial cells (LSEC), as well as upregulated hepatic expression of FcγRIIb in LLC TB. However, hIgG1 CL was unaffected by whole body knockout of FcγRIIb.
CONCLUSION: Reduced CL of D265A versus IgG1 in LLC TB mice, but not TF mice, suggests FcγRs are involved in catabolic CL of IgG antibodies in the presence of LLC tumors and cancer cachexia. This suggest that in the presence of LLC tumors, changes in FcγR expression and/or function lead to significantly altered antibody CL mediated by FcγR. This apparent role of FcγRs in antibody catabolism cannot be solely explained by FcγRIIb, but instead suggests the significance of other FcγRs in cachexia-associated increases in antibody CL.

DOI: 10.3389/fimmu.2026.1676732
PMCID: PMC13076527
PMID: 41988202 [Indexed for MEDLINE]

Conflict of interest statement: DO receives research funding from Merck, Pfizer, Onc.AI, Genentech, Palobiofarma, Turning Point Therapeutic, Bristol Myers Squibb and Travel Funding from Astrazeneca, Genentech and Janssen. These funders were not involved in the study design, collection, analysis, interpretation of data, the writing of this article or the decision to submit it for publication. The remaining author(s) declared that this work was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

58. Population pharmacokinetics of TBAJ-587 and its main metabolites-Evaluation of different loading dose strategies and early dose selection.

Br J Clin Pharmacol. 2026 Apr;92(4):1058-1068. doi: 10.1002/bcp.70333. Epub 2025 Nov 19.

Leding AAM(1), Bruinenberg P(2), Conradie A(2), Nedelman J(2), Lombardi A(2), Hickman D(2), Simonsson USH(1).

Author information:
(1)Department of Pharmaceutical Biosciences, Uppsala University, Uppsala, Sweden.
(2)TB Alliance, New York, New York, USA.

BACKGROUND AND AIM: The rise of drug-resistant tuberculosis (TB) poses a need for new drugs and combinations. TBAJ-587, a new diarylquinoline (DARQ), has shown promising efficacy in preclinical studies. This work aimed to describe the pharmacokinetics (PK) of TBAJ-587 and its metabolites M2 and M3 after single ascending dosing in healthy volunteers and to develop a simultaneous population PK model. In addition, to explore different doses in relation to efficacy and safety and to assess the impact of loading doses on exposure levels of TBAJ-587 and its metabolites.
METHODS: Pharmacokinetic samples from 42 healthy volunteers following a single dose (25, 50, 100, 200, 400 or 800 mg) were collected for up to Day 126. Population pharmacokinetic modelling was conducted using nonlinear mixed-effects modelling in NONMEM. Simulations from final model were performed to compare against efficacy targets derived from the first-in-class DARQ bedaquiline and safety references based on preclinical studies.
RESULTS AND CONCLUSIONS: The final model simultaneously described the PK of TBAJ-587, M2 and M3 well. Simulations of final model identified that all simulated doses and regimens resulted in exposures that were below the safety references. A loading dose for 2 weeks resulted in initially higher concentrations, but a limited difference in exposure at 4 weeks and onwards, compared with no loading dose. A 100 mg once daily dose and higher reached the efficacy targets and can be studied further in combinations in phase 2a studies.

Name of trial: Evaluation of the Safety, Tolerability, PK of TBAJ-587 in Healthy Adults.
REGISTRATION NUMBER: NCT04890535.

DOI: 10.1002/bcp.70333
PMCID: PMC13021289
PMID: 41255184 [Indexed for MEDLINE]

Conflict of interest statement: TB Alliance has ownership over TBAJ-587.

59. Artificial intelligence at the frontlines: Emerging infectious and parasitic diseases in the digital era.

New Microbes New Infect. 2026 Apr 10;71:101751. doi: 10.1016/j.nmni.2026.101751. eCollection 2026 Jun.

Nasr DS(1)(2), Alraee NB(3), Katbi SWA(3), Kouli NM(3), Asaad NI(3), Ismail MM(3), Khanday S(1).

Author information:
(1)Biomedical Sciences Department, Dubai Medical College for Girls, Dubai Medical University, Dubai, 19099, United Arab Emirates.
(2)Medical Parasitology Department, Faculty of Medicine, Cairo University, Cairo, Egypt.
(3)Students at Dubai Medical College for Girls, Dubai Medical University, Dubai, 19099, United Arab Emirates.

Emerging infectious diseases are one of the most significant threats to global health, driven by many factors such as zoonotic spillovers, climate change, globalization, and antibiotic resistance. While a great deal of attention is focused on viral and bacterial pathogens (e.g., SARS-CoV-2, influenza, multidrug-resistant TB), parasitic diseases contribute to global morbidity and mortality that remain largely unrecognized. The recent development of artificial intelligence has introduced powerful computational tools that can integrate large and complex datasets to assist with infectious disease surveillance, diagnosis, outbreak prediction, and drug discovery. Artificial intelligence encompasses machine learning, deep learning, and natural language processing techniques, which allow for automated pattern recognition and predictive modeling based on very complex biomedical data sets. This narrative review explores the recent advancements in AI applications in four key areas related to infectious disease: disease surveillance and early-warning systems; diagnostics and clinical decision support; outbreak prediction and modeling; and drug/vaccine discovery. Emphasis will be placed on applications of AI to parasites such as malaria, leishmaniasis, and soil-transmitted helminths. In addition, we discuss several challenges related to AI implementation in endemic regions including limited data availability, algorithmic bias, limited

infrastructure in endemic areas, and ethical issues regarding data governance. Integrating AI into the One Health framework of linking human, animal, and environmental health will potentially enhance global preparedness to respond to emerging infectious and parasitic diseases.

DOI: 10.1016/j.nmni.2026.101751
PMCID: PMC13101621
PMID: 42027758

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.

60. From Lake Victoria to the Tap: Antibiotic Resistance and Pathogenic Contamination of Kisumu City Water Supply and Wastewater Network.

Trop Med Int Health. 2026 Apr;31(4):547-559. doi: 10.1111/tmi.70105. Epub 2026 Feb 16.

Reva ON(1), Sifuna A(2), Orata F(3), Omolo C(4), Iramiot JS(5), Enright MC(6), Mutshembele A(7), Zhou J(6), Shivoga WA(8).

Author information:
(1)Department of Biochemistry, Genetics and Microbiology, Centre for Bioinformatics and Computational Biology, University of Pretoria, Pretoria, South Africa.
(2)Department of Medical Biochemistry, Masinde Muliro University of Science and Technology, Kakamega, Kenya.
(3)Department of Pure and Applied Chemistry, Masinde Muliro University of Science and Technology, Kakamega, Kenya.
(4)Water and Sanitation Company (KIWASCO), Kisumu, Kenya.
(5)Department of Microbiology and Immunology, Busitema University, Faculty of Health Sciences, Mbale Campus, Mbale, Uganda.
(6)Manchester Metropolitan University, Manchester, UK.
(7)South African Medical Research Council-Office of AIDS and TB (SAMRC-OATB), Pretoria, South Africa.
(8)Department of Biological Sciences, Centre of Excellence for Water and Environment Resources Management, Masinde Muliro University of Science and Technology, Kakamega, Kenya.

Waterborne diseases and antimicrobial resistance (AMR) pose mounting public health threats across sub-Saharan Africa, particularly in rapidly urbanising regions dependent on untreated or poorly treated surface waters. This study applied shotgun metagenomic sequencing to characterise microbial communities, virulence factors and antibiotic resistance genes (ARGs) in water samples collected from Lake Victoria, River Wigwa, Dunga Water Treatment Plant, Nyalenda Wastewater Stabilisation Ponds and the tap water outlet in post-treatment supply

pipe in Kisumu city (Kenya). Bacterial taxa dominated all metagenomes, with 121 classes represented. Cyanobacteria, particularly Planktothrix, were highly abundant in lake and tap water, whereas wastewater and river samples exhibited greater taxonomic diversity. Major human pathogens, including Pseudomonas aeruginosa , Klebsiella pneumoniae , Escherichia coli , Acinetobacter baumannii and Bacillus cereus/anthracis, were detected in nearly all samples, with unexpectedly high prevalence in tap water. Viral indicators of faecal contamination (adenoviruses, enteroviruses and torque teno viruses) corroborated widespread wastewater influence. Functional gene profiling revealed a rich resistome comprising aminoglycoside-modifying enzymes, β-lactamases, vancomycin-resistance operons and disinfectant-resistance determinants. The highest ARG and virulence gene frequencies occurred in tap and treatment-plant water, suggesting that incomplete disinfection and biofilm persistence promote the proliferation and exchange of ARGs between environmental and pathogenic taxa. In contrast, Lake Victoria water exhibited lower ARG abundance, reflecting natural self-purification processes. These findings underscore the inadequate water treatment and open wastewater systems create ecological 'hotspots' for ARG selection and horizontal gene transfer. Metagenomic surveillance integrated into One Health frameworks can enhance risk forecasting and guide interventions to mitigate AMR emergence and dissemination in freshwater systems serving over 35 million people across the Lake Victoria basin.

DOI: 10.1111/tmi.70105
PMCID: PMC13050616
PMID: 41697036 [Indexed for MEDLINE]

Conflict of interest statement: The authors have nothing to report. The authors declare no conflicts of interest.

61. Highly effective isolation of Stenotrophomonas from pharyngeal swabs of infected inpatients and issues in species identification.

Microbiol Spectr. 2026 Apr 7;14(4):e0379825. doi: 10.1128/spectrum.03798-25. Epub 2026 Feb 25.

Xu B(#)(1), Zeng Y(#)(2), Yu Z(1), Jiang Y(1), Zhou Y(2), Wang C(2), Liu J(2), Wang R(1), Qi W(2).

Author information:
(1)National Key Laboratory of Intelligent Tracking and Forecasting for Infectious Disease, Chinese Centre for Disease Control and Prevention, National Institute for Communicable Disease Control and Prevention, Beijing, People's Republic of China.
(2)Beijing Friendship Hospital, Capital Medical University, Beijing, People's Republic of China.
(#)Contributed equally

Stenotrophomonas is a significant opportunistic pathogen associated with high attributable mortality. Notably high isolation rates and species diversity have been observed among tuberculosis patients in Beijing, China. To determine its infection/colonization rate and characteristics in non-TB patients, we conducted a study utilizing a sensitive pre-enrichment PCR assay on pharyngeal swabs from inpatients in the Department of Infectious Diseases. Three Stenotrophomonas strains were isolated from 143 samples (2.10%), and positive cases shared common characteristics-advanced age, invasive procedures, repeated hospitalizations, and broad-spectrum antimicrobial exposure-which are established risk factors for Stenotrophomonas maltophilia infection. Both the isolation rate and common characteristics differed from those of TB patients. Notably, three isolates were identified via average nucleotide identity (ANI) as S. geniculate and S. muris, but both species were misidentified as S. maltophilia by matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF) mass spectrometry, despite achieving reliable identification scores (≥2.0). This misidentification likely explains the exclusive focus on S. maltophilia and the underestimation of other species absent from MALDI-TOF databases. Antibiotic susceptibility testing showed general susceptibility to quinolones, tigecycline, chloramphenicol, and trimethoprim-sulfamethoxazole and partial susceptibility to ceftazidime and ceftazidime/avibactam. Notably, a strain susceptible to ceftazidime and moxifloxacin was isolated from a patient treated with these agents. In conclusion, this study underscores the necessity of developing alternative rapid molecular methods with ANI-equivalent resolution for Stenotrophomonas, alongside expanding mass spectral databases and reevaluating the clinical significance and resistance profiles of the Stenotrophomonas species.IMPORTANCECompounding its inherent pathogenicity, Stenotrophomonas adversely impacts co-infecting pathogens and is associated with high attributable mortality and multidrug resistance. This study demonstrates that through enrichment and PCR of throat swab samples, this elusive pathogen-frequently undetected in routine clinical testing-can be identified with high sensitivity, providing crucial diagnostic alerts for clinicians, particularly in critically ill and etiology-unknown patients. Our analysis reveals that the risk factors for Stenotrophomonas positivity differ between general infectious disease inpatients and tuberculosis patients. Furthermore, our findings highlight a critical issue of species misidentification by routine microbiological methods, which has obscured the true clinical significance and resistance profiles of Stenotrophomonas species.

DOI: 10.1128/spectrum.03798-25
PMCID: PMC13055341
PMID: 41738794 [Indexed for MEDLINE]

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

62. Integrative multimodal transcriptomics identifies a cancer-associated fibroblast membrane signature for predicting prognosis and therapeutic response in pancreatic ductal adenocarcinoma.

J Mol Med (Berl). 2026 Apr 6;104(1):60. doi: 10.1007/s00109-026-02669-7.

Zhuang L(#)(1), Zhang W(#)(2), Wu J(#)(2)(3), Cao J(4), Feng L(4), Cao S(5).

Author information:
(1)Department of Hepatobiliary, Pancreatic and Splenic Surgery, Yiyang Central Hospital, No. 118, Kangfu North Road, Heshan District, Yiyang, 413000, Hunan Province, China.
(2)Institute for Brain Research and Rehabilitation, South China Normal University, Guangzhou, 510631, Guangdong Province, China.
(3)School of Biomedical Science, Hunan University, Hunan Province, Changsha, 410082, China.
(4)General Surgery Department, Yiyang Central Hospital, Hunan Province, Yiyang, 413000, China.
(5)Department of Hepatobiliary, Pancreatic and Splenic Surgery, Yiyang Central Hospital, No. 118, Kangfu North Road, Heshan District, Yiyang, 413000, Hunan Province, China. 13807374946@163.com.
(#)Contributed equally

Cancer-associated fibroblasts (CAFs) are central to the pancreatic ductal adenocarcinoma (PDAC) microenvironment, promoting tumor progression and therapeutic resistance. However, the expression landscape of CAF membrane proteins in PDAC remains poorly defined. We integrated scRNA-seq (n = 33; 87,949 cells), spatial transcriptomics (n = 2; 7,011 spots), and bulk RNA-seq (n = 7; 642 samples) to systematically identify PDAC-specific CAF membrane genes. A LASSO-based Cox model was developed to construct a prognostic signature, PaFMS, and evaluated through multi-cohort validation. Functional enrichment, immune infiltration, drug sensitivity, and immunotherapy response analyses were further conducted. Validation was performed using multiple database-driven analyses. We identified a PDAC-enriched myoCAF-c1 cluster closely associated with epithelial-mesenchymal transition (EMT) and angiogenesis. From this cluster, 33 candidate CAF membrane genes were defined, whose protein-protein interactions were predominantly linked to extracellular matrix organization and collagen remodeling, and spatially colocalized with myoCAF-c1 and EMT regions. An 11-gene prognostic signature, PaFMS that robustly stratified patients across six independent cohorts, achieving high predictive accuracy for overall survival. High-risk patients exhibited proliferative signaling activation, immune suppression, and reduced T/B-cell infiltration. PaFMS was associated with responses to 33 anticancer agents and predicted enhanced benefit from anti-PD-L1 immunotherapy in the low-risk group. Multi-cohort validation confirmed the expression specificity of PaFMS genes, including PLAU, TMEM158, and TRIM59. Together, these findings reveal that myoCAF-c1 promotes angiogenesis and tumor progression, and establish PaFMS as a robust CAF membrane-based prognostic model in PDAC with potential utility for precision prognosis and therapeutic decision-making. KEY MESSAGES: Integrated single-cell, spatial, and bulk RNA-seq analyses identified PDAC-specific CAF membrane genes. Discovered a PDAC-enriched myoCAF-c1 subtype linked to EMT and angiogenesis. Developed an 11-gene CAF membrane-based prognostic model (PaFMS) validated across six cohorts. PaFMS predicts patient survival, drug sensitivity, and immunotherapy response in PDAC.

DOI: 10.1007/s00109-026-02669-7
PMCID: PMC13053443
PMID: 41942785 [Indexed for MEDLINE]

Conflict of interest statement: Declarations. Ethics: Not applicable. Competing interests: The authors declare no competing interests.

Recent TB News

Johns Hopkins team develops therapeutic, nasally delivered DNA vaccine for tuberculosis
https://www.hopkinsmedicine.org/news/newsroom/news-releases/2026/04/johns-hopkins-team-develops-therapeutic-nasally-delivered-dna-vaccine-for-tuberculosis
A research team at Johns Hopkins has recently developed a therapeutic intranasal DNA vaccine against tuberculosis (TB). The vaccine works by fusing two genes (rel_{Mtb} and Mip3a) together with the goal of directing the body's immune system to fight drug-tolerant bacteria that contribute to disease relapse. The vaccine demonstrated success in mice but needs additional studies before clinical trials in humans can be run.

Two new TB vaccines show safety but limited protection
https://www.news-medical.net/news/20260409/Two-new-TB-vaccines-show-safety-but-limited-protection.aspx
A large trial conducted in India demonstrated that two new vaccines, VPM1002 and Immuvac, are safe for use in adults and children but did not provide protection against all forms of tuberculosis (TB). Both vaccines showed an ability to help prevent the progression from latent TB to active TB and VPM1002 did show protection against extrapulmonary TB (EPTB) across all age groups, demonstrating a potential for a real public health benefit.