PubMed Open Access

1. Rifampicin-resistant tuberculosis in Spain.

ERJ Open Res. 2026 Feb 23;12(1):00941-2025. doi: 10.1183/23120541.00941-2025. eCollection 2026 Jan.

García-García JM(1), Rodrigo-Sanz T(1), Gullón-Blanco JA(2), Casas García X(3), Millet JP(3), Quirós Fernández S(4), Martínez Lirola MJ(5), Mangas Moro A(6), Domínguez Castellano Á(7), Navas Elorza E(8), Nieto Marcos M(9), Arasa Panisello F(10), Bermúdez Ruiz P(11), García Cabrera M(12), Sanz Herrero F(13), Suárez Toste I(14), Urrelo Cerrón LA(10), Espiau Guarner M(15), Soriano Arandes A(15), Arias Guillén M(16), Cebrián Gallardo JJ(17), García-Fuertes JA(18), Pérez-Jacoiste Asín MA(19), Somoza González M(20), Palacios Gutiérrez JJ(16)(21), Alcaide F(21)(22), Samper Blasco S(21)(23), Tabernero Huguet E(1), Caylà JA(1), Ruiz Manzano J(1), Caminero Luna JA(24); Working Group on Rifampicin Resistant Tuberculosis of the Tuberculosis Research Programme (PII-TB) SEPAR.

Collaborators: Martínez Robles E, Castillo García M, Izquierdo Alonso JL, Borderías Clau L, Calderón Alcalá M, Carpena Martínez I, Cordero Matía ME, De la Torre Carazo S, Fernández Álvarez P, Álvarez Navascués F, Fernández Infante B, Ferreiro Fernández L, Hernández Egido S, Navas Bueno B, Noguera Julián A, Ozoleto Camacho O, Pérez Mendoza G, Rodríguez González J, Ruiz González A, Seminario Ruiz A, Valiño López P, Zabaleta Murguiondo M, Mínguez Clemente P, Castanera Moros A, Pérez Recio S.

Author information:
(1)Tuberculosis Research Programme (PII-TB), SEPAR (Spanish Society of Pneumology and Thoracic Surgery), Barcelona, Spain.
(2)Hospital Universitario San Agustín, Avilés, Spain.
(3)Serveis Clínics, Barcelona, Spain.
(4)Hospital Universitario Basurto, Bilbao, Spain.
(5)Complejo Hospitalario Torrecárdenas de Almería, Almería, Spain.
(6)Hospital Universitario La Paz-Cantoblanco-Carlos III, Madrid, Spain.
(7)Hospital Universitario Virgen Macarena, Seville, Spain.
(8)Hospital Universitario Ramón y Cajal, Madrid, Spain.
(9)Hospital Doctor Moliner, Serra, Spain.
(10)Hospital de Tortosa Verge de la Cinta, Tortosa, Spain.
(11)Hospital Regional Universitario de Málaga, Málaga, Spain.
(12)Hospital Universitario Doctor José Molina Orosa, Arrecife, Spain.
(13)Hospital General Universitario de Valencia, Valencia, Spain.
(14)Hospital Universitario de Canarias, La Laguna, Spain.
(15)Hospital Universitario Vall d'Hebron, Barcelona, Spain.

(16)Hospital Universitario Central de Asturias, Oviedo, Spain.
(17)Hospital Costa del Sol, Marbella, Spain.
(18)Hospital de Txagorritxu, Vitoria-Gasteiz, Spain.
(19)Hospital Universitario 12 de Octubre, Madrid, Spain.
(20)Consorcio Sanitario de Terrassa, Terrassa, Spain.
(21)Sociedad Española de Enfermedades Infecciosas y Microbiología Clínica (SEIMC), Madrid, Spain.
(22)Hospital Universitario de Bellvitge, Barcelona, Spain.
(23)Instituto Aragonés de Ciencias de la Salud, Zaragoza, Spain.
(24)Hospital Universitario de Gran Canaria Dr Negrín, Las Palmas, Spain.

OBJECTIVE: The aim of the study was to analyse the characteristics of rifampicin-resistant tuberculosis patients in Spain.
METHODS: This was an ambispective observational study of a multicentre cohort of patients diagnosed between January 2019 and July 2023 in most Autonomous Communities (retrospective period 2019-2020, prospective 2021-2023).
RESULTS: 94 patients were included; 83 (88.3%) had pulmonary tuberculosis. The mean age was 38.00±17.8 years; 67 (71.3%) were male, 62 (66.0%) were from countries other than Spain, six (6.4%) were HIV-infected and 24 (25.5%) had previously treated tuberculosis. Nine patients had rifampicin-resistant tuberculosis (RR-TB), 75 multidrug-resistant tuberculosis (MDR-TB), nine pre-extensively drug-resistant tuberculosis (pre-XDR-TB) and one XDR-TB. Treatment included bedaquiline in 39 (41.5%) patients, linezolid in 87 (92.6%), fluoroquinolones in 82 (87.2%), clofazimine in 64 (68.0%) and delamanid in 27 (28.7%). Treatment was supervised by experts in 63 cases (67.0%). In 43 patients (45.7%), there were difficulties obtaining authorisation for drug prescription (bedaquiline or delamanid). 21 patients (22.3%) had difficulties understanding the treatment. The final treatment outcomes were cured in 60 cases (63.8%), treatment completed in 23 (24.5%), deaths in 3 (3.2%), with 2 due to tuberculosis, loss to follow-up in five (5.3%) and not evaluated in three (3.2%). No treatment failures occurred. Successful outcomes were achieved in 83 patients (88.3%). MDR-TB compared with pre-XDR-TB (OR 8.77, 95% CI 1.42-45.55; p=0.01) and no treatment comprehension difficulties (OR 10.61, 95% CI 2.78-40.48; p=0.001) were both associated with successful outcomes.
CONCLUSIONS: Most patients achieved successful outcomes with individualised regimens guided predominantly by experts. Patients with pre-XDR-TB and those with comprehension difficulties had significantly reduced success rates.

DOI: 10.1183/23120541.00941-2025
PMCID: PMC12926829
PMID: 41736728

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

2. Epidemiology of drug-resistant tuberculosis in Hunan China over a 10-year Period.

Front Public Health. 2026 Feb 23;14:1771140. doi: 10.3389/fpubh.2026.1771140. eCollection 2026.

Liu Y(1), Wang J(1), Wan X(1), Peng W(2), Guo J(1), Yang X(1), Zhou D(1), Li W(1), Duan J(1), Zeng X(1), Bai H(1), Chen Z(1), Luo F(3), Tan Y(1).

Author information:
(1)Hunan Provincial Tuberculosis Prevention and Control Institute & Hunan Chest Hospital, Changsha, Hunan, China.
(2)Guangzhou Huazhun Medical Laboratory Co., Ltd., Guangzhou, Guangdong, China.
(3)Hunan Province Cooperative Innovation Center for Molecular Target New Drug Study, School of Pharmaceutical Science, Hengyang Medical School, University of South China, Hengyang, China.

BACKGROUND: Drug-resistant tuberculosis (DR-TB) remains a major public health challenge in China, yet long-term epidemiological data from key regions such as Hunan Province in South-Central China are still limited.
OBJECTIVE: This study aimed to characterize the epidemiological trends, spatial distribution, and risk factors of Single drug-resistant tuberculosis (SDR-TB), poly-drug-resistant tuberculosis (PDR-TB), multidrug-resistant tuberculosis (MDR-TB), rifampicin-resistant tuberculosis (RR-TB), and isoniazid-resistant tuberculosis (INH-R TB) in Hunan Province between 2014 and 2023, to inform region-specific control strategies.
METHODS: It was a retrospective analysis that was conducted on 6,597 laboratory-confirmed DR-TB cases. Data were obtained from the Provincial Tuberculosis Control Institute. All patients underwent phenotypic drug susceptibility testing. Independent risk factors for DR-TB subtypes were identified through multivariable logistic regression, with adjusted odds ratios (ORs) and corresponding 95% confidence intervals (CIs) calculated.
RESULTS: A total of 6,597 patients with DR-TB were included in this 10-year analysis. Among them, 74.97% were male and 64.44% were farmers. The highest case burden was observed in the 50-59 age group (24.78%). Spatially, cases clustered mainly in the Changsha (16.39%), Shaoyang (13.78%), and Loudi (9.05%). The most common resistance subtypes were INH-R TB (56.27%) and MDR-TB (52.37%). The distribution of all DR-TB subtypes varied significantly across age groups ($p < 0.05$), with peaks in middle-aged and older adults. Over time, the detection rate of MDR-TB was highest in 2018, while RR-TB remained the most frequently detected resistance type. Multivariable analysis identified significant regional

and demographic disparities. The eastern region of Hunan was associated with an increased risk of SDR-TB (OR = 1.334) and PDR-TB (OR = 1.208), whereas the western region carried the highest risk for MDR-TB (OR = 1.734). Female patients consistently showed lower risks of MDR-TB (OR = 0.819) and RR-TB (OR = 0.784) compared with males.
CONCLUSION: This study presents a 10-year epidemiological assessment of DR-TB in Hunan Province, China, covering 2014-2023. A disproportionately high burden was observed among middle-aged and older male farmers. The predominance of INH-R TB and MDR-TB, together with distinct regional and demographic risk profiles, underscores an urgent need to strengthen TB control measures. These results support the implementation of targeted interventions, including intensified screening in high-risk populations and in high-incidence areas, along with optimized treatment regimens, to curb the ongoing DR-TB epidemic in South-Central China.

DOI: 10.3389/fpubh.2026.1771140
PMCID: PMC12968256
PMID: 41810308 [Indexed for MEDLINE]

Conflict of interest statement: WP was employed by Guangzhou Huazhun Medical Laboratory Co., Ltd. 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.

3. The lipid language of tuberculosis: Mycobacterium tuberculosis surface molecules in host interaction and drug resistance.

mBio. 2026 Mar 11;17(3):e0395925. doi: 10.1128/mbio.03959-25. Epub 2026 Feb 2.

Radhakrishnan SK(1), Sundaramurthy V(1).

Author information:
(1)National Center for Biological Sciences, Bangalore, India.

Mycobacterium tuberculosis (Mtb), the causative agent of tuberculosis (TB), is a uniquely successful pathogen due in large part to its complex lipid-rich cell envelope. Comprising nearly 40% of its dry weight, Mtb lipids-such as mycolic acids, phthiocerol dimycocerosates (PDIM), trehalose dimycolate (TDM), and sulfolipids (SLs)-play crucial roles in infection, immune evasion, intracellular persistence, granuloma formation, transmission, and drug resistance. These

lipids modulate host-pathogen interactions by altering host membrane biophysics, hijacking phagosome maturation, and interfering with host immune pathways, including autophagy and inflammatory signaling. Upon inhalation, Mtb surface lipids inhibit pulmonary surfactant function and mask pathogen-associated molecular patterns, facilitating uptake by permissive macrophage subsets. Intracellularly, lipoglycans like mannose-capped lipoarabinomannan block phagolysosome fusion, while PDIM and TDM promote phagosomal escape and subversion of vesicular trafficking. Lipid-mediated modulation of autophagy pathways further enhances bacterial survival within host cells. In addition to shaping host immune responses, Mtb lipids orchestrate granuloma development and promote pathological features such as foam cell formation and caseation, which are central to transmission. Specifically, phenolic glycolipids and SLs stimulate neuronal pathways, triggering cough, thereby facilitating aerosol spread. Finally, the lipid-rich envelope acts as a formidable barrier to antibiotics, with resistance partly driven by the altered lipid composition and architecture in multidrug-resistant strains. Targeting lipid biosynthesis and transport pathways offers promising avenues for novel anti-TB therapies. This review highlights the multifaceted roles of Mtb lipids at the host-pathogen interface, recent technical advances enabling these insights, and emerging challenges in translating lipid biology into improved TB control.

DOI: 10.1128/mbio.03959-25
PMCID: PMC12977573
PMID: 41627032 [Indexed for MEDLINE]

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

4. Differences in pulmonary cavity features among drug-sensitive pulmonary tuberculosis and multidrug/extensively-resistant pulmonary tuberculosis: a multi-national multi-center computed tomography-based study.

J Thorac Dis. 2026 Feb 28;18(2):56. doi: 10.21037/jtd-2025-aw-2331. Epub 2026 Feb 26.

Tang SN(1), Huang XL(1)(2)(3), Skrahina A(4), Zheng QT(5), Tarasau A(4), Klimuk D(4), Alexandru S(6), Crudu V(6)(7), Harris M(8), Hurt DE(8), Akhundova I(9), Avaliani Z(10)(11), Vashakidze S(10)(12), Shubladze N(10), Zheng GP(13), Bao XH(13), Muntean AA(14)(15), Strambu I(16), Zaharia DC(15)(16), Ghita E(16), Bogdan M(16), Munteanu R(16), Spinu V(16), Cristea A(16), Ene C(16), Kirichenko V(17), Snezhko E(17), Kovalev V(17), Tuzikov A(17), Gabrielian A(8), Rosenthal A(8), Lu PX(#)(5), Skrahin A(#)(4)(18), Wáng YXJ(#)(1).

Author information:

(1)Department of Imaging and Interventional Radiology, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong SAR, China.
(2)Department of Ultrasonic Medicine, West China Second University Hospital of Sichuan University, Chengdu, China.
(3)Key Laboratory of Birth Defects and Related Diseases of Women and Children (Sichuan University), Ministry of Education, Chengdu, China.
(4)Republican Scientific and Practical Centre of Pulmonology and Tuberculosis, Minsk, Republic of Belarus.
(5)Shenzhen Center for Chronic Disease Control, Shenzhen, China.
(6)Institute of Pneumology, Chisinau, Republic of Moldova.
(7)Nicolae Testemitanu State University of Medicine and Pharmacy, Chișinău, Republic of Moldova.
(8)Office of Cyber Infrastructure and Computational Biology, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD, USA.
(9)Scientific Research Institute of Lung Diseases, Ministry of Health, Baku, Republic of Azerbaijan.
(10)The National Center for Tuberculosis and Lung Diseases, Tbilisi, Republic of Georgia.
(11)Department of Medicine, European University, Tbilisi, Georgia.
(12)Department of Medicine, The University of Georgia, Tbilisi, Georgia.
(13)Department of Radiology, The Third People's Hospital of Shenzhen, Shenzhen, China.
(14)The "Cantacuzino" National Military Medical Institute for Research and Development, Bucharest, Romania.
(15)The "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania.
(16)Marius Nasta Pneumophtisiology Institute, Ministry of Health, Bucharest, Romania.
(17)United Institute of Informatics Problems, National Academy of Sciences of Belarus, Minsk, Republic of Belarus.
(18)Belarusian State Medical University, Minsk, Republic of Belarus.
(#)Contributed equally

BACKGROUND: Pulmonary cavities (PC) are known to be more prevalent among multidrug-resistant pulmonary tuberculosis (MDR)/extensively drug-resistant tuberculosis (XDR) patients than among drug-sensitive tuberculosis (DS) patients. This study aims to clarify how the interaction between Mycobacterium tuberculosis aggressiveness and tuberculosis history causes the PC prevalence and pattern differences between DS patients and MDR/XDR patients.
METHODS: Eastern European patient data were from the NIAID TB (National Institute of Allergy & Infectious Diseases Tuberculosis) Portals Program registered before January 2019. Chinese patients were from Shenzhen, China, treated between April 2017 and February 2019. There were in total 244 DS cases (222 new patients and 22 previously treated patients), 344 MDR cases (188 new

patients and 156 previously treated patients), and 155 XDR cases (36 new patients and 119 previously treated patients). The first chest computed tomography (CT) images were analysed. PC were counted only for those with a lumen diameter >5 mm. Multiple cavities in a single consolidation were counted as one cavity. Calcified lesions in the lungs, as a sign of chronicity, were also recorded.
RESULTS: In new patients, there was no difference in lung lesion calcification prevalence among DS (13.5%), MDR (14.4%), and XDR (13.9%). In previously treated patients, lung calcification prevalence was 36.4% for DS, 44.9% for MDR, and 45.4% for XDR. For new patients, the PC prevalence was higher for MDR cases than for DS cases (41% vs. around 25%). For treated patients, PC prevalence increased to 36.4% for DS cases, to 57% for MDX cases, and to 71.4% for XDR cases. For new patients, the mean PC number for positive cases was DS: 1.66, MDR: 2.79, XDR: 2.69. For treated cases, the mean PC number for positive cases was DS: 2.13, MDR: 2.58, XDR: 2.47. For new patients, the mean PC diameter (in mm) for positive cases was DS: 15.4, MDR: 16.9, XDR: 17.5. For treated cases, the mean PC diameter (in mm) for positive cases was DS: 19.0, MDR: 20.8, XDR: 25.6. The number of lung fields with PC lesion was higher for MDR cases than for DS cases. PC number ≥2 had a specificity of around 92.3% for new patients, and around 81.0% for previously treated patients, suggesting the diagnosis of MDR/XDR.
CONCLUSIONS: MDR/XDR patients exhibit significantly higher PC prevalence and more extensive pulmonary involvement compared to DS patients, which are not totally determined by the length of disease history. Compared with literature reports, the prevalence of PC and the PC number per positive case were comparatively low in this study. Taking all results together, PC number ≥3 offers reasonable specificity for suggesting the diagnosis of MDR, though the sensitivity would be low.

DOI: 10.21037/jtd-2025-aw-2331
PMCID: PMC12972916
PMID: 41816393

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-aw-2331/coif). Y.X.J.W. serves as an unpaid editorial board member of Journal of Thoracic Disease from April 2024 to June 2026. The other authors have no conflicts of interest to declare.

5. Incidence and risk factors of adverse drug reactions in

multidrug-resistant/rifampicin-resistant tuberculosis (MDR/RR-TB) regimens containing new drugs: a retrospective study of two national multicenter cohorts.

J Thorac Dis. 2026 Feb 28;18(2):129. doi: 10.21037/jtd-2025-aw-2411. Epub 2026 Feb 26.

Wang Y(1), Fu L(1), Li Z(1), Liu Y(1), Li L(1).

Author information:
(1)Beijing Chest Hospital, Capital Medical University, Beijing Tuberculosis and Thoracic Tumor Research Institute, Beijing, China.

BACKGROUND: Treatment of multidrug-resistant/rifampicin-resistant tuberculosis (MDR/RR-TB) faces severe challenges, including prolonged courses, marked drug toxicity, and poor patient compliance. While regimens containing new drugs (bedaquiline, delamanid) have substantially improved MDR/RR-TB outcomes, systematic research on the epidemiological characteristics and risk control of adverse drug reactions (ADRs) remains insufficient. This study, based on a national multi-center clinical cohort, retrospectively analyzed data from 2,151 patients, aiming to explore the characteristics and risk factors related to ADR and provide a basis for individualized treatment.
METHODS: This study retrospectively included 2,151 patients with MDR/RR-TB from two national multicenter clinical cohorts in China (including the bedaquiline cohort and the delamanid cohort) from 2017 to 2022. Clinical data were extracted using a standardized process, and patients with missing key data that could not be traced were excluded from the study. Adverse reactions were defined and graded. Potential risk factors were screened through univariate analysis (Chi-squared test), and independent risk factors for ADRs were identified using a multivariate logistic regression model. The association between different types of ADRs and treatment drugs was also analyzed.
RESULTS: Overall ADR incidence was 56.2% (62.2% in bedaquiline cohort vs. 45.7% in delamanid cohort). The most common ADRs were cardiovascular [29.1%, mainly corrected QT interval (QTc) prolongation], hepatic (20.9%), and hematological (12.6%). Independent risk factors included female sex [odds ratio (OR) =1.26], age ≥35 years (OR =1.31), body mass index <18.5 kg/m2 (OR =1.22), diabetes (OR =1.28), retreatment (OR =1.28), extrapulmonary TB (OR =1.62), cavitation (OR =1.24), and pre-extensively drug-resistant (XDR)/XDR-TB (OR =1.14/1.29). Both drugs were linked to QTc prolongation.
CONCLUSIONS: New MDR/RR-TB regimens are effective but carry a high ADR burden. Enhanced monitoring of high-risk groups and QTc/liver function is essential.

DOI: 10.21037/jtd-2025-aw-2411

PMCID: PMC12972814
PMID: 41816479

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-aw-2411/coif). The authors have no conflicts of interest to declare.

6.Extensively drug-resistant tuberculosis in Togo: first reported cases and implications for tuberculosis control.

IJID Reg. 2025 Dec 17;18:100825. doi: 10.1016/j.ijregi.2025.100825. eCollection 2026 Mar.

Zoutené M(1), Ako AME(1), Aziagbe KA(1)(2), Gateu Tadjom NV(1), Adambounou TAS(1)(2), Adjoh KS(1)(2).

Author information:
(1)Department of Pulmonology, Sylvanus Olympio University Hospital, Lomé, Togo.
(2)Faculty of Health Sciences, University of Lomé, Lomé, Togo.

OBJECTIVES: The increasing burden of extensively drug-resistant tuberculosis (XDR-TB) undermines global TB control efforts.
METHODS: This was a case series study conducted from January 1, 2007, to December 31, 2024, in the Department of Pulmonology at Sylvanus Olympio University Teaching Hospital.
RESULTS: We report a series of three cases. Case 1: A 30-year-old man with a history of contact with an XDR-TB case was treated with a 20-month regimen. Culture conversion was achieved at the 3rd month of treatment. A complication in the form of pyopneumothorax occurred during the 6th month of therapy. Case 2: A 51-year-old patient with no significant medical history was diagnosed with XDR-TB after 4 months of treatment for multidrug-resistant TB (MDR-TB). Conversion of follow-up cultures was achieved 2 months after modification of the treatment regimen. Case 3: A 62-year-old woman living with human immunodeficiency virus (HIV), previously treated for MDR-TB, developed XDR-TB during the course of treatment. The patient died on the 29th day of XDR-TB treatment.
CONCLUSIONS: XDR-TB is a curable disease. Early and accurate diagnosis allows for better selection of the most appropriate treatment strategy.

DOI: 10.1016/j.ijregi.2025.100825

PMCID: PMC12874096
PMID: 41657866

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

7. Multidrug-Resistant Anal and Perianal Tuberculosis: A Case Report From the Pneumo-Phthisiology Department of Conakry University Hospital, Guinea.

Case Rep Pulmonol. 2026 Feb 24;2026:3497569. doi: 10.1155/crpu/3497569. eCollection 2026.

Diallo OH(1)(2), Camara MH(1)(2), Diallo BD(1)(2), Bah TM(2), Camara ONN(2), Camara A(1)(2), Camara LM(1)(2).

Author information:
(1)Faculty of Health Sciences and Techniques, Gamal Abdel Nasser University of Conakry, Conakry, Guinea, uganc.org.
(2)Department of Pneumo-Phthisiology, Ignace Deen University Hospital Center, Conakry, Guinea.

INTRODUCTION: Multidrug-resistant (MDR) anal and perianal tuberculosis constitutes an exceptionally rare form of extrapulmonary tuberculosis. We report a case of MDR anal and perianal tuberculosis diagnosed and managed in the Pneumo-Phthisiology Department of Ignace Deen University Hospital in Conakry, Guinea.
CASE PRESENTATION: Mrs. M.B., a 33-year-old housewife residing in Tombolia (Conakry), with no notable medical history, presented to the General Surgery Department of Ignace Deen University Hospital on 24 February 2023 with fever, abdominal pain, constipation, and painful swelling of the anal and perianal region. Following a hemorrhoidectomy, histopathological examination of the surgical specimen initially suggested a diagnosis of diffuse large B-cell lymphoma of the anal region. Consequently, CHOP chemotherapy (Adriamycin, cyclophosphamide, vincristine, and prednisolone) was initiated on 10 March 2023 in the Hematology Department. After three cycles of chemotherapy, the patient showed no clinical improvement, with persistent anal lesions and recurrent fever. A strongly positive tuberculin skin test (15 mm) prompted referral to the Pneumo-Phthisiology Department for suspected anal tuberculosis. GeneXpert MTB/RIF testing performed on stool samples confirmed the presence of MDR Mycobacterium tuberculosis. A 9-month short-course second-line antituberculosis regimen was initiated. After 1 month of treatment, the patient developed abdominal pain, semiliquid diarrhea, anorexia, and abdominal distension with a positive fluid-thrill sign. The anal and perianal lesions, however, showed

significant improvement.
CONCLUSION: MDR anal and perianal tuberculosis is an uncommon manifestation of extrapulmonary tuberculosis. In regions with high tuberculosis endemicity, it should be considered in the differential diagnosis of chronic ulcerative cutaneous or mucosal lesions. Management relies primarily on second-line antituberculosis therapy to prevent complications and ensure complete recovery.

DOI: 10.1155/crpu/3497569
PMCID: PMC12930298
PMID: 41744002

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

8. Lineages of Mycobacterium tuberculosis complex associated with pulmonary drug-resistant tuberculosis in Africa: a systematic review.

BMJ Public Health. 2026 Feb 27;4(1):e002336. doi: 10.1136/bmjph-2024-002336. eCollection 2026.

Gweba C(1)(2), Oyefabi AO(3), Awopeju A(4), Jabaka RD(5), Uzairue LI(6)(7).

Author information:
(1)School of Public Health, University of Port Harcourt, Choba, Nigeria.
(2)Institute of Human Virology, Abuja, Nigeria.
(3)Department of Community Medicine, Kaduna State University, Kaduna, Nigeria.
(4)Department of Medical Microbiology and Parasitology, University of Port Harcourt, Choba, Nigeria.
(5)Microbiology, Kebbi State University of Science and Technology, Aliero, Nigeria.
(6)Former Affiliation: Medical Laboratory Science, Federal University Oye-Ekiti, Oye, Nigeria.
(7)Faculty of Health and Life Sciences, De Montfort University, Leicester, UK.

INTRODUCTION: The emergence of multidrug-resistant tuberculosis has eroded the gains made in the fight against tuberculosis. This review aims to provide current perspectives on the lineages of the Mycobacterium tuberculosis complex (MTBC) associated with drug-resistant tuberculosis (DR-TB) in Africa.
METHOD: Primary studies were retrieved from PubMed, AJOL, Scopus and Africa Index Medicus databases, including worldwide science and Bielefeld Academic Search Engine websites. Retrieved articles were imported into Rayyan.ai for the

selection and screening process. The quality of included studies was assessed using the Joanna Briggs Institute (JBI) critical appraisal checklist for analytical and cross-sectional studies. Articles published between 2013-2023, studies conducted among humans with pulmonary DR-TB that reported MTBC lineages or species were included. On the other hand, studies that reported lineages or species in animals and studies conducted outside Africa were excluded. An Excel sheet was developed and used for data extraction by two independent reviewers, and the extracted data were compared and discrepancies resolved through discussion. Two independent reviewers assessed the risk of bias by applying the eight items on the JBI checklist to each of the included studies.
RESULT: A total of 491 articles were retrieved; however, 73 eligible articles were included in the final analysis after the selection and screening process. The characteristics of the selected studies show that the studies were from 21 countries, and varieties of molecular methods (IS6110-RFLP, MIRU-VNTR-16, Spoiligotyping and whole genome sequencing) were used in the included studies. Of the included studies, 75% were assessed to have low risk of bias using the JBI checklist, indicating that the overall quality of evidence is moderate to high. Across the continent, L4 was the dominant lineage 51% (8244/16 172) associated with DR-TB infection, which was followed by L2 41% (6649/16 172), L3 4.6% (741/16 172).
CONCLUSION: M. tuberculosis genotypes associated with drug-resistant pulmonary tuberculosis in Africa are L4, along with L2 and L3. The review included only studies published in the English language, and authors received no external funding for the review, authorship or publication.
PROSPERO REGISTRATION NUMBER: CRD42024512834.

DOI: 10.1136/bmjph-2024-002336
PMCID: PMC12958978
PMID: 41789376

Conflict of interest statement: Authors have declared that they have no conflicting interests.

9.Screening for heterogeneous drug resistance in tuberculosis and its impact on clinical prognosis: A comprehensive review.

iScience. 2026 Feb 17;29(3):115049. doi: 10.1016/j.isci.2026.115049. eCollection 2026 Mar 20.

Du X(1), Shi K(2), Zhang H(2), Chong Y(2).

Author information:
(1)Weifang People's Hospital, Shandong Second Medical University, Weifang 261053, Shandong, China.
(2)School of Public Health, Shandong Second Medical University, Weifang 261053, Shandong, China.

Tuberculosis (TB) remains a leading global health threat, with the rise of drug-resistant (DR-TB) strains posing a significant impediment to disease control. An increasingly recognized and complex challenge is heteroresistance, the coexistence of drug-susceptible and drug-resistant Mycobacterium tuberculosis subpopulations within a single host. This phenomenon acts as a crucial intermediate in the evolution toward fixed resistance and has been strongly associated with poor clinical prognoses, including treatment failure and the amplification of resistance. This review synthesizes the current state of knowledge regarding the screening methodologies for and the adverse outcomes associated with TB heteroresistance. The diagnostic gap creates a substantial risk of misclassifying patients and prescribing functionally inadequate therapeutic regimens. Further, the presence of heteroresistance significantly correlates with diminished treatment efficacy and an increased likelihood of unfavorable outcomes. Importantly, the precise clinical significance of low-frequency resistant variants remains a critical area of investigation, with an urgent need to establish evidence-based thresholds to guide therapy. Future research must focus on defining clinically relevant heteroresistance thresholds, standardizing advanced diagnostic platforms, and further elucidating the biological mechanisms that govern the emergence and persistence of these heteroresistance bacterial populations to ultimately improve patient outcomes and curb the spread of drug-resistant tuberculosis.

DOI: 10.1016/j.isci.2026.115049
PMCID: PMC12962120
PMID: 41797898

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

10. Evaluating treatment outcomes stratified by regimen among drug-resistant TB patients in Sierra Leone.

Public Health Action. 2026 Mar 6;16(1):28-34. doi: 10.5588/pha.25.0056. eCollection 2026 Mar.

Koroma JA(1), Fofanah BD(2), Nair D(3), Kamau EM(4), Kamara IF(2), Sesay MA(1), Turay IS(1), Sesay N(1), Kanu F(1), Lahai WK(1), Kanu JS(1), Koroma AT(1), Fornah F(1), Seisay AL(1), Bailor SS(1), Harding R(1), Emezue S(1), Tefera GB(5), Ameh G(2), Mazzi M(2), Lakoh S(1), Mahmoud M(1).

Author information:
(1)Ministry of Health, Freetown, Sierra Leone.
(2)World Health Organization Country Office, Freetown, Sierra Leone.
(3)Independent Researcher, Scottsdale, AZ, USA.
(4)UNICEF, UNDP, World Bank, WHO Special Programme for Research and Training in Tropical Diseases (TDR), Geneva, Switzerland.
(5)Partners in Health, Koidu, Sierra Leone.

SETTING: Sierra Leone has a high burden of drug-resistant TB (DR-TB), managed at three treatment centres.
OBJECTIVE: To compare treatment success between BPaL (bedaquiline, pretomanid, and linezolid)/BPaLM (bedaquiline, pretomanid, linezolid, and moxifloxacin) and the standardised short and the individualised long regimens among DR-TB patients and identify predictors of unsuccessful outcomes.
DESIGN: Retrospective cohort study utilising routinely collected national DR-TB data from January 2022 to December 2024.
RESULTS: Among 598 DR-TB patients registered from 2022 to 2024, 571 with complete outcomes were analysed. Overall treatment success was 80.2%, highest with BPaL/BPaLM (87.1%) compared with the standardised short (78.8%) and individualised long regimens (70.4%). Adjusted analyses showed BPaL/BPaLM remained strongly associated with higher success than the individualised long (adjusted risk ratio [aRR] 2.89; 95% confidence interval [CI] 1.80-4.64) and standardised short regimens (aRR 1.46; 95% CI 1.04-2.05). HIV co-infection and underweight body mass index independently predicted poor outcomes. Findings were consistent across propensity-weighted and sensitivity analyses.
CONCLUSION: Under routine programmatic conditions in Sierra Leone, BPaL/BPaLM achieved higher treatment success than standardised short or individualised long regimens. However, HIV co-infection and undernutrition predicted poorer outcomes, underscoring the need for integrated nutritional support, expanded drug-susceptibility testing, and strengthened TB/HIV services.

DOI: 10.5588/pha.25.0056
PMCID: PMC12991776
PMID: 41847580

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

11.Effectiveness and safety of a shortened oral regimen for rifampicin- or multidrug-resistant TB.

IJTLD Open. 2026 Mar 13;3(3):144-150. doi: 10.5588/ijtldopen.25.0553. eCollection 2026 Mar.

Herrera-Flores E(1), Shen E(2), Vargas-Vasquez D(3), Llanos-Tejada F(4), Ruiz-Vargas Z(5), Cornejo-García J(1), Vela-Trejo D(6), Puyen-Guerra ZM(7), Rojas MC(7), Guerra DM(8), Romo ML(9), Jimenez J(8), Osso E(9), Trevisi L(9), LaHood A(9), Rich ML(10)(11), Seung KJ(10)(11), Mitnick CD(9)(11), Franke MF(9)(12), Lecca L(8)(9), Alarcon-Guizado V(6).

Author information:
(1)Hospital Nacional Arzobispo Loayza, Lima, Peru.
(2)Harvard Medical School, Boston, MA, USA.
(3)Hospital Nacional Hipolito Unanue, Lima, Peru.
(4)Hospital Nacional Dos de Mayo, Lima, Peru.
(5)Hospital Nacional Maria Auxiliadora, Lima, Peru.
(6)Dirección de Prevención y Control de la Tuberculosis, Lima, Peru.
(7)Instituto Nacional de Salud, Lima, Peru.
(8)Socios en Salud, Lima, Peru.
(9)Department of Global Health and Social Medicine, Harvard Medical School, Boston, MA, USA.
(10)Division of Global Health Equity, Department of Medicine, Brigham and Women's Hospital, Boston, MA, USA.
(11)Partners in Health, Boston, MA, USA.
(12)Department of Epidemiology, Harvard T.H. Chan School of Public Health, Boston, MA, USA.

BACKGROUND: Multidrug-resistant or rifampicin-resistant TB (MDR/RR-TB) poses significant challenges to patients, providers, and programmes. We evaluated a 9-month, 5-drug all-oral regimen implemented under operational conditions in Peru.
METHODS: Between February and September 2023, we enrolled 50 adults with confirmed pulmonary MDR/RR-TB in a prospective observational study conducted within Peru's National Tuberculosis Programme. The regimen consisted of bedaquiline, linezolid, levofloxacin, clofazimine, and delamanid, administered for 9 months and potentially extended to 12 months. We describe the frequency of clinically relevant adverse events of special interest, sputum culture conversion, end-of-treatment outcomes, and changes in dyspnoea and quality of life.
RESULTS: Of 50 participants, 24 (48%) were women, and median age was 28.5 years (interquartile range [IQR]: 23-59 years); 38 (76%) had cavitary disease, and 29

(58%) had bilateral disease. Adverse events were infrequent and manageable; only one case of linezolid-associated myelosuppression led to permanent drug discontinuation. Of 33 participants with positive sputum culture, 100% experienced culture conversion (median: 39 days, IQR: 31-61). Favourable end-of-treatment outcomes were observed in 40 (85.1%) (95% confidence interval: 72.3%-92.6%). Quality-of-life and dyspnoea scores improved significantly in those with treatment success.
CONCLUSION: This 9-month oral regimen was effective and safe and improved patient-reported outcomes. These results support broader adoption in national TB programmes across Latin America and beyond.

DOI: 10.5588/ijtldopen.25.0553
PMCID: PMC12991560
PMID: 41847327

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

12.Combined Oral Contraceptive Drug-Drug Interaction Study With Ganfeborole, a New Anti-Tuberculosis Agent.

J Clin Pharmacol. 2026 Mar;66(3):e70161. doi: 10.1002/jcph.70161.

Iavarone L(1), Lavezzi SM(2), Carcas AJ(3), Chaychenko T(4), Gabarro-Carrion R(5), Huertas AGLL(3), Gresham S(6), Marín-Candón A(3), Penman SL(4), Rolfe K(4), Tiberi S(4)(7), Barros-Aguirre D(5), Borobia AM(3); ERA4TB consortium.

Author information:
(1)Parexel International, Milan, Italy.
(2)Parexel International, Dublin, Ireland.
(3)Clinical Pharmacology Department, La Paz University Hospital, IdiPAZ, and School of Medicine, Universidad Autónoma de Madrid, Madrid, Spain.
(4)GSK, London, UK.
(5)GSK, Tres Cantos, Spain.
(6)GSK, Stevenage, UK.
(7)Blizard Institute, Barts and The London School of Medicine and Dentistry, Queen Mary University of London, London, UK.

New drugs are urgently needed to treat drug-resistant tuberculosis in combination regimens. Ganfeborole demonstrated bactericidal activity and good tolerability in clinical trials. In preclinical studies, ganfeborole showed embryofetal developmental effects, currently mandating highly effective non-user

dependent contraception in women of childbearing potential. We conducted a Phase 1, open-label, single-center, fixed sequence, 1-way drug-drug interaction (DDI) study in 20 healthy women of non-childbearing potential aged 18-65 years. The primary objective was to assess ganfeborole's effect at steady-state (20 mg daily) on single dose pharmacokinetics of ethinyl estradiol [EE] 0.03 mg/levonorgestrel [LNG] 15 mg (Bayer). Endpoints were EE and LNG area under the plasma concentration-time curve extrapolated to infinity (AUC(0-inf)) and maximum concentration (Cmax). Unexpected fluctuations in individual EE and LNG plasma concentration-time profiles limited the number of acceptable endpoints for the analysis. Geometric mean ratios (GMR; EE/LNG+ganfeborole versus EE/LNG alone) and respective 90% confidence intervals (CI) for EE Cmax (0.96, 0.85-1.09), LNG AUC(0-inf) (1.10, 0.98-1.23) and LNG Cmax (1.08, 0.97-1.19) met criteria for lack of DDI (90% CI 0.80-1.25). However, the GMR for EE AUC(0-inf) was 0.88, with 90% CI 0.55-1.41. While post-hoc analyses on partial AUCs (up to 8 and 24 h) provided GMR 90% CIs within 0.80-1.25, a lack of DDI could not be concluded. No treatment-related adverse events were reported. Further assessments of potential DDI between ganfeborole and combined oral contraceptives are warranted. Future trials will maintain strict contraception requirements. Clinical Trial Registration: NCT06354257 (registration date: 2024-04-03); EudraCT: 2023-507839-38-00.

DOI: 10.1002/jcph.70161
PMCID: PMC12966810
PMID: 41793065 [Indexed for MEDLINE]

Conflict of interest statement: LI, and SML provided consultancy to GSK. TC, RG-C, SG, SLP, KR, ST, and DB-A are GSK employees. RG-C, SG, SLP, KR, ST, and DB-A hold financial equities in GSK. SLP, KR, and DB-A hold financial equities in Haleon. DB-A also reports patents planned, issued or pending and the following grants paid to his institution: ERA4TB (CDTI) (IDI-20200356); bETO-TB supported by the European Union (RIA2019AMR-2657); CLICK-TB - supported by the European Union (RIA2017T-2030). AJC reports the following paid to his institution: industry-funded professional development programme from the Universidad Autónoma de Madrid and AbbVie; investigation grants from European and national funding agencies; and contracts related to research and principal investigator roles in clinical trials. AJC also reports payment for scientific reviews of public investigation calls (ISCIII and others). AGLH received a grant from the Fundación para la Investigación Biomédica Hospital Universitario La Paz within the past 36 months. AM-C declares no conflicts of interest. All authors declare no other financial and non-financial relationships and activities.

13. Dendritic cells in the lung cavities of extensively drug-resistant tuberculosis patients exhibit altered frequency and phenotype.

ERJ Open Res. 2026 Feb 23;12(1):00155-2025. doi: 10.1183/23120541.00155-2025. eCollection 2026 Jan.

Londt R(1)(2), Semple L(1)(2), Pooran A(1)(2), Esmail A(1)(2), Davids M(1)(2), Dheda K(1)(2)(3)(4)(5), Tomasicchio M(1)(2)(5).

Author information:
(1)Centre for Lung Infection and Immunity, Division of Pulmonology, Department of Medicine, University of Cape Town and UCT Lung Institute, Cape Town, South Africa.
(2)South African MRC Centre for the Study of Antimicrobial Resistance, University of Cape Town, Cape Town, South Africa.
(3)Institute of Infectious Diseases and Molecular Medicine, University of Cape Town, Cape Town, South Africa.
(4)Faculty of Infectious and Tropical Diseases, Department of Immunology and Infection, London School of Hygiene and Tropical Medicine, London, UK.
(5)These authors contributed equally.

BACKGROUND: Studies examining dendritic cell (DC) immunobiology in tuberculosis (TB) patients have been conflicting, and no studies have examined DCs in the peripheral blood or lungs of patients with pre- or extensively drug-resistant TB (XDR-TB).
METHODS: To provide insight into DC immunobiology, we first compared the DC subsets in the peripheral blood of XDR-TB patients with that from participants with latent TB infection (LTBI). Second, we compared DC subsets from cavity biopsies from explanted lung sections with normal-appearing lung tissue from pre-XDR/XDR-TB patients undergoing resection surgery. DCs were assessed for phenotypic and functional markers using flow cytometry.
RESULTS: In the peripheral blood of XDR-TB patients, plasmacytoid DCs (pDCs) expressed lower levels of cluster of differentiation 83 (CD83; $p=0.01$), toll-like receptor 2 (TLR-2; $p<0.0001$) and macrophage mannose receptor (MMR; $p<0.0001$), with higher levels of programmed cell death protein 1 (PD-L1; $p=0.007$) than pDCs from LTBI participants ($p=0.01$). MMR expression from the conventional DC1 (cDC1) subset in XDR-TB patients was found to be higher ($p=0.02$) than that from the cDC1 subset in LTBI participants. In the lung compartment (cavity and normal-appearing lung), the dominant DC subset was the pDCs ($p=0.02$), despite the conventional DC subsets (cDCs) expressing higher levels of C-C chemokine receptor 7 (CCR7) ($p=0.02$ for both comparisons), CD83 ($p\leq0.03$ for both comparisons), TLR-2 ($p=0.02$ for both comparison), MMR ($p=0.02$

for both comparisons) and DC-SIGN ($p \leq 0.05$ for both comparisons).

CONCLUSIONS: The low frequency of cDCs in the lung cavity of XDR-TB patients in conjunction with the limited migratory and co-stimulatory expression of pDCs suggests that there is DC dysregulation in the lung mucosal milieu, possibly due to persistent disease.

DOI: 10.1183/23120541.00155-2025
PMCID: PMC12926818
PMID: 41736733

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

14. Potential of Vγ9Vδ2T cells in tuberculosis: integration of innate and adaptive immunity for vaccine development.

PeerJ. 2026 Mar 4;14:e20904. doi: 10.7717/peerj.20904. eCollection 2026.

Di D(1), Gao C(2), Deng Y(3), Li Y(1), Zhang Y(4).

Author information:
(1)Department of Immunology, School of Basic Medical Sciences, Shandong Second Medical University; Key Laboratory of Immune Microenvironment and Inflammatory Disease Research in Universities of Shandong Province, Shandong Second Medical University, Weifang, Shandong Province, China.
(2)Department of Respiratory Critical Care Medicine, Weifang No. 2 People's Hospital, Weifang, Shandong Province, China.
(3)Ultrasound Medicine Department, Weifang No. 2 People's Hospital, Weifang, Shandong Province, China.
(4)Department of Rheumatology and Immunology, Weifang No. 2 People's Hospital, Weifang, Shandong Province, China.

Tuberculosis (TB) is a chronic infectious disease caused by Mycobacterium tuberculosis that poses major global health challenges. The Bacillus Calmette-Guérin (BCG) vaccine provides only limited protection against TB in adults and the current therapeutic regimens for TB are constrained by prolonged treatment cycles and the emergence of drug-resistant strains. Consequently, the role of Vγ9Vδ2 T cells in anti-TB immunity has increasingly garnered attention. These nonconventional T lymphocytes rapidly recognize Mtb-infected cells and exert effector functions through a unique T-cell receptor that directly recognizes phosphorylated antigens independent of the major histocompatibility

complex. Vγ9Vδ2 T cells mediate direct cytotoxicity against infected cells and coordinate with other immune components to strengthen the host defense against TB. These distinctive attributes highlight the potential of Vγ9Vδ2 T cells as targets in novel TB vaccine strategies. The current understanding of Vγ9Vδ2 T cell-mediated immunity to Mtb, recent advances in TB vaccine research, and prospective directions for future investigation are synthesized in this review.

DOI: 10.7717/peerj.20904
PMCID: PMC12967074
PMID: 41800127 [Indexed for MEDLINE]

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

15. Genetic and immunologic determinants of BCG disease: from mechanism to Prevention.

Ann Med. 2026 Dec;58(1):2634548. doi: 10.1080/07853890.2026.2634548. Epub 2026 Mar 2.

Chen F(1)(2)(3), Shen Y(2), Yan Q(4), Zheng D(2), Chen X(2)(5), Fang L(2)(5), Sun M(2)(5), Zhang Y(6), Chu M(1)(2), Yang E(3), Huang XF(2).

Author information:
(1)Children's Heart Center, Institute of Cardiovascular Development and Translational Medicine, The Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University, Wenzhou, Zhejiang Province, China.
(2)Zhejiang Provincial Clinical Research Center for Pediatric Precision Medicine, The Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University, Wenzhou, Zhejiang Province, China.
(3)Department of Child Healthcare, Wenzhou People's Hospital, Wenzhou, Zhejiang Province, China.
(4)Oujiang Laboratory (Zhejiang Lab for Regenerative Medicine, Vision and Brain Health), Wenzhou Medical University, Wenzhou, Zhejiang Province, China.
(5)Department of Pediatrics, the Second School of Medicine, The Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University, Wenzhou, Zhejiang Province, China.
(6)Department of Traditional Chinese Medicine, Wenzhou Yebo Proctology Hospital, Wenzhou, Zhejiang Province, China.

BACKGROUND: Bacillus Calmette-Guérin (BCG) infection, a disseminated infection

triggered in immunocompromised hosts by the administration of the attenuated BCG vaccine, is characterized by a pathogenic mechanism that involves the synergistic interaction between host immune deficiencies and strain-specific genetic mutations.
METHODS: This review synthesizes published multi-omics and proteomics findings from the past decade, along with reported results from in vitro drug susceptibility assays and molecular diagnostics, to explore key pathogenic genes in BCG strains. We compare differences in pathogen characteristics, host immune responses, and clinical manifestations between BCG disease and tuberculosis (TB) disease caused by Mycobacterium tuberculosis (Mtb). Additionally, we summarize evidence on BCG drug susceptibility and the roles of resistance-related genes in drug resistance mechanisms.
RESULTS: The study revealed the following findings: 1) The occurrence of BCG disease follows the "dual-hit model," where defects in the host interferon-gamma/interleukin-12 (IFN-γ/IL-12) signaling pathway (in 70% of cases) synergize with genetic mutations in BCG strains (such as pks12 and mma3), leading to immune evasion and disseminated infection; 2) Compared to Mtb, BCG strains exhibit reduced virulence due to the loss of the RD1 region, but strain heterogeneity leads to differences in cell wall lipid metabolism, which induces atypical systemic symptoms in immunocompromised hosts; 3) Some BCG strains display low-level resistance to isoniazid and rifampicin, with resistance linked to mma3 mutations (resulting in increased MIC for isoniazid) and inactivation of pncA (resulting in resistance to pyrazinamide); 4) Genetic modifications of strains (such as BCGΔBCG1419c vaccine), delayed vaccination, and individualized immune monitoring can effectively reduce the infection risk in immunocompromised hosts. T-cell receptor excision circles (TREC)/K-cell receptor excision circles (KREC) screening improves the identification rate of immunocompromised hosts.
CONCLUSION: BCG disease represents a typical case of host-pathogen interaction imbalance. Its prevention and control require an integrated approach combining molecular mechanisms and clinical practice improvements.

Plain Language Summary: BCG disease is primarily caused by a combination of host immune deficiencies and genetic mutations in BCG strains, leading to disseminated infections, particularly in immunocompromised hosts.Genetic mutations in BCG strains, such as those in pks12 and mma3, contribute to increased virulence and low-level drug resistance, necessitating tailored treatment strategies for affected individuals.Optimized vaccination strategies, including genetic modifications of BCG strains, immunodeficiency screening, and individualized immune monitoring, are essential to reduce the risk of BCG disease in immunocompromised hosts.

DOI: 10.1080/07853890.2026.2634548
PMCID: PMC12954803
PMID: 41770622 [Indexed for MEDLINE]

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

16. Acquisition of bedaquiline and clofazimine resistance in association with a novel loss-of-function mutation in the pepQ gene during treatment of multidrug-resistant tuberculosis.

ASM Case Rep. 2025 Nov 12;2(2):e00126-25. doi: 10.1128/asmcr.00126-25. eCollection 2026 Mar.

Richard-Greenblatt M(1)(2)(3), Bagga R(3), Duncan C(1), Billick MJ(4), Song H(5), Sabur NF(5)(6)(7), Escuyer V(8), Lam K(1), Brode SK(5)(6).

Author information:
(1)Public Health Ontario, Toronto, Ontario, Canada.
(2)Hospital for Sick Children, Toronto, Ontario, Canada.
(3)Department of Laboratory Medicine and Pathobiology, University of Toronto, Ontario, Canada.
(4)Department of Infectious Diseases, University of Toronto, Ontario, Canada.
(5)University Health Network, Toronto, Ontario, Canada.
(6)Division of Respirology, University of Toronto, Toronto, Ontario, Canada.
(7)Unity Health-St. Michael's Hospital, Toronto, Ontario, Canada.
(8)Wadsworth Centre, New York State Department of Health, Albany, New York, USA.

BACKGROUND: Bedaquiline (BDQ) has transformed the management of multidrug-resistant (MDR) and rifampin-resistant tuberculosis (TB). Unfortunately, the expanded use of BDQ in these regimens has been accompanied by resistance, which is steadily increasing in certain regions of the world. Nonetheless, our understanding of the mechanisms behind BDQ resistance remains poor, limiting the utility of more rapid molecular or genomic-based diagnostics for the detection of BDQ-resistant isolates.
CASE SUMMARY: We describe an unusual case of a rapid, 2-year evolution of a fully susceptible Mycobacterium tuberculosis strain to extensively drug-resistant TB in a 44-year-old Canadian-born woman with Crohn's disease. Comparative whole-genome sequencing captured the progressive development of resistance mutations and identified a novel loss-of-function mutation (Glu-177-STOP) in the M. tuberculosis pepQ gene that was associated with treatment failure while on BDQ and phenotypic BDQ/clofazimine (CFZ) cross-resistance. Therapeutic drug monitoring while on MDR therapy (daily ethambutol, pyrazinamide, linezolid, CFZ, and intravenous amikacin) detected low serum levels of CFZ, which was not addressed prior to the addition of BDQ to her 5-drug regimen and may have selected for BDQ/CFZ cross-resistance.

CONCLUSION: This case contributes to the limited clinical data implicating pepQ in BDQ/CFZ cross-resistance and describes a novel loss-of-function mutation associated with resistance. As our understanding of genotypic BDQ resistance remains elementary, when novel drug mutations arise, practitioners should consider their significance in the context of phenotypic drug susceptibility test results and the patient's clinical response.

DOI: 10.1128/asmcr.00126-25
PMCID: PMC12955440
PMID: 41853115

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

17. Advancing global health access through market shaping: Cases and learnings.

PLOS Glob Public Health. 2026 Feb 24;6(2):e0004523. doi: 10.1371/journal.pgph.0004523. eCollection 2026.

Wagner CM(1), Lin A(2), Nsanzimana S(3), Ginnard JK(4), Iyer JK(5), Etiebet MA(6), Ripin D(7), Juneja S(8), Hein D(9), Gandhi G(10), Holmes CB(11).

Author information:
(1)Avenir Management Partners, Boston, Massachusetts, United States of America.
(2)Center for Innovation and Impact, USAID, Washington, DC, United States of America.
(3)Ministry of Health, Government of Rwanda, Kigali, Rwanda.
(4)Unitaid, Geneva, Switzerland.
(5)Access to Medicine Foundation, Amsterdam, Netherlands.
(6)Vital Strategies, New York, New York, United States of America.
(7)Clinton Health Access Initiative, Dorchester, Massachusetts, United States of America.
(8)Market Access, TB Alliance, New York, New York, United States of America.
(9)Vaccine Programmes & Markets, Gavi, The Vaccine Alliance, Geneva, Switzerland.
(10)Global Development, Gates Foundation, Seattle, Washington, United States of America.
(11)Center for Innovation in Global Health, Georgetown University, Washington District of Columbia, United States of America.

New health products have contributed to major improvements in public health, but many clinically effective interventions still face delays in reaching low- and

middle-income countries (LMICs). Market shaping approaches have emerged as a set of tools designed to address such access gaps by influencing prices, supply, and demand. Drawing on practitioner experience and illustrative cases, this paper examines how market shaping mechanisms have been used to expand access to pharmaceutical products in LMICs. We review examples including dolutegravir, rifapentine-based tuberculosis preventive therapy, pretomanid for drug-resistant tuberculosis, the RTS,S malaria vaccine, and Rwanda's hepatitis C program, alongside ecosystem-level interventions such as revolving funds and initiatives to strengthen regional manufacturing. Across these cases, we suggest generalizable lessons and describe trade-offs related to donor dependence, supplier concentration, and timing of interventions. The paper identifies priorities for empirical research to assess the performance, risks, and applicability of market shaping tools as global health needs and resource environments evolve.

DOI: 10.1371/journal.pgph.0004523
PMCID: PMC12931745
PMID: 41734147

Conflict of interest statement: Authors note their paid employment by respective organizations and agencies as funders, operators, and policymakers in global health, and the related role of those institutions in some of the transactions and cases described in this article. In addition, MAE is a previous employee and stockholder of Merck & Co, Inc (12/2016 – 08/2024) and a current member of the Board of Directors of Center for Global Development. The authors confirm employment does not affect adherence to PLOS Global Public Health’s policies on data and material sharing. There are no patents, products in development or marketed products associated with this research to declare.

18. Population-based study of pharmacogenetics and pharmacokinetics in Southern African patients with multidrug-resistant tuberculosis (PoPG): a protocol for the Namibian cohort.

BMJ Open. 2026 Mar 3;16(3):e109764. doi: 10.1136/bmjopen-2025-109764.

Boois L(1), Ekandjo H(1), Shavuka O(1), Nepolo E(1), Ndong Sima CA(2), Oelofse C(3), Uren C(2)(4), Petersen DC(3), Möller M(2), Wijk M(5), Kellermann T(6),

Decloedt E(6), McIlleron H(5), Denti P(5), Claassens MM(7)(8).

Author information:
(1)Faculty of Health Sciences and Veterinary Medicine, University of Namibia, Windhoek, Namibia.
(2)Department of Biomedical Sciences, Stellenbosch University Faculty of Medicine and Health Sciences, Cape Town, South Africa.
(3)South African Medical Research Council Centre for Tuberculosis Research, Stellenbosch University, Stellenbosch, South Africa.
(4)Centre of Bioinformatics and Computational Biology, Stellenbosch University, Stellenbosch, South Africa.
(5)Division of Clinical Pharmacology, University of Cape Town, Rondebosch, South Africa.
(6)Division of Clinical Pharmacology, Stellenbosch University, Stellenbosch, South Africa.
(7)Faculty of Health Sciences and Veterinary Medicine, University of Namibia, Windhoek, Namibia mcla@sun.ac.za.
(8)Desmond Tutu TB Centre, Department of Pediatrics and Child Health, Stellenbosch University, Tygerberg, South Africa.

BACKGROUND: Multidrug-resistant tuberculosis (MDR-TB) is an urgent public health challenge in Namibia, with profound socioeconomic consequences. The high burden of both tuberculosis and HIV complicates treatment and underscores the need for optimised drug therapies. Precision medicine, which leverages patient-specific genetic and molecular information, offers promise for improving MDR-TB outcomes. However, its effective application relies on population-specific data, particularly understanding how individuals metabolise tuberculosis drugs and how genetic diversity drives variability in treatment response. Currently, no pharmacokinetic (PK) or pharmacogenetic (PG) data on TB treatment exist for Namibian populations. This gap is particularly concerning, given the country's genetic diversity, environmental factors and comorbidities that may uniquely influence drug metabolism. This study aims to generate PK and PG data to inform dose optimisation and support personalised treatment strategies for MDR-TB in Namibia. The findings will contribute to improved patient care and inform health system strengthening based on locally relevant evidence.
METHODS: This cross-sectional study will consist of 100 Namibian participants with matched human DNA and PK data of MDR-TB cases receiving isoniazid, clofazimine, bedaquiline and the fluoroquinolones (levofloxacin or moxifloxacin). PK sampling will be divided as follows: 30 individuals will undergo intensive PK sampling, while the remaining (n=70) will undergo sparse PK sampling. DNA will be extracted at Stellenbosch University (SU), and samples will be genotyped using the H3Africa microarray. Sequences will be aligned to the human reference genome, hg38 (GRCh38p13), using the freely available Burrows-Wheeler Aligner. A subset of the samples (n=20-30) will undergo whole

genome sequencing (WGS) to verify imputation results and identify novel genetic variants potentially affecting PK in this population.
DATA ANALYSIS: Quality control and variant call format file generation will be performed using the Genome Analysis Toolkit best practices (V.3.5). Intensive and sparse PK data will be pooled for the development of a population PK (popPK) model using a non-linear mixed-effects modelling approach. The popPK model will characterise the relationship between TB drug dose and exposure, including quantifying covariates, including genetic variation, explaining PK variability, providing a foundation for dose optimisation and personalised treatment strategies.
ETHICS AND DISSEMINATION: Ethics approval was obtained from the University of Namibia Human Research Ethics Committee for Health (Ref. SOM18/2024), the Ministry of Health and Social Services (Ref. 22/4/2/3), the SU Health Research Ethics Committee (Ref. N21/11/136) and the University of Cape Town Human Research Ethics Committee (Ref. 500/2022).

DOI: 10.1136/bmjopen-2025-109764
PMCID: PMC12959021
PMID: 41775468 [Indexed for MEDLINE]

Conflict of interest statement: Competing interests: None declared.

19. Drug-Resistant Tuberculous Meningitis (DR-TBM) in a Low-Incidence Setting: Two Cases and an Evidence Review Highlighting Key Advances and Knowledge Gaps in Clinical Management.

Open Forum Infect Dis. 2026 Feb 25;13(2):ofag046. doi: 10.1093/ofid/ofag046. eCollection 2026 Feb.

Boschung KF(1), Wong PHP(1)(2), Werry D(2), Sekirov I(3), Turvey SL(1)(4), Cook VJ(1)(4), Johnston J(1)(4), Connors WJA(1)(4).

Author information:
(1)Department of Medicine, University of British Columbia, Vancouver, British Columbia, Canada.
(2)Division of Infectious Diseases, Surrey Memorial Hospital, Surrey, British Columbia, Canada.
(3)BCCDC Public Health Laboratory, BC Centre for Disease Control, Vancouver, British Columbia, Canada.
(4)Tuberculosis Services, BC Centre for Disease Control, Vancouver, British

Columbia, Canada.

We report on 2 patients with drug-resistant tuberculous meningitis diagnosed and treated in a high-resource, low-incidence setting. Both patients were treated with multidrug regimens including bedaquiline, a nitroimidazole, cycloserine, and linezolid. Drug selection was informed by molecular diagnostics, susceptibility testing, and pharmacokinetic and clinical data. Adverse events included suicidal ideation, cytopenias, ototoxicity, and neuropathy. There was discordance between phenotypic (susceptible) and genotypic (resistant) drug susceptibility testing for rifampin. After treatment, both patients had excellent clinical outcomes, with at least 12 months of post-treatment follow-up. These clinical cases provide an opportunity to explore the role of molecular diagnostics in the diagnosis of drug-resistant tuberculous meningitis, drug regimen selection in the era of novel oral regimens, and clinical decision-making in the setting of discordance between genotypic and phenotypic drug susceptibility testing.

DOI: 10.1093/ofid/ofag046
PMCID: PMC12933500
PMID: 41756205

Conflict of interest statement: Potential conflicts of interest. All authors: no reported conflicts.

20. A 9-Year-Old Boy With Right-Sided Extrapulmonary Drug-Resistant Tuberculosis Subphrenic Abscess: A Case Report From Woldia, Northeast Ethiopia.

Clin Case Rep. 2026 Feb 28;14(3):e72165. doi: 10.1002/ccr3.72165. eCollection 2026 Mar.

Lingerew A(1), Addis S(2), Atnafu A(3), Siyoum Z(4), Deribessa SJ(5).

Author information:
(1)Department of Pediatrics and Child Health School of Medicine, College of Medicine and Health Sciences, Woldia University Woldia Ethiopia.
(2)Department of Radiology Woldia University Woldia Ethiopia.
(3)Department of Pathology School of Medicine, College of Medicine and Health Sciences, Woldia University Woldia Ethiopia.
(4)School of Medicine, College of Medicine and Health Sciences, Woldia University Woldia Ethiopia.

(5)Division of Infectious Disease, Department of Pediatrics and Child Health St Paul's Hospital Millennium Medical College Addis Ababa Ethiopia.

Diagnosing extrapulmonary and drug-resistant tuberculosis in children is challenging. Early recognition and treatment improve outcomes and reduce transmission. In this 9-year-old boy, diagnosis of drug-resistant subphrenic TB required a high index of suspicion, appropriate diagnostic testing, and timely initiation of second-line anti-tuberculosis therapy.

DOI: 10.1002/ccr3.72165
PMCID: PMC12949426
PMID: 41767065

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

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

Lancet Reg Health Southeast Asia. 2026 Feb 14;46:100730. doi: 10.1016/j.lansea.2026.100730. eCollection 2026 Mar.

Basu S(1), Vashist A(2), Chandra S(3), Sharma N(4).

Author information:
(1)Dept. of Community Medicine, ESI-PGIMSR & ESIC Medical College, Joka, Kolkata, India.
(2)Dept. of Biotechnology, School of Engineering and Applied Sciences, Bennett University, Greater Noida, India.
(3)Ministry of Health and Family Welfare, Government of India, India.
(4)Dept. of Community Medicine, SGT University, Gurugram, India.

India's pursuit of Tuberculosis (TB) elimination is contingent on the rapid universal scale-up of TB Preventive Treatment (TPT) for household contacts. However, current strategies largely neglect the asymptomatic active (subclinical) TB stage in terms of standardized diagnosis and optimized management. Consequently, administering TPT to individuals with unrecognized subclinical TB constitutes inadequate therapy that provides no patient benefit, enables community transmission, and risks minimal chances of iatrogenic drug resistance-violating the fundamental ethical principle of non-maleficence. We examine the tension between utilitarian public health goals and individual

biomedical ethics, arguing for a transition within the National TB Elimination Program (NTEP) toward a rights-based framework prioritizing the clinical safety of household contacts. Crucially, the NTEP must institutionalize robust health education for contacts regarding the persistent risk of progression for at least 24 months post-TPT completion, coupled with sustained clinical surveillance to mitigate delayed health-seeking behavior. Further, sustained investment in digital diagnostics and translational research apart from addressing implementation gaps in the private sector is paramount to making TPT safe, evidence-driven, and ethically responsible.

DOI: 10.1016/j.lansea.2026.100730
PMCID: PMC12925466
PMID: 41732188

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

22. Effect of the COVID-19 pandemic on drug-resistant tuberculosis treatment outcomes at a national referral hospital in Sierra Leone, 2017 to 2022: A retrospective cohort study.

PLOS Glob Public Health. 2026 Mar 4;6(3):e0004472. doi: 10.1371/journal.pgph.0004472. eCollection 2026.

Koroma JA(1), Mahmoud M(1), Molleh B(2), Sevalie S(2)(3)(4), Chan AK(5), Mishra S(5), Lakoh S(1)(2)(3), Kanu JS(3)(6).

Author information:
(1)Ministry of Health, Government of Sierra Leone, Freetown, Sierra Leone.
(2)Research and Scientific Division, Sustainable Health Systems, Freetown, Sierra Leone.
(3)College of Medicine and Allied Health Sciences, University of Sierra Leone, Freetown, Sierra Leon.
(4)34 Military Hospital, Republic of Sierra Leone Armed Forces, Freetown, Sierra Leone.
(5)Division of Infectious Diseases, Department of Medicine, University of Toronto, Toronto, Ontario, Canada.
(6)National Public Health Agency, Government of Sierra Leone, Freetown, Sierra Leone.

Sierra Leone is one of the 30 high TB burden countries in the world, with an incidence rate in 2023 of 273 per 100,000 population. Despite progress in case

notification and treatment coverage, around 5,000 cases of TB in Sierra Leone are missing each year. The COVID-19 pandemic has further compounded these challenges. We highlight its effect on drug-resistant TB treatment outcomes. We conducted a retrospective cohort study of drug-resistant TB cases using national data from January 2017 to December 2022. Data was analyzed using STATA. Descriptive analysis summarized demographic, clinical characteristics and treatment outcomes. Logistic regression examined the association between time-period and outcomes, adjusting for age, gender, nutritional status, HIV status and regimen. Of 701 patients, 383 (54.6%) were registered pre-COVID-19, 228 (32.5%) during, and 92 (13.1%) post-COVID-19. Pre-treatment TB cases reduced from 359 (92.5%) in the pre-COVID-19 period to 80 (30.9%) in the COVID-19 period. New treatment cases increased from 29 (7.5%) to 159 (61.4%) during COVID-19. Treatment completion decreased from 74.7% pre-COVID-19 to 63.3% during and 68.5% post-COVID-19). Malnourished patients had higher odds of success (aOR: 1.482, 95% CI: 1.007-2.183), while those on short regimen had lower odds (aOR: 0.51, 95% CI: 0.321-0.810). We observed a decline in drug-resistant TB treatment success rate during COVID-19, which was primarily influenced by concurrent shifts in treatment protocols and underlying secular trends. The pandemic itself did not emerge as an independent determinant of poor treatment outcomes, highlighting the resilience of the TB care system. Nonetheless, the pandemic had significant indirect consequences, including worsening rates of malnutrition and HIV co-infection. These trends point to deeper systemic vulnerabilities, such as weak social protection mechanisms, increased food insecurity, and disruptions in HIV service delivery, all of which contributed to delay in diagnosis and compromised treatment adherence.

DOI: 10.1371/journal.pgph.0004472
PMCID: PMC12959693
PMID: 41779701

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

23. Designing and evaluating the acceptability of a psychosocial and socioeconomic support package for people with drug-resistant tuberculosis in Johannesburg, South Africa.

PLoS One. 2026 Mar 3;21(3):e0343154. doi: 10.1371/journal.pone.0343154.

eCollection 2026.

Mphothulo N(1), Loveday M(2).

Author information:
(1)School of Public Health and Nursing, University of KwaZulu Natal, Durban, South Africa.
(2)HIV and other Infectious Diseases Research Unit (HIDRU), South African Medical Research Council, CAPRISA-MRC HIV-TB Pathogenesis and Treatment Research Unit, Durban, South Africa.

Drug-resistant tuberculosis (DR-TB) is a global health problem that presents multifaceted challenges to people living with the disease. These challenges lead to sub-optimal adherence in some DR-TB patients who are then not cured of their TB. Besides the challenges associated with taking treatment, many patients with DR-TB also have to contend with psychosocial and socioeconomic challenges. The objective of this study was to develop a psychosocial and socioeconomic intervention for people with DR-TB in Johannesburg, South Africa, and evaluate if they find it acceptable. Guided by the Behaviour Change Wheel (BCW) and Perceptions and Practicalities Approach (PaPA) frameworks, and utilising a participatory research approach, We developed a support package with input from a qualitative needs assessment with DR-TB patients (n = 16) and family members (n = 8) and input from various stakeholders (n = 18), (health managers, clinicians and officials from social security departments). The support package was then evaluated for acceptability by patients who had successfully completed DR-TB treatment (n = 13) and their families (n = 6), using an exploratory qualitative method. Both successfully treated DR-TB patients and their family members found the intervention to be acceptable and believed it will reduce the barriers to retention in care that they faced during their treatment journey.

DOI: 10.1371/journal.pone.0343154
PMCID: PMC12956097
PMID: 41774734 [Indexed for MEDLINE]

Conflict of interest statement: The author has declared that no competing interests exist.

24. The antimycobacterial and healing effect of sorafenib through pro-apoptotic and immunomodulatory activities.

Microbiol Spectr. 2026 Mar 3;14(3):e0165725. doi: 10.1128/spectrum.01657-25. Epub 2026 Jan 26.

Rajmani RS(1), Rani N(1), Surolia A(1)(2).

Author information:
(1)Molecular Biophysics Unit, Indian Institute of Science, Bangalore, India.
(2)Dr. Reddy's Institute of Life Sciences, Hyderabad, India.

Tuberculosis is caused by the bacterium Mycobacterium tuberculosis (Mtb). Emergence of drug resistance in Mtb requires continuous enrichment of anti-tubercular medication. Inclusion of host-directed therapies holds considerable promise in this context. Sorafenib (SRB) is a multi-kinase inhibitor targeting VEGF receptor kinase, Raf, MEK, and extracellular signal-regulated kinase (ERK) signaling cascade to treat several types of cancer, including hepatocellular carcinoma. We have previously established that SRB allosterically inhibits ornithine acetyltransferase (MtArgJ), an essential enzyme in the arginine biosynthesis pathway of Mtb, thereby limiting bacterial growth in culture at a minimum inhibitory concentration of 10 µg/mL. The current work focuses on how SRB at the dose of 30 mg/kg body wt inhibits the pathogenicity and survival of bacteria in a preclinical mouse model of tuberculosis by inducing pro-apoptotic and immunomodulatory mechanisms in the host. We observed that SRB treatment promotes apoptosis in Mtb-infected and -uninfected THP-1 cells, human monocyte-derived macrophages. Concomitantly, SRB treatment reduces infection-associated necrosis in the Mtb-infected THP-1 cells. We further noted the upregulated expression of pro-apoptotic proteins during SRB treatment in preclinical mouse models. In addition, we investigated the expression of pro- and anti-inflammatory cytokines and immunomodulation in lung tissues treated with SRB. Interestingly, SRB treatment increased the number of arginase 1-positive macrophages, which are reckoned to enhance tissue healing. In conclusion, our research discloses that SRB is helpful in both lowering the tubercular burden and accelerating recovery of damaged tissue by harnessing the host immune response.IMPORTANCEHost-directed therapies hold considerable promise for treating drug-resistant Mycobacterium tuberculosis (Mtb). In this context, the induction of apoptotic and immunomodulatory responses in the host by sorafenib (SRB) is demonstrated here to compromise the survival and pathogenic potential of Mtb in a preclinical mouse model of TB and in Mtb-infected and -uninfected THP-1 cells. Concurrently, the infection-associated necrosis in the Mtb-infected THP-1 cells is also reduced. Furthermore, arginase 1-positive macrophages, which are known to enhance tissue healing, are increased in SRB-treated groups. Thus, SRB treatment not only lowers the tubercular load but

also aids in healing damaged tissues by leveraging the host immunity.

DOI: 10.1128/spectrum.01657-25
PMCID: PMC12955432
PMID: 41586623 [Indexed for MEDLINE]

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

25. Targeted and whole-genome sequencing for drug resistance and genetic relatedness inference of rifampicin-resistant Mycobacterium tuberculosis: an in-depth comparison.

ERJ Open Res. 2026 Feb 23;12(1):00630-2025. doi: 10.1183/23120541.00630-2025. eCollection 2026 Jan.

de Diego Fuertes M(1), Costa Conceição E(2), Wells F(2), Rennie V(1), Heupink T(1), Churchyard G(3), Ndebele F(3), Van der Spoel Van Dijk A(3), Fanampe B(3), Charalombous S(3), Ayodeji Ogunbayo E(3), Quispe Rojas W(1), Warren RM(2), Van Rie A(1), Dippenaar A(1).

Author information:
(1)Department of Family Medicine and Population Health, Global Health Institute, Faculty of Medicine and Health Sciences, University of Antwerp, Antwerp, Belgium.
(2)South African Medical Research Council Centre for Tuberculosis Research, Division of Molecular Biology and Human Genetics, Faculty of Medicine and Health Sciences, Stellenbosch University, Cape Town, South Africa.
(3)The Aurum Institute, Parktown, South Africa.

BACKGROUND: Challenges in tuberculosis (TB) control have fuelled interest in routine next generation sequencing (NGS). However, the comparative performance of targeted NGS (tNGS) and whole genome sequencing (WGS) for drug resistance and genetic relatedness inference remains unclear.
METHODS: In this cross-sectional study, we compared WGS (MICK-MAGMA platform) and the Deeplex MycTB tNGS assay in 90 patients with rifampicin-resistant TB in South Africa. A pairwise analysis was conducted for a total of 60 isolates, for which tNGS was conducted directly on DNA from sputum, and WGS on cultured isolates from the same samples.
RESULTS: Drug resistance inference was highly concordant (≥92%) for most drugs, but lower for isoniazid (82%) and ethionamide (78%). Mixed infections were more commonly detected in tNGS (6.7%) than WGS (1.7%), though likely due to

analytical errors. tNGS detected more minor variants (allelic frequency <25%) than WGS (76 versus 32), with minimal overlap. Most minor variants were of unknown significance; some likely stemmed from contamination or sequencing errors. Heteroresistance involving minor variants was rare (4.7% in tNGS, 0% in WGS). WGS provided lineage and sublineage information for all samples, while tNGS reported lineage for 67% and sublineage for 20%. WGS classified more samples as genetically unrelated (76%) than tNGS (40%).
CONCLUSION: In this cohort, drug resistance inference was largely concordant between tNGS and WGS. WGS offered higher resolution for genetic relatedness, while tNGS showed greater sensitivity for minor variants. Further research is needed to clarify the clinical relevance of minor variants and assess the utility of WGS for transmission control.

DOI: 10.1183/23120541.00630-2025
PMCID: PMC12926815
PMID: 41736736

Conflict of interest statement: Conflict of interest: All authors of the study declare that they have no conflicts of interest to disclose. The University of Antwerp, as licenser of the MICK-MAGMA technologies, receives a royalty fee on all commercial activities of the MIC-MAGMA platform.

26. 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.

27. Towards universal social protection for people affected by tuberculosis in the Western Pacific Region: a social protection baseline assessment and policy entry points.

Trop Med Health. 2026 Mar 12;54(1):47. doi: 10.1186/s41182-025-00887-2.

Boccia D(#)(1), Rahevar K(#)(2), Carter DJ(3), Pescarini JM(4)(5), Schwalb A(4)(6)(7), Islam T(8), Oh KH(2), Morishita F(2), Yadav RP(2).

Author information:
(1)Faculty of Epidemiology and Population Health, London School of Hygiene and Tropical Medicine, London, UK. delia.boccia@lshtm.ac.uk.
(2)World Health Organization Regional Office for the Western Pacific, Manila, Philippines.
(3)Faculty of Population Health and Policy, London School of Hygiene and Tropical Medicine, London, UK.
(4)Faculty of Epidemiology and Population Health, London School of Hygiene and Tropical Medicine, London, UK.
(5)Centro de Integracao de Dados e Conhecimentos Para Saude, Instituto Goncalo Moniz, Fundacao Oswaldo Cruz, Salvador, Brazil.
(6)TB Modelling Group, TB Centre, London School of Hygiene and Tropical Medicine, London, UK.
(7)Instituto de Medicina Tropical Alexander von Humboldt, Universidad Peruana Cayetano Heredia, Lima, Peru.
(8)Department for HIV, TB, Hepatitis and STIs, World Health Organization, Geneva, Switzerland.
(#)Contributed equally

BACKGROUND: Achieving universal social protection (SP) coverage for people affected by tuberculosis (TB) is increasingly recognised as an essential component of its response, as well as other diseases of poverty. Realising this goal requires to clearly understand the SP needs of people affected by TB and to identify means to maximise their access to existing or new SP benefits in an efficient, effective, and sustainable manner.
MAIN BODY: To address these questions, between 2022 and 2023, the WHO Western Pacific Regional office conducted the first SP baseline assessment for people affected by TB in Mongolia, Lao People's Democratic Republic, the Philippines, Cambodia, and Viet Nam. This exercise encompassed a desk review of SP programmes operating in these countries, followed by an expert consultation to discuss barriers and entry points to expand SP coverage among people affected by TB. Overall evidence gathered from publicly available reports and publications suggests that existing SP programmes in these countries are insufficiently

accessible and inadequate to meet the needs of people affected by TB. Most countries provide TB-specific benefits only to people with multidrug-resistant TB, leaving most people with TB unserved. The most reported barriers to access to SP included lack of awareness, stigma, poverty, as well as programmes' fragmentation, and administrative and financial constraints. Identified solutions included raising awareness about SP, extending TB-specific SP benefits to all people with TB in need, advocating for a better inclusion of people with TB into existing governmental programmes, and strengthening the referral system across the health and SP sectors.
CONCLUSIONS: By identifying concrete policy entry points and actionable solutions, this SP baseline assessment provided a foundation for these five countries to embed social protection more systematically into their national TB responses. Ideally, this effort should now be replicated in all high TB-burden countries willing to achieve universal SP coverage among people affected by TB. The lessons that emerged from this baseline assessment are consistent with the recommended actions and principles underlying the Western Pacific Regional Framework for Reaching the Unreached and are thus transferrable to other diseases of poverty.

DOI: 10.1186/s41182-025-00887-2
PMCID: PMC12980936
PMID: 41821111

Conflict of interest statement: Declarations. Ethics approval and consent to participate: Not applicable. Consent for publication: Not applicable. Competing interests: The authors declare no competing interests.

28. Multicentre field evaluation of Xpert MTB/XDR in sub-Saharan Africa.

ERJ Open Res. 2026 Mar 9;12(2):00427-2025. doi: 10.1183/23120541.00427-2025. eCollection 2026 Mar.

Massou F(1)(2)(3), Diarra B(4)(5), Ba Diallo A(6), Bah KS(7), Vuchas C(8), Neh A(8), Sander M(8), Adebiyi EO(9), Aderemi BO(10), Agbla SC(11), Floyd S(12), Kaswa MK(13)(14), Aloni M(15), Sissy M(15), Ushizimpumu B(16), Niyigena EB(16), Ngabonziza JCS(2)(17)(18), Abebe G(19), Tadesse M(19), Bah B(7), Camara L(7), Gaye Diallo A(6), Camara M(6), Diallo F(4)(5), Togo ACG(4)(5), Ferré A(20), Badalato N(20), Penn-Nicholson A(21)(22), Schumacher SG(22), Odjougbele ST(1), Houeto S(1), Mulders W(2), Frissette K(2), Kebede W(23), El Tayeb O(24), Merle CS(25)(26), de Jong BC(2)(26), Supply P(27)(26), Affolabi D(1)(26), Rigouts

L(2)(3)(26).

Author information:
(1)Supranational Reference Laboratory of Tuberculosis, Cotonou, Benin.
(2)Mycobacteriology Unit, Department of Biomedical Sciences, Institute of Tropical Medicine, Antwerp, Belgium.
(3)Faculty of Pharmaceutical, Biomedical and Veterinary Sciences, University of Antwerp, Antwerp, Belgium.
(4)University Clinical Research Center, Bamako, Mali.
(5)University of Sciences, Techniques and Technologies of Bamako, Bamako, Mali.
(6)Department of Biological and Applied Pharmaceutical Sciences, Laboratory of Bacteriology and Virology, Cheikh Anta Diop Dakar University, Dakar, Senegal.
(7)Service de Pneumo-phtisiologie, Hôpital National Ignace-Deen, Conakry, Guinee.
(8)Center for Health Promotion and Research, Bamenda, Cameroon.
(9)South West Zonal TB Ref Laboratory, University College Hospital, Ibadan, Nigeria.
(10)Government Chest Hospital, Hospitals Management Board, Ibadan, Nigeria.
(11)Department of Health Data Science, University of Liverpool, Liverpool, UK.
(12)London School of Hygiene and Tropical Medicine, London, UK.
(13)National TB Program, Kinshasa, Democratic Republic of the Congo.
(14)Département de Biologie Médicale, Faculté de Médecine, Université de Kinshasa, Kinshasa, Democratic Republic of the Congo.
(15)Laboratoire National de Référence des Mycobactéries, PNLT, Kinshasa, Democratic Republic of the Congo.
(16)National Reference Laboratory, Rwanda Biomedical Centre, Kigali, Rwanda.
(17)Research Innovation and Data Science Division, Rwanda Biomedical Centre, Kigali, Rwanda.
(18)Department of Clinical Biology, University of Rwanda, Kigali, Rwanda.
(19)Mycobacteriology Research Center, Jimma University, Jimma, Ethiopia.
(20)GenoScreen, Lille, France.
(21)Foundation for Innovative New Diagnostics, Geneva, Switzerland.
(22)University of Cape Town, Western Cape, South Africa.
(23)Institute of Health, Jimma University, Jimma, Ethiopia.
(24)Damien Foundation, Ibadan, Nigeria.
(25)Special Programme for Research and Training in Tropical Diseases, World Health Organization, Geneva, Switzerland.
(26)These authors contributed equally.
(27)University Lille, CNRS, Inserm, CHU Lille, Institut Pasteur de Lille, U1019-UMR 9017, Center for Infection and Immunity of Lille, Lille, France.

BACKGROUND: The World Health Organization-endorsed Xpert MTB/XDR assay provides a rapid method to detect resistance to isoniazid, fluoroquinolones, injectables aminoglycosides and ethionamide, yet evaluation of its performance, particularly

in endemic settings, remains limited.
METHODS: We conducted a prospective multicentre study (June 2017 to March 2021) in nine sub-Saharan African countries, enrolling adults with pulmonary tuberculosis confirmed by Xpert MTB/RIF or Ultra. Xpert MTB/XDR results were compared to a World Health Organization-endorsed targeted next-generation sequencing reference used on the same sputum, with discordance resolved using whole genome sequencing and phenotypic drug-susceptibility testing when available. Diagnostic accuracy for each drug was calculated, also accounting for genotypic heteroresistance detection.
RESULTS: Among 1238 included patients, Xpert MTB/XDR demonstrated high specificity (≥98%) across all drugs yet showed variable sensitivity, detecting 606 out of 637 isoniazid-resistant (95%, 95% CI 94-97%), 22 out of 33 fluoroquinolones-resistant (67%, 95% CI 48-81%) and 159 out of 279 ethionamide-resistant (57%, 95% CI 51-63%) samples. The assay reliably detected most common resistance-conferring mutations, such as katG_S315T, fabG1_C-15T, and gyrA_A90V and D94G, yet failed to detect low-frequency heteroresistance (≤10-35%) and off-target mutations, mostly for ethionamide. Amikacin resistance was rare (0.2%). Sensitivity for fluoroquinolones was higher (78%) among rifampicin-resistant samples, highlighting its utility as a reflex test in rifampicin-resistant patients.
CONCLUSIONS: Xpert MTB/XDR offers rapid diagnosis of resistance with high specificity. While limitations in detecting low-frequency and off-target variants affect its sensitivity, most frequent, fixed in-target mutations are readily detected. Future studies should evaluate strategies to integrate Xpert MTB/XDR with other diagnostic approaches in national tuberculosis programmes.

DOI: 10.1183/23120541.00427-2025
PMCID: PMC12969699
PMID: 41809859

Conflict of interest statement: Conflict of interest: A. Ferré and N. Badalato are employees of GenoScreen, which developed the targeted next-generation sequencing assay used as a reference standard. A. Penn-Nicholson is employee of the Foundation for Innovative New Diagnostics (FIND), which provided the Xpert MTB/XDR cartridges free of charge, and S.G. Schumacher is a former employee of FIND. P. Supply is a scientific adviser for GenoScreen. The other authors declare no conflicts of interest.

29. Point-of-care molecular diagnostics and drug-resistance mechanisms in neglected

infectious diseases: current advances and future therapeutic opportunities.

Front Cell Infect Microbiol. 2026 Feb 26;16:1769679. doi: 10.3389/fcimb.2026.1769679. eCollection 2026.

Zhang Q(#)(1), Zhang X(#)(1), Yang J(1), Li H(2).

Author information:
(1)Department Clinical Laboratory, The People's Hospital of Danyang, Danyang Hospital Affiliated to Nantong University, Jiangsu, China.
(2)Department Infectious Diseases, The People's Hospital of Danyang, Danyang Hospital Affiliated to Nantong University, Jiangsu, China.
(#)Contributed equally

The rising burden of neglected infectious diseases and the accelerating spread of antimicrobial resistance (AMR) demand rapid, accurate, and decentralized diagnostic solutions. Point-of-care (POC) molecular diagnostics enable early diagnosis and resistance profiling during the clinical encounter, without reliance on centralized laboratories, which is particularly important in low-resource settings. Molecular POC technologies are being developed around the following advances: isothermal nucleic acid amplification technologies, rapid polymerase chain reaction (PCR), CRISPR-based diagnostic detection technologies, nanomaterials-enabled biosensors, and microfluidic platforms for sample-to-results with near laboratory-quality accuracy within clinically relevant timeframes (typically < 30 minutes). The combination of artificial intelligence (AI) and cloud-based digital health systems supports the automated interpretation and provision of real-time surveillance and antimicrobial stewardship. Next-generation molecular POC platforms provide higher sensitivity and mechanistic insights into drug-resistance in TB, malaria, and bacterial infections. Barriers include clinical validation, cost, scalability, and equitable access. The convergence of molecular diagnostics, nanotechnology and AI-powered analytics leads to future-oriented, transformative opportunities in precision therapy areas, AMR surveillance and infectious disease preparedness.

DOI: 10.3389/fcimb.2026.1769679
PMCID: PMC12979382
PMID: 41834999 [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.

30. A tiled amplicon protocol for culture-free whole-genome sequencing of M. tuberculosis from clinical specimens.

J Clin Microbiol. 2026 Mar 11;64(3):e0182325. doi: 10.1128/jcm.01823-25. Epub 2026 Feb 9.

Kalinich CC(#)(1), Gonzalez FL(#)(2), Osmaston A(3)(4), Breban MI(1), Distefano I(1), Leon C(4), Coronel J(4), Tan G(3), Crudu V(5), Ciobanu N(5), Codreanu A(5), Solano W(4), Ráez J(4), Sheen P(4), Zimic M(4), Allicock OM(1)(6), Chaguza C(1), Wyllie AL(1), Brandt M(1), Weinberger DM(1)(6)(7), Sobkowiak B(3)(7), Cohen T(1)(7), Grandjean L(3)(4), Grubaugh ND(1)(2)(6)(7), Redmond SN(1)(6)(7).

Author information:
(1)Department of Epidemiology of Microbial Diseases, Yale School of Public Health, New Haven, Connecticut, USA.
(2)Department of Ecology and Evolutionary Biology, Yale University, New Haven, Connecticut, USA.
(3)Department of Infection, Immunity, and Inflammation, Institute of Child Health, University College London, London, England.
(4)Universidad Peruana Cayetano Heredia, Lima, Peru.
(5)Institute of Phthisiopneumology, Chisinau, Moldova.
(6)Yale Institute for Global Health, Yale University, New Haven, Connecticut, USA.
(7)Public Health Modeling Unit, Yale School of Public Health, New Haven, Connecticut, USA.
(#)Contributed equally

Update of
bioRxiv. 2024 Dec 20:2024.12.19.629550. doi: 10.1101/2024.12.19.629550.

Whole-genome sequencing of Mycobacterium tuberculosis can be a valuable tool for TB surveillance and treatment, providing insights into transmission patterns and comprehensive drug susceptibility testing. However, the slow growth of M. tuberculosis means traditional culture-based sequencing methods can take weeks to return results, which has limited the widespread adoption of these techniques and limited their use in clinical decision-making. Tiled amplicon sequencing is a fast, reliable, and cost-effective method of whole-genome sequencing that can be done directly on clinical specimens and has been implemented at scale in academic and public health laboratories across the world; it was the cornerstone of SARS-CoV-2 sequencing and has been adapted for a wide range of viral pathogens. However, similar methods are not yet available for far larger bacterial genomes. Extending this approach to M. tuberculosis would significantly reduce the cost, labor, and turnaround time for whole-genome

sequencing. We designed a tiled amplicon panel consisting of 5,128 primers that covers the entire M. tuberculosis genome, the largest tiled amplicon sequencing panel we are aware of to date. Applying our amplicon panels to clinical samples of sputum, we show the ability to recover whole-genome bacterial sequences without the need for culture. The resulting sequence data can be used to determine M. tuberculosis lineage and reliably identify markers of drug resistance. Using this approach in clinical settings could reduce the time needed for comprehensive drug susceptibility testing from weeks to days and enable genomic epidemiology to be performed at scale, even in resource-limited settings.IMPORTANCEWe have developed and tested an amplicon panel, TB-seq, for the priority pathogen Mycobacterium tuberculosis, demonstrating recovery of near-full genomes directly from patient sputum, including mixed and low-concentration samples. This approach significantly reduces the turnaround time for this slow-growing bacterium while maintaining high accuracy in detecting clinically relevant mutations, including those associated with drug resistance. Given the global burden of tuberculosis and the critical need for faster diagnostic solutions, we believe our method has the potential to improve clinical decision-making and public health strategies.

DOI: 10.1128/jcm.01823-25
PMCID: PMC12977623
PMID: 41660836 [Indexed for MEDLINE]

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

31. Risk factors for complications after complete debridement in patients with thoracolumbar spinal tuberculosis: A retrospective study.

Medicine (Baltimore). 2026 Mar 6;105(10):e47551. doi: 10.1097/MD.0000000000047551.

Huang R(1), Yang Z(1)(2), Shi J(1), Niu N(1).

Author information:
(1)Department of Orthopedic Surgery, General Hospital of Ningxia Medical University, Yinchuan, Ningxia, People's Republic of China.
(2)Department of Orthopedic Surgery, General Hospital of Ningxia Medical University, The First School of Clinical Medicine, Yinchuan, Ningxia, People's Republic of China.

Many studies have been published on the characteristics of spinal tuberculosis, but not yet on the risk factors for complications after complete debridement.

This study aimed to investigate the risk factors of postoperative complications in patients with thoracolumbar spinal tuberculosis (TB) after complete debridement. The clinical data of patients with thoracolumbar spinal TB after complete debridement admitted to General Hospital of Ningxia Medical University from January 2013 to December 2021 were included in this retrospective study. Patients were included if they had complete clinical data and a minimum follow-up duration of 1 year to ensure adequate assessment of postoperative complications. The study cohort was divided into 2 groups, including complication group and non-complication group according to the presence or absence of postoperative complications. The clinical characteristics of thoracolumbar spinal TB patients who developed postoperative complications were evaluated, and risk factors were analyzed by using univariate and binary multivariate logistic regression analysis. A total of 571 patients were included in this study: 92 patients with complications and 479 patients without complications. The results of the univariate analysis and multivariate binary logistic regression analysis showed that preoperative albumin <35 g/L (odds ratio [OR] = 1.855; 95% confidence interval [CI], 1.106-3.111, P = .019), the number of diseased segments ≥3 (OR = 2.072; CI, 1.183-3.629, P = .011), anemia (OR = 1.691; CI, 1.047-2.731, P = .032) and drug resistance (OR = 1.768; CI, 1.011-3.091, P = .046) were independent risk factors for postoperative complications in patients with thoracolumbar spinal TB after complete debridement. Our findings support that the level of preoperative serum albumin, number of diseased segments, anemia, and drug-resistant TB are independent risk factors for postoperative complications in patients with thoracolumbar spinal TB after complete debridement. Therefore, improving preoperative serum albumin level, correcting anemia, actively preventing and monitoring drug-resistance may effectively reduce the risk of postoperative complications in patients with thoracolumbar spinal TB after complete debridement.

DOI: 10.1097/MD.0000000000047551
PMCID: PMC12975241
PMID: 41790653 [Indexed for MEDLINE]

Conflict of interest statement: The authors have no conflicts of interest to disclose.

32. Interim Effectiveness and Safety of Prolonged Bedaquiline Use in Comparison to Standard 24-Week Treatment for MDR-TB: A Multicenter Cohort Study in China.

Infect Drug Resist. 2026 Mar 10;19:572423. doi: 10.2147/IDR.S572423. eCollection 2026.

Hu X(#)(1), Gao M(#)(2), Liu Y(#)(3), Pei Y(#)(4), Du J(#)(5), Wu G(#)(6), Wang A(#)(7), Li L(3), Gao J(1).

Author information:
(1)GCP Administration Office, Beijing Chest Hospital, Capital Medical University/Beijing Tuberculosis & Thoracic Tumor Research Institute, Beijing, People's Republic of China.
(2)Department of Tuberculosis, Beijing Chest Hospital, Capital Medical University/Beijing Tuberculosis and Thoracic Tumor Research Institute, Beijing, People's Republic of China.
(3)Clinical Center on TB, Beijing Chest Hospital, Capital Medical University/Beijing Tuberculosis & Thoracic Tumor Research Institute, Beijing, People's Republic of China.
(4)Department of Tuberculosis, Changsha Central Hospital, Changsha, People's Republic of China.
(5)Department of Tuberculosis, Wuhan Pulmonary Hospital, Wuhan, People's Republic of China.
(6)Department of Tuberculosis, Chengdu Public Health Clinical Centre, Chengdu, People's Republic of China.
(7)Department of Tuberculosis, Shenyang Chest Hospital, Shenyang, People's Republic of China.
(#)Contributed equally

PURPOSE: Limited evidence exists regarding impacts of prolonged bedaquiline use in the treatment of multidrug-resistant (MDR) tuberculosis (TB). This study evaluated the effectiveness and safety of prolonged bedaquiline use (>24 weeks) compared to the standard 24-week in MDR/extensively drug-resistant (XDR)-TB treatment with longer regimen.
PATIENTS AND METHODS: This retrospective study analysed a prospective cohort of drug-resistant pulmonary TB patients treated with bedaquiline provided by the Global Drug Facility in China. Patients were enrolled from February 2018 to April 2020 across 21 hospitals under the New Drug Introduction and Protection Program. Prolonged use decisions were made by a central expert committee based on individual treatment responses. Effectiveness was assessed through cumulative culture conversion rates and time; safety was evaluated by monitoring adverse events (AEs).
RESULTS: Of 481 patients, 421 received standard bedaquiline treatment, and 60 received prolonged treatment. Median culture conversion time was 4 weeks in both groups (P = 0.443), with one patient in the prolonged group achieving culture conversion after 24 weeks. Rates of QT prolongation (30.0% vs 28.5%), deaths (0% vs 2.1%), and other AEs were comparable. During the first 24 weeks, the prolonged group had a lower AE rate overall (35.0% vs 51.3%), including serious AEs (1.7% vs 13.8%), grade >3 AEs (13.3% vs 30.4%), AEs leading to death (0% vs

2.1%), bedaquiline-related AEs (16.7% vs 26.6%), and AEs leading to bedaquiline discontinuation (0% vs 5.7%).
CONCLUSION: Prolonged bedaquiline use is effective and well-tolerated without significantly increased toxicity, potentially benefitting bedaquiline-tolerant patients with positive sputum cultures after the standard 6-month treatment.

DOI: 10.2147/IDR.S572423
PMCID: PMC12988734
PMID: 41835202

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

33. Late-Stage Functionalization of the Rifamycin Core via Click Chemistry Toward New Antibacterial Derivatives.

Molecules. 2026 Mar 3;31(5):847. doi: 10.3390/molecules31050847.

Beeser L(1), Armstrong D(1), Fullerton MS(2), Beasley I(1), Treadway W(1), Nikkel C(1), Ho ML(1), Glenn B(1), Mills C(1), Budhathoki S(3), Parchman J(1), Holdiness R(1), Smith J(1), Hodge Z(1), Dragan AL(2), Alam MA(3)(4), Shields RC(5), Voth DE(2), Nawarathne IN(1).

Author information:
(1)Division of Natural Sciences, Lyon College, Batesville, AR 72501, USA.
(2)Department of Microbiology and Immunology, University of Arkansas for Medical Sciences, Little Rock, AR 72205, USA.
(3)Molecular Biosciences Program, Arkansas State University, Jonesboro, AR 72401, USA.
(4)Department of Chemistry and Physics, The Beck College of Sciences and Mathematics, Arkansas State University, Jonesboro, AR 72467, USA.
(5)Department of Oral Biology, University of Florida, Gainesville, FL 32610, USA.

Antimicrobial resistance (AMR) threatens global health, particularly through the rise of multidrug-resistant tuberculosis (MDR-TB) and other critical bacterial infections such as methicillin-resistant Staphylococcus aureus (MRSA). Rifamycins remain frontline antibiotics but are increasingly undermined by resistance. Here, we introduce a click-enabled platform for the synthesis of C8-functionalized rifamycins, which can be converted in a single additional step into efficacious 3'-hydroxy-5'-aminobenzoxazinorifamycins (bxRifs) and

enzymatically into 25-deacetylated rifamycins (deAcRifs), providing access to novel antibacterial scaffolds that expand beyond the scope of traditional C8 modifications. Accordingly, we establish a modular strategy for late-stage analog development of the complex natural product rifamycin S, wherein azido and alkyne functionalities are installed via tailored core chemistry and converted into 1,2,3-triazoles through copper(I)-catalyzed click chemistry. Another key feature of this work is the development of systematic HPLC purification methods, enabling the isolation of analytically pure compounds despite structural complexity. The resulting analogs exhibit distinct antibacterial profiles, notably against Gram-positive bacteria including MRSA and Streptococcus mutans, informing structure-activity relationships and offering a foundation for further optimization. This approach supports the rapid diversification of rifamycin scaffolds to combat the escalating threat of AMR, while also establishing a foundation for future discovery through bioorthogonal applications.

DOI: 10.3390/molecules31050847
PMCID: PMC12985754
PMID: 41828835 [Indexed for MEDLINE]

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

34. Computational and Experimental Characterization of Mycobacterium marinum β-Carbonic Anhydrase Inhibitors.

Bioinform Biol Insights. 2026 Feb 26;20:11779322261427120. doi: 10.1177/11779322261427120. eCollection 2026.

Morshed N(1), Reza MS(2), Bhowmik R(3), Aspatwar A(3).

Author information:
(1)Department of Pharmacy, Faculty of Pharmacy, University of Dhaka, Dhaka, Bangladesh.
(2)Department of Pharmaceutical Technology, Faculty of Pharmacy, University of Dhaka, Dhaka, Bangladesh.
(3)Faculty of Medicine and Health Technology, Tampere University, Tampere, Finland.

Carbonic anhydrases in Mycobacterium tuberculosis are increasingly recognized as promising therapeutic targets in drug-resistant tuberculosis. In this study, a homology model of β-carbonic anhydrase was developed using the closely related Mycobacterium marinum sequence as a structural basis. A focused antituberculosis compound library was screened, identifying 2 ligands, F2686-0257 and F1011-1367,

with strong binding affinities and distinct interaction patterns. Molecular dynamics simulations more than 100 ns confirmed stable backbones and conserved binding pockets, with F2686-0257 stabilized by aromatic anchoring and F1011-1367 by polar interactions. Structure-activity relationship analysis highlighted rigid aromatic scaffolds, controlled molecular size, and balanced polarity as favorable features. In M marinum growth assays, F2686-0257 inhibited bacterial proliferation at 100 μM and enhanced rifampicin activity, whereas F1011-1367 showed weaker inhibition without synergy. The compounds also showed favorable ADMET and drug-likeliness properties. These results support β-carbonic anhydrase as a viable target and provide scaffolds for the rational development of novel antitubercular agents.

DOI: 10.1177/11779322261427120
PMCID: PMC12949308
PMID: 41768140

Conflict of interest statement: The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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

RSC Adv. 2026 Mar 2;16(13):11647. doi: 10.1039/d6ra90025a. eCollection 2026 Feb 26.

Nguyen HT(1)(2), Badavath VN(3), Maji S(4), Polimati H(5), Okello E(6), Bunce RA(4), Thuan NH(1)(2), Nuzul Hakimi Wan Salleh WM(7), Tatipamula VB(1)(2).

Author information:
(1)Center for Pharmaceutical Biotechnology, Duy Tan University Da Nang 550000 Vietnam.
(2)Institute of Research and Development, Duy Tan University Da Nang 550000 Vietnam vinaybharadwajtatipamula@duytan.edu.vn.
(3)School of Pharmacy and Technology Management, SVKM's Narsee Monjee Institute of Management Studies (NMIMS), Deemed-to-be-University Green Industrial Park TSIIC Jadcherla Hyderabad 509301 India.
(4)Department of Chemistry, Oklahoma State University Stillwater 74078 Oklahoma USA.
(5)Pharmacology Department, AU College of Pharmaceutical Sciences, Andhra University Visakhapatnam 530003 Andhra Pradesh India.

(6)Veterinary Medicine Teaching and Research Center, School of Veterinary Medicine, University of California Davis Tulare CA USA.
(7)Department of Chemistry, Faculty of Science and Mathematics, Universiti Pendidikan Sultan Idris Tanjong Malim 35900 Perak Malaysia.

Erratum for
RSC Adv. 2026 Feb 16;16(10):8960-8970. doi: 10.1039/d5ra05774d.

[This corrects the article DOI: 10.1039/D5RA05774D.].

DOI: 10.1039/d6ra90025a
PMCID: PMC12951841
PMID: 41777831

36. Identification of novel pyrazolo[4,3-c]pyridine and diazepane derivatives as potent inhibitors of Mycobacterium tuberculosis protein tyrosine phosphatase B.

Infect Immun. 2026 Mar 10;94(3):e0073825. doi: 10.1128/iai.00738-25. Epub 2026 Feb 9.

Raunak R(#)(1), Bahl A(#)(1), Srivastava S(2), Rakshit R(1), Bansal S(3), Kant S(4), Mandal CC(3), Pandey S(5), Tripathi D(1).

Author information:
(1)Microbial Pathogenesis and Microbiome Lab, Department of Microbiology, School of Life Sciences, Central University of Rajasthan, Ajmer, Rajasthan, India.
(2)Department of Pharmacy, School of Chemical Sciences and Pharmacy, Central University of Rajasthan, Ajmer, Rajasthan, India.
(3)Department of Biochemistry, School of Life Sciences, Central University of Rajasthan, Ajmer, Rajasthan, India.
(4)Department of Immunology and Microbiology, University of Colorado School of Medicine, Anschutz Medical Campus, Aurora, Colorado, USA.
(5)Department of Biochemistry, School of Chemical and Life Sciences, Jamia Hamdard, New Delhi, Delhi, India.
(#)Contributed equally

Tuberculosis (TB), caused by Mycobacterium tuberculosis (M.tb), continues to pose a critical global health threat as a leading infectious cause of mortality. Therapeutic efficacy is increasingly compromised by the emergence of multidrug-resistant strains and the limitations of existing regimens, which necessitate treatment durations of six months or longer. Protein tyrosine

phosphatase B from Mtb (PtpB-Mtb) has been recognized as a critical virulence factor, representing a promising target for novel antitubercular therapies due to its unique structural and functional properties. In this study, a comprehensive structure-based virtual screening approach was employed to identify novel small-molecule scaffolds with inhibitory potential against PtpB-Mtb. The ChemBridge compound library was curated and filtered for drug-like properties, followed by hierarchical molecular docking and molecular dynamics simulations to prioritize candidates with high predicted affinity and stability within the PtpB-Mtb active site. Quantum mechanical calculations further characterized the electronic properties of top hits. Recombinant PtpB-Mtb was expressed and purified to homogeneity, and in vitro enzymatic assays were performed to evaluate the inhibitory potency and selectivity of shortlisted compounds. Two derivatives bearing pyrazolo[4,3-c]pyridine and 1,4-diazepane ring nuclei demonstrated significant inhibition of PtpB-Mtb activity, exhibiting IC_{50} values of 14.4 μM and 32.6 μM, respectively. Biolayer interferometry confirmed strong and specific binding to PtpB-Mtb, with dissociation constants (Kd) of 0.012 μM and 0.57 μM. The integrated workflow presented herein highlights the potential of these novel scaffolds as starting points for the development of selective, cell-permeable PtpB-Mtb inhibitors, offering a promising avenue for next-generation anti-tubercular drug discovery.

DOI: 10.1128/iai.00738-25
PMCID: PMC12974134
PMID: 41661129 [Indexed for MEDLINE]

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

37. From clinical phenotypes to genomic signatures: machine learning integration for precision tuberculosis treatment prediction.

Front Bioinform. 2026 Mar 3;6:1787360. doi: 10.3389/fbinf.2026.1787360. eCollection 2026.

Li L(1), Liu H(2), Lei Q(3), Li T(4).

Author information:
(1)Yizhi School of Agriculture and Forestry, Xianyang Vocational Technical College, Xian Yang, Shaanxi, China.
(2)Information Management Office, Northwestern Polytechnical University, Xi'an, Shaanxi, China.
(3)Department of Pharmacy, Xi'an Chest Hospital, Xi'an, Shaanxi, China.

(4)Drug Clinical Trial Institution Office, Xi'an Chest Hospital, Xi'an, Shaanxi, China.

BACKGROUND: Tuberculosis (TB) remains a major global health threat, causing approximately 1.5 million deaths each year. Despite progress in treatment, 15%-20% of patients still experience treatment failure or relapse, highlighting the urgent need for precise predictive tools for early identification of high-risk patients. Current methods based on clinical parameters have limitations in prediction accuracy and revealing potential biological mechanisms.
METHODS: This study developed and validated an innovative multi-omics integration prediction model. We retrospectively collected clinical data from 467 tuberculosis patients and integrated transcriptomic data from three independent public cohorts (GSE19491, GSE31312, GSE83456), involving 3,240 differentially expressed genes. Through advanced feature engineering and bioinformatics analysis, key features were selected. We systematically evaluated 12 machine learning algorithms and adopted an ensemble learning strategy to construct the final model. Model performance was evaluated through strict cross-validation and prospective validation cohorts.
RESULTS: Clinical data analysis identified age, body mass index (BMI), and C-reactive protein (CRP) levels as significant predictors of treatment response. Transcriptomic analysis revealed 1,247 differentially expressed genes between responders and non-responders, enriched in immune response and metabolic pathways. Among the tested algorithms, the ensemble model based on Extra Trees performed the best, with an area under the curve (AUC) of 0.986, significantly superior to models using only clinical data (AUC = 0.850) or only genomic data (AUC = 0.820). Feature importance analysis confirmed CRP, specific gene features (such as DNA repair and interferon response pathways), age, and BMI as the most important predictors. External validation confirmed the model's robustness (AUC = 0.972).
CONCLUSION: This study successfully developed a high-precision prediction model integrating clinical and genomics data, capable of early identification of high-risk patients with poor treatment response. The model demonstrates excellent prediction performance and generalization ability, providing a powerful tool for moving towards tuberculosis precision medicine, guiding individualized treatment strategies to improve patient prognosis and control the spread of drug resistance.
CLINICAL TRIAL REGISTRATION: https://www.chictr.org.cn/, ChiCTR2300074328, 03/08/2023.

DOI: 10.3389/fbinf.2026.1787360
PMCID: PMC12993280

PMID: 41852497

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. The handling editor XW declared a past co-authorship with the authors LL.

38. Cardiodynamic evaluation of sorfequiline (TBAJ-876): results from a first-in-human study.

Antimicrob Agents Chemother. 2026 Mar 4;70(3):e0127325. doi: 10.1128/aac.01273-25. Epub 2026 Jan 30.

Darpo B(1), Nedelman J(2), Bruning-Barry R(3), Hickman D(2), Kleiman R(1), Lombardi A(2), Xue H(1).

Author information:
(1)Clario, Philadelphia, Pennsylvania, USA.
(2)TB Alliance, New York, New York, USA.
(3)RTI International, Durham, North Carolina, USA.

Sorfequiline (TBAJ-876) is a novel diarylquinoline under development for tuberculosis. In a first-in-human, multiple-ascending-dose study, electrocardiogram and pharmacokinetic data were analyzed to assess cardiac repolarization. Placebo-corrected change-from-baseline in QTcF (ΔΔQTcF) ranged from -11.4 to +2.4 ms without dose dependency. Concentration-QTc modeling showed a shallow, non-significant slope. The predicted mean effect on ΔΔQTcF at the maximum geometric mean Cmax of sorfequiline's M3 metabolite was -1.1 ms (90% CI -9.5 to 7.4).CLINICAL TRIALSThis study is registered with ClinicalTrials.gov as NCT06058299.

DOI: 10.1128/aac.01273-25
PMCID: PMC12959150
PMID: 41616265 [Indexed for MEDLINE]

Conflict of interest statement: B.D. and R.K. are employees and stockholders of Clario. H.X. is an employee of Clario. J.N. and D.H. are employees of TB Alliance. A.L. is a consultant for TB Alliance. R.B.-B. is a consultant for TB Alliance.

39. Development of a point-of-care dual one-step recombinase-aided PCR assay for rapid identification of Mycobacterium tuberculosis gyrA mutations conferring

fluoroquinolone resistance.

Front Microbiol. 2026 Mar 2;17:1772984. doi: 10.3389/fmicb.2026.1772984. eCollection 2026.

Liu X(1)(2)(3)(4)(5), Peng K(2)(3)(4), Li Y(6), Jiao S(2)(3)(4)(5)(7), Wu J(2)(3)(4)(5)(8), Zhang D(2)(3)(4)(5)(8), Gao S(5), Xiang Y(5), Ren J(5), Ma Q(2)(3)(4), Li X(2)(3)(4), Zhao Z(2)(3)(4), Han Z(2)(3)(4), Shen X(5), Ma X(5), Tie Y(2)(3)(4).

Author information:
(1)Hebei Medical University, Shijiazhuang, Hebei, China.
(2)Department of Clinical Laboratory, Hebei General Hospital, Shijiazhuang, Hebei, China.
(3)Hebei Key Laboratory of Molecular Medicine, Shijiazhuang, Hebei, China.
(4)Hebei Clinical Research Center for Laboratory Medicine, Shijiazhuang, Hebei, China.
(5)National Key Laboratory of Intelligent Tracking and Forecasting for Infectious Diseases, NHC Key Laboratory of Medical Virology and Viral Diseases, National Institute for Viral Disease Control and Prevention, Chinese Center for Disease Control and Prevention, Beijing, China.
(6)Health Science Center, Ningbo University, Ningbo, Zhejiang, China.
(7)North China University of Science and Technology, Tangshan, Hebei, China.
(8)Hebei North University, Zhangjiakou, Hebei, China.

BACKGROUND: Fluoroquinolone (FQ) resistance in Mycobacterium tuberculosis (MTB) is a major cause of treatment failure in multidrug-resistant tuberculosis (MDR-TB). This resistance primarily results from mutations within the quinolone resistance-determining region (QRDR) of the gyrA gene encoding DNA gyrase. Conventional phenotypic drug susceptibility testing (DST) is labor-intensive and time-consuming, making it unsuitable for rapid clinical decision-making. Therefore, developing a rapid, sensitive, and point-of-care testing (POCT) assay is of great importance.
METHODS: A cartridge-based POCT dual one-step recombinase-aided PCR (POCT-DO-RAP) assay was established for rapid detection of FQ resistance-associated mutations in MTB. Locked nucleic acid (LNA) probes were designed to enhance single-nucleotide discrimination for gyrA A90V and D94G mutations. Magnetic bead-based extraction enabled fully automated nucleic acid purification, while recombinase-aided amplification (RAA) and quantitative PCR (qPCR) were sequentially performed within a real-time PCR-based POCT device. The analytical performance of the POCT-DO-RAP assay was evaluated using recombinant plasmids (1-105 copies/μL), H37Rv-simulated sputum samples and 128 clinical isolates. The POCT-DO-RAP assay was further validated using 88 clinical samples and the results were compared with the conventional qPCR and the nested PCR

followed by Sanger sequencing.
RESULTS: The optimized POCT-DO-RAP assay achieved limits of detection of 1 copy/reaction for the wild-type (WT) tube and 10 CFU/mL for the mutant-type (MT) tube, representing a 10-fold increase in sensitivity compared with conventional qPCR. The assay reliably detected mutant alleles even when they represented only 1% of mixed templates. Among 128 clinical isolates, the assay accurately differentiated 50 wild-type and 78 resistant strains, showing complete concordance with Sanger sequencing and no cross-reactivity. In clinical validation,9 samples negative by qPCR were confirmed as positive by both DO-RAP assay and nested PCR followed by Sanger sequencing.
CONCLUSION: The POCT-DO-RAP assay developed in this study achieves a fully integrated "sample-in, result-out" workflow on a single device, offering ultra-high sensitivity, precise mutation discrimination, and excellent clinical concordance. This approach provides a promising molecular diagnostic tool for rapid detection of drug-resistant tuberculosis, particularly suitable for primary healthcare and resource-limited settings.

DOI: 10.3389/fmicb.2026.1772984
PMCID: PMC12989489
PMID: 41847197

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.

40. Factors accelerating time to death among persons with Tuberculosis in Western India: Evidence from a community-based retrospective death audit.

PLoS One. 2026 Feb 27;21(2):e0343271. doi: 10.1371/journal.pone.0343271. eCollection 2026.

Shah H(1), Patel J(1), Saha S(1), Modi B(2), Nimavat P(1).

Author information:
(1)Department of Public Health Science, Indian Institute of Public Health Gandhinagar (IIPHG), Gandhinagar, India.
(2)Scientist G & Director, National Institute of Occupational Health, Ahmedabad, India.

INTRODUCTION: Tuberculosis (TB) remains a leading cause of death globally. India aims to eliminate TB by 2025; however, persistently high mortality rates suggest critical failures in early intervention, particularly among vulnerable populations. This study examined the clinical, social, and system factors associated with accelerated mortality among notified persons with TB (PwTB) in Western India.
METHODS: A cross-sectional study was conducted in six districts of Gujarat, India, during 2023-2024 using Community-Based Verbal Autopsy (CBVA) among relatives of 149 deceased PwTB. Sociodemographic, clinical, and TB care cascade data were collected, and a retrospective time-to-event analysis was performed. A Cox proportional hazards model was used to assess the factors associated with a shorter time from diagnosis to death.
RESULTS: Majority of deceased belonged to 26-50 years age group (40%), with a high male predominance (81.9%). Nearly half (48.3%) had comorbidities, and 65.8% had a history of addiction. A substantial median delay of approximately five weeks was observed between symptom onset and treatment initiation. Following a confirmed diagnosis, the majority of deaths (nearly 80%) occurred within the first 16 weeks. A comparable trend was noted after the start of treatment, with about 78% of fatalities occurring within 15 weeks. In the adjusted Cox regression model, key population status (HR = 1.5, $p = 0.01$), presence of comorbidities (HR = 2.0, $p < 0.001$), and drug-resistant tuberculosis (HR = 1.7, $p = 0.003$) were independently associated with a shorter time from diagnosis to death.
DISCUSSION: The findings highlighted the convergence of clinical complexity, social vulnerability, and persistent system constraints that shorten survival, even after treatment initiation. Strengthening early case diagnosis, integrating comorbidity management, improving health system responsiveness, and implementing targeted strategies for vulnerable populations are critical. A systematic TB Death Surveillance and Response System (TBDSR), integrating facility-, community-based reviews, and digital reporting, would provide actionable insights to inform timely intervention and support progress towards TB elimination in India and other high-burden settings.

DOI: 10.1371/journal.pone.0343271
PMCID: PMC12948073
PMID: 41758813 [Indexed for MEDLINE]

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

41. Establishing a Neisseria gonorrhoeae whole-genome sequencing external quality assessment for the Antimicrobial Resistance Laboratory Network (AR Lab Network) regional laboratories.

Microbiol Spectr. 2026 Mar 3;14(3):e0225625. doi: 10.1128/spectrum.02256-25. Epub 2026 Jan 30.

Reimche JL(1)(2), Smith AC(1), Pham CD(1)(3), Schmerer MW(1), Cartee JC(1), Bolden CB(1)(4), Kersh EN(1), Gernert KM(1); Antimicrobial Resistance Laboratory Network GC Working Group.

Collaborators: Burks A, Qian X, Montgomery GE, Thomas L, Hargrove A, Lemon A, Spann M, Rossi A, Oakeson K, Neff L, Young E, Casey R, Hiatt B, Tran ML, Hun S, Hua C, Veliz K, Soge OO, Torpey DJ, Klein L, Myers R, Keller EN, Maruca T, Moore TL, Eklund E, Taylor D, Critchfield H, Stamper P, Chapel N, Lee B, Patel A, Loomis J.

Author information:
(1)STD Laboratory Reference and Research Branch, Division of STD Prevention, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, Centers for Disease Control and Prevention, Atlanta, Georgia, USA.
(2)Oak Ridge Institute for Science and Education, Oak Ridge Associated Universities, Oak Ridge, Tennessee, USA.
(3)Division of Healthcare Quality Promotion, National Center for Emerging and Zoonotic Infectious Disease, Centers for Disease Control and Prevention, Atlanta, Georgia, USA.
(4)Division of Parasitic Diseases and Malaria, Global Health Center, Centers for Disease Control and Prevention, Atlanta, Georgia, USA.

Drug-resistant Neisseria gonorrhoeae (GC) is classified by the Centers for Disease Control and Prevention (CDC) as an urgent threat. Effective surveillance of antimicrobial resistance and strain types through whole-genome sequencing (WGS) is essential to preserve existing antibiotics for treatment. To ensure consistent, high-quality data, we implemented an External Quality Assessment (EQA) program within the Antimicrobial Resistance Laboratory Network in fall 2020. This biannual program distributes five blinded GC reference isolates in triplicate to four regional laboratories for antimicrobial susceptibility testing and WGS. Data were transferred to the CDC for taxonomic classification, assembly, phylogenetics, and quality evaluation. During fall 2020 (pilot)-spring (Cycle 1) 2023, five laboratories (four external; one at CDC) participated in a

pilot and five EQA cycles. In the pilot cycle, all laboratories met all quality metrics. However, in 2021 Cycle 1, one laboratory scored below passing (<80%), highlighting the need for ongoing assessment. Issues were due to low coverage and poor-quality assemblies. Multilocus sequence typing and single-nucleotide polymorphism distances identified sample-swapping errors. In 2022 Cycle 1, two laboratories scored <80% due to sample handling issues and low sequence quality. After identifying the root cause and implementing corrective actions, all laboratories achieved 100% pass rates in 2022 Cycle 2 and 2023 Cycle 1. The EQAs identified shortcomings in WGS and sample management workflows not evident in routine processing and supported continual improvement of the participating laboratories and WGS quality management. This approach supports effective surveillance of drug-resistant GC, which informs the development of CDC's sexually transmitted infection treatment guidelines.IMPORTANCEThe External Quality Assessment (EQA) program for whole-genome sequencing (WGS) of Neisseria gonorrhoeae (GC) is necessary for robust surveillance of antimicrobial resistance (AR)-associated genomic markers and strain prevalence. By ensuring high-quality, consistent WGS data across laboratories participating in genomic surveillance, this program addresses issues identified in sequencing workflows and sample management that were not apparent in routine processing. Eight sequence quality metrics and alignment of phenotypic and genotypic data enhance data reliability, supporting the Centers for Disease Control and Prevention's efforts to monitor and control drug-resistant GC. The successful implementation of corrective actions after issues discovered in some EQA cycles demonstrates the program's effectiveness in improving laboratory performance. This program contributes to the fidelity of and capacity for genomic surveillance, identification of AR genomic variants, and public health strategies to reduce GC infections.

DOI: 10.1128/spectrum.02256-25
PMCID: PMC12955492
PMID: 41616250 [Indexed for MEDLINE]

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

42. Safety pharmacology and toxicology of a novel nitroimidazooxazole antitubercular agent in SD rat and Beagle dogs.

Mol Biomed. 2026 Mar 2;7(1):18. doi: 10.1186/s43556-026-00414-7.

Peng D(#)(1), Qin F(#)(1), Fu M(#)(1), Jiang N(2), Wang M(3), Wang Z(4), Wei X(5)(6).

Author information:

(1)Laboratory of Aging Research and Cancer Drug Target, State Key Laboratory of Biotherapy and Cancer Center, National Clinical Research Center for Geriatrics, West China Hospital, Sichuan University, No. 17, Block 3, Southern Renmin Road, Chengdu, Sichuan, 610041, People's Republic of China.
(2)Jumbo Drug Bank Co., Ltd., Chengdu, China.
(3)Laboratory of Aging Research and Cancer Drug Target, State Key Laboratory of Biotherapy and Cancer Center, National Clinical Research Center for Geriatrics, West China Hospital, Sichuan University, No. 17, Block 3, Southern Renmin Road, Chengdu, Sichuan, 610041, People's Republic of China. wangmanni@scu.edu.cn.
(4)Laboratory of Aging Research and Cancer Drug Target, State Key Laboratory of Biotherapy and Cancer Center, National Clinical Research Center for Geriatrics, West China Hospital, Sichuan University, No. 17, Block 3, Southern Renmin Road, Chengdu, Sichuan, 610041, People's Republic of China. wangzhenling@scu.edu.cn.
(5)Laboratory of Aging Research and Cancer Drug Target, State Key Laboratory of Biotherapy and Cancer Center, National Clinical Research Center for Geriatrics, West China Hospital, Sichuan University, No. 17, Block 3, Southern Renmin Road, Chengdu, Sichuan, 610041, People's Republic of China. xiaweiwei@scu.edu.cn.
(6)Jumbo Drug Bank Co., Ltd., Chengdu, China. xiaweiwei@scu.edu.cn.
(#)Contributed equally

We developed JBD0131, a novel nitroimidazooxazole antitubercular agent, and conducted a comprehensive preclinical evaluation of its safety pharmacology, toxicology, and pharmacokinetics in SD rats and Beagle dogs. JBD0131 was well-tolerated in repeated-dose oral studies, with no treatment-related mortality or significant alterations in organ weights or significant alterations in organ-to-body weight ratios observed. The no-observed-adverse-effect level (NOAEL) was established at 480 mg/kg/day in rats and 300 mg/kg/day in female dogs. In male dogs, the NOAEL was determined to be 15 mg/kg/day, a discrepancy primarily attributed to a slight trend toward Corrected QT interval (QTc) prolongation at higher doses (60 and 300 mg/kg/day) to which males exhibited greater cardiovascular sensitivity. Pharmacokinetic analysis revealed dose-proportional systemic exposure with no accumulation of JBD0131. Although the metabolite DM131 showed moderate accumulation, it was identified as the amino-reduction detoxification product of JBD0131, a conversion that yields a more stable species and is supported by favorable clinical safety data. While Phase I clinical trials of JBD0131 have been reported, this preclinical study remains indispensable as it establishes the toxicological "ceiling" and defines safety margins through supra-therapeutic dosing. By identifying sex-specific sensitivities and clarifying metabolite safety, this work provides a critical scientific foundation for long-term clinical monitoring and risk assessment. Based on indirect comparisons with reported historical data for clinical agents such as bedaquiline and pretomanid, JBD0131 demonstrated a favorable preclinical safety profile in the models tested, supporting its continued development for multidrug-resistant tuberculosis.

DOI: 10.1186/s43556-026-00414-7
PMCID: PMC12950821
PMID: 41766049 [Indexed for MEDLINE]

Conflict of interest statement: Declarations. Ethics approval and consent to participate: The study was conducted at Chengdu Huaxi Haichi Pharmaceutical Technology Co., Ltd. (Chengdu, China) in strict accordance with the approved study protocol, institutional standard operating procedures, and relevant animal welfare regulations. All procedures complied with the Principles of Good Laboratory Practice (GLP) as defined by the CFDA (2003), FDA (21 CFR Part 58), and OECD (ENV/MC/CHEM(98)17). The facility is GLP-certified by both the National Medical Products Administration (NMPA, formerly CFDA) and OECD, and is fully accredited by the AAALAC International. All animal experimental protocols were reviewed and approved by the Institutional Animal Care and Use Committee (IACUC) of the facility (Approval No.: IACUC-A2017007). Consent for publication: Not applicable. Competing interests: Jumbo Drug Bank Co. Ltd. provided the financial support to this preclinical trial. Ning Jiang and Xiawei Wei are employees of this Company and declare a potential conflict of interest. The other authors have no conflicts of interest to declare.

43. iFIND INH/FQ: a LC-aNAAT assay for rapid simultaneous detection of isoniazid and fluoroquinolone resistance in Mycobacterium tuberculosis.

Microbiol Spectr. 2026 Mar 3;14(3):e0374325. doi: 10.1128/spectrum.03743-25. Epub 2026 Feb 6.

Ou X(#)(1), Ma Y(#)(2), Zheng H(#)(3), Li Y(2), Zeng J(2), Chen Y(3), Huang L(2), Guo Y(3), Zhao B(1), Li J(3), Xing R(1), Xia H(1), Zhao Y(1).

Author information:
(1)National Key Laboratory of Intelligent Tracking and Forecasting for Infectious Diseases, National Center for Tuberculosis Control and Prevention, Chinese Center for Disease Control and Prevention (Chinese Academy of Preventive Medicine), Beijing, China.
(2)Tuberculosis Prevention and Control Division, Chengde Center for Disease Control and Prevention (Chengde Health Inspection Institute), Chengde, China.
(3)Beijing Key Laboratory of Pediatric Respiratory Infection Diseases, Key Laboratory of Major Diseases in Children, Ministry of Education, National Clinical Research Center for Respiratory Diseases, Laboratory of Respiratory Diseases, Beijing Pediatric Research Institute, Beijing Children's Hospital,

Capital Medical University, National Center for Children's Health, Beijing, China.
(#)Contributed equally

To evaluate the performance of the iFIND INH/FQ, a low-complexity molecular assay, for the rapid and simultaneous detection of resistance to isoniazid (INH) and fluoroquinolones (FQs) in Mycobacterium tuberculosis. Frozen sputum specimens stored at the Chengde Center for Disease Control and Prevention laboratory were used. Phenotypic drug susceptibility testing (pDST) and DNA sequencing served as reference standards. The limit of detection (LOD) was determined using probit regression with spiked samples. The assay's ability to detect resistance-conferring mutations in katG, inhA, and gyrA genes was assessed using genotypically characterized strains. Diagnostic accuracy was evaluated against pDST. The LOD was 20.79 CFU/mL for INH and 9.34 CFU/mL for FQs. The assay detected all targeted mutations except ahpC c.-6 associated with INH resistance. Compared to pDST, the iFIND INH/FQ assay demonstrated a sensitivity of 97.59% (95% confidence interval [CI]: 91.63-99.34%) and specificity of 98.10% (95% CI: 94.57-99.35%) for INH resistance. For FQ resistance, sensitivity was 92.16% (95% CI: 81.50-96.91%) for levofloxacin and 92.00% (95% CI: 81.16-96.85%) for moxifloxacin, with specificities of 97.33% (95% CI: 93.89-98.85%) and 96.81% (95% CI: 93.21-98.53%), respectively. Sequencing confirmed iFIND results in the majority of discrepant cases (100% for INH and 55.65% for FQs). The iFIND INH/FQ LC-aNAAT is a highly accurate and rapid molecular assay for simultaneous detection of INH and FQ resistance. It is a promising tool for scaling up rapid drug susceptibility testing in clinical and peripheral laboratory settings.
IMPORTANCE: As a low-complexity automated nucleic acid amplification test, the iFIND assay achieves the goal of simultaneously detecting isoniazid and fluoroquinolone resistance in approximately 90 min, perfectly meeting the TPP's core requirements for "rapid" and "simple operation." Its fully integrated system minimizes manual steps and contamination risk, making it highly suitable for use in resource-limited, lower-biosafety-level primary laboratories.

DOI: 10.1128/spectrum.03743-25
PMCID: PMC12955496
PMID: 41649261 [Indexed for MEDLINE]

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

44. Efficacy and predictors of virological non-suppression in Thailand's rollout of dolutegravir-based first-line antiretroviral therapy: A nationwide cohort Analysis.

HIV Med. 2026 Mar;27(3):459-470. doi: 10.1111/hiv.70178. Epub 2025 Dec 19.

Hiranburana N(1)(2), Sophonphan J(1)(3), Kerr SJ(1)(3)(4), Lertpiriyasuwat C(5), Noknoy S(5), Jirajariyavej S(6), Fujitnirun C(7), Chetchotisakd P(8), Lolekha R(9), Bowonwatanuwong C(9), Ruxrungtham K(1)(10)(11), Putcharoen O(12), Avihingsanon A(1)(2).

Author information:
(1)HIVNAT, Thai Red Cross AIDS and Infectious Diseases Research Centre, Bangkok, Thailand.
(2)Center of Excellence in Tuberculosis, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand.
(3)Research Affairs, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand.
(4)The Kirby Institute, University of New South Wales, Sydney, New South Wales, Australia.
(5)Division of AIDS and STI, Department of Disease Control, Ministry of Public Health, Nonthaburi, Thailand.
(6)Taksin Hospital, Bangkok, Thailand.
(7)Bhumibol Adulyadej Hospital, Bangkok, Thailand.
(8)Faculty of Medicine, Srinagarind Hospital, Khon Kaen University, Khon Kaen, Thailand.
(9)Thai AIDS Society, Bangkok, Thailand.
(10)Center of Excellence in Vaccine Research and Development, Chula Vaccine Research Center (Chula VRC), Bangkok, Thailand.
(11)School of Global Health, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand.
(12)Division of Infectious Diseases, Department of Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand.

OBJECTIVE: To evaluate real-world outcomes of dolutegravir (DTG)-based first-line antiretroviral therapy (ART) among people with HIV in Thailand, where baseline HIV-1 RNA and resistance testing is not routinely available.
METHODS: This retrospective cohort study enrolled ART-naive Thai people with HIV aged ≥15 years who initiated DTG-based ART between 2020 and 2023 under the national Universal Health Coverage programme. People with HIV with ≥1 post-baseline HIV viral load (VL) measurement were included. Virological non-suppression (VNS) was defined as VL ≥1000 copies/mL after ≥6 months of ART. The primary outcome was the proportion achieving virological suppression (VL <50 copies/mL). Competing-risk regression was used to identify factors associated with VNS, accounting for death and loss to follow-up (LTFU). Mortality data were confirmed via the national death registry.
RESULTS: Of 10 475 people with HIV initiating DTG-based ART, 84.5% achieved

virological suppression and 95.3% achieved VL < 200 copies/mL within 1 year. The cumulative VNS incidence was 10.1% (95% confidence interval [CI]: 9.6%-10.5%), and highest among those with late ART initiation (10.6% [95% CI: 7.4%-14.3%]). VNS was significantly associated with younger age, 15-24 years (aSHR 2.28, 95% CI:1.66-3.12), 25-34 years (aSHR1.43, 95% CI:1.07-1.90), baseline CD4 < 100 cells/mm3 (aSHR 2.11, 95% CI: 1.36-3.27) and residence in northern (aSHR 1.64, 95% CI: 1.12-2.40) or southern Thailand (aSHR 1.99, 95%: 1.30-3.04). Same-day/rapid ART initiation, sex and WHO HIV clinical staging were not associated with VNS.
CONCLUSIONS: Nationwide rollout of DTG-based ART achieved excellent virological outcomes in Thailand. However, higher VNS risk among adolescents, individuals with advanced HIV disease and those in specific regions underscores the need for targeted interventions to improve treatment equity and long-term viral suppression.

DOI: 10.1111/hiv.70178
PMCID: PMC12847068
PMID: 41420262 [Indexed for MEDLINE]

Conflict of interest statement: CONFLICT OF INTEREST STATEMENT AA has received research grants for HIVNAT from Gilead Science, ViiV/GSK, Roche, MSD, Janssen Research and Development; transportation costs to attend meetings/conferences from Gilead Sciences; and other non-financial interests (unpaid) for working with: (1) Strategic and Technical Advisory group to WHO for HIV/hepatitis/STI, (2) Thai AIDS society committee; and (3) Thailand National ART, TB, HIV, Hepatitis program committee. The rest of the authors declare no conflicts of interest.

45. The Efficacy and Safety of Hepatic Arterial Infusion Chemotherapy for Mismatch Repair Proficient (pMMR)/Microsatellite Stable (MSS) Colorectal Cancer Liver Metastases (CRLM).

Cancer Med. 2026 Mar;15(3):e71663. doi: 10.1002/cam4.71663.

Li Y(1), Xi J(1), Huang X(1), Luo Y(1), Zhang X(1), Li X(1).

Author information:
(1)Department of Interventional Therapy, National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China.

PURPOSE: To assess the effectiveness and safety of hepatic arterial infusion chemotherapy (HAIC) in patients with mismatch repair proficient (pMMR)/microsatellite stable (MSS) colorectal cancer liver metastases (CRLM) who are resistant to standard treatments.
METHODS: This study retrospectively evaluated 137 consecutive patients with pMMR/MSS CRLM who underwent HAIC from July 2019 to September 2023. Progression-free survival (PFS) was the primary outcome, with secondary outcomes being overall survival (OS), objective response rate (ORR), disease control rate (DCR), and safety. The Cox proportional hazards model was used to identify prognostic factors for survival.
RESULTS: In total, 78 patients participated, with a median age of 58 years (IQR, 50.75-64.00), and 50 were male. Among these, 28 were treated with a combination of HAIC and targeted therapy, whereas 50 were given HAIC monotherapy. For all patients, the median PFS and OS were 5.10 months (95% CI: 2.85, 7.35) and 16.80 months (95% CI: 13.07, 20.53), respectively. The ORR and DCR for intrahepatic lesions were 1.37% and 58.9%, respectively. All lesions had an ORR of 2.74% and a DCR of 30.14%. The 1-year OS rate was 67.63 (95% CI, 57.22, 79.91). Patients undergoing HAIC, whether with or without targeted therapy, showed no significant differences in ORR and DCR. Multivariable analysis showed that the combination of HAIC and targeted therapy was not an independent risk factor for PFS and OS. No adverse events of grade 4 or higher were observed.
CONCLUSION: HAIC shows effectiveness and tolerance in pMMR/MSS CRLM patients who are refractory to systemic therapy. However, the additive value of targeted therapy for HAIC in these patients needs to be further investigated.

DOI: 10.1002/cam4.71663
PMCID: PMC12967907
PMID: 41796273 [Indexed for MEDLINE]

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

46. Women and TB/HIV coinfection in Brazil: regional inequalities and trends in a scenario of vulnerability.

Rev Bras Enferm. 2026 Feb 23;79:e20250259. doi: 10.1590/0034-7167-2025-0259. eCollection 2026.

Oliveira EV(1), Ziani JDS(2), Corcini LMCDS(2), Pieri FM(3), Alves JD(4), Melo EC(1), Moreira RC(1), Scholze AR(2).

Author information:

(1)Universidade Estadual do Norte do Paraná. Bandeirantes, Paraná, Brazil.
(2)Universidade Federal de Santa Maria. Santa Maria, Rio Grande do Sul, Brazil.
(3)Universidade Estadual de Londrina. Londrina, Paraná, Brazil.
(4)Universidade Federal do Mato Grosso. Cuiabá, Mato Grosso, Brazil.

OBJECTIVES: to identify the clinical-epidemiological profile of women with TB/HIV coinfection and classify the temporal trend of coinfection in the regions of Brazil.
METHODS: ecological study of time series of records from the Notifiable Diseases Information System carried out from 2012 to 2023. The analysis was performed using the Prais-Winsten autoregression method.
RESULTS: a total of 31,171 cases were recorded in the country, with the highest concentration in the Southeast. Coinfection showed a steady trend, with higher rates in the South and North regions. Regional disparities are related to factors such as low education level, age between 20 and 39 years, and black race/skin color. In the South, drug resistance and substance use disorders also stood out.
CONCLUSIONS: the need for regional, equitable and integrated public policies is evident, focusing on expanding access to diagnosis and treatment, considering the specific vulnerabilities of women affected by coinfection.

OBJECTIVES: identificar o perfil clínico-epidemiológico das mulheres com coinfecção TB/HIV e classificar a tendência temporal da coinfecção nas regiões do Brasil.
MÉTODOS: estudo ecológico de séries temporais de registros do Sistema de Informação de Agravos de Notificação realizado no período de 2012 a 2023. A análise foi realizada utilizando o método de autorregressão Prais-Winsten.
RESULTADOS: foram registrados 31.171 casos no país, com maior concentração no Sudeste. A coinfecção apresentou tendência estacionária, com taxasmais altas nas regiões Sul e Norte. As disparidades regionais se relacionam a fatores comobaixa escolaridade, idade entre 20 e 39 anos, e raça/cor preta. No Sul, destacaram-se ainda a resistência medicamentosa e transtornos por uso de substâncias.
CONCLUSÕES: evidencia-se a necessidade de políticas públicas regionais, equitativas e integradas, com foco na ampliação do acesso ao diagnóstico e tratamento, considerando as vulnerabilidades específicas dasmulheres afetadas pela coinfecção.

DOI: 10.1590/0034-7167-2025-0259
PMCID: PMC12933940
PMID: 41739680

Recent TB News

Trials to watch: Phase III TB vaccines and MDR-TB treatments
https://www.clinicaltrialsarena.com/features/trials-to-watch-phase-iii-tb-vaccines-and-mdr-tb-treatments/?cf-view

After years without much advancement in new TB drug trials, a vaccine and two treatments are progressing through late-stage studies. As researchers predict the number of TB cases in the 16 major markets (US, France, Germany, Italy, Spain, UK, Japan, Australia, Brazil, Canada, China, India, Mexico, Russia, South Africa, and South Korea) to increase to 4.4 million in 2033, this article highlights a few current trials that could have major impacts on TB globally.

More than 1 in 5 new TB cases in Europe are missed, analysis finds.
https://www.cidrap.umn.edu/tuberculosis/more-1-5-new-tb-cases-europe-are-missed-analysis-finds
According to a new report from Europe, incidence of TB in the continent has dropped by around 40% in the last decade but over 20% of new TB cases are going undetected. While this issue is highlighted in Europe, this continues to be an ongoing problem globally. To fill this gap, researchers and the WHO encourage better TB prevention and early case detection, especially through better/more rapid diagnostics and drug-susceptibility tests.