PubMed Open Access

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

Eur Respir J. 2025 Aug 22;66(2):2500315. doi: 10.1183/13993003.00315-2025. Print 2025 Aug.

Kwak N(1)(2), Kim JY(1)(3)(2), Han A(4)(5), Berry C(6), Beumont M(7), Tweed C(8), Crook A(8), Dheda K(9)(10), Fabiane S(8), Fadeyi MO(11), Foraida S(7), Gils T(12)(13), Hoang TTT(14), Jham MA(15), Murphy RA(16), Nguyen BH(14), Nguyen TMP(14), Nyang'wa BT(17)(18), Oelofse S(10), Hahn S(19)(20)(21), Yim JJ(22).

Author information:
(1)Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine, Seoul National University Hospital, Seoul National University College of Medicine, Seoul, Republic of Korea.
(2)N. Kwak and J-Y. Kim contributed equally.
(3)Department of Microbiology, Harvard Medical School, Boston, MA, USA.
(4)Interdisciplinary Program of Medical Informatics, Seoul National University College of Medicine, Seoul, Republic of Korea.
(5)Integrated Major in Innovative Medical Science, Seoul National University College of Medicine, Seoul, Republic of Korea.
(6)Médecins Sans Frontières, London, UK.
(7)TB Alliance, New York, NY, USA.
(8)MRC Clinical Trials Unit, University College London, London, UK.
(9)Department of Immunology and Infection, Faculty of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, London, UK.
(10)Centre for Lung Infection and Immunity, University of Cape Town, Cape Town, South Africa.
(11)Damien Foundation Belgium (Nigeria Project), Ibadan, Nigeria.
(12)Unit of HIV and Coinfections, Department of Clinical Sciences, Institute of Tropical Medicine, Antwerp, Belgium.
(13)Global Health Institute, University of Antwerp, Wilrijk, Belgium.
(14)National Lung Hospital, Hanoi, Vietnam.
(15)UMMA Community Clinic, Los Angeles, CA, USA.
(16)Division of Infectious Diseases, Dartmouth Geisel School of Medicine, Hanover, NH, USA.
(17)Médecins Sans Frontières, Amsterdam, The Netherlands.
(18)Clinical Research Department, London School of Hygiene and Tropical Medicine, London, UK.
(19)Medical Bigdata Research Center, Medical Research Center, Seoul National

University, Seoul, Republic of Korea.
(20)Institute of Health Policy and Management, Medical Research Center, Seoul National University, Seoul, South Korea.
(21)Department of Human Systems Medicine, Seoul National University College of Medicine, Seoul, Republic of Korea.
(22)Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine, Seoul National University Hospital, Seoul National University College of Medicine, Seoul, Republic of Korea yimjj@snu.ac.kr.

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

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

DOI: 10.1183/13993003.00315-2025
PMCID: PMC12371315
PMID: 40675768 [Indexed for MEDLINE]

Conflict of interest statement: Conflict of interest: M. Beumont and S. Foraida

are employees of TB Alliance. R.A. Murphy reports payment for expert testimony and support for attending meetings from the University of Nevada. J-J. Yim has participated or is currently participating as the overall or institutional principal investigator in multiple clinical trials sponsored by Insmed Incorporated, AN2 Therapeutics and LigaChem Biosciences Inc. The remaining authors have no potential conflicts of interest to disclose.

2. Targeting de novo purine biosynthesis for tuberculosis treatment.

Nature. 2025 Aug;644(8075):214-220. doi: 10.1038/s41586-025-09177-7. Epub 2025 Jun 18.

Lamprecht DA(#)(1)(2), Wall RJ(#)(3), Leemans A(#)(4), Truebody B(5), Sprangers J(4)(6), Fiogbe P(4)(6), Davies C(3), Wetzel J(4), Daems S(4), Pearson W(3), Pillay V(5), Saylock S(7), Ricketts MD(7), Davis E(3), Huff A(7), Grell T(7), Lin S(8), Gerber M(8), Vos A(9), Dallow J(3), Willcocks SJ(3)(10), Roubert C(11), Sans S(11), Desorme A(11), Chappat N(11), Ray A(11), Pereira Moraes M(12), Washington T(12), D'Erasmo H(12), Sancheti P(9), Everaerts M(9), Monshouwer M(4), Esquivias J(13), Larrouy-Maumus G(14), Draghia Akli R(7)(15), Fletcher H(3)(16), Pym AS(16), Aldridge BB(12)(17), Sarathy JP(18), Clancy KW(7), Stoops B(9), Dhar N(8), Steyn AJC(5)(19)(20), Jackson P(21), Aguilar-Pérez C(4), Koul A(22)(23).

Author information:
(1)Janssen Global Public Health, LLC, Janssen Pharmaceutica NV, Antwerp, Belgium. dirk.lamprecht@uct.ac.za.
(2)Holistic Drug Discovery and Development (H3D) Centre, University of Cape Town, Rondebosch, South Africa. dirk.lamprecht@uct.ac.za.
(3)Department of Infection Biology, Faculty of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, London, UK.
(4)Janssen Global Public Health, LLC, Janssen Pharmaceutica NV, Antwerp, Belgium.
(5)Africa Health Research Institute, University of KwaZulu Natal, Durban, South Africa.
(6)Charles River Laboratories, Antwerp, Belgium.
(7)Janssen Research and Development, LLC, Janssen Pharmaceutica, Spring House, PA, USA.
(8)Vaccine and Infectious Disease Organization, University of Saskatchewan, Saskatoon, Saskatchewan, Canada.
(9)Janssen Research and Development, LLC, Janssen Pharmaceutica NV, Antwerp, Belgium.
(10)Department of Life Sciences, College of Health, Medicine and Life Sciences, Brunel University of London, Uxbridge, UK.

(11)Evotec ID (LYON) SAS, Lyon, France.
(12)Department of Molecular Biology and Microbiology, Tufts University School of Medicine and Stuart B. Levy Center for Integrated Management of Antimicrobial Resistance, Boston, MA, USA.
(13)Janssen Research and Development, LLC, Janssen Pharmaceutica, Toledo, Spain.
(14)Centre for Bacterial Resistance Biology, Department of Life Sciences, Faculty of Natural Sciences, Imperial College London, London, UK.
(15)Research and Development, Novavax, Inc., Gaithersburg, MD, USA.
(16)Janssen Global Public Health, LLC, Janssen Pharmaceutica, High Wycombe, UK.
(17)Department of Biomedical Engineering, Tufts University School of Engineering, Medford, MA, USA.
(18)Center for Discovery and Innovation, Hackensack Meridian Health, Nutley, NJ, USA.
(19)Department of Microbiology, University of Alabama at Birmingham, Birmingham, AL, USA.
(20)Centers for AIDS Research and Free Radical Biology, University of Alabama at Birmingham, Birmingham, AL, USA.
(21)Janssen Global Public Health, LLC, Janssen Pharmaceutica, La Jolla, CA, USA.
(22)Janssen Global Public Health, LLC, Janssen Pharmaceutica NV, Antwerp, Belgium. anil.koul@lshtm.ac.uk.
(23)Department of Infection Biology, Faculty of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, London, UK. anil.koul@lshtm.ac.uk.
(#)Contributed equally

Tuberculosis remains the leading cause of death from an infectious disease1,2. Here we report the discovery of a first-in-class small-molecule inhibitor targeting PurF, the first enzyme in the mycobacterial de novo purine biosynthesis pathway. The lead candidate, JNJ-6640, exhibited nanomolar bactericidal activity in vitro. Comprehensive genetic and biochemical approaches confirmed that JNJ-6640 was highly selective for mycobacterial PurF. Single-cell-level microscopy demonstrated a downstream effect on DNA replication. We determined the physiologically relevant concentrations of nucleobases in human and mouse lung tissue, showing that these levels were insufficient to salvage PurF inhibition. Indeed, proof-of-concept studies using a long-acting injectable formulation demonstrated the in vivo efficacy of the compound. Finally, we show that inclusion of JNJ-6640 could have a crucial role in improving current treatment regimens for drug-resistant tuberculosis. Together, we demonstrate that JNJ-6640 is a promising chemical lead and that targeting de novo purine biosynthesis represents a novel strategy for tuberculosis drug development.

DOI: 10.1038/s41586-025-09177-7
PMCID: PMC12328218
PMID: 40533558 [Indexed for MEDLINE]

Conflict of interest statement: Competing interests: D.A.L., A.L., J.S., P.F., J.W., S.D., S. Saylock, M.D.R., A.H., T.G., A.V., K.W.C., P.S., M.E., M.M., J.E., R.D.A., H.F., A.S.P., B.S., C.A.-P., P.J. and A.K. were or are all full-time employees of Janssen Pharmaceutica, a Johnson & Johnson company, and/or potential stockholders of Johnson & Johnson. J.S. and P.F. were or are employees of Charles River Laboratories, a contract research organization. A.R., C.R., N.C. and S. Sans were or are all full-time employees of Evotec. R.J.W., C.D., W.P., E.D., S.L., M.G., J.D., S.J.W., G.L.-M., N.D. and A.K. received funding from Janssen Pharmaceutica to perform contract research. The other authors declare no competing interests.

3. Prevalence and contributing factors of drug-resistant tuberculosis (DR-TB) in iran: a systematic review.

BMC Infect Dis. 2025 Aug 8;25(1):1004. doi: 10.1186/s12879-025-11439-8.

Daneshi S(1), Mehni EB(2), Kamali M(3), Barfar E(4), Barahouei FB(5), Hushmandi K(6), Raesi R(7)(8).

Author information:
(1)Department of Public Health, School of Health, Jiroft University of Medical Sciences, Jiroft, Iran.
(2)Department of Nursing, Nursing and Midwifery School, Jiroft University of Medical Sciences, Jiroft, Iran.
(3)Department of Ophthalmology, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran.
(4)Health Promotion Research Center, Zahedan University of Medical Sciences, Zahedan, Iran.
(5)Student Research Committee, Zahedan University of Medical Sciences, Zahedan, Iran.
(6)Nephrology and Urology Research Center, Clinical Sciences Institute, Baqiyatallah University of Medical Sciences, Tehran, Iran. kiavash.hushmandi@gmail.com.
(7)Department of Public Health, School of Health, Torbat Jam Faculty of Medical Sciences, Torbat Jam, Iran. Raesi.br881@gmail.com.
(8)Department of Public Health, School of Health, Mashhad University of Medical Sciences, Mashhad, Iran. Raesi.br881@gmail.com.

INTRODUCTION: Drug-resistant tuberculosis (DR-TB) is an increasing public health

concern in Iran, with multidrug-resistant tuberculosis (MDR-TB) posing significant challenges to disease control efforts. This study examines the prevalence of DR-TB in Iran from January 2000 to October 2023.
METHODS: A comprehensive systematic search was conducted across multiple databases, including PubMed, Scopus, Google Scholar, EMBASE, BioMed Central, and Web of Science. The search utilized specific keywords such as "drug-resistant tuberculosis," "DR-TB," "MDR-TB," "XDR-TB," "Iran," "prevalence," and "risk factors," among others. Boolean operators (AND/OR) were employed to refine the search results. Only articles published between January 2000 and October 2023 were considered for inclusion. The search strategy followed the PRISMA guidelines, and the review questions were formulated based on the PICO model. The initial search identified 750 records. After removing duplicates and screening the titles, abstracts, and full texts, a total of 9 articles that met the inclusion criteria were included in the systematic review.
RESULTS: Between 2000 and 2023, the prevalence of MDR-TB in Iran ranged from 5.1 to 11.3% among general TB cases, increasing to 36% among retreatment cases and 18.5% in border provinces such as Sistan-Baluchestan. Retreatment patients had a sixfold higher risk of MDR-TB compared to new cases. Comorbidities such as diabetes (OR: 2.3) and HIV (OR: 3.1), along with male sex and older age, were significant contributing factors-particularly in XDR-TB cases. Despite the rising trend in drug resistance, diagnostic and laboratory limitations remain major challenges. Key risk factors include a history of previous treatment, diabetes mellitus, limited access to healthcare, and socioeconomic barriers. Diagnostic difficulties, including inadequate laboratory capacity and underutilization of molecular diagnostic tools, further complicate TB control and management.
CONCLUSION: Addressing the rising prevalence of DR-TB in Iran requires urgent public health interventions, including strengthening healthcare infrastructure, improving access to diagnostic services, and implementing community-based education programs to reduce stigma and enhance treatment adherence. Without these measures, the burden of DR-TB is likely to increase, further complicating efforts to control this public health crisis.

DOI: 10.1186/s12879-025-11439-8
PMCID: PMC12335167
PMID: 40781658 [Indexed for MEDLINE]

Conflict of interest statement: Declarations. Ethics approval and consent to participate: Not applicable. Consent for publication: Not applicable.
Disclosure: During the preparation of this work, the authors used ChatGPT in order to check the grammar and improve readability. After using this tool, the authors reviewed and edited the content as needed and take full responsibility

for the content of the publication. Competing interests: The authors declare no competing interests.

4. Exploring β-lactam interactions with DacB1: unraveling optimal therapies for combating drug-resistant Mycobacterium tuberculosis.

mBio. 2025 Aug 13;16(8):e0137225. doi: 10.1128/mbio.01372-25. Epub 2025 Jul 10.

Nantongo M(1)(2), Nguyen DC(3), Shin E(2)(4), Bethel CR(2), Taracila MA(2)(4), Dousa KM(4)(5), Li Q(4), Fletcher S(4), Kurz SG(6), Kreiswirth BN(7), Boom WH(1)(4)(8), Holland S(9), Rubin EJ(10), Bonomo RA(1)(4)(5)(11).

Author information:
(1)Department of Molecular Biology and Microbiology, Case Western Reserve University (CWRU), Cleveland, Ohio, USA.
(2)Research Service, Louis Stokes Veterans Affairs Medical Center, Cleveland, Ohio, USA.
(3)Division of Infectious Diseases, Department of Pediatrics and Division of Infectious Diseases, Department of Internal Medicine, Rush University Medical Center, Chicago, Illinois, USA.
(4)Department of Medicine, CWRU, Cleveland, Ohio, USA.
(5)Medical Service, Veterans Affairs Northeast Ohio Healthcare System (VANEOHS), Cleveland, Ohio, USA.
(6)Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine, Yale School of Medicine, New Haven, Connecticut, USA.
(7)Center for Discovery and Innovation, Hackensack, New Jersey, USA.
(8)Division of Infectious Diseases and HIV Medicine, University Hospitals Cleveland Medical Center, Cleveland, Ohio, USA.
(9)Laboratory of Clinical Immunology and Microbiology, National Institutes of Health, National Institute of Allergy and Infectious Diseases, Bethesda, Maryland, USA.
(10)Department of Immunology and Infectious Diseases, Harvard T. H. Chan School of Public Health, Boston, Massachusetts, USA.
(11)Departments of Biochemistry, Pharmacology, and Proteomics and Bioinformatics, CWRU; Cleveland Geriatrics Research Education and Clinical Center (GRECC), VANEOHS; CWRU Cleveland VAMC Center for Antibiotic Resistance and Epidemiology (Case VA CARES), Cleveland, Ohio, USA.

Tuberculosis (TB) continues to pose a global public health threat, exacerbated by rising drug-resistant strains of Mycobacterium tuberculosis (Mtb). DacB1, a D,D-carboxypeptidase critical in Mtb peptidoglycan biosynthesis, is a promising target for β-lactam antibiotics (BLs), which remain underutilized in TB treatment. Dual BL therapy may enhance efficacy by inactivating multiple targets

within the peptidoglyan synthesis pathway. Minimum inhibitory concentrations (MICs) for β-lactams and β-lactamase inhibitors against Mtb H37Ra, H37Rv, and clinical isolates showed that imipenem, meropenem, or tebipenem MICs were reduced when combined with amoxicillin or ceftriaxone or β-lactamase inhibitors such as clavulanate or durlobactam. Timed electrospray ionization mass spectrometry (ESI-MS) captured acyl-enzyme adducts between DacB1 and BLs, revealing binding interactions with carbapenems (imipenem, meropenem, and tebipenem) but not most penicillins or cephalosporins except cloxacillin and cefoxitin. Differential scanning fluorimetry (DSF) combined with circular dichroism (CD) confirmed physical and structural changes in DacB1 upon BL binding despite no alteration in melting temperature. Carbapenem-DacB1 interactions were notably faster with imipenem, likely due to reduced steric hindrance compared to meropenem and tebipenem. Molecular modeling revealed conserved penicillin-binding protein motifs within the active site of DacB1: S121XXK124, S176XN178, and K282TG284 (PDB ID # 4PPR). Building on this, molecular docking suggested favorable interactions between these motifs and the carbapenems: the carbapenem carbonyl group aids in positioning within DacB1's oxyanion hole, ready for acylation, while hydrophobic interactions with the cyclic R2 side chains and C1 methyl groups in meropenem and tebipenem contribute to steric hindrance hence slow acyl-enzyme formation. These findings enhance our understanding of DacB1 inhibition and suggest that carbapenems, particularly in combination therapies, hold promise as effective TB treatments.
IMPORTANCE: TB remains a significant public health threat, particularly due to the rising prevalence of drug-resistant Mtb strains. Current treatment options for drug-resistant TB are costly, toxic, and often ineffective, necessitating the exploration of alternative therapeutic strategies. This study is of critical importance as it investigates the potential of β-lactam antibiotics (BLs), a class historically considered ineffective against Mtb, for repurposing in TB treatment. By targeting DacB1, a key enzyme in Mtb peptidoglycan biosynthesis, this research provides new insights into the mechanism of β-lactam interactions and their potential to disrupt cell wall synthesis. The findings demonstrate that dual β-lactam therapy and β-lactam/β-lactamase inhibitor combinations enhance antibiotic efficacy, suggesting a promising avenue for combating drug-resistant TB. Furthermore, structural and molecular analyses confirm that carbapenems, particularly imipenem, meropenem, and tebipenem, effectively bind to DacB1, paving the way for optimized treatment strategies. Given the challenges in developing new TB drugs, repurposing β-lactams offers a cost-effective and readily implementable solution to address antimicrobial resistance. This study contributes valuable knowledge that could accelerate the development of novel TB therapies, improve treatment success rates, and ultimately reduce TB-related mortality worldwide.

DOI: 10.1128/mbio.01372-25
PMCID: PMC12345272

PMID: 40637416 [Indexed for MEDLINE]

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

5. Vitamin C potentiates the killing of Mycobacterium tuberculosis by bedaquiline through metabolic disruption.

mBio. 2025 Aug 13;16(8):e0148425. doi: 10.1128/mbio.01484-25. Epub 2025 Jun 25.

Vilchèze C(1), Rajagopalan S(1), Kalluru RS(2), Banaei N(2), Jacobs WR Jr(1).

Author information:
(1)Department of Microbiology and Immunology, Albert Einstein College of Medicine, Bronx, New York, USA.
(2)Department of Pathology, Stanford University School of Medicine, Stanford, California, USA.

Tuberculosis (TB), a disease caused by the bacterium Mycobacterium tuberculosis (Mtb), continues to pose a major global health threat, exacerbated by the emergence of drug-resistant strains and the lengthy treatment regimens required for effective management. Bedaquiline (BDQ), a key component in novel regimens for multidrug-resistant (MDR) TB, has demonstrated significant efficacy but is threatened by rising resistance. Our study investigates the potential of vitamin C to enhance BDQ's activity and prevent resistance. We found that combining BDQ with vitamin C sterilized drug-susceptible and MDR Mtb cultures in vitro within 21 days, achieving a 6-log reduction in colony-forming units. This combination also enhanced Mtb killing in infected human macrophages and peripheral blood mononuclear cells. Transcriptomic analysis revealed that the BDQ/vitamin C combination induces widespread metabolic disruption in Mtb, characterized by upregulation of stress response and metal ion homeostasis genes and downregulation of energy metabolism and cell wall biosynthesis genes. Mechanistic studies implicated reactive oxygen species and disrupted copper homeostasis as contributing factors to the sterilization effect. These findings highlight the potential of using vitamin C as an adjunct therapy with BDQ, offering a promising strategy to enhance drug efficacy and mitigate emerging drug resistance during MDR-TB treatment.
IMPORTANCE: Tuberculosis (TB) remains a major global health problem, especially as drug-resistant forms become more common and harder to treat. Bedaquiline is one of the most important new drugs for treating these resistant infections, but resistance to bedaquiline is also starting to appear. This study found that the combination of vitamin C and bedaquiline sterilizes Mycobacterium tuberculosis cultures in vitro while potentiating bedaquiline activity in infected human macrophage cells. The combination appears to overwhelm the bacteria by creating

stress and disrupting essential functions, like energy production and metal balance. These results suggest that vitamin C, a safe and inexpensive supplement, could be used alongside existing drugs to make treatment faster and more effective while also helping to prevent resistance.

DOI: 10.1128/mbio.01484-25
PMCID: PMC12345178
PMID: 40558048 [Indexed for MEDLINE]

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

6. Mixed infections and heteroresistance of Mycobacterium tuberculosis among multidrug-resistant tuberculosis in China: a genomic epidemiology study.

Emerg Microbes Infect. 2025 Dec;14(1):2534656. doi: 10.1080/22221751.2025.2534656. Epub 2025 Aug 1.

Liu Y(1), Zhang Y(2), Lu X(1), Wu Z(2), Li M(1), Zhang R(1), Lu Y(1), Hou R(1), Ji Y(1), Zhang Q(1), Jiang Q(3), Li J(2), Jiang Y(2), Wang Y(4), Yuan J(5), Takiff HE(6), Chen X(7), Shen X(2), Yang C(1)(8).

Author information:
(1)School of Public Health (Shenzhen), Shenzhen Key Laboratory of Pathogenic Microbes and Biosafety, Shenzhen Campus of Sun Yat-sen University, Sun Yat-sen University, Guangdong, People's Republic of China.
(2)Division of TB and HIV/AIDS Prevention, Shanghai Municipal Center for Disease Control and Prevention, Shanghai, People's Republic of China.
(3)Department of Epidemiology and Biostatistics, School of Public Health, Wuhan University, Wuhan, People's Republic of China.
(4)Department of Tuberculosis Prevention and Control, Bao'An Chronic Disease Prevention and Cure Hospital in Shenzhen, Shenzhen, People's Republic of China.
(5)Nanshan District Center for Disease Control and Prevention, Shenzhen, People's Republic of China.
(6)CMBC, Instituto Venezolano de Investigaciones Científicas, IVIC, Caracas, Venezuela.
(7)Shanghai Municipal Center for Disease Control and Prevention, Shanghai, People's Republic of China.
(8)Guangdong Provincial Highly Pathogenic Microorganism Science Data Center, Key Laboratory of Tropical Disease Control, Ministry of Education, Sun Yat-sen University, Guangdong, People's Republic of China.

Mixed infection refers to the presence of multiple Mycobacterium tuberculosis strains within one host, while heteroresistance denotes the coexistence of

drug-susceptible and drug-resistant strains or genotypes. Mixed infections and heteroresistance with Mycobacterium tuberculosis can complicate drug resistance diagnosis, treatment options, and transmission inference. We conducted a population-based genomic epidemiological study of multidrug-resistant tuberculosis (MDR-TB) in Shanghai, China, between January 1, 2005, and December 31, 2018, to evaluate the prevalence and impact of mixed infection and heteroresistance on MDR-TB diagnosis and treatment outcomes. Demographic, clinical, and laboratory data were collected, and factors associated with mixed infections and heteroresistance were identified with multivariable logistic regression analysis. Among the 936 MDR-TB patients in our study, 10.8% (101/936) had mixed infections and 16.5% (154/936) exhibited heteroresistance, which was more frequent with second-line anti-TB drugs ($P < 0.01$). There was a higher risk of heteroresistance in older patients (≥60 years: aOR 1.91, 95% CI 1.02-3.57), patients with diabetes (2.59, 1.36-4.91), and mixed infections (2.85, 1.67-4.88). Mixed infections and heteroresistance accounted for 22.6% (58/257) of the strains with discrepancies between phenotypic and genotypic drug susceptibility testing (DST). Strains with heteroresistance to EMB had a higher discordance rate than those without (29.1% VS 17.2%, $P < 0.05$). Isolates that were phenotypically susceptible but genotypically resistant harboured minority or low-frequency resistance mutations and were more common in patients with mixed infections and heteroresistance. In summary, mixed infections are significantly associated with heteroresistance, and both mixed infections and heteroresistance can lead to discrepancies between phenotypic and genotypic DST.

DOI: 10.1080/22221751.2025.2534656
PMCID: PMC12320256
PMID: 40748858 [Indexed for MEDLINE]

Conflict of interest statement: No potential conflict of interest was reported by the authors.

7. Global, regional, and national burden and trends of multidrug-resistant tuberculosis and extensively drug-resistant tuberculosis in adolescents and adults aged 15-49 years from 2010 to 2021: insights from the global burden of disease study 2021.

BMC Med. 2025 Jul 28;23(1):445. doi: 10.1186/s12916-025-04269-7.

Cui K(1), Zhao X(1), Liu W(1), Bai L(2).

Author information:
(1)Center of Infectious Diseases, West China Hospital of Sichuan University, Chengdu, China.

(2)Center of Infectious Diseases, West China Hospital of Sichuan University, Chengdu, China. pangbailang@163.com.

BACKGROUND: Multidrug-resistant tuberculosis (MDR-TB) and extensively drug-resistant tuberculosis (XDR-TB) among those aged 15-49 years pose a severe public health challenge, yet our understanding of the burden of these diseases in this age group remains limited. This study aimed to evaluate the trends in MDR-TB and XDR-TB burden among this population from 2010 to 2021 across global, regional, and national levels.
METHODS: This study extracted four key indicators-incidence, prevalence, deaths, and disability-adjusted life years (DALYs) per 100,000 population-for MDR-TB and XDR-TB among 15-49 years from the 2021 Global Burden of Disease (GBD) study. It assessed the burden trends using percentage change (PC) and estimated annual percentage change (EAPC), with further analysis by age, sex, and sociodemographic index (SDI).
RESULTS: In 2021, the global incidence, prevalence, deaths, and DALYs of MDR-TB among adolescents and young adults were 241,399, 336,746, 33,285, and 1,896,002, respectively. Global MDR-TB incidence and DALYs rates showed slight decreases since 2010, with EAPCs of -0.76 and -2.61, respectively. In 2021, the global incidence, prevalence, deaths, and DALYs of XDR-TB among adolescents and young adults were 12,861, 14,039, 2442, and 133,610, respectively. Since 2010, global XDR-TB incidence rates have increased, with an EAPC of 0.57, while prevalence and death rates have decreased, with EAPCs of - 2.67 and - 2.87, respectively. The incidence and prevalence rates of MDR-TB were significantly decreased since 2010 in high SDI, high-middle SDI, and low SDI regions. The prevalence rate of XDR-TB was significantly decreased since 2010 in the high SDI and high-middle SDI regions, while a significant increase was observed in the middle SDI, low-middle SDI, and low SDI regions. Furthermore, a gradual decline was observed in the burden of MDR-TB and XDR-TB as the SDI level increases. The burden of MDR-TB and XDR-TB showed an upward trend during the COVID-19 epidemic.
CONCLUSIONS: The burden of MDR-TB and XDR-TB among adolescents and young adults remained very severe, particularly in the middle SDI and low-middle SDI regions. The COVID-19 pandemic may impact the global burden of these drug-resistant tuberculosis. Targeted interventions are crucial to address this issue.

DOI: 10.1186/s12916-025-04269-7
PMCID: PMC12305936
PMID: 40721781 [Indexed for MEDLINE]

Conflict of interest statement: Declarations. Ethics approval and consent to participate: Ethical approval and informed consent were waived because the GBD 2021 study is publicly available and no identifiable information was included in

the analyses. Consent for publication: Not applicable. Competing interests: The authors declare no competing interests.

8. Operational considerations of select new treatment recommendations for drug-susceptible and drug-resistant tuberculosis.

J Clin Tuberc Other Mycobact Dis. 2025 May 24;40:100536. doi: 10.1016/j.jctube.2025.100536. eCollection 2025 Aug.

Wilson JW(1), Temesgen Z(1), Gaensbauer JT(2).

Author information:
(1)Division of Public Health, Infectious Diseases, Occupational Medicine, Section of Infectious Diseases, Mayo Clinic College of Medicine, USA.
(2)Division of Pediatric Infectious Diseases, Mayo Clinic College of Medicine, USA.

A number of management updates recently have been published for both drug-susceptible and drug-resistant tuberculosis (TB), TB in children, and contacts of patients with drug-resistant TB. The operationalization and application of these recommendations, which reflect favorable clinical trial outcomes, may vary significantly for different patient groups and in different settings. Defining the best treatment approach for each patient requires the integration of multiple data points including organism culture growth and corresponding drug susceptibility profiles, specific TB syndrome, concurrent patient co-morbidities and available public health resources. We review several updated TB treatment recommendations and discuss applicable strengths, select limitations and corresponding precautions as they pertain to diverging patient groups, TB syndromes, and public health capacity.

DOI: 10.1016/j.jctube.2025.100536
PMCID: PMC12166396
PMID: 40520337

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.

9. Xpert MTB/RIF Ultra assay for pulmonary tuberculosis and rifampicin resistance in adults and adolescents.

Cochrane Database Syst Rev. 2025 Jul 29;7(7):CD009593. doi: 10.1002/14651858.CD009593.pub6.

Horne DJ(1), Zifodya JS(2), Shapiro AE(3), Church EC(4), Kreniske JS(5), Kay AW(6), Scandrett K(7), Steingart KR(8), Takwoingi Y(7).

Author information:
(1)Department of Medicine, Division of Pulmonary, Critical Care & Sleep Medicine, University of Washington, Seattle, Washington, USA.
(2)Department of Medicine, Section of Pulmonary, Critical Care & Environmental Medicine, Tulane University, New Orleans, Louisiana, USA.
(3)Departments of Global Health and Medicine, Division of Allergy and Infectious Diseases, University of Washington, Seattle, Washington, USA.
(4)Division of Vaccines and Infectious Diseases, Fred Hutchinson Cancer Center, Seattle, Washington, USA.
(5)Department of Medicine, Division of Pulmonary & Critical Care Medicine, Weill Cornell Medical College, New York, New York, USA.
(6)The Global Tuberculosis Program, Texas Children's Hospital, Section of Global and Immigrant Health, Department of Pediatrics, Baylor College of Medicine, Houston, Texas, USA.
(7)Department of Applied Health Sciences, University of Birmingham, Birmingham, UK.
(8)Honorary Research Fellow (retired), Department of Clinical Sciences, Liverpool School of Tropical Medicine, Liverpool, UK.

Update of
doi: 10.1002/14651858.CD009593.pub5.

BACKGROUND: Xpert MTB/RIF Ultra (Xpert Ultra) is a molecular World Health Organization (WHO)-recommended rapid diagnostic test that simultaneously detects tuberculosis and rifampicin resistance. This review updates a comparative accuracy Cochrane review of Xpert MTB/RIF and Xpert Ultra as Xpert Ultra has replaced Xpert MTB/RIF.
OBJECTIVES: To determine the diagnostic accuracy of Xpert MTB/RIF Ultra (Xpert Ultra) for detecting pulmonary tuberculosis and rifampicin resistance in adults and adolescents with presumptive tuberculosis based on signs or symptoms or with an abnormal chest x-ray suggestive of tuberculosis.
SEARCH METHODS: We searched seven databases including CENTRAL, MEDLINE, and Embase, plus two trial registers (ClinicalTrials.gov and the WHO ICTRP) to 16 October 2023 without language restrictions. A WHO Public Call for ongoing and unpublished studies was made between 30 November 2023 and 15 February 2024.
SELECTION CRITERIA: We included cross-sectional studies, cohort studies, and randomised controlled trials that provided data on the diagnostic accuracy of

Xpert Ultra using respiratory specimens in adolescents (aged 10 to 14 years) and adults (aged 15 years and older) with presumptive pulmonary tuberculosis. For pulmonary tuberculosis detection, the reference standards were culture and a composite reference standard. For rifampicin resistance, the reference standards were culture-based phenotypic drug susceptibility testing with or without whole genome sequencing.

DATA COLLECTION AND ANALYSIS: Two review authors independently extracted data using a standardised form. We assessed risk of bias using QUADAS-2. We performed meta-analyses using a bivariate model to produce summary sensitivities and specificities, separately for pulmonary tuberculosis detection and rifampicin resistance detection. We performed subgroup analyses by smear status, HIV status, and history of tuberculosis. We summarised Xpert Ultra trace-positive results.

MAIN RESULTS: Pulmonary tuberculosis detection For detection of pulmonary tuberculosis, Xpert Ultra summary sensitivity and specificity against culture were 90.7% (95% confidence interval (CI) 88.2 to 92.7) and 94.8% (95% CI 92.8 to 96.3) (32 studies, 12,529 participants; high-certainty evidence). Most studies had low risk of bias in all QUADAS-2 domains. If the point estimates for Xpert Ultra are applied to a hypothetical cohort of 1000 people, where 100 of those presenting with symptoms have pulmonary tuberculosis, Xpert Ultra will miss nine cases. The number of people wrongly diagnosed with pulmonary tuberculosis would be 47. In people living with HIV, Xpert Ultra summary sensitivity and specificity were 87.7% (82.0 to 91.7) and 95.3% (92.2 to 97.2) (11 studies, 1164 participants). Amongst people with smear-negative, culture-positive pulmonary tuberculosis, Xpert Ultra summary sensitivity and specificity were 80.7% (75.4 to 85.0) and 94.0% (91.3 to 95.9) (16 studies, 6460 participants). In people with a history of tuberculosis, Xpert Ultra summary sensitivity and specificity were 84.8% (78.2 to 89.7) and 86.2% (78.9 to 91.3) (9 studies, 809 participants). The proportion of Ultra trace-positive results that were true positives compared to the microbiological reference standard was 38.8%. Reclassifying trace-positive results as Xpert Ultra-negative led to a reduction in sensitivity and modest increase in specificity. Rifampicin resistance detection For detection of rifampicin resistance, Xpert Ultra summary sensitivity and specificity were 95.8% (93.2 to 97.4) and 98.3% (97.0 to 99.0) (10 studies, 1644 participants; high-certainty evidence). Most studies had low risk of bias in all QUADAS-2 domains. If the point estimates for Xpert Ultra are applied to a hypothetical cohort of 1000 people, where 100 of those presenting with symptoms have rifampicin resistance, Xpert Ultra will miss four cases. The number of people wrongly diagnosed with rifampicin resistance would be 16 out of the 900 who do not have rifampicin resistance. Xpert Ultra performed similarly, for rifampicin resistance, in people with smear-positive and smear-negative tuberculosis.

AUTHORS' CONCLUSIONS: Xpert Ultra has high sensitivity and specificity for detection of pulmonary tuberculosis rifampicin resistance. Xpert Ultra for the

detection of pulmonary tuberculosis has lower sensitivity in people with smear-negative/culture-positive tuberculosis and lower sensitivity and specificity in people with a history of tuberculosis. Xpert Ultra trace-positive results were common. Strengths of this review include the approach to identifying relevant studies, the number of studies and participants included in this systematic review, and that most studies were at low risk of bias. The small number of studies (six) and participants who were adolescents is a limitation to our accuracy estimates in this age group. Xpert Ultra testing provides accurate results and can allow rapid initiation of treatment for rifampicin-resistant and multiple-drug-resistant tuberculosis.
FUNDING: The WHO supported this systematic review. Liverpool School of Tropical Medicine hosted the Cochrane Infectious Diseases Group (CIDG) editorial base, which supported the authors in the development of this review update. The Foreign, Commonwealth and Development Office funded the CIDG.
REGISTRATION: Generic protocol available on Open Science Framework via https://osf.io/26wg7/wiki/home/. Previous protocol and review versions available via DOI 10.1002/14651858.CD009593 and DOI 10.1002/14651858.CD009593.pub5.

DOI: 10.1002/14651858.CD009593.pub6
PMCID: PMC12305759
PMID: 40728034 [Indexed for MEDLINE]

Conflict of interest statement: DJH received funding from the World Health Organization Global Tuberculosis Programme, Switzerland. JSZ received funding from the World Health Organization Global Tuberculosis Programme, Switzerland. In addition, JSZ has served as an expert witness for Hautot and Hautot Law and is the Fiduciary Officer for The 18th Ward Sports Club. AES received funding from the World Health Organization Global Tuberculosis Programme, Switzerland. AES is a member of International Union Against Tuberculosis and Lung Disease, Infectious Diseases Society of America, and International AIDS Society. ECC received funding from the World Health Organization Global Tuberculosis Programme, Switzerland and has contributed to a systematic review commissioned by Foundation for Innovative New Diagnostics. ECC is employed by Public Health – Seattle & King County. JSK received funding from the World Health Organization Global Tuberculosis Programme, Switzerland. KS received funding from the World Health Organization Global Tuberculosis Programme, Switzerland. AWK received funding from the World Health Organization Global Tuberculosis Programme, Switzerland. KRS received funding from the World Health Organization Global Tuberculosis Programme, Switzerland. In addition, KRS has served as a consultant for Amsterdam UMC, Foundation for Innovative New Diagnostics, University of Birmingham, and World Health Organization. KRS is a Cochrane Editor but was not

involved in the editorial process for this review. YT received funding from the World Health Organization Global Tuberculosis Programme, Switzerland. YT is a Cochrane Editor but was not involved in the editorial process for this review. The authors have no financial involvement with any organisation or entity with a financial interest in or financial conflict with the subject matter or materials discussed in this review apart from those disclosed.

10. Genomic decoding of drug-resistant tuberculosis transmission in Thailand over three decades.

Sci Rep. 2025 Aug 13;15(1):29617. doi: 10.1038/s41598-025-15093-7.

Thawong N(#)(1)(2), Srilohasin P(#)(3), Phelan JE(1), Phornsiricharoenphant W(4), Tongsima S(4), Suriyaphol P(3), Prammananan T(4), Faksri K(5), Sawaengdee W(2), Wang L(1), Hinthong W(1), Hibberd ML(1), Campino S(1), Wattanapokayakit S(2), Mahasirimongkol S(#)(2), Chaiprasert A(#)(6), Clark TG(#)(7)(8).

Author information:
(1)Department of Infection Biology, Faculty of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, London, WC1E 7HT, UK.
(2)Department of Medical Sciences, Ministry of Public Health, Nonthaburi, Thailand.
(3)Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok, 10700, Thailand.
(4)Ministry of Higher Education, Science, Research and Innovation, National Science and Technology Development Agency, Bangkok, Thailand.
(5)Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand.
(6)Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok, 10700, Thailand. Angkana.cha@mahidol.ac.th.
(7)Department of Infection Biology, Faculty of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, London, WC1E 7HT, UK. taane.clark@lshtm.ac.uk.
(8)Faculty of Epidemiology and Population Health, London School of Hygiene & Tropical Medicine, London, UK. taane.clark@lshtm.ac.uk.
(#)Contributed equally

Thailand has a high burden of tuberculosis, with control efforts hindered by drug-resistant Mycobacterium tuberculosis (Mtb). The increasing use of whole-genome sequencing (WGS) of Mtb offers valuable insights for clinical management and public health surveillance. WGS can be used to profile drug resistance, identify circulating sub-lineages, and trace transmission pathways or outbreaks. We analysed WGS data from 2,005 Mtb isolates collected across Thailand from 1994-2020, including 816 retrieved and 1,189 newly sequenced

samples, with most isolates being multidrug-resistant (MDR-TB). Most isolates are lineage two strains (78·3%), primarily the Beijing sub-lineage (L2.2.1). Drug resistance profiling revealed substantial isoniazid and rifampicin resistance, and 67·3% classified as MDR-TB. Phenotypic and genotypic drug susceptibility testing showed high concordance (91·1%). Clustering analysis identified 206 transmission clades (maximum size 288), predominantly with MDR-TB, especially in Central and Northeastern regions. One cluster (n = 22) contains the ddn Gly81Ser mutation, linked to delamanid resistance, with some members pre-dating drug roll-out. In the largest cluster (n = 288), containing isolates spanning two decades, we applied transmission reconstruction methods to estimate a mutation rate of 1·1 × 10-7 substitutions per site per year. Overall, this study demonstrates the value of WGS in uncovering TB transmission and drug resistance, offering key data to inform better control strategies in Thailand and elsewhere.

DOI: 10.1038/s41598-025-15093-7
PMCID: PMC12344131
PMID: 40796628

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

11. Bactericidal activity of gallic acid against multidrug-resistant Mycobacterium Tuberculosis.

Arch Microbiol. 2025 Aug 11;207(9):218. doi: 10.1007/s00203-025-04422-z.

Wei M(1), Bostani A(2), Jamalsi N(2), Baqin H(2), Wen P(3).

Author information:
(1)Department of Respiratory and Critical Care Medicine, Shandong Public Health Clinical Center, Shandong University, Shandong, 250013, China.
(2)Medical Laboratory Department, Amir A'lam Hospital, Tehran, Iran.
(3)Department of Respiratory and Critical Care Medicine, Shandong Public Health Clinical Center, Shandong University, Shandong, 250013, China.
wp1980jn@sina.com.

The persistent rise of multidrug-resistant (MDR) bacteria represents a significant public health challenge, necessitating the exploration of alternative therapeutic options. The slow pace of approval for new anti-tuberculosis (TB) medications underscores the urgent need to identify

potential alternative agents. Gallic acid (GA) possesses numerous biological properties, including antibacterial and antiseptic effects. In this study, both standard and MDR strains of M. tuberculosis were utilized to assess the antibacterial efficacy of GA and related mechanisms. GA achieved minimum inhibitory and minimum bactericidal concentrations comparable to those of the examined antibiotics with significantly lower cytotoxicity in the THLE-3 cell line (p-value < 0.05). Furthermore, GA displayed bactericidal properties, enhanced the effectiveness of moxifloxacin and levofloxacin against MDR M. tuberculosis, and modulated the expression of efflux pump genes, specifically Rv1410c and Rv1258c (p-value < 0.001). These results contribute to a deeper understanding of GA's antibacterial potential and suggest a novel alternative approach for managing MDR bacterial infections.

DOI: 10.1007/s00203-025-04422-z
PMCID: PMC12339633
PMID: 40788398 [Indexed for MEDLINE]

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

12. Tuberculosis infection control in MDR-TB designated hospitals in Jiangsu Province, China.

J Clin Tuberc Other Mycobact Dis. 2025 Jul 29;41:100555. doi: 10.1016/j.jctube.2025.100555. eCollection 2025 Dec.

Song H(1), Li G(1), Xu Z(2), Wang F(3), Wang X(4), Dai B(5), Zhang X(6), Li J(7), Li Y(1), Zhu L(1).

Author information:
(1)Department of Chronic Communicable Disease, Jiangsu Provincial Center for Disease Control and Prevention, People's Republic of China.
(2)Department of Chronic Communicable Disease, Wuxi Municipal Center for Disease Control and Prevention, People's Republic of China.
(3)Tuberculosis Control Center, Suzhou Municipal Center for Disease Control and Prevention Tuberculosis Control Center, People's Republic of China.
(4)Department of Chronic Communicable Disease, Nantong Municipal Center for Disease Control and Prevention, People's Republic of China.
(5)Department of Chronic Communicable Disease, Zhenjiang Municipal Center for Disease Control and Prevention, People's Republic of China.
(6)Department of Chronic Communicable Disease, Changzhou Municipal Center for

Disease Control and Prevention, People's Republic of China.
(7)Department of Chronic Communicable Disease, Yangzhou Municipal Center for Disease Control and Prevention, People's Republic of China.

BACKGROUND: Hospital-acquired Tuberculosis (TB) infections among healthcare workers (HCWs) and patients present a significant challenge due to the increased risk of TB infection within healthcare settings.
METHODS: A standardized assessment tool was applied for the evaluation, which involved direct observation, document review, and interviews with facility heads. A baseline evaluation of TB infection control (TBIC) measures in TB outpatient and inpatient departments, as well as laboratories, was completed by January 2019. Based on the results, a comprehensive intervention package was implemented, incorporating a three-tiered hierarchy of controls: administrative control (AC), environmental control (EC), and respiratory protection (RP). Subsequent monitoring was conducted quarterly, with corrective actions accordingly. More than two years of follow-up data were collected, with the collaboration of local hospitals, the municipality Centers for Disease Control and Prevention (CDC), and the Jiangsu Provincial CDC, concluding on August 31, 2021.
RESULTS: At baseline, the average implementation rates of AC, EC and RP were 57.3 %, 59.2 %, and 66.6 %, respectively. After the intervention, significant improvements were observed in key infection control measures. A triage process for cough patients was established, mechanical ventilation systems were installed, and the use of masks was improved. In addition, ultraviolet (UV) and upper-room ultraviolet germicidal irradiation (UVGI) systems were installed where required. As a result, the average implementation rates of AC, EC and RP significantly increased to 86.3 %, 87.4 %, and 98.4 % ($P < 0.05$), respectively. However, at the study's conclusion, Suzhou Fifth People's Hospital reported a lower AC implementation rate of 70.7 %, while Changzhou Third People's Hospital had an EC implementation rate of 68.1 %. These discrepancies were primarily attributed to suboptimal architectural designs that hindered proper ventilation in the wards.
CONCLUSIONS: This study demonstrates that designated hospitals still face persistent gaps in tuberculosis infection control (TBIC). However, over the course of one and a half years of targeted and standardized interventions, substantial improvements in TBIC practices were achieved across most participating institutions. Despite the suboptimal availability of dedicated TB wards, strengthening TBIC measures remains crucial to reducing TB transmission among healthcare workers and non-TB patients. This approach is both practical and scalable, particularly in high-burden TB settings. Nevertheless, the long-term efficacy and sustainability of these TBIC practices warrant ongoing evaluation.

DOI: 10.1016/j.jctube.2025.100555
PMCID: PMC12340389
PMID: 40809299

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.

13. Global prevalence of tuberculosis and drug-resistant forms: A 30-year analysis from 1990 to 2019.

J Glob Antimicrob Resist. 2025 Jul 23;44:411-419. doi: 10.1016/j.jgar.2025.07.012. Online ahead of print.

Lv X(1), Ji X(2), Xiong L(1), Chen Y(3), Wang H(3), Yang Y(4).

Author information:
(1)Zhongshan Hospital, Fudan University (Xiamen Branch), Xiamen, China.
(2)The Second Affiliated Hospital of Shantou University Medical College, Shantou, China.
(3)Xiang'an Hospital of Xiamen University, Xiamen, China.
(4)Xiang'an Hospital of Xiamen University, Xiamen, China. Electronic address: yangying77777@xmu.edu.cn.

OBJECTIVES: Tuberculosis (TB) remains a major global health threat. Multidrug-resistant (MDRTB) and extensively drug-resistant TB (XDRTB) present growing challenges. This study aims to analyze the global and national prevalence trends of TB and its subtypes from 1990 to 2019.
METHODS: This study utilised Global Burden of Disease data to analyse age-standardised prevalence rates (ASPR) and evaluate the global and national prevalence trends of TB and its subtypes from 1990 to 2019.
RESULTS: Global TB prevalence is declining but MDRTB and XDRTB are rising sharply. In 2019, TB ASPR was 23 085 per 100 000, falling 1.044% annually since 1990. Latent TB infection decreased 1.044% yearly to 22 906 per 100 000 in 2019. Drug-susceptible TB fell 1.692% annually to 169 per 100 000 in 2019. MDRTB rose 6.008% yearly, reaching 8.6 per 100 000 in 2019. XDRTB increased 71.746% yearly to 0.4 per 100 000. Rates varied widely between countries. ASPR tended to be higher in males and poorer regions. Pace of change differed by sex, socioeconomics and geography.
CONCLUSIONS: Substantial variations exist in TB prevalence and trends globally, reflecting inequities. Findings provide comprehensive long-term TB assessments, with rising multidrug resistance threatening progress and elimination goals.

Urgent targeted strategies are needed for high-risk groups, surveillance, resources, commitment and political will, especially in disadvantaged populations.

DOI: 10.1016/j.jgar.2025.07.012
PMID: 40712777

14. The Frequency and Incidence of QT Prolongation With Extended Use of Bedaquiline or Delamanid in a Large, Multi-Country Multidrug-Resistant/Rifampicin-Resistant Tuberculosis Cohort.

Clin Infect Dis. 2025 Aug 1;81(1):153-158. doi: 10.1093/cid/ciae601.

Khan U(1)(2), Rich M(3)(4), Franke MF(4)(5), Lachenal N(6), Ahmed S(7), Bekele A(8), Isani AK(9), Hewison C(10), Sari CYI(11), Tan CL(12), Varaine F(10), Flores EH(13), Putri FA(14), Faqirzai J(15), Beauchamp J(16), Vo LNQ(17)(18), Siddiqui MR(19), Seung K(3)(4), Bastard M(20), Nkunkanyirazo P(21), Kiria N(22), Khan M(23), Algozhin Y(24), Melikyan N(20), Saki NA(25), Vilbrun SC(26), Fatima R(27), Naing YY(28), Islam S(29), Mamsa S(30), Mitnick CD(4)(5), Huerga H(20), Khan PY(1)(31).

Author information:
(1)Interactive Research & Development (IRD) Global, Singapore, Singapore.
(2)Department of Epidemiology, Biostatistics and Occupational Health, McGill University, Montreal, Quebec, Canada.
(3)Division of Global Health Equity, Brigham and Women's Hospital, Boston, Massachusetts, USA.
(4)Partners In Health, Boston, Massachusetts, USA.
(5)Department of Global Health and Social Medicine, Harvard Medical School, Boston, Massachusetts, USA.
(6)Pharmacovigilance Unit, Médecins Sans Frontières, Geneva, Switzerland.
(7)Interactive Research & Development (IRD), Karachi, Pakistan.
(8)Addis Ababa University College of Health Sciences, Addis Ababa, Ethiopia.
(9)Communicable Disease Control (CDC), Directorate General Health Services, Sindh, Pakistan.
(10)Medical Department, Médecins Sans Frontières, Paris, France.
(11)RS Islam Jakarta Cempaka Putih, Jakarta, Indonesia.
(12)Médecins Sans Frontières, Minsk, Belarus.
(13)Arzobispo Loayza Hospital, Lima, Peru.
(14)Interactive Research & Development (IRD), Jakarta, Indonesia.
(15)Médecins Sans Frontières, Yerevan, Armenia.

(16)Zanmi Lasante, Cange, Haiti.
(17)Friends for International TB Relief, Hanoi, Vietnam.
(18)Department of Global Public Health, WHO Collaboration Centre on Tuberculosis and Social Medicine, Karolinska Institute, Stockholm, Sweden.
(19)Institute of Chest Diseases (ICD) Kotri, Sindh, Pakistan.
(20)Field Epidemiology Department, Epicentre, Paris, France.
(21)Partners In Health, Lesotho, Maseru, Lesotho.
(22)Médecins Sans Frontières, Tbilisi, Georgia.
(23)Interactive Research & Development (IRD), Durban, South Africa.
(24)Partners In Health, Almaty, Kazakhstan.
(25)National TB Programme, Dhaka, Bangladesh.
(26)GHESKIO Institute of Infectious Diseases and Reproductive Health, NTP, Port-au-Prince, Haiti.
(27)National TB Control Program, Common Management Unit (HIV, TB, Malaria), Islamabad, Pakistan.
(28)Médecins Sans Frontières, Yangon, Myanmar.
(29)Interactive Research & Development (IRD), Dhaka, Bangladesh.
(30)Indus Hospital and Health Network (IHHN), Karachi, Pakistan.
(31)Clinical Research Department, Faculty of Infectious and Tropical Diseases, London School of Hygiene & Tropical Medicine, London, United Kingdom.

BACKGROUND: The 2022 World Health Organization (WHO) guidelines on multidrug-resistant/rifampicin-resistant tuberculosis (MDR/RR-TB) recommend 6 months of bedaquiline (Bdq) in the all-oral 9-month shorter regimen and 6 months or longer for Bdq and delamanid (Dlm) in the 18-20-month longer regimen. However, lack of evidence on extended treatment using Bdq or Dlm has limited their use to 6 months. We examine the frequency and incidence of QT prolongation based on duration of Bdq and/or Dlm use in longer regimens.
METHODS: We analyzed a prospective cohort of MDR/RR-TB patients from 16 countries who initiated treatment with Bdq and/or Dlm containing regimens from 1 April 2015 to 30 September 2018. Data were systematically collected using a shared protocol. The outcome of interest was the first clinically relevant prolonged QT interval (grade 3 or above) or a serious adverse event (SAE) involving prolonged QT of any grade.
RESULTS: Among 2553 patients, 59% received >6 months of Bdq and/or Dlm. Of these, 579 (20.9%) patients experienced a prolonged QT event, the majority (95.5%) being grade 1 or 2. Sixty-four (2.5%) patients experienced the outcome of interest with only 12 (0.5%) having ≥1 QT prolonging drugs permanently suspended. The incidence rate of the first prolonged QT event was highest in the first six months of treatment and lower in subsequent 6-month periods.
CONCLUSIONS: We demonstrate that Bdq and/or Dlm use beyond 6 months is safe in longer MDR/RR-TB regimens with most clinically relevant QT prolongation events occurring in the first 6 months. Electrocardiogram (ECG) monitoring for early identification of QT prolongating events is possible in programmatic conditions.

DOI: 10.1093/cid/ciae601
PMCID: PMC12314499
PMID: 39658125 [Indexed for MEDLINE]

Conflict of interest statement: Potential conflicts of interest. M. F. F. declares support through a National Institutes of Health (NIH)-funded grant. P. Y. K. declares participation on a DSMB board for an NIH R01 study. All other authors report no potential conflicts. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

15. Improving Treatment Adherence in Youths With Multidrug-Resistant Tuberculosis With Psychosocial Intervention.

Brain Behav. 2025 Aug;15(8):e70665. doi: 10.1002/brb3.70665.

Dhumal G(1)(2), Nevrekar N(1)(2), Gupte N(1), Shrisunder R(1)(2), Kulkarni P(1)(2), Sarpotdar S(2), Pm A(1), Hosmani A(3), Lokhande R(4), Gupta A(5), Suryavanshi N(1)(2).

Author information:
(1)Johns Hopkins Center for Infectious Diseases in India, Pune, Maharashtra, India.
(2)Byramjee Jeejeebhoy Government Medical College Clinical Trial Unit-Johns Hopkins University, Pune, Maharashtra, India.
(3)Aundh Chest Hospital, Pune, India.
(4)Byramjee Jeejeebhoy Government Medical College and Sassoon General Hospitals, Pune, India.
(5)Johns Hopkins University, Baltimore, USA.

INTRODUCTION: Multidrug-resistant tuberculosis (MDR-TB) deeply impacts the well-being of adolescents and young adults (AYA), resulting in poor treatment adherence. Identifying psychosocial challenges and preferred interventions is essential to enhance treatment adherence and outcomes in this unique group.
METHODS: This was a mixed-method study where participants aged between 15 and 24 years, diagnosed with MDR-TB, were recruited for in-depth interviews and a semi-structured questionnaire.
RESULTS: The individual-level psychosocial challenges included mental stress, suicidal ideation, reluctance to continue medication, perceived and experienced

stigma, and socio-economic burdens. Health system-related challenges encompassed delayed diagnosis, drug stockouts, and negative experiences with Health Care Providers (HCPs). Among 75 participants, the median age was 20.5 years, with 57% (n = 41) females, 85% (n = 62) single, and a median treatment duration of 8 months at the interview. Seventy-two percent (n = 54) of the participants reported psychological issues such as irritation, loneliness, anxiety, sleep disorder, suicidal ideation, and stigma. Individual-level interventions were preferred by 61% (n = 46) of participants, including social media, deep breathing, and exercise training.
CONCLUSIONS: To enhance results in MDR-TB, it is crucial to develop and assess personalized psychosocial interventions with tailored adjustments to tackle the psychosocial obstacles encountered by adolescents and young adults with MDR-TB.

DOI: 10.1002/brb3.70665
PMCID: PMC12321948
PMID: 40760794 [Indexed for MEDLINE]

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

16. Pakistan's path forward in DR-TB management: insights from global implementation of BPaL/BPaLM regimen.

Ann Med Surg (Lond). 2025 Jul 10;87(8):4713-4717. doi: 10.1097/MS9.0000000000003548. eCollection 2025 Aug.

Sah S(1), Ahsan A(1), Yadav T(2).

Author information:
(1)Department of Internal Medicine, Dow University of Health Sciences, Karachi, Pakistan.
(2)Primary Healthcare Centre (PHCC) Jhorahat, Koshi, Nepal.

Drug-resistant tuberculosis (DR-TB) is a serious public health threat, and Pakistan is one of the most impacted nations. The long treatment duration of traditional regimens puts a great burden on healthcare systems, especially in resource-constrained environments. Accordingly, the World Health Organization launched the Bedaquiline, Pretomanid, and Linezolid (BPaL)/Bedaquiline, Pretomanid, Linezolid, and Moxifloxacin (BPaLM) regimen - a 6-month, all-oral therapy consisting of BPaLM. With stated success rates as high as 90%, these regimens present an exciting alternative to traditional treatments. Yet, their integration into current treatment programs is hindered by policy lags, poor

diagnostic infrastructure, and difficulty in maintaining patient compliance. This brief communication explores the promise of BPaL/BPaLM to enhance DR-TB cure rates while pinpointing major hurdles to its use in Pakistan. Enhancing diagnostic capacity, upgrading healthcare infrastructure, and accelerating policy adjustment are crucial steps toward maximizing DR-TB management in high-burden countries.

DOI: 10.1097/MS9.0000000000003548
PMCID: PMC12333698
PMID: 40787500

Conflict of interest statement: Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article. Not applicable.

17. High risk of drug-resistant tuberculosis in IGRA-negative contacts: should preventive treatment be considered?

Infection. 2025 Aug;53(4):1501-1506. doi: 10.1007/s15010-024-02470-z. Epub 2025 Jan 21.

Brehm TT(1)(2)(3), Köhler N(1)(2)(3), Grobbel HP(1)(2), Welling J(4), Mandalakas AM(1)(2)(5), Fava V(6)(7), Schurr E(6)(7)(8), Lange C(9)(10)(11)(12)(13).

Author information:
(1)Department of Clinical Infectious Diseases, Research Center Borstel, Leibniz Lung Center, Parkallee 35, Borstel, Germany.
(2)German Center for Infection Research (DZIF), Partner Site Hamburg-Lübeck-Borstel-Riems, Germany.
(3)Division of Infectious Diseases, I. Department of Internal Medicine, University Medical Center Hamburg-Eppendorf, Hamburg, Germany.
(4)Pneumologische Schwerpunktpraxis Lübeck, Lübeck, Germany.
(5)Global Tuberculosis Program, Baylor College of Medicine and Texas Children's Hospital, Houston, TX, USA.
(6)Program in Infectious Diseases and Immunity in Global Health, The Research Institute of the McGill University Health Centre, Montréal, Canada.
(7)McGill International TB Centre, McGill University, Montréal, Canada.
(8)Department of Human Genetics and Medicine, McGill University, Montréal, Canada.
(9)Department of Clinical Infectious Diseases, Research Center Borstel, Leibniz Lung Center, Parkallee 35, Borstel, Germany. clange@fz-borstel.de.
(10)German Center for Infection Research (DZIF), Partner Site

Hamburg-Lübeck-Borstel-Riems, Germany. clange@fz-borstel.de.
(11)Global Tuberculosis Program, Baylor College of Medicine and Texas Children's Hospital, Houston, TX, USA. clange@fz-borstel.de.
(12)Respiratory Medicine & International Health, University of Lübeck, Lübeck, Germany. clange@fz-borstel.de.
(13)Institute for Infection Research and Vaccine Development (IIRVD), University Medical Center Hamburg-Eppendorf, Hamburg, Germany. clange@fz-borstel.de.

PURPOSE: Deciding whether to provide preventive treatment to contacts of individuals with multidrug-resistant (MDR) tuberculosis is complex.
METHODS: We present the diagnostic pathways, clinical course and outcome of tuberculosis treatment in eight siblings from a single family. Tuberculosis disease was diagnosed by Mycobacterium tuberculosis culture and molecular detection of M. tuberculosis-specific DNA from bronchopulmonary specimens using GeneXpert® MTB/RIF. M. tuberculosis infection was diagnosed by an interferon-gamma release assay (IGRA; QuantiFERON®-TB Gold Plus). Whole exome sequencing for genetic predisposition to mycobacterial infection was performed in one patient.
RESULTS: Six of eight siblings aged 16-20 years from a migrant family of Somali origin were diagnosed with pulmonary MDR tuberculosis over a 12-month period. The remaining male siblings, aged 11 and 14 years, were asymptomatic during contact investigation. Chest radiographs, computed tomography (CT) scans, sputum cultures and nucleic acid amplification tests were negative, and the IGRA did not detect M. tuberculosis infection. A repeat CT scan eight months later was unremarkable, and repeated sputum cultures remained negative. In the absence of sufficient evidence of M. tuberculosis infection, no preventive treatment was offered. At month seven of consistent clinical observation, both children were diagnosed with pulmonary tuberculosis; the older with advanced disease and subsequent post-tuberculosis lung disease. Whole exome sequencing revealed no Mendelian variant associated with susceptibility to mycobacterial infection.
CONCLUSION: When significant risk of tuberculosis transmission exists, close contacts of MDR tuberculosis patients should be offered preventive treatment with levofloxacin despite a negative IGRA test result.

DOI: 10.1007/s15010-024-02470-z
PMCID: PMC12316788
PMID: 39836352 [Indexed for MEDLINE]

Conflict of interest statement: Declarations. Ethical approval: Not applicable. Consent to participate: Not applicable. Consent to publish: Informed consent for publication of their data was obtained from all participants (or their legal guardians, in the case of minors). This includes consent for the publication of

any identifiable data, images, or information contained in the manuscript.
Competing interests: The authors declare no competing interests.

18. Enhanced tuberculosis control via leveraging dendritic cell-mediated Th1 responses in preventive and immunotherapeutic vaccine strategies.

J Adv Res. 2025 Jul 30:S2090-1232(25)00585-5. doi: 10.1016/j.jare.2025.07.056. Online ahead of print.

Kim H(1), Kim JS(2), Kwon KW(3), Kim WS(4), Park M(5), Ha SJ(5), Choi S(6), Kim J(7), Shin SJ(8).

Author information:
(1)Department of Microbiology, Institute for Immunology and Immunological Disease, Yonsei University College of Medicine, Seoul, South Korea.
(2)Department of Microbiology, Institute for Immunology and Immunological Disease, Yonsei University College of Medicine, Seoul, South Korea; Myunggok Medical Research Institute, College of Medicine, Konyang University, Daejeon, South Korea.
(3)Department of Microbiology, Institute for Immunology and Immunological Disease, Yonsei University College of Medicine, Seoul, South Korea; Department of Microbiology, College of Medicine, Gyeongsang National University, Jinju, South Korea.
(4)Department of Microbiology, Institute for Immunology and Immunological Disease, Yonsei University College of Medicine, Seoul, South Korea; Functional Biomaterial Research Center, Korea Research Institute of Bioscience and Biotechnology, Jeongeup-si, Jeollabuk-do, South Korea.
(5)Department of Biochemistry, College of Life Science and Biotechnology, Yonsei University, Seoul, South Korea; Brain Korea 21(BK21) Four program, Yonsei Education & Research Center for Biosystems, Yonsei University, Seoul, South Korea.
(6)Department of Microbiology, Institute for Immunology and Immunological Disease, Yonsei University College of Medicine, Seoul, South Korea; Graduate School of Medical Science, Brain Korea 21 Project, Yonsei University College of Medicine, Seoul, South Korea.
(7)Department of Biomedical Sciences, Graduate School of Medical Science, Brain Korea 21 Project, Yonsei University College of Medicine, Seoul, South Korea.
(8)Department of Microbiology, Institute for Immunology and Immunological Disease, Yonsei University College of Medicine, Seoul, South Korea; Graduate School of Medical Science, Brain Korea 21 Project, Yonsei University College of Medicine, Seoul, South Korea. Electronic address: sjshin@yuhs.ac.

INTRODUCTION: Insufficient vaccine efficacy of the Bacillus Calmette-Guérin

(BCG) and long, expensive tuberculosis (TB) treatments highlight the need for better TB control measures.
METHODS: This study evaluated whether the adoptive transfer of dendritic cell (DC)-based vaccines pulsed with culture filtrate antigens (CFA) of Mycobacterium tuberculosis (Mtb) could enhance BCG efficacy and support anti-TB drug therapy.
RESULTS: In BCG-vaccinated mice, adoptive transfer of CFA-pulsed DCs promoted swift T cell recruitment to the lung parenchyma, reducing bacterial load within 1 week post-infection, promoting the generation of tissue-resident T cells and expansion of CD4+ T cells co-producing IFN-γ, IL-2, and/or TNF-α. The vaccine efficacy persisted for a prolonged period post-infection, with protection found in both high dose and low dose Mtb infection models. Additionally, CFA-DC administration during chemotherapy enhanced treatment efficacy, maintaining CD4+ T cell responses. In latent TB models, mice were protected from Mtb reactivation in both drug-sensitive and multidrug-resistant TB models.
CONCLUSIONS: DC-based prophylactic and immunotherapeutic vaccine strategies enhance protective immunity during BCG vaccination and chemotherapy, offering new insights into TB control strategies.

DOI: 10.1016/j.jare.2025.07.056
PMID: 40749789

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

19. Factors influencing the risk of developing multidrug-resistant pulmonary tuberculosis in Northeast Thailand.

J Clin Tuberc Other Mycobact Dis. 2025 Jul 2;40:100549. doi: 10.1016/j.jctube.2025.100549. eCollection 2025 Aug.

Leeka N(1), Laohasiriwong W(1), Mahato RK(1), Amprarat K(2), Chaisuksant S(3).

Author information:
(1)Faculty of Public Health, Khon Kaen University, Khon Kaen 40002, Thailand.
(2)Chum-Phae hospital Khon Kaen 40130, Thailand.
(3)Khon Kaen hospital, Khon Kaen 40000, Thailand.

BACKGROUND: This study aimed to identify the factors influencing Multidrug-Resistant Pulmonary Tuberculosis (MDR-TB) in Northeast Thailand.

METHODS: A case-control study was conducted by reviewing medical record and collecting primary data using a structured questionnaire. The study population comprised the case group of patients with MDR-TB and the control group consisted of other pulmonary tuberculosis patients aged 18 years and over with ratio 1 case: 3 controls. The factors influencing MDR-TB in the Northeast of Thailand were identified by multivariable analysis.
RESULTS: The results revealed that the majority of the cases and controls were males (73.79 % and 59.87 %, respectively) with mean ages of 50.50 years and 56.30 years. Cases had more moderate self-care behaviors (40.78 %) compared with controls (17.15 %). Nearly half (48.54 %) of the cases had a limited level of health literacy. Multivariable analysis demonstrated that education level (Adjusted Odd Ratio (AOR) = 1.12; 95 % CI = 1.14-1.96, p = 0.04), average monthly family income (AOR = 1.78; 95 % CI = 1.19-2.97, p = 0.01), number of windows (AOR = 2.03; 95 % CI = 1.34-3.91, p = 0.001), being diagnosed with tuberculosis two or more times (AOR = 4.63; 95 % CI = 2.51-12.35, p < 0.001), poor attitude towards tuberculosis illness (AOR = 1.32; 95 % CI = 1.05-2.48, p = 0.03), mild to moderate self-care behavior levels (AOR = 1.47; 95 % CI = 1.14-3.05, p < 0.001), and inadequate to problematic levels of health literacy (AOR = 2.11; 95 % CI = 1.36-3.63, p < 0.001) were significant determinants of MDR-TB.
CONCLUSIONS: This study concluded that education level, monthly family income, number of windows, recurrence of TB diagnosis, attitude towards TB illness, self-care behavior level and limited health literacy level were risk factors of MDR-TB. Inadequate health literacy was particularly associated with a high risk of developing MDR-TB. In order to increase treatment success rates, the results from this study should be used to improve targeted interventions and health education strategies.

DOI: 10.1016/j.jctube.2025.100549
PMCID: PMC12272133
PMID: 40688755

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.

20. Whole-genome sequencing and machine learning reveal key drivers of delayed sputum conversion in rifampicin-resistant tuberculosis.

Front Cell Infect Microbiol. 2025 Aug 7;15:1641385. doi: 10.3389/fcimb.2025.1641385. eCollection 2025.

Fang Q(#)(1), Li X(#)(2)(3), Lu Y(3), Gao J(3), Wu Y(4), Chen Y(5), Che Y(5).

Author information:
(1)Departments of Pulmonary Medicine, The First Affiliated Hospital of Ningbo University, Ningbo, Zhejiang, China.
(2)Jiaxing Key Laboratory of Clinical Laboratory Diagnostics and Translational Research, Affiliated Hospital of Jiaxing University, Jiaxing, Zhejiang, China.
(3)Cosmos Wisdom Mass Spectrometry Center of Zhejiang University Medical School, Hangzhou, Zhejiang, China.
(4)Fountain Valley School, Colorado Springs, CO, United States.
(5)Institute of Tuberculosis Prevention and Control, Ningbo Municipal Center for Disease Control and Prevention, Ningbo, Zhejiang, China.
(#)Contributed equally

Rifampicin-resistant tuberculosis (RR-TB) remains a major global health challenge, with delayed sputum culture conversion (SCC) predicting poor treatment outcomes. This study integrated whole-genome sequencing (WGS) and machine learning to identify clinical and genomic determinants of SCC failure in 150 RR-TB patients (2019-2023). Phenotypic and genotypic analysis revealed high rates of isoniazid resistance (74.0%) and rpoB mutations (97.3%, predominantly Ser450Leu), with 90% of strains belonging to Lineage 2 (Beijing family). While 64.7% achieved 2-month SCC, 18.0% remained culture-positive at 6 months. Univariate analysis linked 2-month SCC failure to smear positivity, resistance to isoniazid, amikacin, capreomycin, and levofloxacin, and pre-XDR-TB status, though only smear positivity (aOR=2.41, P=0.008) and levofloxacin resistance (aOR=2.83, P=0.003) persisted as independent predictors in multivariable analysis. A Random Forest model achieved robust prediction of SCC failure (AUC: 0.86 ± 0.06 at 2 months; 0.76 ± 0.10 at 6 months), identifying levofloxacin resistance (feature importance: 6.37), embB_p.Met306Ile (5.94), and smear positivity (5.12) as top 2-month predictors, while katG_p.Ser315Thr (4.85) and gyrA_p.Asp94Gly (3.43) dominated 6-month predictions. These findings underscore smear positivity, levofloxacin resistance, and specific resistance mutations as critical drivers of SCC failure, guiding targeted RR-TB treatment strategies.

DOI: 10.3389/fcimb.2025.1641385
PMCID: PMC12367658
PMID: 40851801 [Indexed for MEDLINE]

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

21. Rifampicin-resistant Mycobacterium tuberculosis and unsuccessful results from Xpert® MTB/Rif-Ultra assay in Amhara Region, Ethiopia.

J Clin Tuberc Other Mycobact Dis. 2025 Apr 25;40:100528. doi: 10.1016/j.jctube.2025.100528. eCollection 2025 Aug.

Belay G(1), Getachew H(1), Birku T(1), Tadese A(2), Gashaw Y(3), Getie M(1), Molla T(1), Tarekegn M(1), Mekonnen D(4), Abate A(5).

Author information:
(1)Department of Medical Microbiology, Amhara National Regional State Public Health Institute, Bahir Dar, Ethiopia.
(2)Department of Tropical and Infectious Disease, Amhara National Regional State Public Health Institute, Bahir Dar, Ethiopia.
(3)Regional TB Laboratory System Strengthening and EQA Technical Advisor, Amhara National Regional State Public Health Institute, Bahir Dar, Ethiopia.
(4)Department of Medical Laboratory Sciences, School of Health Science, College of Medicine and Health Sciences, Bahir Dar University, Bahir Dar, Ethiopia.
(5)Laboratory Director, Amhara National Regional State Public Health Institute, Bahir Dar, Ethiopia.

BACKGROUND: Tuberculosis, an infectious disease caused by Mycobacterium tuberculosis (Mtb), causes 10 million new infections and 1.3 million deaths annually. The treatment of TB is hampered by the increasing incidence rate of drug resistance associated with TB. To diagnose TB and identify drug-resistant TB cases, rapid molecular technologies such as Xpert MTB/RIF, Truenat MTB, MTB Plus, and MTB-RIF Dx tests are recommended by the World Health Organization (WHO) and rolled out globally. Xpert MTB/RIF-Ultra assay is the most widely used in developing countries like Ethiopia. However, this rapid technology has inherent limitations, such as error reports, invalid results, and no results collectively reported as unsuccessful tuberculosis results. The purpose of this study was to retrospectively evaluate the trend of rifampicin resistance and unsuccessful results in the Xpert MTB/RIF-Ultra assay facility of Northwest Ethiopia.
METHODS: Retrospective data archived in the Amhara Public Health Institute (APHI) TB laboratory from 2019 to 2024 were reviewed. Xpert MTB/RIF-Ultra software data were retrieved and transferred to Microsoft Excel. Then, it was checked for completeness, cleaned manually, and imported to Statistical Package for the Social Sciences (SPSS) version 25 software. The rate of mycobacterium tuberculosis (Mtb.) positives, multi-drug resistance tuberculosis (MDR-TB), and Unsuccessful results were analyzed from the total and year-wise. The final results were depicted using tables and different charts.

RESULTS: From June 30, 2019, to June 30, 2024, a total of 587,128 sputum samples were obtained from presumptive TB patients in 111 GeneXpert sites in the Amhara Region. Of these samples analyzed using Xpert MTB/RIF-Ultra, 6.17 % (36,212/587,128) were Mtb positive. Furthermore, the overall proportion of rifampicin resistance (RR) among Mtb-confirmed cases decreased to 3.03 % (1,096/36,212) and showed a downward trend from 4.62 % (184/3979) in 2020 to 2 % (176/8806) in 2024. The overall unsuccessful results (error, invalid & no result) were 6.48 %. The rate of unsuccessful results remained above the national target of < 5 % throughout the study periods.
CONCLUSION AND RECOMMENDATION: The rate of Mtb and MDR-TB showed a decreasing trend in the last six years in Northwest Ethiopia. However, unsuccessful results remained above the national target. The cause of unsuccessful results should be investigated, and the Xpert MTB/RIF-Ultra-related quality assurance system must be enhanced to reduce the rate of Xpert MTB/RIF-Ultra unsuccessful results.

DOI: 10.1016/j.jctube.2025.100528
PMCID: PMC12063118
PMID: 40351513

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.

22. Adverse effects of linezolid in the treatment of drug-resistant tuberculosis combined with diabetic peripheral neuropathy.

Eur J Med Res. 2025 Aug 12;30(1):737. doi: 10.1186/s40001-025-03011-6.

Li Y(1), Feng Y(2), Yin Z(3), Wang X(4), Hou Y(3), Yu L(3).

Author information:
(1)Department of Respiratory Medicine, Hebei Provincial Key Laboratory of Pulmonary Diseases, Hebei Chest Hospital, Shijiazhuang, China.
(2)Department of Endocrinology, Hebei Provincial Key Laboratory of Pulmonary Diseases, Hebei Chest Hospital, Shijiazhuang, China. chaofeichongjing@163.com.
(3)Department of Endocrinology, Hebei Provincial Key Laboratory of Pulmonary Diseases, Hebei Chest Hospital, Shijiazhuang, China.
(4)Department of Tuberculosis , Hebei Provincial Key Laboratory of Pulmonary Diseases, Hebei Chest Hospital, Shijiazhang, China.

OBJECTIVE: This aimed to observe the adverse effects of linezolid on nerve conduction velocity in patients with drug-resistant tuberculosis combined with diabetic peripheral neuropathy.
METHODS: Patients hospitalized in our hospital from March 2018 to March 2022 were divided into the drug-resistant tuberculosis (DRTB) group, type 2 diabetes peripheral neuropathy (DPN) group, and type 2 diabetic peripheral neuropathy combined with drug-resistant tuberculosis (DM-DRTB) group. The drug-resistant TB treatment regimen used linezolid with antituberculous drugs. Neurophysiological examinations were performed on the patients before and 2 months after treatment, the conduction velocities of the superficial peroneal nerve and peroneal nerve of the lower limbs of the three groups were recorded, and the conduction velocities of the deep peroneal nerve, superficial peroneal nerve, common peroneal nerve, tibial nerve, and femoral nerve of the lower limb motor nerves of the three groups were compared and statistically analyzed.
RESULTS: After 2 months of linezolid treatment, the sensory nerve conduction velocities of the superficial peroneal nerve and sural nerve of the lower limb in the DRTB group and the DM-DRTB group significantly decreased, and the difference was statistically significant ($p < 0.05$). There was no significant decrease in the motor nerve conduction velocities of the deep peroneal nerve, superficial peroneal nerve, common peroneal nerve, tibial nerve, or femoral nerve of the lower limb in the DRTB and the DM-DRTB groups, and the differences were not statistically significant ($p > 0.05$).
CONCLUSION: Linezolid can slow lower limb sensory nerve conduction velocity in patients with DRTB and DM-DRTB; however, the effect on lower limb motor nerves was not significant.

DOI: 10.1186/s40001-025-03011-6
PMCID: PMC12341100
PMID: 40797354 [Indexed for MEDLINE]

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

23. BCG vaccination: historical role, modern applications, and future perspectives in tuberculosis and beyond.

Front Pediatr. 2025 Jul 31;13:1603732. doi: 10.3389/fped.2025.1603732. eCollection 2025.

Starshinova A(1)(2)(3), Kudryavtsev I(4), Rubinstein A(4), Dovgalyuk I(5), Kulpina A(1)(2)(3), Churilov LP(1)(2), Kudlay D(6)(7)(8)(9).

Author information:
(1)Department of Mathematics and Computer Science, Saint Petersburg State University, St. Petersburg, Russia.
(2)Medical Department, Saint Petersburg State University, St. Petersburg, Russia.
(3)Medical Department, Almazov National Medical Research Centre, Saint-Petersburg, Russia.
(4)Department of Immunology, Institution of Experimental Medicine, St. Petersburg, Russia.
(5)Phthisiopulmonology Department, Research Institute of Phthisiopulmonology, St. Petersburg, Russia.
(6)Department of Pharmacology, Institute of Pharmacy, I.M. Sechenov First Moscow State Medical University, Moscow, Russia.
(7)Laboratory of Personalized Medicine and Molecular Immunology, Institute of Immunology FMBA of Russia, Moscow, Russia.
(8)Department of Pharmacognosy and Industrial Pharmacy, Faculty of Fundamental Medicine, Lomonosov Moscow State University, Moscow, Russia.
(9)Laboratory of Comparative Sensory Physiology, Sechenov Institute of Evolutionary Physiology and Biochemistry of the Russian Academy of Sciences, St. Petersburg, Russia.

Tuberculosis (TB) remains a fatal disease primarily transmitted through airborne droplets, with children who are the most susceptible, particularly in the areas with poor tuberculosis control. The BCG vaccine, developed by Albert Calmette and Camille Guérin, has a history spanning a century. This vaccine has been implemented in numerous countries, significantly reducing child mortality in regions heavily affected by TB. In this review, we aim to revisit the vaccine's development and rollout, while also highlighting its current attributes and the successful application in the Russian Federation, where 90% of newborns receive the anti-tuberculosis vaccination. Due to that practice, only a few isolated cases of young children with generalized tuberculosis (about five to seven annually) are observed in Russia. Research on the BCG vaccine is ongoing, revealing significant genetic alterations in BCG strains that have evolved from the original variant. These genetic differences may contribute to variations in vaccine efficacy, making screening important to predict effectiveness. The BCG vaccine can initiate a localized mucosal immune response, offering, besides the anti-TB effect, some protection against infections involving mucous membranes, including salmonellosis, HIV, and acute viral respiratory infections. It is essential to investigate the role of BCG in various applications; however, this exploration should not detract from its main protective benefits against tuberculosis (TB). Future studies may provide evidence of the vaccine's safety and efficacy to support its use beyond TB prevention. While BCG vaccination does not lower the risk of infection with Mycobacterium tuberculosis, it does prevent

the progression to the most severe clinical manifestations (such as miliary TB and tuberculous meningitis) caused by hematogenous spread of M.tuberculosis. The challenge of protecting HIV-infected children from TB remains urgent, especially in regions burdened with drug-resistant TB, highlighting the need for robust protective measures.

DOI: 10.3389/fped.2025.1603732
PMCID: PMC12350428
PMID: 40822692

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

24. Navigating the complexities of drug development for metallo-β-lactamase Inhibitors.

RSC Med Chem. 2025 May 27;16(8):3393-3415. doi: 10.1039/d5md00035a. eCollection 2025 Aug 13.

Reddy N(1)(2), Balieiro AM(3), Silva JRA(1)(3), Gouws CA(1), Mutshembele A(2), Arvidsson PI(1)(4), Kruger HG(1), Govender T(5), Naicker T(1).

Author information:
(1)Catalysis and Peptide Research Unit, University of KwaZulu-Natal Durban 4000 South Africa naickert1@ukzn.ac.za.
(2)Office of AIDS and TB, South African Medical Research Council Pretoria 0084 South Africa.
(3)Laboratory of Computer Modeling of Molecular Biosystems, Federal University of Pará Belém 66075-110 Pará Brazil.
(4)Science for Life Laboratory, Drug Discovery & Development Platform & Division of Translational Medicine and Chemical Biology, Department of Medical Biochemistry and Biophysics, Karolinska Institutet Stockholm 17177 Sweden.
(5)Department of Chemistry, University of Zululand Private Bag X1001 KwaDlangezwa 3886 South Africa govenderthav@icloud.com.

The rising antibiotic resistance rates, especially among carbapenem-resistant Enterobacterales with metallo-β-lactamases (MBLs), highlight the urgent need for effective MBL inhibitors (MBLIs). Navigating the complexities of drug development for MBLIs requires addressing the significant challenges that have

hindered its progress. Despite numerous efforts in pre-clinical development, the lack of standardized approaches has led to disparities, stalling the translation of potential MBLIs from research into clinical use. Alarmingly, there is only one metallo-β-lactamase inhibitory candidate in the pre-registration phase of development. This review highlights the need for a global consensus on key aspects of MBLI development, including standardized in vitro testing, refined animal models, harmonized toxicity assessments, consistent pharmacokinetic data, and uniform in silico methods. It also proposes solutions to these challenges, aiming to bridge the gap between research and clinical application.

DOI: 10.1039/d5md00035a
PMCID: PMC12159872
PMID: 40521342

Conflict of interest statement: There are none to declare.

25. Harnessing Actinobacteria secondary metabolites for tuberculosis drug discovery: Historical trends, current status and future outlooks.

Nat Prod Bioprospect. 2025 Aug 11;15(1):52. doi: 10.1007/s13659-025-00533-8.

de Almeida LLC(1), Fernandes SP(1), de Oliveira GD(2)(3), da Silveira Silva M(1), de Souza TA(2), Rodrigues-Junior VS(3), Cibulski SP(4)(5).

Author information:
(1)Programa de Pós-Graduação em Ciências Farmacêuticas, Departamento de Farmácia, Universidade Estadual da Paraíba (UEPB), Campina Grande, Paraíba, Brazil.
(2)Laboratório Multiusuário de Caracterização e Análise (LMCA), Instituto de Pesquisa em Fármacos e Medicamentos, Universidade Federal da Paraíba (UFPB), João Pessoa Paraíba, Brazil.
(3)Programa de Pós-Graduação em Produtos Naturais e Sintéticos Bioativos, Universidade Federal da Paraíba (UFPB), João Pessoa, Paraíba, Brazil.
(4)Programa de Pós-Graduação em Ciências Farmacêuticas, Departamento de Farmácia, Universidade Estadual da Paraíba (UEPB), Campina Grande, Paraíba, Brazil. samuel.cibulski@ufrn.br.
(5)FACISA-Faculdade de Ciências da Saúde do Trairi, Universidade Federal do Rio Grande do Norte (UFRN), Santa Cruz, Rio Grande do Norte, Brazil. samuel.cibulski@ufrn.br.

Tuberculosis (TB) is a leading infectious disease killer and one of the major

causes of deaths worldwide. Although TB is a curable and preventable disease, in 2023, approximately 10.8 million people fell ill with TB and there were an estimated 1.25 million of deaths worldwide. Despite some research progress for new drug candidates, drug repurposing, and new regimens, there is still an urgent need for the new medicins to treat TB, especially due to the growing cases of multidrug and extensively drug-resistant (MDR/XDR) strains. Drug resistance is a challenging obstacle to TB care and prevention globally, making TB harder and longer to treat, often with poorer outcomes for patients. The Actinomycetota encompass Gram-positive bacteria that produce a milieu of bioactive metabolites, including antibiotics, antiproliferative drugs, immunosuppressive agents, and other important medical molecules. Actinomycetota have a special place in the therapeutic arsenal to fight TB, as rifamycins, aminoglycosides, and cycloserine are derived from Streptomyces species, one of the most important genera in this phylum. Furthermore, hundreds of antimycobacterial metabolites have been isolated from Actinomycetota and can serve as effective drugs or useful agents for the discovery of new lead compounds to combat TB. The present review covers more than 171 isolated substances as potential antimycobacterial agents discovered between the years 1972 to 2024. Among the most potent compounds, with MIC in the submicromolar range, steffimycins, ilamycins/rufomycins, nosiheptide, actinomycins, lassomycin and boromycin are the most promising compounds. These compounds represent highly promising candidates for development of new antitubercular drugs. Additionally, some of these substances also demonstrated activity against resistant Mycobacterium tuberculosis (Mtb) strains, which is particularly relevant given the difficulty of treating MDR and XDR strains. Thus, actinobacteria have played and continue to play an important role in fight TB, remaining a promising source of antibiotic metabolites. Their unique metabolic diversity enables the production of metabolites with innovative mechanisms of action, making them a strategic reservoir for discovering therapies against untreatable forms of the disease.

DOI: 10.1007/s13659-025-00533-8
PMCID: PMC12339860
PMID: 40788464

Conflict of interest statement: Declarations. Competing interests: The authors declare do not have any commercial or associative interest that represents a conflict of interest in connection with the work submitted. Informed consent: All authors have read the final manuscript and approved the submission.

26. Targeted sputum sequencing for rapid and broad drug resistance of Mycobacterium

Tuberculosis.

Infection. 2025 Aug;53(4):1413-1423. doi: 10.1007/s15010-024-02463-y. Epub 2025 Jan 16.

Dou HY(#)(1), Huang TS(#)(2), Wu HC(1), Hsu CH(1), Chen FJ(3)(4), Liao YC(5).

Author information:
(1)National Institute of Infectious Diseases and Vaccinology, National Health Research Institutes, No. 35, Keyan Road, Zhunan Town, Miaoli County, 35053, Taiwan.
(2)Division of Microbiology, Department of Pathology and Laboratory Medicine, Kaohsiung Veterans General Hospital, Kaohsiung, 81362, Taiwan.
(3)National Institute of Infectious Diseases and Vaccinology, National Health Research Institutes, No. 35, Keyan Road, Zhunan Town, Miaoli County, 35053, Taiwan. frchen@nhri.edu.tw.
(4)Department of Biological Science and Technology, National Yang Ming Chiao Tung University, Hsinchu, 30010, Taiwan. frchen@nhri.edu.tw.
(5)Institute of Population Health Sciences, National Health Research Institutes, No. 35, Keyan Road, Zhunan Town, Miaoli County, 35053, Taiwan. jade@nhri.edu.tw.
(#)Contributed equally

PURPOSE: Rapid detection of drug resistance in Mycobacterium tuberculosis (Mtb) from clinical samples facilitates the timely provision of optimal treatment regimens for tuberculosis (TB) patients.
METHODS: In November, 2023, the WHO released its second catalogue of resistance-conferring mutations in Mtb. Utilizing this information, we developed a single 17-plex PCR assay covering 16 key resistance genes and modified thermo-protection buffer to amplify 30 kbp DNA directly from sputum samples for nanopore sequencing. We implemented our protocol using rapid barcoding for sequencing with both a Flongle and a MinION flow cell.
RESULTS: The single multiplex PCR assay was successfully validated on clinical sputum samples using the thermo-protection buffer. The protocol was applied to both Flongle and MinION flow cells, analyzing 12 and 40 samples, respectively. Data analysis suggested that optimal performance could be achieved by processing 6 and 12 samples with similar microscope staining scores on these two platforms. This approach facilitated rapid antimicrobial resistance (AMR) predictions directly from sputum on the day of collection or the following day, with a cost of less than $35 per sample. Compared to AMR predictions based on whole-genome sequencing (WGS) using Mykrobe and TBProfiler, our amplicon-based analysis tool, ARapidTb, demonstrated superior resistance detection capabilities. When analyzing publicly available nanopore WGS datasets for 442 isolates, ARapidTb achieved agreement rates of 95.8% and 98.0%, outperforming Mykrobe (89.4% and 98.3%) and TBProfiler (75.6% and 89.8%).

CONCLUSIONS: Our study significantly reduces the time required for drug resistance detection, enabling quicker initiation of appropriate treatments and potentially improving patient outcomes and TB management.

DOI: 10.1007/s15010-024-02463-y
PMCID: PMC12316706
PMID: 39821740 [Indexed for MEDLINE]

Conflict of interest statement: Declarations. Ethical approval: The study was approved by the KSVGH Institutional Review Board (KSVGH20-CT9-03) and the Human Ethics Committee of the National Health Research Institutes, Taiwan (EC1090902-E and EC1100105). All participants provided written informed consent prior to participation. The research conformed to the principles of the Helsinki Declaration. Competing interests: The authors declare no competing interests.

27. Integration of multi-modal measurements identifies critical mechanisms of tuberculosis drug action.

Cell Syst. 2025 Aug 20;16(8):101348. doi: 10.1016/j.cels.2025.101348. Epub 2025 Jul 29.

Johnson WC(1), Alivisatos A(2), Smith TC 2nd(3), Van N(2), Soni V(4), Wallach JB(5), Clark NA(6), Fitzgerald TA(1), Whiteley JJ(7), Tan S(1), Sokolov A(8), Ando DM(9), Schnappinger D(5), Rhee KY(4), Aldridge BB(10).

Author information:
(1)Department of Molecular Biology and Microbiology, Tufts University School of Medicine, Boston, MA 02111, USA; Tufts University School of Graduate Biomedical Sciences, Boston, MA 02111, USA.
(2)Department of Molecular Biology and Microbiology, Tufts University School of Medicine, Boston, MA 02111, USA.
(3)Department of Molecular Biology and Microbiology, Tufts University School of Medicine, Boston, MA 02111, USA; Stuart B. Levy Center for Integrated Management of Antimicrobial Resistance (CIMAR), Tufts University, Boston, MA 02111, USA.
(4)Division of Infectious Diseases, Weill Department of Medicine, Weill Cornell Medicine, New York, NY 10021, USA.
(5)Department of Microbiology and Immunology, Weill Cornell Medicine, New York, NY 10021, USA.
(6)Department of Systems Biology, Laboratory of Systems Pharmacology, Harvard Medical School, Boston, MA 02115, USA.
(7)Department of Biomedical Engineering, Tufts University School of Engineering,

Medford, MA 02155, USA.
(8)Laboratory of Systems Pharmacology, Harvard Medical School, Boston, MA 02115, USA.
(9)Calico Life Sciences LLC, South San Francisco, CA 94080, USA.
(10)Department of Molecular Biology and Microbiology, Tufts University School of Medicine, Boston, MA 02111, USA; Tufts University School of Graduate Biomedical Sciences, Boston, MA 02111, USA; Stuart B. Levy Center for Integrated Management of Antimicrobial Resistance (CIMAR), Tufts University, Boston, MA 02111, USA; Department of Biomedical Engineering, Tufts University School of Engineering, Medford, MA 02155, USA. Electronic address: bree.aldridge@tufts.edu.

Treatments for tuberculosis remain lengthy, motivating a search for new drugs with novel mechanisms of action. However, it remains challenging to determine the direct targets of a drug and which disrupted cellular processes lead to bacterial killing. We developed a computational tool, DECIPHAER (decoding cross-modal information of pharmacologies via autoencoders), to select the important correlated transcriptional and morphological responses of Mycobacterium tuberculosis to treatment. By finding a reduced feature space, DECIPHAER highlighted essential features of cellular damage. DECIPHAER provides cell-death-relevant insight into uni-modal datasets, enabling interrogation of drug treatment responses for which transcriptional data are unavailable. Using morphological data alone with DECIPHAER, we discovered that respiration inhibition by the polypharmacological drugs SQ109 and BM212 can influence cell death more than their effects on the cell wall. This study demonstrates that DECIPHAER can extract the critical shared information from multi-modal measurements to identify cell-death-relevant mechanisms of TB drugs. A record of this paper's transparent peer review process is included in the supplemental information.

DOI: 10.1016/j.cels.2025.101348
PMCID: PMC12365861
PMID: 40738114 [Indexed for MEDLINE]

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

28. Design of a multi-epitope vaccine against drug-resistant mycobacterium tuberculosis and mycobacterium bovis using reverse vaccinology.

Sci Rep. 2025 Jul 26;15(1):27298. doi: 10.1038/s41598-025-11768-3.

Akurut E(1)(2), Gavamukulya Y(3)(4), Mulindwa J(5), Isiagi M(6)(7), Galiwango R(8)(9), Bbuye M(10), Lujumba I(8)(9), Kiberu D(11)(12), Nabisubi P(11)(8), Kebirungi G(8)(9), Kambugu A(9), Castelnuovo B(9), Nkurununngi G(12), Jjingo D(8)(13), Oketch B(14), Kateete DP(11), Mboowa G(15)(16).

Author information:
(1)Department of Immunology and Molecular Biology, College of Health Sciences, Makerere University, P.O Box 7072, Kampala, Uganda. akuruteva@gmail.com.
(2)The African Center of Excellence in Bioinformatics and Data-Intensive Sciences, P.O. Box 22418, Kampala, Uganda. akuruteva@gmail.com.
(3)Department of Biochemistry and Molecular Biology, Faculty of Health Sciences, Busitema University, P.O. Box, 1460, Mbale, Uganda.
(4)Natural Products Research and Innovation Centre (NaPRiC), Faculty of Health Sciences, Busitema University, P.O. Box, 1460, Mbale, Uganda.
(5)Department of Biochemistry and Sports Science, College of Natural Sciences, Makerere University, P.O Box 7062, Kampala, Uganda.
(6)Department of Medicine, Division of Pulmonology, University of Cape Town, Private bag X3, Rondebosch, 7701, South Africa.
(7)Department of Surgery, Division of Global Surgery, University of Cape Town, Private bag X3, Rondebosh, 7701, South Africa.
(8)The African Center of Excellence in Bioinformatics and Data-Intensive Sciences, P.O. Box 22418, Kampala, Uganda.
(9)The Infectious Diseases Institute, Makerere University, P.O. Box 22418, Kampala, Uganda.
(10)Vaccine and Epidemics Research group, College of Health Sciences, Makerere University Lung Institute, P.O. Box 7749, Kampala, Uganda.
(11)Department of Immunology and Molecular Biology, College of Health Sciences, Makerere University, P.O Box 7072, Kampala, Uganda.
(12)Medical Research Council, School of Hygiene and Tropical Medicine, Virus Research Institute and London, Entebbe, Uganda.
(13)The Department of Computer Science, College of Computing and Information Sciences, Makerere University, Kampala, Uganda.
(14)Medical Research Council, Virus Research Institute and London School of Hygiene & Tropical Medicine Uganda Research Unit | International AIDS Vaccine Initiative, Entebbe, Uganda.
(15)The African Center of Excellence in Bioinformatics and Data-Intensive Sciences, P.O. Box 22418, Kampala, Uganda. gmboowa@gmail.com.
(16)The Infectious Diseases Institute, Makerere University, P.O. Box 22418, Kampala, Uganda. gmboowa@gmail.com.

The global burden of Mycobacterium tuberculosis (M. tuberculosis) and Mycobacterium bovis (M. bovis), the rise of drug-resistant strains, necessitates an urgent need for developing more effective vaccines. This study employed an in-silico approach to design a multi-epitope vaccine targeting the PE_PGRS16

protein, a conserved virulence factor found across both species, including drug-resistant strains. PE_PGRS16 was chosen due to its extracellular localization, adhesion properties, and virulence characteristics, making it a promising vaccine target. Epitopes for B-cells, Cytotoxic T Lymphocytes, and Helper T Lymphocytes were selected based on antigenicity, non-toxicity, and immune response potential. The vaccine construct demonstrated favorable properties, including high antigenicity, solubility, and stability, with a low instability index (-31.31) and binding energy (-44.566) when docked to TLR4, suggesting its potential for immune activation. Griselimycin was incorporated as an adjuvant to enhance immunogenicity, as predicted by C-ImmSim simulations. Population coverage analysis for East Africa revealed high applicability, with 98.35% coverage for Class I epitopes, 100% coverage for Class II epitopes, and 100% combined coverage, with average hit values of 8.4, 12.26, and 20.66, respectively. These results suggest broad potential for global vaccine deployment. This study presents a novel multi-epitope vaccine targeting PE_PGRS16, with the potential to combat Mycobacterium tuberculosis and Mycobacterium bovis infections, including drug-resistant forms. Further experimental validation is necessary to confirm its efficacy and safety.

DOI: 10.1038/s41598-025-11768-3
PMCID: PMC12297362
PMID: 40715271 [Indexed for MEDLINE]

Conflict of interest statement: Declarations. Competing interests: The authors declare no competing interests. Ethical consideration: The study was approved by the School of Biomedical Sciences Research and Ethics Committee (Reference: SBSREC-2021-67) at Makerere University College of Health Sciences.

29. Prediction of risk factors associated with the development of multidrug-resistant tuberculosis in patients with tuberculosis.

Front Public Health. 2025 Jul 22;13:1588196. doi: 10.3389/fpubh.2025.1588196. eCollection 2025.

Chen H(1)(2), Tong Z(1), Zhong J(1), Tong Y(1), Zeng Q(1), Shen B(1), Song Q(1), Qian F(2)(3), Xiao X(3).

Author information:
(1)Department of Infection, Huzhou Central Hospital, Huzhou, Zhejiang, China.
(2)Department of Clinical Medicine, Huzhou University, Huzhou, Zhejiang, China.
(3)Huzhou Key Laboratory of Precision Medicine Research and Translation for

Infectious Diseases, Huzhou Central Hospital, Huzhou, Zhejiang, China.

OBJECTIVE: This study aimed to develop and validate a reliable nomogram based on clinical factors to predict development of multidrug-resistant tuberculosis (MDR-TB) associated with individuals with tuberculosis (TB), so as to reduce the harm and economic burden caused by disease progression.
METHODS: The study included 4,251 individuals with TB who received treatment at Huzhou Central Hospital between January 2016 and December 2023, excluding 87 individuals because of infection with non-TB mycobacterium or incomplete information (including missing laboratory or clinical data). A total of 4,164 individuals (2,261 sputum smear-positive and 1,903 sputum smear-negative patients) were ultimately included in the analysis. This analysis incorporated clinical baseline presentations, demographic information, imaging findings, laboratory results, and clinical diagnoses to develop a predictive model for MDR-TB.
RESULTS: This study demonstrated that sex, age, a history of anti-TB therapy, body mass index (BMI) ≤ 18.5, smoking history, occupation, previously diagnosed TB, pulmonary cavitation, comorbidities, poverty, and C-reactive protein (CRP) ≥ 37.3 mg/L were major risk factors for MDR-TB in patients with TB. The area under the receiver operating characteristic (ROC) curve was 0.902 for the training group and 0.909 for the validation group. Calibration curve analysis revealed that the predicted and actual incidence rates of MDR-TB in the two groups were in good agreement, whereas decision curve analysis (DCA) indicated that the predictive model resulted in better clinical benefit.
CONCLUSION: The nomogram model established in this study included 11 clinical characteristics and demographic features of patients with TB, which may be valuable for predicting MDR-TB.

DOI: 10.3389/fpubh.2025.1588196
PMCID: PMC12321860
PMID: 40766036 [Indexed for MEDLINE]

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

30. Nurse-led palliative care for multidrug-resistant tuberculosis: a parallel, single-blind, pragmatic, randomised controlled trial in Uganda.

Lancet Glob Health. 2025 Aug;13(8):e1448-e1457. doi: 10.1016/S2214-109X(25)00173-1. Epub 2025 May 21.

Buyinza N(1), Nkhoma K(2), Namisango E(3), Maddocks M(2), Downing J(4), Prevost AT(2), Chukwusa E(2), Harding R(5).

Author information:
(1)Hospice Africa Uganda, Makindye, Kampala, Uganda.
(2)Florence Nightingale Faculty of Nursing Midwifery & Palliative Care, King's College London, London, UK.
(3)African Palliative Care Association, Kampala, Uganda.
(4)International Children's Palliative Care Network, Bristol, UK.
(5)Florence Nightingale Faculty of Nursing Midwifery & Palliative Care, King's College London, London, UK. Electronic address: richard.harding@kcl.ac.uk.

BACKGROUND: People with multidrug-resistant tuberculosis experience burdensome symptoms, clinical uncertainty, and high mortality. Palliative care is a designated essential health service under Universal Health Coverage. We aimed to test the hypothesis that receipt of additional nurse-led palliative care would improve patient-reported outcomes for patients with multidrug-resistant tuberculosis, compared with usual care.
METHODS: This single-masked, parallel pragmatic randomised controlled trial recruited adults from three public hospitals in Uganda (Mulago National Referral Hospital Kampala, Gulu Regional Referral Hospital, and Mbale Regional Referral Hospital). Inclusion criteria for the study were adults aged 18 years and older with a confirmed bacteriological diagnosis of multidrug-resistant tuberculosis (not responsive to isoniazid or rifampicin) who were registered at the respective study site clinics and who were able to give informed consent. Participants were randomly assigned (1:1) to the intervention (additional nurse-led care) or the standard care control group using randomly permuted blocks stratified by treatment centre. Intervention group participants received nurse-led person-centred holistic assessment, care planning, symptom control, and psychosocial support delivered on inpatient wards or at home. Fortnightly appointments alternated between face-to-face visits and telephone follow-up. Researchers were masked to participant group allocation. The primary outcome was multidimensional palliative care-related symptoms and concerns measured using the African Palliative Care Association Integrated Palliative Outcome Scale, measured monthly from baseline to the primary 4-month endpoint, analysed using a linear mixed-effect model, applying the intention-to-treat principle to analyse participants by allocated group. The trial was registered on the ISRCTN registry (ISRCTN13664346) and is complete.
FINDINGS: Between Dec 18, 2019, and Sept 10, 2020, 178 individuals were initially assessed for eligibility, 24 were excluded for not meeting inclusion criteria, declining to participate, or being too ill to participate, and 154 participants were recruited and randomly assigned to the intervention group or the control group. 76 were assigned to the nurse-led palliative care group and

78 were assigned to the control group. 52 (34%) participants were female and 102 (66%) were male and participants had an overall median age of 38 years (IQR 31-46). From the linear mixed-effects model the intervention had a significant positive effect compared with standard care (5·12 scale-points [95% CI 2·89-7·21], p<0·0001) at the 4-month follow-up. The standardised effect size was 0·61 (95% CI 0·35-0·86).
INTERPRETATION: Additional nurse-led palliative care for patients with multidrug-resistant tuberculosis improved self-reported outcomes spanning physical, psychological, social, and spiritual domains, and increased medication adherence. Person-centred assessment and holistic care with pain and symptom control should be task-shifted into routine tuberculosis care.
FUNDING: Open Society Foundations.

DOI: 10.1016/S2214-109X(25)00173-1
PMID: 40412430 [Indexed for MEDLINE]

Conflict of interest statement: Declaration of interests We declare no competing interests.

31. Epidemiological Characteristics of Tuberculosis Among Interprovincial Migrants - China, 2019-2023.

China CDC Wkly. 2025 Aug 15;7(33):1079-1086. doi: 10.46234/ccdcw2025.180.

Xu D(#)(1)(2), Li X(#)(3), Tian F(#)(4), Cui Z(5), Chen W(2)(3).

Author information:
(1)National Institute for Communicable Disease Control and Prevention, Chinese Center for Disease Control and Prevention, Beijing, China.
(2)Chinese Field Epidemiology Training Program, Chinese Centre for Disease Control and Prevention, Beijing, China.
(3)National Center for Tuberculosis Control and Prevention, Chinese Centre for Disease Control and Prevention, Beijing, China.
(4)Daxing Center for Disease Control and Prevention, Beijing, China.
(5)Guangxi Zhuang Autonomous Region Center for Disease Control and Prevention, Nanning City, Guangxi Zhuang Autonomous Region, China.
(#)Contributed equally

INTRODUCTION: Tuberculosis (TB) represents one of China's most significant

infectious disease, with inter-provincial population migration posing a challenge to controlling its spread. This study examined TB cases among inter-provincial migrants across China from 2019 to 2023.
METHODS: TB surveillance data were extracted from China's Tuberculosis Information Management System and analyzed using R software (version 4.4.0). After information desensitization, the relevant information of TB patients with differing current and permanent address codes was extracted.
RESULTS: Between 2019 and 2023, we identified 123,945 TB cases among inter-provincial migrants, representing 4.03% (123,945/3,077,951) of all reported TB cases. The primary destination provincial-level administrative divisions (PLADs) for TB patients were Guangdong (48,183 cases, 38.9%), Zhejiang (27,383 cases, 22.1%), Fujian (8,582 cases, 6.9%), Beijing (7,959 cases, 6.4%), and Shanghai (7,403 cases, 5.9%), collectively accounting for 80.3% of all inter-provincial migrant TB cases. The PLADs with the highest outflow of TB migrants were Sichuan (15,155 cases, 12.23%), Hunan (14,707 cases, 11.87%), Guizhou (13,927 cases, 11.24%), Jiangxi (8,892 cases, 7.17%), and Hubei (8,441 cases, 6.81%). Among these migrant cases, 66.2% were male, 93.0% were newly diagnosed, 2.4% exhibited drug resistance. The proportion of individuals aged 45-64, aged ≥65 and re-treated exhibited a significant annual increase ($P<0.001$). The overall successful treatment rate was 89.5%, while 5.3% experienced adverse treatment outcomes. Throughout the study period, the lowest proportion of TB cases among inter-provincial migrants occurred in February.
CONCLUSION: From 2019 to 2023, the characteristics of TB among inter-PLADs migrant patients have undergone certain changes. The migration of TB primarily flows from economically weaker regions to more developed areas, with the main destination PLADs relatively stable. Effective TB control among inter-PLADs migrants requires targeted screening programs focusing on individuals from major source and destination PLADs. Tailored strategies should be developed based on the migration patterns of different PLADs.

DOI: 10.46234/ccdcw2025.180
PMCID: PMC12365652
PMID: 40843138

Conflict of interest statement: No conflicts of interest.

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

EBioMedicine. 2025 Aug 4;119:105875. doi: 10.1016/j.ebiom.2025.105875. Online ahead of print.

Carpi G(1), Seifert M(2), De la Rossa A(1), Uplekar S(1), Rodrigues C(3), Tukvadze N(4), Omar SV(5), Suresh A(1), Rodwell TC(2), Colman RE(6).

Author information:
(1)FIND, Geneva, Switzerland.
(2)FIND, Geneva, Switzerland; Division of Pulmonary, Critical Care, Sleep Medicine, and Physiology, University of San Diego, San Diego, CA, USA.
(3)Hinduja Hospital and Medical Research Centre, Tuberculosis, Mumbai, India.
(4)National Center for Tuberculosis and Lung Diseases, Tuberculosis, Tbilisi, Georgia; Swiss Tropical and Public Health Institute, Allschwil, Switzerland.
(5)Centre for Tuberculosis, National & WHO Supranational TB Reference Laboratory, National Institute for Communicable Diseases, A Division of the National Health Laboratory Service, Johannesburg, South Africa.
(6)FIND, Geneva, Switzerland; Division of Pulmonary, Critical Care, Sleep Medicine, and Physiology, University of San Diego, San Diego, CA, USA.
Electronic address: rcolman@health.ucsd.edu.

BACKGROUND: Rapid and accurate detection of drug-resistant tuberculosis (DR-TB) is crucial for ensuring effective treatment, halting transmission and preventing the amplification of resistance. Comparative evaluations of molecular diagnostic assays in high-burden settings are essential for informing clinical decision-making for DR-TB treatment.
METHODS: The Seq&Treat clinical study previously evaluated the performance of two targeted next-generation sequencing (tNGS) workflows, GenoScreen Deeplex Myc-TB and Oxford Nanopore Technologies Tuberculosis Drug Resistance Test, on direct sediment samples from persons at risk for DR-TB. Hain Line Probe Assay (LPAs-MTBDRplus and MTBDRsl) were run as a comparator test using an aliquot of the same sediment samples. Diagnostic performance of the LPAs and previously established tNGS performance were compared, including sensitivity and specificity, for rifampicin, isoniazid, fluoroquinolones (moxifloxacin, levofloxacin), and amikacin, using a composite reference standard of phenotypic drug susceptibility testing and whole-genome sequencing.
FINDINGS: Among 720 clinical samples tested, MTBDRplus LPA sensitivity for rifampicin and isoniazid was 92.3% (95% CI 88.9-94.8) and 91.9% (88.4-94.4), each significantly lower than ≥95% achieved by both tNGS workflows ($p < 0.01$). For fluoroquinolones (moxifloxacin and levofloxacin), the MTBDRsl LPA and ONT had similar sensitivities (94.3% and 92.7%, and 94.8% and 93.9%, respectively), while GenoScreen outperformed both (97.3% and 96.6%). GenoScreen also demonstrated the highest sensitivity for amikacin resistance (94.6%) compared to LPAs (88.7%) and ONT (88.3%). Complete assay failure rates were low for LPAs (4.9%) and ONT (5.0%) and moderately higher for GenoScreen (8.6%), with differences in single-target failures across all assays.
INTERPRETATION: LPAs demonstrated lower sensitivity and more limited drug

resistance detection compared to tNGS workflows, underscoring the advantages of tNGS for improving DR-TB diagnostic algorithms. These findings provide critical evidence to guide updates in DR-TB diagnostic programs.
FUNDING: Support for the Seq&Treat project was provided through funding from Unitaid (2019-32-FIND MDR).

DOI: 10.1016/j.ebiom.2025.105875
PMCID: PMC12344966
PMID: 40763426

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

33. Factors associated with unfavourable treatment outcomes among patients with Multidrug-resistant Tuberculosis receiving outpatients care.

Sci Rep. 2025 Aug 4;15(1):28335. doi: 10.1038/s41598-025-13227-5.

Vadakunnel MJ(1), Nehru VJ(1), Brammacharry U(1), Ramachandra V(1), Palavesam S(1), Muthukumar A(2), Mani BR(3), Pradhabane G(4), Sriramkumar SR(5), Venkatchalam K(6), Muthaiah M(7).

Author information:
(1)Institute of Basic Medical Sciences, University of Madras, Chennai, Tamil Nadu, India.

(2)Department of Environmental Science, Central University, Kasaragod, Kerala, India.
(3)Department of Biochemistry, Queen Mary's College, Madras, Tamil Nadu, India.
(4)Department of Biotechnology, Indira Gandhi College of Arts and Science, Indira Nagar, Puducherry, India.
(5)Centre for Global Health Research, Saveetha Institute of Medical and Technical Sciences, Saveetha Nagar, Thandalam, Chennai, 602105, India.
(6)Department of Microbiology, State TB Training and Demonstration Centre, Intermediate Reference Laboratory, Government Hospital for Chest Diseases, Puducherry, India.
(7)Department of Microbiology, State TB Training and Demonstration Centre, Intermediate Reference Laboratory, Government Hospital for Chest Diseases, Puducherry, India. drmuthurajm@gmail.com.

Enhancing treatment outcomes for drug-resistant tuberculosis is a major global priority for tuberculosis control programs. India has the highest number of Multidrug-resistant Tuberculosis cases worldwide, yet no longitudinal studies have assessed the factors affecting treatment outcomes in public sector conditions. This study aimed to evaluate factors associated with ineffective treatment outcomes in patients with Multidrug-resistant Tuberculosis receiving outpatient care under the National Tuberculosis Elimination Programme in Puducherry, India, from January 2020 to December 2023. We employed multivariate regression methods to calculate odds ratios with 95% confidence intervals to identify factors linked to unsuccessful treatment outcomes. Clinical data from patients with Multidrug-resistant Tuberculosis revealed an overall treatment success rate of 60.42%. The findings showed that patients undergoing retreatment were more likely to experience unsuccessful outcomes. Additionally, co-infection with HIV, as well as the use of alcohol or tobacco, increased the odds of treatment failure. Patients with heteroresistant patterns had 2.72 times higher odds of unsuccessful treatment outcomes compared to those with inferred and true-resistant patterns. Furthermore, patients living in rural areas typically experienced worse treatment outcomes than those in urban areas, with higher rates of loss to follow-up. Patients on longer treatment regimens were also more likely to be lost to follow-up compared to those on shorter regimens. Notably, true resistance due to rpoB gene mutations accounted for 65.9% (29 out of 44) of total deaths, with mutations at codon S450L contributing to 47.7% of these fatalities, a finding that has not been reported elsewhere. The study highlighted a strong association between heteroresistance in the rpoB gene and poor treatment outcomes. These results emphasize the need for detailed molecular-level studies to improve treatment outcomes by ensuring appropriate drug selection for MDR/RR Tuberculosis. Additionally, further research is necessary to determine the impact of heteroresistance on treatment outcomes in individual patients.

DOI: 10.1038/s41598-025-13227-5
PMCID: PMC12322265
PMID: 40760140 [Indexed for MEDLINE]

Conflict of interest statement: Declarations. Competing interests: The authors declare no competing interests. Ethics approval and consent to participate: Before starting the study, we received ethical clearance from the General Hospital Institution Ethics Committee at the Indira Gandhi Government General Hospital and Postgraduate Institute (Ref. No/GHIEC/2020/243; June 2020). Before collecting data, we informed the hospital director and laboratory personnel about the study objectives. Since we used secondary data, we did not need the patients' informed consent. We did not include personal identifiers on the data collection sheet to protect the confidentiality of the participant's records. Additionally, access to secured data from participant records was restricted to the investigators only.

34. Evaluation of antiretroviral regimen switching options in adults with HIV with sustained viral load non-suppression on dolutegravir, lamivudine, and tenofovir in eastern, central, southern, and western Africa: a modelling study.

Lancet HIV. 2025 Aug;12(8):e578-e586. doi: 10.1016/S2352-3018(25)00068-2. Epub 2025 Jun 24.

Phillips AN(1), Bansi-Matharu L(2), van Oosterhout JJ(3), Hyle E(4), van de Vijver D(5), Kouyos R(6), Hong SY(7), Chun H(7), Raizes E(7), Kantor R(8), Jordan MR(9), Vitoria M(10), Ford N(11), Mugurungi O(12), Apollo T(12), Chimberengwa P(13), Meintjes G(14), Siedner M(4), Lundgren J(15), Schapiro J(16), Flexner C(17), Loosli T(6), Cambiano V(2), Smith J(2), Xia R(2), McCluskey S(4), Mewoabi S(18), Calmy A(19), Eholie SP(20), Revill P(21).

Author information:
(1)Institute for Global Health, UCL, London, UK. Electronic address: andrew.phillips@ucl.ac.uk.
(2)Institute for Global Health, UCL, London, UK.
(3)Partners in Hope, Lilongwe, Malawi; David Geffen School of Medicine, University of California Los Angeles, Los Angeles, CA, USA.
(4)Massachusetts General Hospital, Boston, MA, USA; Harvard Medical School, Boston, MA, USA.
(5)Erasmus Medical Centre, Erasmus University, Rotterdam, Netherlands.
(6)Department of Infectious Diseases and Hospital Epidemiology, University Hospital Zurich, Zurich, Switzerland; Institute of Medical Virology, University

of Zurich, Zurich, Switzerland.
(7)Division of Global HIV and TB, Global Health Center, Centers for Disease Control and Prevention, Atlanta, GA, USA.
(8)Department of Medicine, Brown University Warren Alpert Medical School, Providence, RI, USA.
(9)Department of Medicine and Department of Public Health and Community Medicine, Tufts University School of Medicine, Boston, MA, USA; Global Health and Tropical Medicine, LA-REAL, Instituto de Higiene e Medicina Tropical, Universidade NOVA de Lisboa, Lisbon, Portugal.
(10)Department of Global HIV, Hepatitis, and Sexually Transmitted Infections Programmes, World Health Organization, Geneva, Switzerland.
(11)Department of Global HIV, Hepatitis, and Sexually Transmitted Infections Programmes, World Health Organization, Geneva, Switzerland; Centre for Integrated Data and Epidemiological Research, University of Cape Town, Cape Town, South Africa.
(12)Ministry of Health and Child Care, Harare, Zimbabwe.
(13)Department of Community Medicine, National University of Science and Technology, Bulawayo, Zimbabwe.
(14)Department of Medicine, University of Cape Town, Cape Town, South Africa; Blizard Institute, Queen Mary University of London, London, UK.
(15)Centre of Excellence for Health, Immunity, and Infections, Department of Infectious Diseases, Copenhagen University Hospital-Rigshospitalet, Copenhagen, Denmark; Department of Clinical Medicine, University of Copenhagen, Copenhagen, Denmark.
(16)National Hemophilia Center, Sheba Medical Center, Ramat Gan, Israel.
(17)Johns Hopkins University School of Medicine, Baltimore, MD, USA.
(18)Department of Microbiology and Parasitology, University of Buea, Buea, Cameroon.
(19)Geneva University Hospitals, Geneva, Switzerland.
(20)Unit of Infectious and Tropical Diseases, Treichville University Teaching Hospital, Abidjan, Côte d'Ivoire.
(21)Centre for Health Economics, University of York, York, UK.

BACKGROUND: In Africa, for people with HIV on a dolutegravir-based regimen with a viral load of more than 1000 copies per mL despite enhanced adherence counselling, the appropriate course of action is uncertain. We aimed to evaluate the predicted effects of alternative antiretroviral regimen switching options in this population, including consideration of cost-effectiveness.
METHODS: We used an existing individual-based model to simulate risk and experience of HIV in 100 000 adults alive between 1989 and 2076. Using sampling of parameter values, we created 1000 setting-scenarios, reflecting the uncertainty in assumptions and a range of settings similar to those seen in eastern, central, southern, and western Africa. For each setting-scenario, we predicted the outcomes from the three alternative policies for people with

sustained viral load non-suppression on a dolutegravir-containing regimen from 2026: a switch to a protease inhibitor-based regimen (switch policy), a switch to a protease inhibitor-based regimen only if HIV drug resistance testing beforehand shows integrase inhibitor resistance (resistance test policy), and no switch with no HIV drug resistance test (no switch policy). We considered predicted outcomes over 10-year and 50-year periods from 2026, used a 3% discount rate, and a cost-effectiveness threshold of US$500 per disability-adjusted life-year (DALY) averted. Ritonavir-boosted darunavir costs $210 per year, and dolutegravir less than $20. We assumed a cost of HIV drug resistance testing of $200 and considered variations around this. For comparing policies, we calculated net DALYs, which account for the health consequences of differences in costs and provide a measure of the impact of a policy on overall population burden of disease.
FINDINGS: Across setting-scenarios, there was a mean of 14 480 deaths per year (95% CI 13 750-15 210) over 50 years with a mean annual discounted cost of $103·2 million (95·8-106·5) with the switch policy in the context of having scaled to a setting with an adult population of 10 million in 2024. Compared with the switch policy, the no switch policy was predicted to lead to an overall increased number of DALYs incurred (mean 4400 per year, 95% CI 3200-5500), although it resulted in the lowest overall cost, with a difference in annual discounted costs of $5·1 million (95% CI 4·6-5·6) lower than the switch policy. The resistance test policy led to a similar risk of death and DALYs to the switch policy at a lower overall cost (difference in annual discounted costs $3·5 million per year, 95% CI 3·1-3·9), leading to 6900 (95% CI 5500-8200) fewer net DALYs per year. Net DALYs for the resistance test versus no switch policies were similar (-1000 net DALYs, 95% CI 400 to -2300). The incremental cost-effectiveness ratio when comparing the resistance test policy with the no switch policy was $376 per DALY averted; the switch policy was dominated.
INTERPRETATION: Introduction of HIV drug resistance testing for people with sustained viral load non-suppression on dolutegravir-based antiretroviral therapy is likely to be cost-effective. We suggest that exploratory planning for increased access and scale-up of high-quality, low-cost drug resistance testing for the region is undertaken.
FUNDING: Gates Foundation as part of the HIV Modelling Consortium.

DOI: 10.1016/S2352-3018(25)00068-2
PMID: 40578374 [Indexed for MEDLINE]

Conflict of interest statement: Declaration of interests ANP declares grants for his institution from Wellcome, National Institutes of Health (NIH), National

Institute for Health and Care Research, and Gates Foundation, and consultancy fees from WHO. JSc declares consulting fees, honoraria, and support for travel from and serves on advisory boards for AbbVie, Merck, Gilead Sciences, GSK, ViiV, Pfizer, Moderna, and Teva. AC declares that she has been an investigator of studies sponsored by ViiV, Gilead Sciences, and MSD (per patient fees paid to the hospital). DvdV declares grants from ViiV, Gilead Sciences, NIH, NWO (Dutch research council), Aids fonds, and consulting fees from ViiV to his institution. RKa declares grants from Gilead and NIH, honoraria from Thermofisher, and support for travel from WHO. LB-M declares grants from Gates Foundation and consultancy fees from WHO. RKo declares grants from Swiss National Science Foundation, NIH, and Gilead Sciences. SMc declares a grant from ViiV to her institution. VC declares a grant from UKRI and consultancy fees from Source Market Access. CF declares consulting fees from Gilead Sciences, Johnson & Johnson, Merck, Theratechnologies, and ViiV Healthcare. EH declares grants to her institution from Massachusetts General Hospital and NIH. All other authors declare no competing interests.

35. Evaluating the cost-effectiveness of levofloxacin therapy for household contacts of multidrug-resistant tuberculosis in Vietnam.

Lancet Reg Health West Pac. 2025 Aug 8;61:101666. doi: 10.1016/j.lanwpc.2025.101666. eCollection 2025 Aug.

Hasan T(1)(2), Thu Anh N(3)(4), Binh Hoa N(5), Viet Nhung N(6), Yapa HM(1)(2), Graham SM(7), Marais BJ(2)(3), Marks GB(4)(8), Lung T(9)(10), Fox GJ(1)(11).

Author information:
(1)NHMRC Clinical Trials Centre, Faculty of Medicine and Health, University of Sydney, Sydney, Australia.
(2)The Sydney Infectious Diseases Institute (Sydney ID), The University of Sydney, Sydney, Australia.
(3)The University of Sydney Vietnam Institute, University of Sydney, Ho Chi Minh City, Vietnam.
(4)Woolcock Institute of Medical Research, Hanoi, Vietnam.
(5)National Lung Hospital, Hanoi, Vietnam.
(6)University Medical Centre, Ho Chi Minh, Vietnam.
(7)Melbourne Children's Global Health, University of Melbourne Department of Paediatrics and Murdoch Children's Research Institute, Royal Children's Hospital, Melbourne, Australia.
(8)Burnet Institute, Melbourne, Australia.
(9)School of Public Health, Faculty of Health and Medicine, University of Sydney, Sydney, Australia.
(10)The George Institute for Global Health, University of New South Wales,

Sydney, Australia.
(11)Royal Prince Alfred Hospital, Sydney Local Health District, Camperdown, Australia.

BACKGROUND: Multidrug-resistant tuberculosis (TB) threatens global TB control, on account of poor treatment outcomes, high treatment toxicity and costs. Recent trials demonstrated the effectiveness of six-months of levofloxacin (6Lfx) to prevent TB disease among high-risk contacts. However, the cost-effectiveness of this strategy has not previously been evaluated.
METHODS: The VQUIN study was a double-blinded randomised control trial in Vietnam assessing the effectiveness of 6Lfx in household contacts of multidrug resistant/rifampicin resistant TB (MDR/RR-TB) to prevent progression to TB disease. Incorporating in-trial costs and effectiveness outcomes from the VQUIN trial, we developed a closed cohort, decision-analytic Markov model to assess the cost effectiveness of 6Lfx versus placebo in a cohort exposed to MDR/RR-TB in Vietnam.
FINDINGS: Over a 20-year time horizon, the provision of 6Lfx preventative therapy to household contacts of people infected with MDR/RR-TB was found to gain a total of 40.1 QALYs per 1000 population and save US$23,145 per 1000 population, indicating the strategy was cost saving. MDR/RR-TB cases averted over 20 years was 19.9 per 1000 population treated with 6Lfx, and the number of deaths averted was 3.2 per 1000 people treated.
INTERPRETATION: 6Lfx therapy is a cost-saving strategy to reduce the incidence of active disease in household contacts of MDR/RR-TB in a resource-limited setting.
FUNDING: National Health and Medical Research Council Project Grant (#1081443). GJF was supported by a NHMRC Leadership Fellowship (Level 1) (#2007920).

DOI: 10.1016/j.lanwpc.2025.101666
PMCID: PMC12355538
PMID: 40822287

Conflict of interest statement: GM received a grant from the National Health and Medical Research Council which supported this work. He is also the President, International Union Against TB and Lung Disease. GF is a member of the data safety and monitoring board of the DRAMATIC trial. He is also a board member of the Australian Respiratory Council. GF has received budesonide/formoterol from Astra-Zeneca for a clinical trial of asthma and COPD. NVN received a grant from the National Health and Medical Research Council which supported this work (grant #1081443). TAN received a grant from the National Health and Medical Research Council which supported this work (grant #1081443).

36. Whole-genome sequencing for analyzing the transmission characteristics of drug-resistant Mycobacterium tuberculosis in Ganzhou, China.

BMC Infect Dis. 2025 Jul 28;25(1):950. doi: 10.1186/s12879-025-11356-w.

Wang J(#)(1), Chen C(#)(2), Fang H(1), Liao Y(1), Lei Q(1), Feng D(1), Wang M(1), Li B(3).

Author information:
(1)Ganzhou Center for Disease Control and Prevention, Ganzhou, Jiangxi Province, China.
(2)Department of Clinical Laboratory, Shenzhen Baoan Hospital, The Second Affiliated Hospital of Shenzhen University, Shenzhen, Guangdong Province, China.
(3)Guangdong Provincial Center for Disease Control and Prevention, Guangzhou, Guangdong Province, China. libsn@126.com.
(#)Contributed equally

OBJECTIVE: The study aimed to understand the drug resistance profile and transmission characteristics of drug-resistant Mycobacterium tuberculosis (MTB) in Ganzhou, China, to provide a scientific basis for developing prevention and control strategies.
METHODS: DNA extracted from re-cultured positive strains underwent whole-genome sequencing (WGS). The online platform SAM-TB was used to identify drug resistance-related mutations in each strain, construct a phylogenetic tree, and calculate the pairwise strain single-nucleotide polymorphism (SNP) distances. A threshold of 12 SNPs between pairwise strains was set to identify transmission clusters. Epidemiological investigations were conducted for patients within these transmission clusters to analyze the characteristics of drug-resistant tuberculosis (TB) transmission.
RESULTS: A total of 82 strains were analyzed. The most common mutations observed for isoniazid, rifampicin, ethambutol, and streptomycin were katG (S315T, 32/61), rpoB (S450L, 13/37), embB (M306V, 5/12), and rpsL (K43R, 18/26), respectively. Mutations were also observed in genes conferring resistance to other drugs, including pncA (pyrazinamide), gyrA (ofloxacin), rrs, and eis (aminoglycosides). The strains belonged to lineage 2 (75.61%, 62/82) and 4 (24.39%, 20/82). Three clusters containing 12 drug-resistant strains were identified as transmission clusters, ranging in size from 2 to 8, with a clustering rate of 14.63% (12/82). Notably, lineage 2 strains were more prevalent in clustered cases than lineage 4 strains (19.35%, 12/62 vs. 0%, 0/20, Fisher’s exact test, P = 0.033). The isoniazid resistance rate was significantly higher in clustered strains (100%, 12/12) than in non-clustered strains (70.00%, 49/70) (Fisher’s exact test, P = 0.031). Two potential transmission chains of drug-resistant TB were identified.

CONCLUSION: This study utilized WGS technology to provide important data on the genetic mutation types and transmission dynamics of drug-resistant TB in Ganzhou. WGS demonstrates significant potential in early prediction of drug resistance in TB and identification of recent transmission events, offering essential support for monitoring public health events and intervening in drug-resistant tuberculosis.
SUPPLEMENTARY INFORMATION: The online version contains supplementary material available at 10.1186/s12879-025-11356-w.

DOI: 10.1186/s12879-025-11356-w
PMCID: PMC12306122
PMID: 40722062

Conflict of interest statement: Declarations. Ethics approval and consent to participate: This study received ethical approval from the Ethics Committee of the Ganzhou Centers for Disease Control and Prevention (grant number 20221207, December 7, 2022).This study was conducted in accordance with the Declaration of Helsinki. Informed consent was obtained from each participant or respondent.All methods followed the relevant guidelines and regulations. Consent for publication: Not applicable. Competing interests: The authors declare no competing interests.

37. Assessing the determinants of drug-resistant tuberculosis in selected hospitals in Tigray region, Northern Ethiopia: a case-control study.

J Health Popul Nutr. 2025 Jul 24;44(1):267. doi: 10.1186/s41043-025-01021-y.

Meresa D(1), Berhe G(1), Tadesse K(1), Gebru M(2), Gebrezgabiher G(3).

Author information:
(1)School of Public Health, College of Health Sciences, Mekelle University, Mekelle, Ethiopia.
(2)Department of Veterinary Diagnostic Sciences, College of Veterinary Sciences, Mekelle University, Mekelle, Ethiopia.
(3)Department of Veterinary Medicine, College of Veterinary Medicine and Animal Sciences, Samara University, Samara, Ethiopia. gebruska2012@yahoo.com.

BACKGROUND: Drug-resistant tuberculosis (DR-TB) is a significant challenge to the national tuberculosis (TB) control program in Ethiopia. The Tigray region in northern Ethiopia has shown a surge in the incidence of DR-TB cases. However, the determinants of DR-TB in the region are not studied. This study is aimed at identifying the factors associated with the development of DR-TB in the Tigray region of northern Ethiopia.

METHODS: The study used an unmatched case-control design to identify determinants of DR-TB in the Tigray region, northern Ethiopia, whereby 86 patients and 86 controls who registered for TB treatment follow-up in selected hospitals were recruited. Trained nurses collected both primary and secondary data, which were analyzed using descriptive statistics and binary logistic regression. The test statistics was conducted with a 95% confidence level, and a p-value of less than 0.05 was considered significant.
RESULTS: The study included 86 patients with DR-TB (cases) and an equal number of patients with drug-susceptible (controls). The case and control groups had 38 (44.2%) and 47 (54.7%) males, respectively. The study revealed the study participants with male gender (adjusted odds ratio [AOR] = 4.9, 95% confidence interval [CI: 1.2-19.9), single marital status (AOR = 13.6, 95% CI: 2.3-81.2), history of TB treatment (AOR = 58.2, 95% CI: 11.2-302.1), experienced a delay of more than 60 days before TB diagnosis (AOR = 4.8, 95% CI: 1.2-19.3), interrupted treatment at least once (AOR = 4.9, 95% CI: 1.02-23.9), and unsuccessful treatment outcome at first treatment (AOR = 7.6, 95% CI: 1.8-35.9) had a higher risk of DR-TB.
CONCLUSIONS: The study highlights determinants of DR-TB in the region, including gender, marital status, delayed diagnosis (over 60 days), previous treatment history, interrupted treatment, and unsuccessful treatment outcomes during initial treatment. It is recommended that healthcare providers focus on targeted interventions, such as supporting males and unmarried individuals, ensuring early diagnosis and prompt initiation of treatment, improving treatment adherence, and providing tailored support for patients with histories of incomplete treatment and unsuccessful initial treatment outcomes.

DOI: 10.1186/s41043-025-01021-y
PMCID: PMC12291359
PMID: 40708047 [Indexed for MEDLINE]

Conflict of interest statement: Declarations. Ethics approval and consent to participate: Ethical clearance was obtained from the Ethical Review and Research Committee of College of Health Sciences at Mekelle University (ERC 0830/2016). Participants were informed of the study's objective and were invited to participate voluntarily. They were also assured that their information would be kept confidential. Interviews were conducted privately with only those who provided verbal consent to participate. Consent for publication: Not applicable. Competing interests: The authors declare no competing interests.

38. Imaging of post-tuberculosis lung disease cases in children and adolescent survivors: a systematic review.

Eur Clin Respir J. 2025 Aug 18;12(1):2547515. doi: 10.1080/20018525.2025.2547515. eCollection 2025.

Nataprawira HM(1), Dewi IMW(2)(3), Wiraningrat IGAAN(1), Cesilia C(1).

Author information:
(1)Department of Child Health, Faculty of Medicine Universitas Padjadjaran, Hasan Sadikin General Hospital, Bandung, Indonesia.
(2)Department of Biomedical Sciences, Faculty of Medicine Universitas Padjadjaran, Bandung, Indonesia.
(3)Research Centre for Care and Control of Infectious Diseases (RC3ID), Universitas Padjadjaran, Bandung, Indonesia.

INTRODUCTION: Post-tuberculosis lung disease (PTLD) causes health problems among pulmonary TB (PTB) survivors. Post-TB patients may suffer from chronic respiratory symptoms, declining lung function, and persistent radiological abnormalities. However, studies regarding PTLD in children and adolescents are still scarce. Patterns of radiological abnormalities, including chest X-ray (CXR) imaging, high-resolution computed tomography (HRCT), and magnetic resonance imaging (MRI) in post-TB children, and adolescents are not fully understood.
AIM: In this study, we aim to review and analyse radiological features in children and adolescent TB survivors of the literature on the differences in imaging findings in drug-resistant (DR) and drug-sensitive tuberculosis (DS TB) children and adolescent TB survivors.
METHOD: We performed a systematic review to determine imaging patterns of DR and DS TB in children and adolescent survivors. Data collected include study design, number of subjects, age, TB category, treatment duration, time of evaluation, and imaging patterns. We searched MEDLINE/Pubmed, Google Scholar, Science Direct, Wiley Online Library, Cochrane Library, and Proquest and included four studies for data analysis. Study quality was assessed using a modified Newcastle-Ottawa score.
RESULT: Studies included 151 children and adolescents aged 0-17 years. Three out of four studies were conducted on DS-TB patients and one study compared DS- and DR-TB. Radiological abnormalities observed by CXR at TB treatment completion include calcification in the presence or absence of fibrosis, bronchiectasis, and destroyed lung, or lymphoid interstitial pneumonitis. Micronodules are most often seen in HRCT in the acute early stages of TB and were not seen in standard chest radiography. Cavities persisted in almost 50% of patients after TB treatment and fibrotic changes increased after treatment.
CONCLUSION: Imaging abnormalities after TB treatment are often seen in children and adolescents. Imaging evaluation should be performed in PTB survivors, especially in those with moderate or advanced lesions during active disease and

those with severe clinical manifestations.

DOI: 10.1080/20018525.2025.2547515
PMCID: PMC12364111
PMID: 40837550

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

39. Artificial intelligence for tuberculosis control: a scoping review of applications in public health.

J Glob Health. 2025 Jul 25;15:04192. doi: 10.7189/jogh.15.04192.

Menon S(1)(2), Koura KG(1)(3).

Author information:
(1)International Union against Tuberculosis and Lung Disease, Paris, France.
(2)Epitech Research, Auderghem, Belgium.
(3)UMR261 MERIT, Université Paris Cité, IRD, Paris, France.

BACKGROUND: Artificial intelligence (AI) has become an important tool in global health, improving disease diagnosis and management. Despite advancements, tuberculosis (TB) remains a public health challenge, particularly in low- and middle-income countries where diagnostic methods are limited. In this scoping review, we aim to examine the potential role of AI in TB control.
METHODS: We conducted a search on 25 August 2024 for the past five years, in the PubMed database using keywords related to AI and TB. We included laboratory-based and observational studies focussing on AI applications in TB, excluding non-original research.
RESULTS: There were 34 eligible studies, identifying eight overarching aspects associated with TB control, including active case finding (ACF), triage, pleural effusion diagnosis, multidrug-resistant (MDR) TB and extensively drug-resistant (XDR) TB, differential diagnosis distinguishing active TB from TB infection and other pulmonary communicable diseases, TB and other pulmonary communicable and non-communicable diseases (NCDs), treatment outcome prediction, pleural effusion, and predictions of regional and national trends. AI may transform TB control through enhanced ACF methods and triage, improving detection rates in high-burden regions. With high accuracy, AI may diagnose pleural diagnosis, differentiate TB active and TB infection, TB and non-tuberculous mycobacterial

lung disease, COVID-19, and pulmonary NCDs. AI applications may facilitate the prediction of treatment success and adverse effects. Furthermore, AI-driven hotspot mapping may identify undiagnosed TB cases at rates surpassing traditional notification methods. Lastly, predictive modelling and clinical decision support systems may improve the management of MDR-TB.
CONCLUSIONS: This scoping review highlights the potential of AI-driven predictions in national TB programmes to enhance diagnostics, track trends, and strengthen public health surveillance. While promising for reducing transmission and supporting TB care in low-resource settings, these models require large-scale validation to ensure real-world applicability, especially for high-risk groups.

DOI: 10.7189/jogh.15.04192
PMCID: PMC12290985
PMID: 40709592 [Indexed for MEDLINE]

Conflict of interest statement: Disclosure of interest: The authors completed the ICMJE Disclosure of Interest Form (available upon request from the corresponding author) and disclose no relevant interest.

40. Effects of intense exercise on innate bacterial killing in close contacts of patients with TB/MDR-TB.

J Infect Public Health. 2025 Jul 24;18(11):102902. doi: 10.1016/j.jiph.2025.102902. Online ahead of print.

Chuachan S(1), Sriplung H(2), Ponpuak M(3), Chongsuvivatwong V(4).

Author information:
(1)Department of Physical Therapy, Faculty of Medicine, Prince of Songkla University, Hatyai, Songkhla, Thailand.
(2)Department of Epidemiology, Faculty of Medicine, Prince of Songkla University, Hatyai, Songkhla, Thailand. Electronic address: hutcha.s@gmail.com.
(3)Department of Microbiology, Faculty of Science, Mahidol University, Bangkok, Thailand.
(4)Department of Epidemiology, Faculty of Medicine, Prince of Songkla University, Hatyai, Songkhla, Thailand. Electronic address: cvirasak@medicine.psu.ac.th.

BACKGROUND: Close contacts of patients with multidrug-resistant tuberculosis (MDR-TB) face a high infection risk due to limited chemoprophylaxis. Exercise is

known to enhance the lung defense mechanisms. This study evaluated whether intense exercise can boost innate bacterial immunity in close contact by improving the in vitro killing of intracellular Mycobacterium tuberculosis.
METHODS: Twelve males (20-40 years) from a tuberculosis clinic were randomly assigned to exercise or no-exercise groups. The exercise group performed high-intensity cycling at 70-80 % of heart rate reserve (HRR) for 30-60 min, three days/week for 12 weeks. The no-exercise group engaged in self-directed exercise. Blood monocytes were isolated before and after the program and differentiated into inflammatory M1 and anti-inflammatory M2 macrophages. We infected the isolated monocytes and M1 and M2 macrophages with the mCherry-expressing laboratory reference M. tuberculosis strain H37Rv and a local strain of MDR-TB with a multiplicity of infection (MOI) is 10 for 0 and 72 h, and mycobacterial survival was determined via high content imaging.
RESULTS: Mycobacterial survival percentages were normalized to the 0-h infection control. In the exercise group, H37Rv survival was significantly decreased in monocytes, M1, and M2 macrophages compared to that in the no-exercise group. However, the local MDR strain reduced the survival of M1 macrophages but not that of monocytes or M2 macrophages. Additionally, cytokine secretion after H37Rv infection in monocytes showed a significant reduction in IL-1β levels, whereas no significant changes were observed in M1 and M2 macrophages.
CONCLUSION: Intense exercise may enhance mycobacterial killing in individuals exposed to TB, particularly inflammatory M1 macrophages. Promoting intense exercise among close contacts of patients with TB may be beneficial.

DOI: 10.1016/j.jiph.2025.102902
PMID: 40773852

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

41. The effects of decentralisation on patient and service outcomes: a case of the 2018 decentralisation of multidrug-resistant tuberculosis in Zambia.

Arch Public Health. 2025 Jul 24;83(1):193. doi: 10.1186/s13690-025-01672-7.

Matenga TFL(1), Chavula MP(2)(3), Zulu JM(1)(4), Silumbwe A(4), Maritim P(4)(5), Munakampe MN(4)(5), Habib B(1), Liusha N(6), Banda J(7), Sinyangwe NN(8), Mweemba C(4), Mubanga A(9), Kaonga P(7), Musukuma M(7), Phiri H(9), Halwiindi H(10).

Author information:
(1)Department of Health Promotion, School of Public Health, University of Zambia, Lusaka, Zambia.
(2)Department of Community and Family Medicine, School of Public Health, University of Zambia, Lusaka, Zambia. paul.malizgani@umu.se.
(3)Department of Epidemiology and Global Health, Umeå University, 901 87, Umeå, Sweden. paul.malizgani@umu.se.
(4)Department of Health Policy and Management, School of Public Health, University of Zambia, Lusaka, Zambia.
(5)Yakini Health Research Institute, Lusaka, Zambia.
(6)Ministry of Health, Kitwe Teaching Hospital, Off Kumboka Drive, P.O. Box 20969, Kitwe, Zambia.
(7)Department of Epidemiology and Biostatistics, School of Public Health, University of Zambia, Lusaka, Zambia.
(8)Department of Environmental Health, School of Public Health, University of Zambia, Lusaka, Zambia.
(9)Ministry of Health, Ndeke House, Haile Selassie Avenue, P.O. Box 30205, Lusaka, Zambia.
(10)Department of Epidemiology and Global Health, Umeå University, 901 87, Umeå, Sweden.

INTRODUCTION: The Zambian government decentralised tuberculosis control programs by transferring responsibility for the care and treatment of multidrug-resistant tuberculosis (MDR-TB) patients from a two-national hospital model to provincial hospitals and other lower-level healthcare structures. Limited evidence exists on the effects of decentralisation on the quality of TB care provided through public sector decentralisation. In this paper, we explored the impact of decentralising MDR-TB on patient and service outcomes.
METHODS: This study used a mixed-methods approach. Quantitative data were collected through a survey of 244 MDR-TB patients, while qualitative data was collected through interviews with TB coordinators, healthcare providers, patients, and caregivers. Participants were drawn from health facilities and the Ministry of Health. Quantitative data was analysed in STATA version 16.0, while thematic analysis was used for the qualitative data.
RESULTS: Decentralisation has improved patient care and management by increasing access to essential commodities such as medication and diagnostic testing. It has led to more equitable distribution of MDR-TB healthcare services and resources across different population groups, regardless of social, economic, or demographic factors. Furthermore, the quality of life for MDR-TB patients has improved, with better adherence to medication resulting from increased family support. Due to decentralisation, tailored community and patient-centred services have been integrated resulting in reduced congestion at facilities. The study also identified challenges, including heavy workload for healthcare staff,

fragmented coordination of supervisory responsibilities, and confusion over roles in patient management, which negatively impacted the decentralisation process.
CONCLUSION: The decentralisation of MDR TB services offers significant benefits but is not a guaranteed solution, as poor planning or implementation can lead to challenges in service delivery.

DOI: 10.1186/s13690-025-01672-7
PMCID: PMC12288269
PMID: 40707989

Conflict of interest statement: Declarations. Ethics approval and consent to participate: Ethical clearance for this study was sought from the University of Zambia Biomedical Research Ethics Committee (UNZABREC), Reference number 3003–2022. Permission to conduct the study was obtained from the Zambia National Health Research Authority and the Ministry of Health. All participants were given informed consent forms, which were read aloud to them and thoroughly explained before they were signed. Participants were informed about the study's goals, procedures, risks, benefits, and their rights as participants. Consent for publication: Not applicable. Competing interests: The authors declare no competing interests.

42. Surveillance and analysis of drug resistance and drug resistance levels in multidrug resistant tuberculosis on the tropical islands of China.

BMC Infect Dis. 2025 Aug 1;25(1):973. doi: 10.1186/s12879-025-11312-8.

Wang J(#)(1), Dong J(#)(1), Chen Z(1), Xu Y(1), Qiu W(1), Chen S(1), Pei H(2), Zhong Y(3).

Author information:
(1)Department of Clinical Laboratory, The Second Affiliated Hospital of Hainan Medical University, Haikou, 570311, People's Republic of China.
(2)Department of Clinical Laboratory, The Second Affiliated Hospital of Hainan Medical University, Haikou, 570311, People's Republic of China. phzmh61@aliyun.com.
(3)Department of Clinical Laboratory, The Second Affiliated Hospital of Hainan Medical University, Haikou, 570311, People's Republic of China. zhongyeteng@163.com.
(#)Contributed equally

OBJECTIVE: Multidrug-resistant tuberculosis (MDR-TB) remains a major public health challenge in China. Hainan, China's largest tropical island, possesses distinct socio-geographical features. However, the drug resistance patterns and molecular epidemiology of MDR-TB in this region have not been fully elucidated. This study aimed to assess the correlation between drug resistance genotypes and phenotypic resistance levels in multidrug-resistant Mycobacterium tuberculosis (MDR-MTB) strains collected from Hainan Island, using whole-genome sequencing (WGS) and phenotypic drug susceptibility testing (DST).
METHODS: MDR-MTB strains isolated from patients on Hainan Island (2019-2021) were analyzed. Minimum inhibitory concentrations (MIC) for 15 anti-TB drugs were determined by broth microdilution (BMD). Whole-genome sequencing (WGS) was performed using Illumina NovaSeq 6000. Genotypic resistance was predicted via TB-Profiler, and correlations between resistance mutations and MIC levels were assessed.
RESULTS: A total of 209 MDR-MTB strains were analyzed. Strains of lineage 2.2 exhibited significantly higher resistance to ethambutol (EMB) compared to non-lineage 2 strains ($P < 0.05$). The sensitivity of WGS in predicting resistance to first-line drugs isoniazid (INH), rifampicin (RIF), EMB, and pyrazinamide (PZA) was 94.7%, 99.0%, 96.5%, and 80.8%, respectively. However, specificity for EMB and PZA was lower at 60.2% and 79.4%. WGS also demonstrated high sensitivity and specificity (> 95%) for second-line injectable aminoglycosides (amikacin [AMK], capreomycin [CPM], and kanamycin [KM]), but sensitivity for other second-line drugs except for fluoroquinolone drug moxifloxacin (MOX, 94.4%) was below 80.0%. Notably, mutations in katG_S315T, rpoB_S450L, and gyrA_D94G were strongly associated with high-level resistance, while mutations in fabG1, ahpC, embA promoters, and gyrA at codon 90 were linked to low-level resistance.
CONCLUSIONS: This study quantitatively demonstrates the relationship between specific drug resistance genotypes and resistance levels. It is the first to characterize the regional resistance spectrum of MDR-MTB strains on Hainan Island. These findings offer a novel foundation for MIC-based dose adjustment and the optimization of treatment strategies in this region. TRIAL REGISTRATION: MR-46-23-020530. Date of registration:2023-07-03.

DOI: 10.1186/s12879-025-11312-8
PMCID: PMC12317541
PMID: 40750855 [Indexed for MEDLINE]

Conflict of interest statement: Declarations. Ethics approval and consent to participate: This study was approved by the Ethics Committee of the University of the Second Affiliated Hospital of Hainan Medical University, China (No.LW2020226) and waived the requirement for informed consent.This study

complies with the Declaration of Helsinki. Consent for publication: Not applicable. Competing interests: The authors declare no competing interests.

43. Pre-treatment loss to follow-up and associated factors among drug-resistant tuberculosis patients diagnosed in Wakiso district, central Uganda.

BMC Infect Dis. 2025 Jul 31;25(1):967. doi: 10.1186/s12879-025-11295-6.

Arinaitwe J(1)(2), Muleme J(3), Ochanda PN(3), Nuwematsiko R(3), Omongot S(3)(4), Bakamutumaho B(3)(5), Buregyeya E(3).

Author information:
(1)School of Public Health, College of Health Sciences, Makerere University, Kampala, Uganda. arinaitwejim@gmail.com.
(2)Makerere University Lung Institute, College of Health Science, Makerere University, Kampala, Uganda. arinaitwejim@gmail.com.
(3)School of Public Health, College of Health Sciences, Makerere University, Kampala, Uganda.
(4)Makerere University Lung Institute, College of Health Science, Makerere University, Kampala, Uganda.
(5)Uganda Virus Research Institute, Vaccine Preventable Diseases-EPI, Entebbe, Uganda.

BACKGROUND: Tuberculosis ranks among the top ten causes of death worldwide. The Sub-Saharan African region faces increasing trends of Drug-Resistant Tuberculosis (DR-TB), further complicating the existing efforts for prevention, control, and eradication. Pre-treatment loss to follow-up (LTFU) among diagnosed DR-TB patients also signifies a setback in the timely prevention of disease progression and transmission, especially in low-resource settings. This study assessed the magnitude of and factors associated with pre-treatment LTFU among DR-TB patients within Wakiso district, central Uganda.
METHOD: A sequential explanatory study design was adopted to analyze electronic case-based surveillance (eCBSS) data between 2017 to 2022 from the Ministry of Health, Uganda. Participants for qualitative data comprised of six (6) key informant interviews and 2 focus group discussions among health workers and DR-TB patients respectively.
RESULTS: Out of the 972 records retrieved from the eCBSS system for patients treated at Mulago National Referral Hospital from 2017 to 2022; 253 were analyzed. The majority of the participants, 62% (157/253), were male. The median age of study participants was 34 years (range: 18- 85). The prevalence of pretreatment LTFU was 13.4% (34/253). The qualitative findings reinforced and provided context to the quantitative results, revealing how behavioral, social, and system-level factors contribute to pre-treatment loss to follow-up (LTFU)

among DR-TB patients. Significant associations were observed in patients who lacked a recorded telephone contact in TB register (adjusted PR = 0.47, 95% CI: 0.27-0.80) and those without documented home address (adjusted PR = 0.52, 95% CI: 0.27-0.97); qualitatively, this was linked to patients' fear of stigma, lack of trust in the health system, and unstable living conditions, leading them to avoid being traced. The analysis also showed that tobacco use (adjusted PR = 1.96, 95% CI: 1.00-3.87) and illicit drug use (adjusted PR = 4.00, 95% CI: 1.76-9.08) significantly increased the risk of LTFU, which was supported by narratives describing substance use as contributing to hopelessness and neglect of health. Furthermore, patients with a history of treatment failure had 2.4 times the risk of being lost to follow-up (adjusted PR = 2.40, 95% CI: 1.08-5.36), consistent with qualitative reports of discouragement, denial, and lack of awareness about the severity of DR-TB. Relapse cases had 69% higher prevalence of loss to follow-up (adjusted PR = 1.69, 95% CI 0.78-3.70) compared to new cases. Although factors such as alcohol use and family support did not reach statistical significance in the quantitative model, they were prominent in the qualitative data, suggesting under-recognized barriers related to psychosocial distress and poverty. Together, these findings demonstrate a strong convergence between data strands while highlighting that some influential factors particularly social and psychological may be underrepresented in routine health data.

CONCLUSION: The study found a 13.4% prevalence of pre-treatment LTFU among DR-TB patients in Wakiso District. Quantitative analysis identified significant predictors, including lack of contact information, prior treatment failure, tobacco use, and illicit drug use, while protective factors included having a recorded home address and telephone contact recorded in relevant TB registers/electronic systems. These findings were reinforced by qualitative insights, which revealed that fear of stigma, denial of illness, substance abuse, poor health system responsiveness, and lack of social support contributed to patient disengagement. The integration of both data strands highlights the need for a patient-centered approach that strengthens communication, addresses behavioral health needs, and improves follow-up systems to reduce pre-treatment LTFU and improve DR-TB outcomes.

DOI: 10.1186/s12879-025-11295-6
PMCID: PMC12312580
PMID: 40745635 [Indexed for MEDLINE]

Conflict of interest statement: Declarations. Ethics approval and consent to participate: This study was conducted in accordance with the Declaration of Helsinki. The study was reviewed by Makerere University School of Public Health Research and Ethical Committee, located at the School of Public Health, Makerere

University, which is an accredited Institutional Review Board (IRB) for approval (number MakSPH-REC 068). Permission was then sought from the Ministry of Health to access eCBSS platform; from the office of the District Health officer and the health facility in charge before the collection. The secondary data extracted was de-identified and assigned a decoy participant ID. Participants for KIIs and FGDs received information about the study objectives, procedures, and benefits; and asked to consent to participate in the study. Informed consent for participants interviewed was obtained before being interviewed. Privacy and confidentiality of data were ensured by masking participants with personal identifiers like name, and was addressed by assigning a unique code to each participant. Participants were free to accept or refuse to participate in the study. There was no anticipated harm to the participants during this study except for the time they gave in during data collection. Consent for publication: Not applicable. Competing interests: The authors declare no competing interests.

44. Exploration of plasma exosomal miR-122-5p and its related targets KNG1 and C3 in the diagnosis of drug-resistant tuberculosis.

Sci Rep. 2025 Jul 22;15(1):26620. doi: 10.1038/s41598-025-10639-1.

Yao X(1), Zhang L(2).

Author information:
(1)Department of Clinical Medicine, Hangzhou Normal University, Hangzhou, China.
(2)Department of Clinical laboratory, The Affiliated Hospital of Hangzhou Normal University, Hangzhou, China. zjhzzlh2007@163.com.

Drug-resistant tuberculosis (DR-TB) poses significant challenges not only to public health but also imposes substantial psychological and economic burdens on individuals and their families. As a severe infectious disease that jeopardizes both physical and mental well-being, DR-TB frequently spreads in underdeveloped regions due to inadequate diagnostic technologies.In this study, we validated the binding interaction between miR-122-5p and the proteins kininogen-1 (KNG1)/complement C3 using a dual-luciferase reporter assay. Furthermore, we employed liquid biopsy techniques to quantify miR-122-5p expression in plasma exosomes from DR-TB patients, alongside measuring plasma levels of KNG1, complement C3, and other coagulation and immune function parameters. This approach aims to identify efficient, non-invasive laboratory biomarkers for the early diagnosis of DR-TB. 50 patients with drug-susceptible tuberculosis (DS-TB) and 50 patients with DR-TB who were diagnosed in the nearby hospital between April 2024 and January 2025 were chosen. 51 healthy people who had physical exams over the same time frame were also selected as the control group. In the

early morning, 5 ml of fasting venous blood was drawn from each of all subjects and centrifuged for standby. Informed consent was obtained from all Participants, who then signed the informed consent forms. We used Western blotting (WB), transmission electron microscopy (TEM), and nanoparticle tracking analysis (NTA) to find the biomarkers in the exosomes that were taken from each of the three groups' plasma. The dual-luciferase experiment was used to verify the targeting relationship between miR-122-5p and protein KNG1 and complement C3. The RNA level of the miR-122-5p gene in plasma exosomes was detected by real-time fluorescence quantitative PCR (qRT-PCR). The KNG1 level in the plasma of the subjects was measured by ELISA, and the clinical indicators of the patients were also collected. To assess the diagnostic effectiveness of the genes found in the plasma exosomes, we used the receiver operating characteristic (ROC) curve. We found that there is a targeting relationship between miR-122-5p and protein KNG1 as well as complement C3. Meanwhile, the level of miR-122-5p in the DR-TB group was significantly higher than that in the DS-TB group and the HCs group, indicating a relatively high diagnostic efficacy. A useful biomarker to enhance the diagnosis of DR-TB is the level of miR-122-5p in plasma exosomes.

DOI: 10.1038/s41598-025-10639-1
PMCID: PMC12284156
PMID: 40695929 [Indexed for MEDLINE]

Conflict of interest statement: Declarations. Competing interests: The authors declare no competing interests. Ethical approval and consent to participate: The study was approved by the Human Ethics Committee of the Affiliated Hospital of Hangzhou Normal University, and the ethics number was 2024(E2)-KS-069. Consent for publication: Yes.

45. RpoB mutation patterns in Rifampicin-resistant tuberculosis: a Jiangxi Province study, 2021-2023.

Sci Rep. 2025 Jul 31;15(1):27988. doi: 10.1038/s41598-025-11949-0.

Mao ZQ(#)(1)(2), Zhang QL(#)(1)(3), Zheng H(#)(4)(2), Liu ZQ(1), Li FM(1), Xu LS(1), Liang LC(1), Shu LH(1), Yang HQ(5).

Author information:
(1)Jiangxi Chest Hospital (Jiangxi Third People's Hospital), Nanchang, 330103, P R China.
(2)Jiangxi Provincial Key Laboratory of Preventive Medicine, Jiangxi Medical

College, Nanchang University, Nanchang, 330006, P R China.
(3)Jiangxi Provincial Key Laboratory of Health Sciences, Jiangxi Chest Hospital (Jiangxi Third People's Hospital), Nanchang, 330103, P R China.
(4)School of Public Health, Jiangxi Medical College, Nanchang University, Nanchang, 330006, P R China.
(5)Jiangxi Chest Hospital (Jiangxi Third People's Hospital), Nanchang, 330103, P R China. 13879158355@163.com.
(#)Contributed equally

Antimicrobial resistance in Mycobacterium tuberculosis (M.tb) strains presents a significant challenge to global tuberculosis (TB) control efforts. This study was conducted to explore the distribution and prevalence of mutations at various sites within the 81 bp Rifampicin (RIF) resistance-determining region (RRDR) of the rpoB gene in M.tb, as detected by the Xpert MTB/RIF assay. This retrospective analysis encompassed 9,867 non-repeating patients diagnosed with TB between 2021 and 2023. Cases with RR detected by the Xpert were included in further detailed analysis. The study utilized Chi-square tests or Fisher's exact tests to identify statistically significant differences in demographic variables and the prevalence of rpoB gene mutations between RResistant TB (RR-TB) and non-RR-TB groups. Multiple logistic regression analysis was employed to examine the relationship between probe types and demographic variables, with a P-value of less than 0.05 considered statistically significant. Over the three-year study period, M. tb was identified in 2,927 cases, with 485 being RR-TB. While individuals aged ≥ 65 years constituted the largest absolute number of RR-TB cases, the highest relative risk was observed in children aged 5-14 years (OR = 2.68, 95% CI 1.16-6.22, P = 0.02) compared to the ≥ 65 reference group. probe E missing emerged as the predominant mutation site, particularly prevalent in pulmonary specimens and among individuals aged 55-64 years, with a statistically significant difference (P < 0.001). An upward trend in probe B mutations was also observed, reaching statistical significance ($\chi 2 = 6.614$, P = 0.037).This molecular epidemiological study has identified the mutation patterns within the rpoB gene that contribute to RR, as identified through the use of Xpert technology over a three-year span in Jiangxi Province. The insights gained are instrumental in informing individualized treatment regimens for RR-TB patients by correlating mutation locations with resistance levels (e.g., probe E mutations confer high-level resistance requiring second-line drugs, while probe B mutations like D435Y may confer low-level "disputed" resistance). This facilitates precision therapy, avoids unnecessary second-line treatments, and reduces transmission. Future advancements in technology, such as large-scale sequencing studies, could build upon these findings to further elucidate the genetic variations at play. Ultimately, these discoveries could be corroborated through rigorous in vitro and in vivo experimental research, reinforcing the foundation of our understanding and response to antimicrobial resistance in M.tb.

DOI: 10.1038/s41598-025-11949-0
PMCID: PMC12313984
PMID: 40745428 [Indexed for MEDLINE]

Conflict of interest statement: Declarations. Competing interests: The authors declare no competing interests. Institutional review board statement: Ethical approval was waived by the local Ethics Committee of Jiangxi Province Chest Hospital in view of the retrospective nature of the study and all the procedures had been performed were part of the routine care.

46. Assessment of comorbidities, risk factors, and post tuberculosis lung disease in National Tuberculosis Guidelines: A scoping review.

PLOS Glob Public Health. 2025 Jul 23;5(7):e0004935. doi: 10.1371/journal.pgph.0004935. eCollection 2025.

Bah MS(1), Htet KKK(2), Bisson GP(3), Khosa C(4)(5), Masekela R(6)(7), Meghji J(8), Mochankana K(6), Rachow A(9)(10)(11), Navuluri N(12)(13).

Author information:
(1)Department of Population Health Science, Duke University, Durham, North Carolina, United States of America.
(2)Department of Epidemiology, Faculty of Medicine, Prince of Songkla University, Hat Yai, Songkhla, Thailand.
(3)Department of Medicine, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, Pennsylvania, United States of America.
(4)Instituto Nacional de Saúde, Marracuene, Mozambique.
(5)Department of Clinical Sciences, Liverpool School of Tropical Medicine, Liverpool, New York, United Kingdom.
(6)Department of Paediatrics and Child Health, School of Clinical Medicine, College of Health Sciences, University of KwaZulu-Natal, Durban, South Africa.
(7)Africa Health Research Institute, Durban, South Africa.
(8)National Heart and Lung Institute, Imperial College London, London, United Kingdom.
(9)Division of Infectious Diseases and Tropical Medicine, University Hospital, LMU Munich, Munich, Germany.
(10)German Center for Infection Research (DZIF), Partner Site Munich, Munich, Germany.
(11)Unit Global Health, Helmholtz Zentrum München, German Research Center for Environmental Health (HMGU), Neuherberg, Germany.

(12)Division of Pulmonary, Allergy and Critical Care, Department of Medicine, Duke University, Durham, North Carolina, United States of America.
(13)Duke Global Health Institute, Duke University, Durham, North Carolina, United States of America.

Tuberculosis (TB) remains a major public health issue across the world and national TB guidelines are an important resource for diagnosis and treatment. This scoping review aimed to analyze how countries with the highest TB burdens approach the integration of comorbidity and risk factor screening, diagnosis and treatment, TB recurrence, and post-TB lung disease (PTLD) diagnosis and management, within their TB guidelines. We used the Arksey and O'Malley methodological framework to conduct a scoping review of TB guidelines among the WHO list of highest-TB burden countries. We identified drug-susceptible, drug-resistant, and consolidated guidelines through web searches and personal contacts within TB programs. We translated guidelines into English as needed and systematically extracted, recorded, and reviewed the guidelines to aggregate and describe our findings. Among the 49 countries with the highest TB burden, we successfully identified, translated, and analyzed 43 guidelines (24 drug-sensitive, 9 drug-resistance, and 10 consolidated) from 34 countries. Recommendations for screening varied by comorbidity or risk factor with the four most recommended being HIV/AIDS (100%), pregnancy (73%) and liver disease (59%) and mental health (59%). Recommendations for linkage to care were more infrequent and also varied with the top four being HIV (88%), liver disease (47%), diabetes (44%), and mental health (44%). Only 27 (79%) countries specified diagnostic tests to assess for TB recurrence among individuals presenting with symptoms post-TB treatment, with 25 recommending GeneXpert MTB/RIF. Notably, only 7 (21%) countries mentioned PTLD in their guidelines, with wide variations in their specific recommendations regarding screening, diagnosis, and management. Our findings highlight the lack of detailed guidance on how to properly diagnose and refer patients to appropriate care for various comorbidities or risk factors which may significantly impact microbiological and clinical TB treatment outcomes, including PTLD and ultimately point to an important opportunity for improvement in future guidelines.

DOI: 10.1371/journal.pgph.0004935
PMCID: PMC12286338
PMID: 40700421

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

interests exist.

47. Whole genome sequencing reveals novel resistance-conferring mutations and large genome deletions in drug-resistant Mycobacterium tuberculosis isolates from Indonesia.

J Glob Antimicrob Resist. 2025 Jul 22;44:314-318. doi: 10.1016/j.jgar.2025.07.017. Online ahead of print.

Aung HL(1), Chaidir L(2), Pitaloka DAE(3), Miyahara Y(4), Kumar N(5), Soeroto AY(6), Cook GM(4), van Crevel R(7), Alisjahbana B(8), Peacock SJ(5), Hill PC(9).

Author information:
(1)Department of Microbiology and Immunology, Division of Health Sciences, University of Otago, Dunedin, New Zealand. Electronic address: htin.aung@otago.ac.nz.
(2)Department of Biomedical Sciences, Faculty of Medicine, Universitas Padjadjaran, Bandung, Indonesia; Research Center for Care and Control of Infectious Disease, Universitas Padjadjaran, Bandung, Indonesia.
(3)Department of Pharmacology and Clinical Pharmacy, Faculty of Pharmacy, Universitas Padjadjaran, Bandung, Indonesia; Center for Translational Biomarker Research, Universitas Padjadjaran, Bandung, Indonesia.
(4)Department of Microbiology and Immunology, Division of Health Sciences, University of Otago, Dunedin, New Zealand.
(5)Department of Medicine, University of Cambridge, Cambridge, United Kingdom.
(6)Department of Internal Medicine, Faculty of Medicine, Universitas Padjadjaran/Hasan Sadikin Hospital, Bandung, Indonesia.
(7)Department of Internal Medicine, Radboud University Medical Centre, Nijmegen, the Netherlands.
(8)Research Center for Care and Control of Infectious Disease, Universitas Padjadjaran, Bandung, Indonesia; Department of Internal Medicine, Faculty of Medicine, Universitas Padjadjaran/Hasan Sadikin Hospital, Bandung, Indonesia.
(9)Centre for International Health, Division of Health Sciences, University of Otago, Dunedin, New Zealand.

OBJECTIVE: This study evaluated drug resistance profiles of Mycobacterium tuberculosis (Mtb) isolates in West Java, Indonesia through phenotypic and genomic approaches.
METHODS: We performed phenotypic drug-susceptibility testing (DST), coupled with whole-genome sequencing (WGS) of 142 Mtb isolates identified as RIF-R (Rifampicin resistant) using the Xpert MTB/RIF platform.
RESULTS: We found 107/142 (75%) isolates had high-level isoniazid resistance (INH-R) and rifampicin resistance (RIF-R). Of 107 isolates, we found two had

novel katG mutations and three had large genome deletions encompassing the katG gene conferring INH-R. We also did not detect pre-existing mutations resistant to new and repurposed oral drugs bedaquiline (BDQ), pretomanid (Pa) and linezolid (LZD).
CONCLUSIONS: Known drug-resistance conferring mutations reported in this study can be detected by the newly launched Xpert MTB/XDR together with Xpert MTB/RIF, providing clinicians with an expanded drug-susceptibility report without the need for culturing and WGS. On the other hand,the novel mutations and deletions found in this study are escaping routine diagnostics and could drive outbreaks of MDR-TB in Indonesia. The mass rollout of new and repurposed drugs for the treatment of drug-resistant TB in Indonesia is reassured by the absence of pre-existing mutations in this study. However, tools for rapid detection of resistance to these new drugs are urgently required to circumvent treatment-emergent resistance.

DOI: 10.1016/j.jgar.2025.07.017
PMID: 40706998

48.Effect of Bdq-Containing Regimen and Molecular Detection of Bdq Resistance among Pre-XDR-TB Patients with Unfavorable Outcomes.

Int J Gen Med. 2025 Aug 14;18:4469-4480. doi: 10.2147/IJGM.S538660. eCollection 2025.

Ding F(1)(2), Li S(2)(3), Liu X(1)(2), Shao G(2)(3), Su Y(2)(3), Qian Y(1)(2), Mao Z(2)(3), Zeng J(2)(3), Lu S(1)(2)(3), Fang M(2)(3).

Author information:
(1)National Clinical Research Center for Infectious Diseases, Shenzhen Third People's Hospital, Shenzhen, Guangdong Province, People's Republic of China.
(2)The Second Affiliated Hospital, Southern University of Science and Technology, Shenzhen, Guangdong Province, People's Republic of China.
(3)Department of Pulmonary Diseases, Shenzhen Third People's Hospital, Shenzhen, Guangdong Province, People's Republic of China.

PURPOSE: The objective of this study was to evaluate the efficacy of bedaquiline (Bdq)-containing regimens in pre-extensively drug-resistant tuberculosis (pre-XDR-TB) patients in Shenzhen, China, and to investigate the association between Bdq resistance and unfavorable outcomes.
METHODS: Data were collected from 84 pre-XDR-TB patients categorized into Bdq (n = 46) and non-Bdq (n = 38) groups. Individuals in the Bdq group were treated

with Bdq alongside individualized background drugs. Commonly used drugs (>50% of patients) in both groups were linezolid (Lzd), clofazimine (Cfz), cycloserine (Cs) and pyrazinamide (Pza). Treatment outcomes were classified as cure, treatment completion, treatment failure, loss to follow-up, or death. Logistic regression analysis was conducted to determine independent predictors of treatment success using potential risk factors, including age, sex, body mass index (BMI), TB treatment history, and other factors. Whole-genome sequencing (WGS) was conducted on clinical isolates from 4 patients with unfavorable outcomes and 4 patients with favorable outcomes in the Bdq group.
RESULTS: Favorable treatment outcomes were observed in 89.13% (41/46) of the Bdq group and 52.63% (20/38) of the non-Bdq group (P = 0.0005). Univariate and multivariate analyses identified Bdq was an independent factor associated with treatment success (odds ratio [OR] = 11.572, 95% CI: 2.183-61.343, P = 0.004). WGS identified an atpE_Ala63Pro mutation conferring Bdq resistance in one patient with an unfavorable outcome. Additional resistance mutations included Rv0678_Arg156fs (Bdq and Cfz resistance) and rplC_Cys154Arg (Lzd resistance).
CONCLUSION: Bdq-containing regimens significantly improved the treatment outcomes among pre-XDR-TB patients. The emergence of resistance mutations highlights the importance of routine drug resistance monitoring and rational drug use. Expanding access to Bdq and other novel drugs at affordable prices is vital for improving the success of pre-XDR-TB treatment.

DOI: 10.2147/IJGM.S538660
PMCID: PMC12361352
PMID: 40837941

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

49. Chest x-ray features and their associated factors among rifampicin/multi-drug-resistant tuberculosis patients in drug-resistant tuberculosis treatment initiating centers in Addis Ababa, Ethiopia: a retrospective study.

BMC Infect Dis. 2025 Aug 2;25(1):974. doi: 10.1186/s12879-025-11344-0.

Beshaw MA(1), Siraj EM(2), Demass TB(3), Lakew AM(4).

Author information:
(1)Department of Internal Medicine, College of Medicine and Health Sciences, University of Gondar, Gondar, Ethiopia. mulataddis100@gmail.com.

(2)Department of Internal Medicine, Alert Comprehensive Specialized Hospital, Addis Ababa, Ethiopia.
(3)Department of Internal Medicine, College of Medicine and Health Sciences, University of Gondar, Gondar, Ethiopia.
(4)Department of Epidemiology and Biostatistics, Institute of Public Health, College of Medicine and Health Sciences, University of Gondar, Gondar, Ethiopia.

INTRODUCTION: Rifampicin/multi-drug resistant tuberculosis (RR/MDR-TB) treatment regimen selection and its treatment duration are significantly influenced by the degree of lung damage identified with baseline chest x-rays (CXR). Hence, this study was aimed at determining baseline CXR features and their associated factors in Addis Ababa, Ethiopia.
METHODS: The data was collected from 324 RR/MDR-TB patients who had baseline chest x-rays. The data was collected using a structured checklist containing socio-demographics, baseline chest x-rays, and other clinical variables. It was entered into Epi Data 4.1 and then exported to SPSS version 25 for data cleaning and analysis. A binary logistic regression model was fitted. Bivariate logistic regression was done first, then variables with a p-value ≤ 0.2 were taken into the multivariable logistic regression analysis. Variables with a p-value < 0.05 were reported as statistically significant.
RESULTS: Of the 324 study participants, nearly 74% (239) of them had abnormal baseline CXR features. The most common abnormal CXR feature was cavitation, followed by consolidation. In RR/MDR-TB patients with malnutrition, anemia, and any previous TB treatment history, the most common abnormal radiologic feature was cavitation. Daily laborer [AOR = 0.1 (95% CI: 0.01, 0.55)], BMI < 18.5 kg/m2 [AOR = 1.8 (95% CI: 1.02, 3.17)], HIV-positive [AOR = 0.41 (95% CI: 0.2, 0.86)], and comorbidities [AOR = 0.32 (95% CI: 0.15, 0.67)] were significantly associated with abnormal CXR features in RR/MDR-TB patients.
CONCLUSIONS AND RECOMMENDATIONS: In our study, the majority of RR/MDR-TB patients had abnormal CXR features, of which cavitation was the most common. Therefore, further study needs to be done prospectively at the multi-center level since the extent of lung damage identified by CXR is one of the determining factors for DR-TB treatment regimen selection, DR-TB treatment duration, help diagnose DR-TB clinically, and TB sequelae.

DOI: 10.1186/s12879-025-11344-0
PMCID: PMC12317462
PMID: 40753370 [Indexed for MEDLINE]

Conflict of interest statement: Declarations. Ethics approval and consent to participate: Ethical clearance was obtained from the University of Gondar Ethical Review Board. The ethical clearance was presented to the Armour Hanssen

Research Institute (AHRI)/ALERT Ethics Review Committee and the Research Ethical Review Committee Office of St. Peter's Specialized Hospital. The ethical clearance obtained from AHRI/ALERT Ethics Review Committee and the Research Ethical Review Committee Office of St. Peter's Specialized Hospital were submitted to the medical directors and then to the department heads of Internal Medicine of both hospitals. Data was collected after we obtained oral informed consent. Personal identifiers were removed. All the information collected was kept confidential. This study was conducted according to the ethical principles of the Helsinki declaration of 1964. Competing interests: The authors declare no competing interests.

50. Integrating Early Tuberculosis States Into Contact Management in Peru.

JAMA Netw Open. 2025 Aug 1;8(8):e2525207. doi: 10.1001/jamanetworkopen.2025.25207.

Tan Q(1), Huang CC(1)(2), Madden A(1), Murray MB(1)(2)(3).

Author information:
(1)Department of Global Health and Social Medicine, Harvard Medical School, Boston, Massachusetts.
(2)Division of Global Health Equity, Department of Medicine, Brigham and Women's Hospital, Boston, Massachusetts.
(3)Department of Epidemiology, Harvard T. H. Chan School of Public Health, Boston, Massachusetts.

IMPORTANCE: Tuberculosis (TB) is now understood to exist on a spectrum from TB infection to active TB disease. While World Health Organization guidelines target TB infection and TB disease, they overlook individuals with early TB in the middle of this spectrum.
OBJECTIVE: To evaluate chest radiograph (CR)-guided screening strategies among household contacts (HHCs) of patients with TB in a high-burden setting.
DESIGN, SETTING, AND PARTICIPANTS: This decision analytical model was constructed from June 1 to November 31, 2024. Community-based care in an environment with high TB burden and limited resources was used as the setting in Lima, Peru. Participants included a hypothetical cohort of 1000 HHCs with positive results of a tuberculin skin test and negative results of a sputum culture who were cleared of TB disease based on a clinician's evaluation. The hypothetical cohort was based on the clinical and demographic features of a cohort studied between September 1, 2009, and August 29, 2012.
INTERVENTIONS: Strategy 1 included CR screening to rule out TB disease followed by TB preventive therapy for all; strategy 2, CR screening with treatment for TB disease for those with abnormal CR findings and TB preventive therapy for those

without; and strategy 3, observation without pharmacological intervention. We modeled 6 intervention scenarios by applying strategies 1 and 2 to the entire HHC population, to HHCs younger than 35 years, and to HHCs younger than 19 years (Peru's national TB policy).
MAIN OUTCOMES AND MEASURES: TB cases averted, serious adverse events (SAEs), and drug resistance.
RESULTS: A simulated cohort of 1000 HHCs with age and clinical status distributions was based on a previously published cohort of 12 767 TB HHCs in Lima, Peru. Of these, 7661 (60.0%) were male, 4212 (33.0%) were younger than 15 years, and 444 (3.4%) developed TB during 1 year of follow-up. Strategy 2 applied to all HHCs reduced TB cases by 71% to 81%, outperforming strategy 1 applied to all HHCs, which reduced cases by 49% to 69%. Strategy 2 reduced acquired isoniazid resistance but increased SAEs. When both strategies were restricted to HHCs younger than 19 years, strategy 2 reduced TB cases by 42% to 50%. Expanding treatment to older adults further reduced cases but also increased SAEs (19-22 additional SAEs).
CONCLUSIONS AND RELEVANCE: In this model of TB HHC management, CR-guided identification and treatment of early TB was more effective than universal isoniazid preventive therapy, especially in children and young adults. Trade-offs between benefit and harm must be carefully considered in older adults.

DOI: 10.1001/jamanetworkopen.2025.25207
PMCID: PMC12329612
PMID: 40768149 [Indexed for MEDLINE]

Conflict of interest statement: Conflict of Interest Disclosures: Dr Huang reported receiving grant support from Brigham and Women’s Hospital and Harvard Medical School during the conduct of the study. No other conflicts were disclosed.

51.Using linezolid as a substitute for the injectable in case of ototoxicity is safer and as effective as all-oral treatment for rifampicin-resistant TB.

IJTLD Open. 2025 Aug 13;2(8):450-458. doi: 10.5588/ijtldopen.25.0151. eCollection 2025 Aug.

Souleymane MB(1)(2), Decroo T(3), Soumana A(4), Lawan IM(1), Aboubacar AC(4), Gagara-Issoufou A(5)(6), Moussa RH(7), Kabirou AA(8), Hamidou I(9)(10), Moussa SH(5), Adamou M(11), Adehossi E(6), Mamadou S(6), de Jong BC(12), Rigouts L(2)(12), Piubello A(13).

Author information:

(1)Damien Foundation, Niamey, Niger.
(2)University of Antwerp, Department of Biomedical Sciences, Antwerp, Belgium.
(3)Institute of Tropical Medicine, TB-HIV Unit, Antwerp, Belgium.
(4)National Tuberculosis Programme, Coordination, Niamey, Niger.
(5)Hopital National Amirou Boubarcar Diallo, Service pneumo-phtysiologie, Niamey, Niger.
(6)Université Abdou Moumouni de Niamey, Faculté des Sciences de la Santé, Niamey, Niger.
(7)Centre Hospitalier Régional de Tahoua, CAT, Tahoua, Niger.
(8)Centre Hospitalier Régional de Maradi, CAT, Maradi, Niger.
(9)Université André Salifou de Zinder, Faculté des Sciences de la Santé, Zinder, Niger.
(10)Hopital National de Zinder, Service pneumo-phtysiologie, Zinder, Niger.
(11)Ministère de la Santé Publique, de la Population et des Affaires Sociales, Direction Générale de la Santé Publique, Niamey, Niger.
(12)Institute of Tropical Medicine, Mycobacteriology Unit, Antwerp, Belgium.
(13)Damien Foundation, Department of DR-TB, Brussels, Belgium.

BACKGROUND: WHO recommends all-oral bedaquiline (BDQ) and linezolid (LZD)-containing regimens for rifampicin-resistant TB (RR-TB). In Niger, high cure rates were achieved using an adaptive short treatment regimen (aSTR) with a second-line injectable drug (SLID) and LZD, where LZD replaced the SLID in case of any ototoxicity detected on monthly audiometry. In 2020, WHO recommended a short oral BDQ/LZD regimen (oSTR). However, the success reported for oSTR was lower than for aSTR in Niger. The 'SHOrt ORal Treatment' trial therefore compared the safety and efficacy between aSTR and oSTR in Niger.
METHODS: In this pragmatic clinical trial, patients with fluoroquinolone-susceptible RR-TB were assigned by alternate months to aSTR or oSTR. Regression models estimated the association between regimen and safety (grade 3-4 adverse events [AEs]) and efficacy (excluding loss to follow-up).
RESULTS: Between 2021-2022, 158 RR-TB patients were included, 80 on oSTR and 78 on aSTR. Overall, 34 patients experienced 43 grade 3-4 AEs (anaemia: 15, neurotoxicity: 11, vomiting: 8, hepatitis: 7, arthralgia: 1, QTc prolongation: 1). Grade 3-4 AEs occurred in 26/80 (32.5 %) on oSTR versus 8/78 (10.3%) on aSTR, with anaemia, neurotoxicity and arthralgia being significantly higher in the oSTR group. Ototoxicity and nephrotoxicity appeared more frequently during the aSTR, but none evolved to grade 3. Patients treated with oSTR had a 3-fold increase in grade 3-4 AE (aHR 3.04;95% CI:1.36-6.80). End-of-treatment success was similar for oSTR compared to aSTR.
CONCLUSION: aSTR was safer than oSTR and both approaches had a similar treatment efficacy.

DOI: 10.5588/ijtldopen.25.0151
PMCID: PMC12352956
PMID: 40821684

52. Real-world effectiveness and safety of prolonged bedaquiline course in the treatment of drug-resistant tuberculosis-a multi-center retrospective cohort study in a country with a high burden of drug-resistant tuberculosis.

Microbiol Spectr. 2025 Aug 5;13(8):e0009725. doi: 10.1128/spectrum.00097-25. Epub 2025 Jul 7.

Yu Y(#)(1), Cao J(#)(1), Pan H(#)(2), Zhong H(3), Wu X(4), Yang J(4), Cheng L(1), Qu Q(1), Wang L(1), Lu F(2), Chen H(2), Wang J(3), Sha W(1), Sun Q(1).

Author information:
(1)Shanghai Clinical Research Center for Infectious Disease (Tuberculosis), Shanghai Key Laboratory of Tuberculosis, Shanghai Pulmonary Hospital, Tongji University School of Medicine, Shanghai, China.
(2)Department of Tuberculosis, The Third People's Hospital of Zhenjiang affiliated to Jiangsu University, Zhenjiang, China.
(3)Department of Infectious Diseases, Shanghai Fengxian Guhua Hospital, Shanghai, China.
(4)Department of Clinical Laboratory, Shanghai Pulmonary Hospital affiliated to Tongji University, Shanghai, China.
(#)Contributed equally

Bedaquiline (BDQ) has gradually become a core drug in drug-resistant tuberculosis (DR-TB) treatment, and the additional benefits of prolonging BDQ use remain unclear. Patients with DR-TB who received a BDQ-containing regimen from three Chinese clinical centers between 1 March 2018 and 31 December 2021 were retrospectively analyzed. Treatment outcomes and adverse drug reactions were compared between 6-month and prolonged BDQ treatment group before and after adjustment by propensity score matching (PSM). A total of 160 patients were enrolled, 72 patients were treated with BDQ for 6 months, and 88 patients were over 6 months, of which the median duration was 9 months (IQR: 8-11 months). After PSM adjustment, there were no significant differences in treatment outcome between the prolonged groups (7-9, 10-12, >12 months) and the 6-month group (all $P > 0.05$). A total of 35 patients met the criteria for BDQ prolongation but did not receive it, resulting in a success rate of 60%, significantly lower than the prolonged group (78.4%, $P = 0.038$); however, after adjustment by PSM, there was no statistically significance ($P > 0.05$). The median treatment duration (23 months, IQR: 18.50-25.00 months) was significantly longer than the prolonged group (18 months, IQR: 15.00-20.25 months, $P < 0.001$). Additionally, two deaths

occurred in the prolonged group, and none in the 6-month group. The cause of death in one patient was adjudicated as anti-TB treatment-related, while the other one was considered not. There were no significant differences in the effectiveness and safety between 6-month and prolonged group, it's still recommended to prolong BDQ use under close monitoring when anti-TB drugs are insufficient to form an effective treatment regimen. Prolonged use of BDQ achieved similar treatment outcomes while potentially shortening the overall anti-TB duration.IMPORTANCEThis real-world retrospective cohort study provides critical evidence on the extended application of Bedaquiline (BDQ) in managing drug-resistant tuberculosis (DR-TB). To date, the effectiveness and safety data regarding prolonged BDQ treatment are still lacking, and the additional benefits of prolonged BDQ use remain unclear. Our findings notably demonstrate that prolonged use of BDQ can achieve similar treatment success rates while potentially shortening the overall anti-TB treatment duration. We conclude that when the anti-TB drugs are insufficient to form an effective treatment regimen, prolonged BDQ use with rigorous safety monitoring is recommended. Our study significantly advances the evidence base for prolonged use of BDQ in clinical practice.

DOI: 10.1128/spectrum.00097-25
PMCID: PMC12323657
PMID: 40621913 [Indexed for MEDLINE]

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

53. Longitudinal phenotypic and genomic evidence revealing increased risk of drug resistance accumulation in tuberculosis patients in the counties of central China.

Microbiol Spectr. 2025 Aug 5;13(8):e0038025. doi: 10.1128/spectrum.00380-25. Epub 2025 Jun 23.

Wang F-L(#)(1), Chen R(#)(2), Xu Q(#)(3), Wang X-Q(3), Tao F-X(4), Huang Z-K(1), Zhang Y-T(1), Chen S-Q(3), Wu X-J(3), Cao H-Y(3), Jiang Q(1).

Author information:
(1)Department of Epidemiology and Biostatistics, School of Public Health, Research Center of Public Health, Renmin Hospital of Wuhan University, Wuhan University, Wuhan, Hubei, China.
(2)Department of Vaccine, Wuchang District Center for Disease Control and Prevention, Wuhan, Hubei, China.
(3)Department of Public Health, Laboratory of Clinical Microbiology, The Second People's Hospital of Xianning City (Xianning Hospital of Tuberculosis Treatment

and Control), Xianning, Hubei, China.
(4)Department of Public Health, The Fourth Hospital of Wuhan, Wuhan, Hubei, China.
(#)Contributed equally

Drug-resistant tuberculosis (DR-TB) disproportionately affects rural China, yet the molecular and epidemiological drivers of this disparity remain inadequately explored. This study investigates resistance evolution and transmission dynamics in Xianning, China, using longitudinal data from 3,865 culture-positive pulmonary tuberculosis patients (2016-2023). Phenotypic drug susceptibility testing for 14 commonly used anti-tuberculosis drugs showed a stable multidrug-resistant tuberculosis (MDR-TB) rate of 6.6%, while mono-resistance increased from 8.5% to 12.9% over the study period. Notably, 19.3% (53/275) of patients with ≥2 months of culture positivity developed new phenotypic resistance during treatment. Whole-genome sequencing of strains from the last two years identified resistance accumulation through two additional mechanisms: (i) acquisition of resistance via unfixed mutations in individuals and (ii) transmitted strains harboring novel resistance-conferring mutations absent in parental clones within genomic clusters. For the combined cases of resistance accumulation, multivariable logistic regression revealed that baseline drug resistance increased the risk more than threefold (aOR = 3.65-5.28, varying by resistance type), while rural residence independently doubled the risk (aOR = 2.60, 95% confidence interval:1.11-6.49). Furthermore, three of five genomic clusters with resistance accumulation exhibited urban-rural transmission, highlighting risks linked to cross-district care-seeking. These findings underscore how systemic healthcare barriers in rural China drive DR-TB through both treatment failures and strain transmission. Urgent action is needed to decentralize rapid resistance screening and implement tiered care models in primary clinics to curb transmission and mitigate the expanding DR-TB threat.IMPORTANCEThe ongoing epidemic of drug-resistant tuberculosis (DR-TB) in resource-poor settings poses a major public health challenge. This study sheds light on the evolution of DR-TB and its community transmission dynamics in central rural China, suggesting that unequal healthcare may exacerbate resistance accumulation risks by driving acquired resistance through inadequate treatment as well as facilitating strain transmission with escalating drug resistance. These findings emphasize the critical need for decentralized, rapid drug-resistance screening, and enhanced diagnosis and treatment strategies in primary care settings, prioritizing vulnerable populations to curb this growing threat.

DOI: 10.1128/spectrum.00380-25
PMCID: PMC12323381
PMID: 40548705 [Indexed for MEDLINE]

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

54. Waste to worth: diagnostic accuracy of Xpert MTB/XDR on contaminated liquid cultures to salvage the detection of drug-resistant tuberculosis.

J Clin Microbiol. 2025 Aug 13;63(8):e0058025. doi: 10.1128/jcm.00580-25. Epub 2025 Jul 1.

Ghebrekristos Y(#)(1)(2), Auma E(#)(1), Mahlobo Z(1), Venter R(1), Beylis N(3), Achar J(1)(4), Derendinger B(1), Singh S(1)(2), Burger M(2), Opperman C(1)(2)(3), Warren R(1), Theron G(1).

Author information:
(1)DSI-NRF Centre of Excellence for Biomedical Tuberculosis Research and SAMRC Centre for Tuberculosis Research, Division of Molecular Biology and Human Genetics, Faculty of Medicine and Health Sciences, Stellenbosch University, Tygerberg, Cape Town, South Africa.
(2)National Health Laboratory Service, Greenpoint Tuberculosis Laboratory, Cape Town, South Africa.
(3)Division of Medical Microbiology, Department of Pathology, University of Cape Town, Cape Town, South Africa.
(4)Department of Global Public Health, Karolinska Institutet, Stockholm, Sweden.
(#)Contributed equally

Update of
Res Sq. 2025 Apr 12:rs.3.rs-6409041. doi: 10.21203/rs.3.rs-6409041/v1.

Mycobacterium Growth Indicator Tube (MGIT) 960 culture is critical for tuberculosis (TB) drug susceptibility testing (DST) but is vulnerable to contamination. We evaluated the accuracy of Xpert MTB/XDR, a molecular DST for isoniazid, fluoroquinolone, amikacin, and ethionamide, on to-be-discarded contaminated growth. Xpert MTB/XDR was applied to acid-fast-bacilli-negative, contaminated cultures from sputum from people with rifampicin-resistant TB when Xpert MTB/XDR on sputum was unsuccessful (not resistant or susceptible for all drugs), either at diagnosis (Cohort A) or during treatment monitoring (Cohort B). Future DSTs within 3 months served as a reference standard. We determined potential care cascade improvements. In Cohort A, 10% (66/650) of people had a contaminated culture; 89% (59/66) of contaminated growths were Xpert MTB/XDR TB-positive. Sensitivity and specificity for isoniazid, fluoroquinolone, amikacin, and ethionamide resistance were 100% (95% confidence interval [CI] 85, 100) and 100% (79, 100); 100% (59, 100) and 100% (89, 100); 100% (16, 100) and 100% (91, 100); and 100% (72, 100) and 96% (78, 100), respectively. In Cohort B,

22% (28/129) of people with a contaminated culture were Xpert MTB/XDR TB-positive. Of these, 57% (16/28), 7% (2/28), and 43% (12/28) were isoniazid-, fluoroquinolone-, and ethionamide-resistant (in two, one, and four people, respectively, this would be the first resistant result). In both cohorts, time-to-DST could improve by a median (IQR) of 22 (12-42) days. Xpert MTB/XDR on contaminated MGIT960 cultures had high sensitivity and specificity for DST. This approach could mitigate culture contamination's negative effects and improve gaps in the drug-resistant TB diagnostic cascade.
IMPORTANCE: Culture contamination is a common impediment to drug susceptibility testing for tuberculosis, the single biggest infectious cause of death globally. Xpert MTB/XDR is a World Health Organization-recommended rapid molecular test for second-line drug resistance. We evaluated Xpert MTB/XDR on contaminated liquid culture growth that would otherwise be discarded, with the people who provided these specimens potentially lost from care cascades. By applying Xpert MTB/XDR to contaminated growth in a high-volume programmatic laboratory, we found the number of people who had second-line DST improved, as did the number of resistant cases diagnosed and time to diagnosis. Furthermore, DST information was generated in people who otherwise would have had none. This approach can therefore reduce the effect of culture contamination on tuberculosis DST, permitting earlier diagnosis and effective treatment initiation and potentially ultimately contributing to improving clinical outcomes and reducing transmission of drug-resistant TB.

DOI: 10.1128/jcm.00580-25
PMCID: PMC12345176
PMID: 40590556

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

55. Incidence of QT interval prolongation in patients receiving bedaquiline for drug-resistant tuberculosis in Sub-Saharan Africa: a protocol for systematic review and meta-analysis.

BMJ Open. 2025 Jul 28;15(7):e096709. doi: 10.1136/bmjopen-2024-096709.

Okello-Obol M(1), Pitua I(2), Okema JN(3), Ekwem D(4)(5), Bongomin F(6)(7), Olum R(8).

Author information:
(1)Faculty of Medicine, Gulu University, Gulu, Uganda
morrishokello2016@gmail.com.
(2)School of Medicine, Makerere University College of Health Sciences, Kampala, Uganda.

(3)Faculty of Medicine, Gulu University, Gulu, Uganda.
(4)Department of Internal Medicine, St. Mary's Hospital, Lacor, Gulu, Uganda.
(5)School of Health Sciences, Cavendish University, Kampala, Uganda.
(6)Department of Medical Microbiology and Immunology, Gulu University, Gulu, Uganda.
(7)Department of Internal Medicine, Gulu Regional Referral Hospital, Gulu, Uganda.
(8)School of Public Health, Makerere University, Kampala, Uganda.

INTRODUCTION: Tuberculosis (TB) remains a major public health challenge in Sub-Saharan Africa, exacerbated by the high prevalence of drug-resistant TB (DR-TB) and its strong association with HIV. Bedaquiline (BDQ), approved by the WHO in 2013, offers a promising treatment for DR-TB, including multidrug-resistant TB (MDR-TB) and extensively DR-TB (XDR-TB). However, BDQ has been associated with QT interval prolongation, a condition that can lead to serious cardiac arrhythmias such as torsades de pointes. This systematic review and meta-analysis aims to quantify the incidence of QT interval prolongation in patients receiving BDQ for DR-TB in Sub-Saharan Africa and identify predictors of this adverse effect.
METHODS AND ANALYSIS: We will conduct a comprehensive search of PubMed, Embase, Cochrane Library, Web of Science and African Journals Online using medical subject headings and keywords related to 'BDQ', 'DR-TB', 'QT interval prolongation' and 'Sub-Saharan Africa'. Eligible studies will include randomised controlled trials, cohort studies, case-control studies and observational studies conducted in Sub-Saharan Africa. Study titles and abstracts will be initially screened, and full texts will be retrieved and reviewed against eligibility criteria. Relevant data will be extracted from the selected articles and assessed for risk of bias. The primary outcome will be the pooled incidence of QT interval prolongation. Data will be synthesised using a random-effects model meta-analysis if significant heterogeneity is present; otherwise, a fixed-effects model will be applied.
ETHICS AND DISSEMINATION: This study will use published data, requiring no ethical approval. Findings will be disseminated through peer-reviewed publications and conference presentations to inform clinical guidelines and DR-TB treatment policies in Sub-Saharan Africa.
PROSPERO REGISTRATION NUMBER: CRD42024560368.

DOI: 10.1136/bmjopen-2024-096709
PMCID: PMC12306456
PMID: 40730389 [Indexed for MEDLINE]

Conflict of interest statement: Competing interests: None declared.

56. Accelerating extrapulmonary tuberculosis diagnosis with a rapid molecular assay.

Microbiol Spectr. 2025 Aug 5;13(8):e0010425. doi: 10.1128/spectrum.00104-25. Epub 2025 Jun 12.

Guillet-Caruba C(1)(2), Bénet C(1)(2), Jmel H(1), Doucet-Populaire F(1)(2)(3), Bourgeois-Nicolaos N(1)(2)(3).

Author information:
(1)AP-HP Université Paris-Saclay Hôpital Antoine Béclère, Service de Bactériologie-Hygiène, Clamart, France.
(2)Laboratoire de Biologie Médicale de Référence, AP-HP Université Paris-Saclay, Orsay, France.
(3)I2BC, CEA, CNRS, Université Paris-Saclay, Gif-sur-Yvette, Île-de-France, France.

Extrapulmonary tuberculosis (EPTB) is characterized by a very low bacterial load and could remain undiagnosed for a long time in a number of cases due to atypical presentation. Conventional methods and their time to results are not always helpful in rapidly making an EPTB diagnosis and initiating appropriate treatment. In order to accelerate the bacteriological confirmation, we evaluated the benefits of systematically using nucleic acid amplification test (NAAT) on extrapulmonary specimens for TB diagnosis in a developed country. From November 2017 to March 2021, all extrapulmonary samples received at the mycobacteriology department were subjected to both conventional methods and Xpert MTB/RIF Ultra. The time savings and the diagnostic performance of reflex tests were evaluated. During the study period, 691 samples were included, 85 (12.3%) were NAAT positive for Mycobacterium tuberculosis complex (MTBC), and only 1 for a rpoB mutation. The overall rate of invalid NAAT results was low, 0.9%. The average time to results of NAAT was 1.3 days compared to 18 days for positive culture, allowed to accelerate the EPTB diagnosis by 16 days. Overall NAAT sensitivity and specificity were 87.9% and 94.6%, respectively. No discrepancy was found among the 67 results involving the detection of rifampicin resistance. NAAT is a quick and consistent diagnostic test for EPTB with a potential turnaround time of 2 hours. Its systematic use could allow EPTB diagnosis and treatment faster by revealing results days to weeks before culture and drug susceptibility testing.IMPORTANCETuberculosis is considered the deadliest infectious disease in the world. Although tuberculosis most commonly affects the lungs, it also affects other sites referred to as extrapulmonary tuberculosis (EPTB). Diagnosis of EPTB is difficult and often delayed. We evaluated the benefits of systematically and routinely using a nucleic acid amplification test on all

extrapulmonary specimens received at the mycobacterial core laboratory for EPTB diagnosis. Using a rapid (80 minutes) and easy-to-perform test, we accelerated the definitive diagnosis by an average of 16 days.

DOI: 10.1128/spectrum.00104-25
PMCID: PMC12323321
PMID: 40503841 [Indexed for MEDLINE]

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

57. Hepatitis B virus resistance to nucleos(t)ide analogue therapy: WHO consultation on questions, challenges, and a roadmap for the field.

Lancet Microbe. 2025 Aug;6(8):101076. doi: 10.1016/j.lanmic.2025.101076. Epub 2025 Apr 9.

Lumley SF(1), Mokaya J(2), Maponga TG(3), Kramvis A(4), Dusheiko G(5), Irving W(6), Delphin M(7), Said Mohammed K(7), Downs LO(8), Waddilove E(7), Anderson M(9), Iwuji C(10), Msomi N(11), Ocama P(12), Hamid S(13), Adda D(14), Halford R(15), Kabagambe K(16), Benschop KSM(17), Inzaule S(18), Chan P(19), Paul MAS(20), Izumi K(21), Nisa T(21), De Dieu Iragena J(20), Girón-Callejas A(20), Kpossou AR(22), Jamiyu G(23), Emmanuel O(23), Balkissa M(24), Keita M(25), Prabdial-Sing N(26), Martinez A(27), Magongo EN(28), Shao Y(29), Sued O(30), Sereno LS(30), Shafer RW(31), Lesi O(32), Faini D(20), Easterbrook P(20), Duncombe C(33), Jordan MR(34), Matthews PC(35).

Author information:
(1)Nuffield Department of Medicine, University of Oxford, Oxford, UK; Department of Infectious Diseases and Microbiology, Oxford University Hospitals, Oxford, UK.
(2)Parasites and Microbes, Wellcome Sanger Institute, Cambridge, UK.
(3)Division of Medical Virology, Faculty of Medicine and Health Sciences, Stellenbosch University, Cape Town, South Africa; National Health Laboratory Service, Tygerberg Business Unit, Cape Town, South Africa.
(4)Hepatitis Virus Diversity Research Unit, Department of Internal Medicine, University of the Witwatersrand, Johannesburg, South Africa.
(5)University of the Witwatersrand, Johannesburg, South Africa; Institute of Liver Studies, King's College Hospital, London, UK.
(6)NIHR Nottingham Biomedical Research Centre, Nottingham University Hospitals NHS Trust, University of Nottingham, Nottingham, UK.
(7)The Francis Crick Institute, London, UK.
(8)Nuffield Department of Medicine, University of Oxford, Oxford, UK; Department of Infectious Diseases and Microbiology, Oxford University Hospitals, Oxford,

UK; Kenya Medical Research Institute Wellcome Trust, Kilifi, Kenya.
(9)The Francis Crick Institute, London, UK; Africa Health Research Institute, Durban, South Africa; Botswana Harvard Health Partnership, Gaborone, Botswana.
(10)Africa Health Research Institute, Durban, South Africa; Department of Global Health and Infection, Brighton and Sussex Medical School, University of Sussex, Brighton, UK.
(11)Discipline of Virology, University of KwaZulu-Natal and National Health Laboratory Service, Durban, South Africa.
(12)Department of Medicine, Makerere University College of Health Sciences, Kampala, Uganda.
(13)Department of Medicine, Aga Khan University, Karachi, Pakistan.
(14)World Hepatitis Alliance, Geneva, Switzerland; Center for Initiative and Development and Chagro-Care Trust, Jalingo, Nigeria.
(15)World Hepatitis Alliance, Geneva, Switzerland.
(16)The National Organisation for People Living with Hepatitis B, Kampala, Uganda.
(17)National Institute for Public Health and the Environment, Bilthoven, Netherlands.
(18)Amsterdam Institute for Global Health and Development and Department of Global Health, Amsterdam University Medical Center, University of Amsterdam, Amsterdam, Netherlands.
(19)Department of Communicable Diseases, WHO South-East Asia Regional Office, New Delhi, India.
(20)Department of Global HIV, Hepatitis and Sexually Transmitted Infections, WHO, Geneva, Switzerland.
(21)Division of Programmes for Disease Control, WHO Western Pacific Regional Office, Manila, Philippines.
(22)University of Abomey-Calavi, Abomey-Calavi, Benin.
(23)National AIDS, Viral Hepatitis and STIs Control Programme, Abuja, Nigeria.
(24)Programme National de Lutte contre le Sida et les Hépatites (PNLSH), Ministère de la Santé Publique, de la Population et des Affaires Sociales, Niamey, Niger.
(25)The Sectoral Unit for the Fight against HIV, Tuberculosis and Viral Hepatitis, Ministry of Health, Bamako, Mali.
(26)National Institute for Communicable Diseases and National Health Laboratory Service and the Faculty of Health Sciences, Witwatersrand University, Johannesburg, South Africa; National Institute for Communicable Diseases, National Health Laboratory Service, Johannesburg, South Africa.
(27)Gorgas Memorial Institute for Health Studies, Panama City, Panama; Department of Microbiology and Immunology, University of Panama, Panama City, Panama.
(28)Ministry of Health, STD/AIDS Control Program, Kampala, Uganda.
(29)National Centre for AIDS/STD Control and Prevention A, Chinese Center for Disease Control and Prevention, Changping Laboratory, Beijing, China.

(30)HIV, STI, Viral Hepatitis and TB Unit, Department of Communicable Disease Prevention, Control, and Elimination, Pan American Health Organization, Washington, DC, USA.
(31)Department of Medicine, Division of Infectious Diseases, Stanford University, Stanford, CA, USA.
(32)Department of Global HIV, Hepatitis and Sexually Transmitted Infections, WHO, Geneva, Switzerland; University of Lagos, Lagos, Nigeria.
(33)International Association of Providers of AIDS Care, Washington DC, USA.
(34)Division of Geographic Medicine and Infectious Diseases, Tufts Medical Center, Boston, MA, USA; Collaboratory for Emerging Infectious Diseases and Response, Tufts University, Medford, MA, USA.
(35)Kenya Medical Research Institute Wellcome Trust, Kilifi, Kenya; Division of Infection and Immunity, University College London, London, UK; Department of Infectious Diseases, University College London Hospital, London, UK. Electronic address: philippa.matthews@crick.ac.uk.

In this Review, we summarise outputs from a multidisciplinary consultation convened by WHO between July 11 and 13, 2023, to discuss hepatitis B virus (HBV) drug resistance (HBVDR). Treatment of chronic HBV infection with highly effective nucleos(t)ide analogue agents, tenofovir and entecavir, is a crucial intervention that supports the global goal of elimination of HBV infection as a public health threat. The risk of HBVDR as a threat to treatment outcomes is currently considered low from a public health perspective; however, drug resistance can influence individual outcomes, particularly among those who are treatment-experienced. We highlight the need to develop appropriate prevention, monitoring, and surveillance approaches for HBVDR, to support investment in the global scale-up of HBV diagnosis and treatment. Recommendations for the HBVDR field will ultimately be incorporated into a WHO integrated Global Action Plan for drug-resistant HIV, viral hepatitis, and priority sexually transmitted infections.

DOI: 10.1016/j.lanmic.2025.101076
PMID: 40220768 [Indexed for MEDLINE]

Conflict of interest statement: Declaration of interests PCM has received funding for a member of her team from GSK. WI has received research funding from Gilead Sciences and speaker and consultancy fees from Roche Diagnostics, Gilead Sciences, and Source Bioscience. CI has received research funding from Gilead Sciences paid to his institution and honorarium for presentations from the International Vaccine Institute. All these fundings are outside the scope of this paper. LSS and OS are staff members of PAHO. The authors alone are responsible for the views expressed in this publication, and they do not

necessarily represent the decisions or policies of PAHO. All other authors declare no competing interests.

58.Hepatic safety of pretomanid- and pyrazinamide-containing regimens in TB Alliance clinical trials.

IJTLD Open. 2025 Aug 13;2(8):464-470. doi: 10.5588/ijtldopen.25.0199. eCollection 2025 Aug.

Nedelman J(1), Li M(1)(2), Olugbosi M(1), Bruning-Barry R(3), Ambroso J(3), Cevik M(4), Gillespie S(4), Sloan DJ(4), Beumont M(1), Sun E(1).

Author information:
(1)TB Alliance, New York, USA.
(2)Current address, Merck & Co., Inc., Rahway, NJ, USA.
(3)RTI International, Research Triangle Park, USA.
(4)University of St. Andrews, St. Andrews, Scotland, UK.

BACKGROUND: In STAND and SimpliciTB, clinical trials for drug-susceptible TB, regimens containing pretomanid, pyrazinamide, and other agents (PaZX) had more hepatotoxicity than the standard-of-care regimen of isoniazid, rifampicin, pyrazinamide, and ethambutol (HRZE). In Nix-TB and ZeNix, clinical trials for drug-resistant TB, the regimen of bedaquiline, pretomanid, and linezolid (BPaL) demonstrated a favorable benefit-risk profile. We compare the hepatic safety of HRZE, PaZX, and BPaL in their respective populations.
METHODS: In this post-hoc analysis of data from six clinical trials, rates of treatment-emergent elevations of alanine transaminase (ALT) during the first 8 weeks of treatment were estimated by Kaplan-Meier (KM) analysis and compared via log-rank testing and Cox modeling.
RESULTS: The KM-estimated probabilities of treatment-emergent ALT elevations greater than 3x the upper limit of normal (>3xULN) were 5.36%, 12.7%, and 11.4% for HRZE, PaZX, and BPaL, respectively. The only significant ($p < 0.05$) difference was HRZE versus PaZX. The probabilities of ALT elevations >8xULN were 2.68%, 4.58%, and 1.05%, with the only significant difference being PaZX versus BPaL.
CONCLUSIONS: BPaL and HRZE have similar hepatic safety profiles in their respective populations. Pretomanid and pyrazinamide should be co-administered only when the benefit outweighs the risk.

DOI: 10.5588/ijtldopen.25.0199
PMCID: PMC12352949

PMID: 40821686

Conflict of interest statement: Conflicts of interest: JA and RB-B are consultants for TB Alliance paid through RTI International. MB, JN, MO, ES are employees of TB Alliance. ML is a former employee of TB Alliance. MB has stock in J&J. SG has grants or contracts from TB Alliance, EDCTP. ML has stock in J&J, Merck. JN has stock in Novartis, Sandoz. DS has a grant from EDCTP and is a member of Medical Monitoring Team for SimpliciTB.

59.Antimycobacterial and immunomodulatory activities of sorafenib in a preclinical mouse model of TB infection through CD4(+)CD25(low) and CD8(+)CD25(low) effector T cells.

Front Immunol. 2025 Jul 23;16:1591026. doi: 10.3389/fimmu.2025.1591026. eCollection 2025.

Rajmani RS(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 a communicable disease caused by Mycobacterium tuberculosis (Mtb). It is one of the major global public health problems that leads to a high morbidity and mortality rate. Drug resistance in Mycobacterium tuberculosis (Mtb) is another significant and persistent public health concern. The development of effective TB vaccines and treatments requires a better understanding of the intricate interactions between M. tuberculosis and host immunity. We previously reported that sorafenib (SRB) reduces bacterial growth by allosterically inhibiting ornithine acetyltransferase (MtArgJ), an essential enzyme in the arginine biosynthesis pathway of Mtb. Here, we report on the antimicrobial activity of sorafenib in preclinical mouse models of tuberculosis. Sorafenib is a potent drug approved by the Food and Drug Administration (FDA) for treating several types of cancer. The current study is focused on the immunomodulation that SRB induces in the host, specifically the immunological response that is triggered to combat the pathogenicity and survival of the bacteria.Here, we show that SRB significantly sterilizes the bacterial burden in chronic infection animal models of tuberculosis by reducing the number of Mtb-susceptible alveolar macrophages (AMs), and that SRB is more effective when combined with rifampicin (RIF). In the current study, we documented a new immune modulatory characteristic of sorafenib that, upon SRB treatment, markedly increased effector T cells (Teff - CD4+CD25low and CD8+CD25low) activity and decreased regulatory T cells, the immunosuppressive T cells (Treg- CD4+CD25high

and CD8+CD25high) function. In conclusion, our studies revealed that SRB is beneficial for both boosting an efficient T cell response and lowering the tubercular load.

DOI: 10.3389/fimmu.2025.1591026
PMCID: PMC12325335
PMID: 40771802 [Indexed for MEDLINE]

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

60. Drug resistance among students with pulmonary tuberculosis: a study based on screening in Henan, China.

BMC Infect Dis. 2025 Aug 8;25(1):1002. doi: 10.1186/s12879-025-11408-1.

Xu J(#)(1)(2), Zhang Y(#)(3), Wang G(4), Jiang J(3), Du W(3), Chen S(5), Meng D(3), Suo W(3), Zhuang Y(3), Wang K(3), Wang W(3), Zhao D(6)(7).

Author information:
(1)Institute of Tuberculosis Control and Prevention, Henan Provincial Center for Disease Control and Prevention, Zhengzhou, Henan, China. xujiyingx@163.com.
(2), No. 105 Nongyenan Road, Zhengzhou New District, Zhengzhou, 450016, Henan, China. xujiyingx@163.com.
(3)Institute of Tuberculosis Control and Prevention, Henan Provincial Center for Disease Control and Prevention, Zhengzhou, Henan, China.
(4)Department of Medicine, Henan Medical College, Zhengzhou, Henan, China.
(5)Department of Human Resources, Henan Provincial Center for Disease Control and Prevention, Zhengzhou, Henan, China.
(6)Institute of Tuberculosis Control and Prevention, Henan Provincial Center for Disease Control and Prevention, Zhengzhou, Henan, China. 13939033990@163.com.
(7), No. 105 Nongyenan Road, Zhengzhou New District, Zhengzhou, 450016, Henan, China. 13939033990@163.com.
(#)Contributed equally

BACKGROUND: Tuberculosis (TB) can easily spread among students and can lead to an outbreak once there is an infection in a school. Outbreaks of drug-resistant TB (DR-TB) in schools have occasionally been reported, but the profile of DR-TB in students in a province has rarely been described. This study was conducted to determine the prevalence of DR-TB and factors associated with it in students in

Henan Province, China.
METHODS: We retrospectively reviewed the data of 3527 pulmonary TB patients among students with culture-confirmed Mycobacterium tuberculosis (M.tb) isolates collected from the Tuberculosis Information Management System of the China Disease Prevention and Control Information System from 2015 to 2021. Prevalence of DR-TB was analyzed. Comparisons between categorical variables were analyzed using the chi-square test or Fisher's exact test as appropriate. Logistic regression models were used to identify the factors associated with DR-TB.
RESULTS: Any DR-, RR (rifampin resistance)- and MDR (multi-drug resistance) -TB rates in students were 10.46%, 7.91% and 6.10%, respectively. And they all showed a downward trend from 2015 to 2021 ($p < 0.001$). Previously treated cases were 7.30 (95% CI: 5.30, 10.05), 8.60 (95% CI: 6.14,12.14) and 9.43 (95% CI: 6.64,13.40) times more likely than the new cases to be diagnosed with Any DR-TB, RR-TB and MDR-TB, respectively. Patients from schools in the western region of Henan had greater odds of having Any DR- (AOR = 2.06, 95% CI: 1.31, 3.24), RR- (AOR = 2.81, 95% CI: 1.66, 4.76) and MDR-TB (AOR = 2.07, 95% CI: 1.13, 3.80) than those from schools in the northern region. Males had a 1.40-fold (95% CI: 1.11, 1.78), 1.34-fold (95% CI: 1.02, 1.75) greater likelihood of being diagnosed with Any DR- and RR-TB, respectively. The risk of being diagnosed with MDR-TB was 1.42 (95% CI: 1.00, 2.02) times greater in students migrant between prefectures of the province than in the locals.
CONCLUSION: The prevalence of DR-TB among students with PTB in Henan, China, significantly decreased from 2015 to 2021. Previous treated cases and those in west-region schools in Henan were at greater risk of being diagnosed with Any DR-, RR- and MDR-TB. In addition, males were more likely to be diagnosed with Any DR- and RR-TB. It requires further study that whether those who migrated between prefectures of the province were more likely to be diagnosed with MDR-TB.

DOI: 10.1186/s12879-025-11408-1
PMCID: PMC12333275
PMID: 40781271 [Indexed for MEDLINE]

Conflict of interest statement: Declarations. Human Ethics and Consent to Participate: Not applicable. Competing interests: The authors declare no competing interests.

61. Diagnostic Accuracy of LiquidArray MTB-XDR VER 1.0 for the Detection of Mycobacterium tuberculosis Complex, Fluoroquinolone, Amikacin, Ethambutol, and Linezolid Susceptibility.

Clin Infect Dis. 2025 Aug 1;81(1):159-166. doi: 10.1093/cid/ciae614.

Auma E(1), Alberts R(1), Derendinger B(1), Venter R(1), Streicher EM(1), Pillay S(1), Ghebrekristos YT(1)(2), Mburu M(3), Ruhwald M(3), Warren R(1), Penn-Nicholson A(3), Theron G(1), de Vos M(3).

Author information:
(1)Department of Science, Technology and Innovation - National Research Foundation, Centre of Excellence for Biomedical Tuberculosis Research, South African Medical Research Council Centre for Molecular and Cellular Biology, Division of Molecular Biology and Human Genetics, Faculty of Medicine and Health Sciences, Stellenbosch University, Cape Town, Western Cape, South Africa.
(2)National Health Laboratory Service, Greenpoint Tuberculosis Laboratory, Cape Town, South Africa.
(3)Tuberculosis Programme, FIND, Geneva, Switzerland.

Update of
Res Sq. 2024 Sep 04:rs.3.rs-4841978. doi: 10.21203/rs.3.rs-4841978/v2.

BACKGROUND: Drug susceptibility testing (DST) is essential for starting people on effective tuberculosis (TB) regimens. No published data exist for the high-throughput LiquidArray MTB-XDR (LA-XDR) test, which detects Mycobacterium tuberculosis complex (MTBC) and fluoroquinolone, amikacin, ethambutol, and linezolid susceptibility (the latter 2 have no rapid DSTs available).
METHODS: We enrolled people (N = 720) with presumptive TB who provided 2 sputum samples for an Xpert MTB/RIF Ultra assay and a culture (MTBC reference standard). Phenotypic DST and Sanger sequencing were the composite reference standards. LA-XDR on the manual FluoroLyse and automated GenoXtract fleXT (fleXT) DNA extraction methods were compared.
RESULTS: For MTBC, LA-XDR had similar sensitivities (85%-87%) and specificities (99%) using each extraction method. Drug susceptibility sensitivities (95% confidence interval) varied: 94% (86%-98%) for fluoroquinolones, 64% (45%-80%) for amikacin, and 88% (79%-93%) for ethambutol (specificities of 97%-100%). Six of 7 (86%) resistant linezolid isolates were detected. LA-XDR with fleXT had indeterminate proportions of 21/251 (8%), 2/251 (1%), 63/251 (25%), and 93/251 (37%) for fluoroquinolones, ethambutol, amikacin, and linezolid, respectively (amikacin and linezolid indeterminates were higher with FluoroLyse-extracted DNA). In a hypothetical population of 100 smear-negative people with fluoroquinolone-resistant TB undergoing fleXT DNA extraction, 25 (25%) would be missed (1 extraction error, 2 invalid results, 15 MTBC-negative, 6 fluoroquinolone-indeterminate, and 1 false-susceptible).
CONCLUSIONS: LA-XDR met the minimum World Health Organization target product profile for a next-generation, sputum-based, moderate-complexity DST with high fluoroquinolone and ethambutol resistance sensitivity, moderate amikacin

resistance sensitivity, and promise for linezolid resistance, for which more data are needed. Improved LA-XDR MTBC detection would reduce missed resistance.

DOI: 10.1093/cid/ciae614
PMCID: PMC12314493
PMID: 39663850 [Indexed for MEDLINE]

62. Construction and Validation of a Nomogram-Based Predictive Model for Acute Kidney Injury Caused by Drug Resistance to Tuberculosis.

Int J Gen Med. 2025 Jul 30;18:4119-4129. doi: 10.2147/IJGM.S527840. eCollection 2025.

Deng M(#)(1), Han N(1), Jia M(1), Zheng Z(1), Tian Y(1), Wang H(#)(1), Feng L(1).

Author information:
(1)Department of Tuberculosis, Affiliated Hospital of Hebei University, Baoding, Hebei, 071000, People's Republic of China.
(#)Contributed equally

OBJECTIVE: Acute kidney injury (AKI) is a common and serious adverse effect during tuberculosis (TB) treatment in clinical settings, particularly in patients with drug-resistant TB. AKI may lead to treatment interruption and poor prognosis. Early identification of patients at high risk for AKI is crucial to improve clinical outcomes.
METHODS: We retrospectively enrolled 571 TB patients, divided into training and validation cohorts. LASSO and multivariate logistic regression were used to identify risk factors, and the nomogram was evaluated using AUC, calibration, and decision curve analysis (DCA).
RESULTS: This study included 571 patients with TB. In this study, five variables (age, hypertension, diabetes, Scr, and ALB) were included to construct a nomogram for predicting AKI caused by drug resistance to TB. The AUC of the training set and validation set were 0.809 (95% CI: 0.7480-0.871, P < 0.001) and 0.841 (95% CI: 0.765-0.918, P < 0.001), respectively, indicating that the prediction model had good discriminative performance. The calibration curve shows that the predicted values of the model are basically consistent with the actual values, indicating good performance. DCA suggests that almost all ranges of TB patients can benefit from this new predictive model, indicating good clinical utility.

CONCLUSION: The nomogram model of AKI caused by drug resistance to TB established in this study has good predictive value and helps identify high-risk populations.

DOI: 10.2147/IJGM.S527840
PMCID: PMC12320139
PMID: 40761921

Conflict of interest statement: The authors declare that there are no conflicts of interest that could be perceived as prejudicing the impartiality of the research reported.

63. Successful Treatment of Multidrug-Resistant Tuberculous Meningitis in a Young Chinese Woman: A Case Study From Japan.

Am J Case Rep. 2025 Aug 16;26:e947502. doi: 10.12659/AJCR.947502.

Tanaka M(1), Hasegawa R(2), Ishikawa K(1), Mori N(1).

Author information:
(1)Department of Infectious Diseases, St. Luke's International Hospital, Tokyo, Japan.
(2)Department of Infection, Allergy, Clinical Immunology and Laboratory Medicine, Akita University, Akita, Japan.

BACKGROUND Multidrug-resistant tuberculosis (MDR-TB) continues to pose a serious public health challenge, especially when associated with tuberculous meningitis (TBM), which complicates treatment due to the need for central nervous system (CNS) penetration and non-oral administration routes. This case report describes a 24-year-old woman with MDR pulmonary tuberculosis and tuberculous meningitis (TBM) successfully treated with a combination of pyrazinamide, levofloxacin, cycloserine, and linezolid. CASE REPORT A previously healthy 24-year-old woman from Jilin Province, China presented with fever, headache, and impaired consciousness. Chest computed tomography (CT) showed centrilobular nodules and tree-in-bud appearances, while magnetic resonance imaging (MRI) revealed basal meningeal enhancement and tuberculomas. Acid-fast bacilli (AFB) were detected on smear microscopy of cerebrospinal fluid (CSF), and culture confirmed Mycobacterium tuberculosis. Drug susceptibility testing confirmed MDR-TB. Due to impaired consciousness, the treatment regimen was selected based on CNS penetration and enteral administration compatibility. A combination of pyrazinamide, levofloxacin, cycloserine, and linezolid was administered over 18

months. Bedaquiline and pretomanid were not used due to insufficient CNS penetration data at the time and limited availability in Japan. The patient required prolonged mechanical ventilation and was discharged in a minimally conscious state after 541 days. CONCLUSIONS This case highlights the importance of individualized drug selection for MDR-TB with CNS involvement. In managing tuberculosis, especially in low-incidence countries, the epidemiological background of the patient's country of origin should also be considered. Early diagnosis and appropriate drug selection were critical to the patient's survival despite severe neurological sequelae.

DOI: 10.12659/AJCR.947502
PMCID: PMC12366473
PMID: 40817574

Conflict of interest statement: Conflict of interest: None declared

64.Characterisation of M. tuberculosis isolates obtained from Tamil Nadu prevalence survey by whole genome sequencing analysis.

Infect Genet Evol. 2025 Aug;132:105763. doi: 10.1016/j.meegid.2025.105763. Epub 2025 May 10.

Rajendran P(1), Giridaran P(2), Thomas SV(1), Nagaraj N(1), Thiruvengadam K(1), Radhika G(1), Samyuktha R(1), Selvaraju S(1), Frederick A(3), Padmapriyadarsini C(1), Shanmugam S(4).

Author information:
(1)ICMR, National Institute for Research in Tuberculosis, India.
(2)ICMR, National Institute for Research in Tuberculosis, India; ICMR, National Institute of Epidemiology, India.
(3)Directorate of Medical and Rural Health Services, Chennai, India.
(4)ICMR, National Institute for Research in Tuberculosis, India. Electronic address: shanmugam.sk@icmr.gov.in.

Recent advances in whole genome sequencing have facilitated the understanding of drug resistance patterns and lineage distribution of M. tuberculosis worldwide. In this study, we aimed to determine the genetic diversity of MTB isolates from presumptive pulmonary TB patients obtained from a state prevalence survey. A total of 124 isolates were available for further characterisation, out of which 71 (57.2 %) and 47 (37.9 %) were subjected to sequencing and phenotypic DST, respectively. The phenotypic resistance profile revealed 3 isolates with multidrug resistance and 3 with mono-INH resistance. Out of 71 isolates, sequencing data were available for 61 (85.9 %), where the lineage distribution

and drug resistance profile were analysed in comparison with phenotypic DST results. All the mutations were significant, accounting for one or the other resistance pattern. The concordance between pDST and gDST for the drugs was above 90 % except for ETH (77 %) and INH (87 %). The phylogenetic analysis of the lineage distribution revealed three clusters with MDR isolates belonging to lineage 1 and lineage 3. While lineage 2 is more frequently associated with MDR distribution both in India and worldwide, we did not find any lineage 2 MDR-TB isolates in our study. The use of WGS analysis improved our understanding of the genetic characteristics of MTB and its correlation with DR-TB transmission.

DOI: 10.1016/j.meegid.2025.105763
PMID: 40354869 [Indexed for MEDLINE]

Conflict of interest statement: Declaration of competing interest The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper titled “Characterisation of M. tuberculosis isolates obtained from Tamil Nadu prevalence survey by whole genome sequencing analysis”.

65. Mechanism of the dual action self-potentiating antitubercular drug Morphazinamide.

PNAS Nexus. 2025 Jul 29;4(8):pgaf242. doi: 10.1093/pnasnexus/pgaf242. eCollection 2025 Aug.

Ostrer L(1), Crooks TA(1), Howe MD(1), Vo S(1)(2), Jia Z(1), Hegde P(2), Schacht N(1), Aldrich CC(2), Baughn AD(1).

Author information:
(1)Department of Microbiology and Immunology, University of Minnesota Medical School, Minneapolis, MN 55455, USA.
(2)Department of Medicinal Chemistry, College of Pharmacy, University of Minnesota Medical School, Minneapolis, MN 55455, USA.

Update of
bioRxiv. 2025 Jan 31:2024.10.08.617272. doi: 10.1101/2024.10.08.617272.

Pyrazinamide (PZA) is a cornerstone of first-line antitubercular drug therapy and is unique in its ability to kill nongrowing populations of Mycobacterium tuberculosis through disruption of coenzyme A (CoA) metabolism. Unlike other drugs, PZA action is conditional and requires potentiation by host-relevant

environmental stressors, such as low pH and nutrient limitation. Despite its pivotal role in tuberculosis therapy, the durability of this crucial drug is challenged by the emergent spread of drug resistance. To advance drug discovery efforts, we characterized the activity of a more potent PZA analog, morphazinamide (MZA). Here, we demonstrate that like PZA, MZA acts in part through impairment of CoA metabolism. Unexpectedly, we find that, in contrast to PZA, MZA does not require potentiation and maintains bactericidal activity against PZA-resistant strains due to an additional mechanism involving aldehyde release. Further, we find that the principal mechanism for resistance to the aldehyde component is through promoter mutations that increase expression of the mycothiol oxidoreductase MscR. Our findings reveal a dual-action synergistic mechanism of MZA that results in a faster kill rate and a higher barrier to resistance. These observations provide new insights for the discovery of improved therapeutic approaches for addressing the growing problem of drug-resistant tuberculosis.

DOI: 10.1093/pnasnexus/pgaf242
PMCID: PMC12342587
PMID: 40799345

66. Validation and clinical application of an LC-MS/MS method designed to simultaneously measure seven second-line TB drugs and two metabolites in human lung tissue.

J Pharm Biomed Anal. 2025 Aug 6;266:117093. doi: 10.1016/j.jpba.2025.117093. Online ahead of print.

Foster KK(1), Pooran A(2), van der Merwe M(1), Castel S(1), Joubert A(1), Zangenberg E(1), Dheda K(3), Wiesner L(4).

Author information:
(1)Division of Clinical Pharmacology, Department of Medicine, University of Cape Town, Cape Town, South Africa.
(2)Centre for Lung Infection and Immunity, Division of Pulmonology, Department of Medicine and UCT Lung Institute & South African MRC/UCT Centre for the Study of Antimicrobial Resistance, University of Cape Town, Cape Town, South Africa.
(3)Centre for Lung Infection and Immunity, Division of Pulmonology, Department of Medicine and UCT Lung Institute & South African MRC/UCT Centre for the Study of Antimicrobial Resistance, University of Cape Town, Cape Town, South Africa; Faculty of Infectious and Tropical Diseases, Department of Immunology and

Infection, London School of Hygiene and Tropical Medicine, London, UK.
(4)Division of Clinical Pharmacology, Department of Medicine, University of Cape Town, Cape Town, South Africa. Electronic address: lubbe.wiesner@uct.ac.za.

We developed and validated a novel bioanalytical method for the simultaneous quantification of levofloxacin, linezolid, moxifloxacin, delamanid, bedaquiline, clofazimine, and pretomanid, along with the metabolites of delamanid (DM-6705) and bedaquiline (N-desmethyl-bedaquiline, M2), in human lung tissue samples. Following homogenization by bead beating and extraction by protein precipitation, the analytes were separated on an Agilent 1260 Infinity II HPLC system using a Poroshell 120 C18 EC (2.1 mm×50 mm, 2.7 μm) column with gradient elution, applying a mobile phase consisting of 0.1 % formic acid in water and 0.1 % formic acid in a mixture of acetonitrile and methanol. Detection and quantification of the analytes and their stable isotope labelled internal standards were performed on a Sciex API 5500 QTrap mass spectrometer using positive electrospray ionization and multiple reaction monitoring. Validation according to the guidelines of the FDA and EMA proved the method to be precise, accurate, and robust with no significant influence of matrix components. The application of the method to the analysis of clinical samples demonstrated the feasibility of quantifying the second-line anti-tuberculosis drugs in human lung tissue and the potential to provide insights into the drug distribution across the infection sites in the lung.

DOI: 10.1016/j.jpba.2025.117093
PMID: 40782709

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

67. Stool-Based Molecular Tuberculosis Treatment Monitoring: A Faster Means for Detecting Persistent Mycobacteria Compared to Phenotypic Culture.

Open Forum Infect Dis. 2025 Jun 24;12(8):ofaf345. doi: 10.1093/ofid/ofaf345. eCollection 2025 Aug.

Adu Gyamfi CG(1)(2)(3)(4), Seeger A(1), Mulengwa D(1)(2), Vasiliu A(1), Carratala-Castro L(5)(6), Mtafya B(7), Maphalala N(1)(2), Munguambe S(6), Saavedra B(6), Ness T(1), Maphalala G(8), Acacio S(6), Mambuque E(6), Ehrlich J(5), Mejia R(9), Ziyane M(2)(8), Kirchner HL(1)(10), Lange C(1)(11)(12)(13),

Kay A(1)(2), Garcia-Basteiro AL(5)(6)(14), Mandalakas A(1), DiNardo AR(1).

Author information:
(1)Global Tuberculosis Program, Department of Pediatrics, Baylor College of Medicine, Houston, Texas, USA.
(2)Department of Global Tuberculosis Program, Baylor Colloge of Medcine Foundation Eswatini, Mbabane, Eswatini.
(3)Centre for Vaccines and Immunology, National Institute for Communicable Diseases, Johannesburg, South Africa.
(4)School of Physiology, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa.
(5)Barcelona Institute for Global Health, Hospital Clínic, Universitat de Barcelona, Barcelona, Spain.
(6)Centro de Investigação em Saude de Manhiça, Maputo, Mozambique.
(7)National Institute for Medical Research-Mbeya Medical Research Center, Mbeya, Tanzania.
(8)Eswatini Health Laboratory Service, Mbabane, Eswatini.
(9)Pediatric Tropical Medicine, Baylor College of Medicine, Houston, Texas, USA.
(10)Department of Population Health Sciences, Geisinger, Danville, Pennsylvania, USA.
(11)Division of Clinical Infectious Diseases, Research Center Borstel, Borstel, Germany.
(12)German Center for Infection Research, partner site Hamburg-Lübeck-Borstel-Riems, Borstel, Germany.
(13)Respiratory Medicine and International Health, University of Lübeck, Lübeck, Germany.
(14)Centro de Investigación Biomédica en Red de Enfermedades Infecciosas, Barcelona, Spain.

BACKGROUND: Tuberculosis (TB) treatment monitoring is hindered by the lack of a rapidly measured biomarker that accurately predicts clinically relevant outcomes. Symptom screening poorly correlates with bacillary burden. Although culture is a direct measure of viable bacillary burden, the long turnaround time makes it clinically irrelevant.
METHODS: The TB treatment monitoring potential of stool-based, quantitative polymerase chain reaction (qPCR) was prospectively assessed among 231 participants of all ages from Eswatini, Tanzania, and Mozambique with microbiologically confirmed TB. Stool qPCR results were compared to sputum culture, persistent symptoms, drug resistance, and World Health Organization TB outcomes.
RESULTS: Quantitative bacillary burden measured by stool qPCR strongly correlated with sputum culture at baseline (Spearman correlation $r_s = 0.79$; $P < .001$). Stool was successfully collected at >90% of all timepoints, while sputum collection decreased to <50% at the end of therapy. Participants with isoniazid

or rifampin resistance demonstrated decreased bacillary clearance by sputum culture and stool qPCR during the first 2 weeks of treatment. Participants who remained culture positive at 2 months had a slower decrease in bacillary burden measured by stool qPCR compared to those who were culture negative by 2 months. The odds of a participant being culture positive at 2 months was associated with a lower initial qPCR cycle threshold (odds ratio [OR], 0.792; P = .004), and a smaller absolute difference between the qPCR cycle threshold measured at 2 weeks and baseline (OR, 0.72; P = .0006). Neither sputum culture, sputum Xpert Ultra, or stool qPCR was associated with resolution of symptoms or in-treatment death. CONCLUSIONS: Stool-based TB treatment monitoring correlates with sputum culture but provides results faster, leverages a more accessible specimen, and identifies patients with TB who are at risk for drug resistance and persistent 2-month culture positivity. None of the quantitative tests of bacillary burden singularly could predict symptom resolution or death.

DOI: 10.1093/ofid/ofaf345
PMCID: PMC12342930
PMID: 40799783

68. Identification of Mycobacterium tuberculosis intracellular survival-related virulence factors via CRISPR-based eukaryotic-like secretory protein mutant library screen.

Microbiol Spectr. 2025 Aug 5;13(8):e0076725. doi: 10.1128/spectrum.00767-25. Epub 2025 Jun 12.

Liu W(1), Wang Y(1), Zhao J(1), Zhang X(1), Li Z, Jia H(1), Zhu C(1), Zhang L(1), Pan L(1), Zhang Z(1).

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

Tuberculosis (TB), caused by Mycobacterium tuberculosis (M.tb), remains a serious infectious disease posing significant global health challenges. A critical evolutionary feature of M.tb is its genome encoding a set of eukaryotic-like secretory proteins, which facilitate intracellular survival by manipulating host immune responses. However, the specific eukaryotic-like secretory proteins that facilitate M.tb intracellular survival and their

regulatory mechanisms on host immunity remain uncharacterized. In this study, a mutant library comprising 137 potential eukaryotic-like secretory proteins was constructed using clustered regularly interspaced short palindromic repeats (CRISPR)-non-homologous end joining genome editing technology. Subsequently, macrophages were infected with the mutant library, and CRISPR sequencing enabled preliminary identification of virulence factors associated with bacterial intracellular persistence. To validate the screen, two genes (Rv0066c and Rv3139) exhibiting the most pronounced reduction in intracellular survival rates when mutated were selected for the construction of large-fragment knockout strains (ΔRv0066c and ΔRv3139). Subsequent macrophage infection assays reconfirmed the impaired intracellular survival of these two mutants. RNA-seq analysis was conducted to characterize host gene expression profiles during ΔRv0066c-infected macrophage interactions. RNA-seq analysis of macrophages infected with wild-type and ΔRv0066c strains identified 138 differentially expressed genes, with 75 upregulated and 63 downregulated in ΔRv0066c. Gene ontology clustering of these differentially expressed genes highlighted molecular functions related to chemokine binding, chemokine-mediated signaling pathways, Ras protein signal transduction, and calcineurin-mediated signaling. Collectively, this work established a potential eukaryotic-like secretory protein mutant library and identified two novel M.tb effectors governing intracellular survival, providing potential new targets for anti-TB drug development.

IMPORTANCE: Eukaryotic-like secretory proteins that subvert host immunity to enable intracellular persistence are a key evolutionary adaptation of Mycobacterium tuberculosis (M.tb). In this study, we established a mutant library targeting 137 potential eukaryotic-like secretory proteins through clustered regularly interspaced short palindromic repeats (CRISPR)-non-homologous end joining genome editing technology. The library was subjected to macrophage infection assays, and CRISPR sequencing enabled identification of M.tb persistence-associated virulence determinants. Validation screens highlighted two genes (Rv0066c and Rv3139) that displayed the most significant intracellular survival defects to generate large-fragment knockout strains (ΔRv0066c and ΔRv3139). Macrophage infection experiments reconfirmed the compromised intracellular viability of both mutants. RNA-seq profiling of ΔRv0066c-infected macrophages identified 138 differentially expressed genes, with functional enrichment in chemokine signaling, Ras protein signal transduction, and calcineurin-mediated signaling. To conclude, this study identified two novel M.tb effectors contributing to intracellular survival as potential new targets for anti-TB drug development.

DOI: 10.1128/spectrum.00767-25
PMCID: PMC12323669
PMID: 40503836 [Indexed for MEDLINE]

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

69. Sterilizing activity of spectinamide MBX-4888A when replacing linezolid in the Nix-TB regimen in the relapsing BALB/c mouse model of tuberculosis.

bioRxiv [Preprint]. 2025 Aug 6:2025.08.04.668403. doi: 10.1101/2025.08.04.668403.

Peroutka-Bigus N(1), Sherman MS(1), Kaya F(2), Waidyarachchi SL(3), Liu J(4), Rushefsky J(1), Butler MM(3), Bowlin T(3), Meibohm B(5), Gonzalez-Juarrero M(1), Lenaerts AJ(1), Zimmerman M(2), Lee RE(4), Robertson GT(1).

Author information:
(1)Mycobacteria Research Laboratories, Department of Microbiology, Immunology and Pathology, Colorado State University, Fort Collins, Colorado, USA.
(2)Center for Discovery and Innovation, Hackensack Meridian School of Medicine, Nutley, New Jersey, USA.
(3)Microbiotix, Inc., Worcester, MA 01605, USA.
(4)Department of Chemical Biology & Therapeutics, St. Jude Children's Research Hospital, Memphis, Tennessee, USA.
(5)Department of Pharmaceutical Sciences, University of Tennessee Health Science Center, Memphis, TN 38163, USA.

Spectinamides have garnered interest as experimental tuberculosis therapeutics owing to their safety profile and efficacy as partner agents when used in conjunction with established regimens in mice. The Nix-TB regimen of bedaquiline, pretomanid, and linezolid represents a short, effective regimen recommended for treatment of pre-extensively drug-resistant tuberculosis. However, linezolid administration is associated with severe adverse events which limits its use. Here we present preclinical data that spectinamide MBX-4888A can replace linezolid in Nix-TB.

DOI: 10.1101/2025.08.04.668403
PMCID: PMC12340861
PMID: 40799565

70. Development, characterization and evaluation of antibacterial efficacy of actively targeted gold-polydopamine nanoparticle formulations for tuberculosis Treatment.

Eur J Pharm Sci. 2025 Aug 7;213:107219. doi: 10.1016/j.ejps.2025.107219. Online ahead of print.

Turan-Ayhan E(1), Çalımcı M(2), Turanlı Y(3), Şahin F(4), Tarhan G(4), Tamer U(2), Ilbasmis-Tamer S(5).

Author information:
(1)Department of Pharmaceutical Technology, Faculty of Pharmacy, Gazi University, Ankara, Türkiye; Department of Pharmaceutical Microbiology, Faculty of Pharmacy, Adıyaman University, Adıyaman, Türkiye.
(2)Department of Analytical Chemistry, Faculty of Pharmacy, Gazi University, Ankara, Türkiye.
(3)Turkish Medicines and Medical Devices Agency, Ankara, Türkiye.
(4)Department of Medical Microbiology, Faculty of Medicine, Adıyaman University, Adıyaman, Türkiye.
(5)Department of Pharmaceutical Technology, Faculty of Pharmacy, Gazi University, Ankara, Türkiye. Electronic address: ilbasm@yahoo.com.

Tuberculosis (TB) is one of the oldest known diseases in the world and it remains a significant public health challenge. The increasing resistance of microorganisms to antibiotics underlines the necessity of appropriate use of antibiotics and correct dosage in treatment. In some cases, frequent and high-dose drug therapy is required, which can lead to serious organ damage in the liver and kidneys in long-term treatment. However, this problem can be overcome by using appropriate drug delivery systems that allow more effective treatments at lower doses. Here, we developed a drug delivery system specifically targeting tuberculosis using gold (Au)-polydopamine (PDA) nanoparticles and modified with polyethylene glycol (PEG), a targeting agent (antibody), and the antibiotic linezolid, resulting in Au-PDA-PEG-Antibody-Linezolid nanoparticles. We successfully developed and characterized these active targeted nanoparticles using UV-Vis absorbance spectroscopy, Fourier-transform infrared spectroscopy (FT-IR), dynamic light scattering (DLS), zeta potential measurements, and surface-enhanced Raman spectroscopy (SERS) measurements. Additionally, the developed formulations were compared with the commercial product through in vitro release studies, and antibacterial efficacy studies were conducted on multidrug-resistant tuberculosis (MDR-TB) strains. The targeted drug delivery system might be able to reduce side effects by increasing treatment effectiveness at lower doses. Additionally, our study is the one of the first example to feature actively targeted nanoparticle formulations using the active ingredient linezolid and PEGs with different chemical structures.

DOI: 10.1016/j.ejps.2025.107219
PMID: 40754012

Conflict of interest statement: Declaration of competing interest The author(s) have declared no conflicts of interest.

71. Visual Recovery Following Linezolid Cessation in an MDR-TB Patient: Detailed Case Analysis.

Case Rep Pulmonol. 2025 Jul 27;2025:9939815. doi: 10.1155/crpu/9939815. eCollection 2025.

Wiyana YB(1), Marhana IA(1), Suhartono G(2), Haryono A(1).

Author information:
(1)Department of Pulmonology and Respiratory Medicine, Faculty of Medicine Universitas Airlangga-Dr. Soetomo General Academic Hospital, Surabaya, Indonesia.
(2)Department of Ophthalmology, Faculty of Medicine Universitas Airlangga-Dr. Soetomo General Academic Hospital, Surabaya, Indonesia.

Multidrug-resistant tuberculosis (MDR-TB) is characterized by resistance to at least isoniazid and rifampicin. Linezolid is an antibiotic used for drug-resistant Gram-positive bacteria and is a treatment option for MDR-TB. However, its use is associated with optic neuropathy, presenting as acute worsening and bilateral vision loss, typically within 4 months of therapy. A 47-year-old male with MDR-TB relapsed during the sixth month of an individualized treatment regimen at Dr. Soetomo General Academic Hospital, Surabaya. The patient presented with weakness and anemia, receiving a regimen including levofloxacin (750 mg), linezolid (600 mg), clofazimine (100 mg), and cycloserine (500 mg). In the ninth month, the patient developed visual disturbances, initially suspected to be caused by an intracranial tumor. Despite various examinations and treatments, there was no improvement until linezolid was discontinued. The patient's visual complaints gradually improved following the cessation of linezolid therapy. This case underscores the potential for linezolid to cause optic neuropathy during prolonged treatment for MDR-TB. Detailed ophthalmologic examinations, including optical coherence tomography (OCT) and magnetic resonance imaging (MRI), confirmed optic neuropathy without intracranial pathology. Despite high-dose steroid therapy, the patient's vision improved only after 1 month since discontinuing linezolid. This highlights the importance of monitoring for ocular toxicity in patients undergoing long-term linezolid therapy and suggests that timely intervention can prevent permanent visual impairment. The case demonstrates the reversible nature of linezolid-induced optic neuropathy upon drug cessation and emphasizes the need for regular ophthalmologic assessments in patients receiving prolonged linezolid

treatment. This report contributes to the understanding of the adverse effects of linezolid and underscores the importance of vigilant monitoring and alternative therapeutic strategies for MDR-TB.

DOI: 10.1155/crpu/9939815
PMCID: PMC12318621
PMID: 40756245

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

72. A timeline of reckoning: Tracking the historical rise of antimicrobial resistance across HIV, TB, and malaria.

J Glob Antimicrob Resist. 2025 Jul 22;44:420-431. doi: 10.1016/j.jgar.2025.07.014. Online ahead of print.

Williamson T(1), Adderley J(1), Quinn K(1), Clark TG(2), Lewin SR(3), Doerig C(4).

Author information:
(1)School of Health and Biomedical Sciences, RMIT University, Bundoora, VIC, Australia.
(2)Department of Infection Biology, Faculty of Infectious and Tropical Diseases, London School of Tropical Medicine and Hygiene, London, UK.
(3)Department of Infectious Diseases, The University of Melbourne at the Peter Doherty Institute for Infection and Immunity, Melbourne, VIC, Australia; Victorian Infectious Diseases Service, Royal Melbourne Hospital at the Peter Doherty Institute for Infection and Immunity, Melbourne, VIC, Australia; Department of Infectious Diseases, Alfred Hospital and Monash University.
(4)School of Health and Biomedical Sciences, RMIT University, Bundoora, VIC, Australia; Burnet Institute, Melbourne, VIC, Australia. Electronic address: christian.doerig@rmit.edu.au.

Antimicrobial resistance is one of the major health challenges of this century. Here, we provide an in-depth perspective on the evolution of antimicrobial resistance in three globally relevant infectious diseases, HIV, tuberculosis (TB), and malaria. Specifically, we scrutinize the timelines between deployment and the subsequent emergence of resistance for all drugs that have been mobilized in the fight against these three diseases. Our data reveals that malaria exhibits a slower rate of resistance development to monotherapies in

comparison to HIV and TB. While the adoption of combination therapies significantly reduces the risk of de novo emergence of resistance, the challenge of pre-existing drug resistance persists, necessitating continuous surveillance and emphasizing the critical need for diverse and innovative approaches to manage and mitigate the ever-growing threat of antimicrobial resistance.

DOI: 10.1016/j.jgar.2025.07.014
PMID: 40706999

73. Bacterial co-occurrence with pulmonary TB, a respiratory tract infection (RTI): A cross-sectional study in a resource-limited setting.

J Clin Tuberc Other Mycobact Dis. 2025 May 10;40:100534. doi: 10.1016/j.jctube.2025.100534. eCollection 2025 Aug.

Magwalivha M(1), Rikhotso MC(1), Kachienga LO(1), Musoliwa R(1), Banda NT(1), Mashilo MS(1), Tshiteme T(1), Mphaphuli AM(1), Mahamud HA(1), Patel S(1), Ngandu JK(1), Patel S(1), Potgieter N(1), Traoré AN(1).

Author information:
(1)Department of Biochemistry and Microbiology, Faculty of Sciences, Engineering & Agriculture, University of Venda, Thohoyandou 0950, South Africa.

BACKGROUND: Bacterial co-infections significantly affect the treatment outcomes of tuberculosis (TB) patients, particularly in resource-limited settings. Misdiagnosis of TB co-infections accelerate disease progression and contribute to the development of drug resistance, leading to higher mortality and morbidity rates, especially in underserved areas. This study aimed to investigate bacterial co-infections in patients with pulmonary tuberculosis in a rural Vhembe region of Limpopo, South Africa.
MATERIALS AND METHODS: A total of 100 sputum together with 100 blood samples were collected from TB patients who were undergoing TB treatment. DNA isolates were used as templates for PCR using the Anyplex™MTB/NTMe Assay kit, and subsequently, the Allplex™ MTB/MDR/XDRe Assay kit was used for the multiple detections of Mycobacterium tuberculosis (MTB) and resistance to first line and second line anti-TB drugs. Co-infections were determined using the Allplex™ Bacteria(I) & (II) Assay kit. HIV status of patients was determined using blood testing kits.
RESULTS: Majority of study participants were male (55 %) and aged between 36 and 55 (54 %), while female were 46 % of the population. Bacterial species detected included non-tuberculous mycobacteria (NTM) in 67 % of participants, Aeromonas

spp. (19 %), Vibrio spp. (2 %), and E. coli (2 %). Multidrug-resistant Mycobacterium tuberculosis (MTB) strains were identified in 2 % of the cohort. There was a significant association between employment status and age ($p = 0.00$), as well as between HIV status and age ($p = 0.03$). While no significant associations were found between HIV status and the presence of NTM or other bacterial co-infections ($p = 0.19$ and 0.21, respectively), the majority of Aeromonas spp. and NTM cases were observed among HIV-positive participants. Notably, 36 of the NTM cases occurred in individuals living with HIV. CONCLUSION: The study findings suggest that age, socioeconomic status, and gender play a role in the development of TB, HIV, and other bacterial infections, which could further complicate treatment outcomes in patients. These factors likely contribute to increased vulnerability to co-infections, emphasizing the complex interplay between TB and HIV in these populations. Additionally, the study emphasises the importance of considering these socio-demographic factors in public health interventions to reduce the burden of TB-HIV co-infection and associated bacterial infections.

DOI: 10.1016/j.jctube.2025.100534
PMCID: PMC12141069
PMID: 40485838

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.

74. Progress on the Global Research Agenda for Antimicrobial Resistance in Human Health in Pakistan: Findings and Implications.

Infect Drug Resist. 2025 Jul 29;18:3795-3828. doi: 10.2147/IDR.S531874. eCollection 2025.

Maryam S(1), Saleem Z(2), Haseeb A(3), Qamar MU(4)(5), Amir A(6)(7), Almarzoky Abuhussain SS(8), Imam MT(9), Afzal S(10), Meyer JC(11)(12), Mudenda S(13), Godman B(11)(14)(15).

Author information:
(1)Department of Pharmaceutical Practices, College of Pharmacy, Umm Al-Qura University, Makkah, Saudi Arabia.
(2)Department of Pharmacy Practice, College of Pharmacy, Qassim University, Qassim, Saudi Arabia.
(3)Clinical Pharmacy Department, Al Rayan National College of Health Sciences

and Nursing, Al Madinah Al Munawarrah, Saudi Arabia.
(4)Institute of Microbiology, Faculty of Life Sciences, Government College University Faisalabad, Faisalabad, 38000, Pakistan.
(5)Division of Infectious Diseases, Department of Medicine, Geneva University Hospitals and Medical School, Geneva, Switzerland.
(6)Department of Microbiology, National University of Medical Sciences, Rawalpindi, 46000, Pakistan.
(7)Department of Microbiology, National Institute of Health, Islamabad, 45501, Pakistan.
(8)Department of Pharmaceutical Practices, College of Pharmacy, Umm Al-Qura University, Makkah, 21955, Saudi Arabia.
(9)Department of Clinical Pharmacy, College of Pharmacy, Prince Sattam Bin Abdulaziz University, Al Kharj, 11942, Saudi Arabia.
(10)Department of Pharmacy, DHQ Hospital Jhelum, Jhelum, Pakistan.
(11)Department of Public Health Pharmacy and Management, School of Pharmacy, Sefako Makgatho Health Sciences University, Pretoria, 0208, South Africa.
(12)South African Vaccination and Immunisation Centre, Sefako Makgatho Health Sciences University, Ga-Rankuwa, 0208, South Africa.
(13)Department of Pharmacy, School of Health Sciences, University of Zambia, Lusaka, 50110, Zambia.
(14)Strathclyde Institute of Pharmacy and Biomedical Science (SIPBS), University of Strathclyde, Glasgow, G4 0RE, UK.
(15)Antibiotic Policy Group, Institute for Infection and Immunity, City St. George's, University of London, London, SW17 0RE, UK.

BACKGROUND AND OBJECTIVE: Antimicrobial resistance (AMR) poses a formidable challenge to global public health, with low- and middle-income countries (LMICs) including Pakistan being particularly vulnerable. This study assesses the progress made in Pakistan following the Global Research Agenda for AMR, which builds on the key activities and goals of its national action plan to reduce AMR. The intention is to identify key gaps, achievements, and future areas of focus to help reduce rising AMR rates in Pakistan.
METHODS: Utilizing a systematic-narrative hybrid literature review methodology approach, recent research publication and policy initiatives related to AMR, including those published on the internet, were examined and documented.
FINDINGS: The findings from 349 published studies were divided into the 40 research priority areas. This included 23 papers (9.95%) specifically related to prevention and 55 (22.9%) to diagnosis, 64 (26.7%) for treatment and care of patients with infectious diseases, 59 (24.5%) for cross-cutting, and 44 (18.33%) for drug-resistant tuberculosis (TB). Currently, research on AMR in Pakistan is primarily concentrated in major urban centers across a limited number of cities. This needs addressing going forward. To effectively combat AMR in Pakistan, prioritizing prevention is crucial to curb disease spread and reduce reliance on prophylactic treatments, especially inappropriate prescribing and dispensing of

antimicrobials. Enhancing diagnostic facilities, strengthening antimicrobial surveillance systems and promoting appropriate management of patients with infectious diseases, supported by robust antimicrobial stewardship programs, can also help enhance judicious antibiotic use in Pakistan and reduce AMR going forward.
CONCLUSION AND INTERPRETATION: There are ongoing concerns regarding current research activities in Pakistan to reduce AMR. The pathway forward in Pakistan includes leveraging global partnerships to share knowledge, resources, and strategies to enhance the use of Access antibiotics as well as reduce AMR to reach agreed United Nations' goals.

Plain Language Summary: Antimicrobial resistance (AMR) poses a substantial threat to public health, as it reduces the number of effective antibiotics to combat infections, as well as increasing costs and the number of deaths. Pakistan is a critical country, with high and growing rates of AMR. Consequently, this issue must be addressed. The Global Research Agenda for AMR provided guidance on approaches that key stakeholders in Pakistan should undertake to reduce AMR. Our findings uncovered 20 published studies covering multiple aspects to reduce AMR. These included studies related to ways to reduce infections and the associated use of antibiotics and improve the care of patients with infectious diseases, including tuberculosis (TB), resistant to the current antimicrobials. Going forward, health authorities and others in Pakistan need to prioritize activities to reduce infections, including better hygiene, as well as reduce unnecessary prescribing and dispensing of antibiotics. This includes activities called antimicrobial stewardship programs to improve antibiotic use. The pathway forward also included leveraging global partnerships to share knowledge, resources, activities and strategies to improve the future use of antibiotics. We believe that this is the first study among low- and middle-income countries to fully explore current activities as part of the Global Research Agenda for AMR to provide guidance to other researchers and countries operating in this field.

DOI: 10.2147/IDR.S531874
PMCID: PMC12318840
PMID: 40761881

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

75.Design and Development of Lysyl tRNA Synthetase Inhibitors, for the Treatment of Tuberculosis.

J Med Chem. 2025 Aug 14;68(15):16459-16482. doi: 10.1021/acs.jmedchem.5c01331. Epub 2025 Aug 1.

Davis SH(1), Mathieson M(1), Buchanan KI(1), Dawson A(1), Smith A(1), Cocco M(1), Tamaki FK(1), Post JM(1), Baragaña B(1), Jansen C(1), Kiczun M(1), Zuccotto F(1), Wood G(1), Scullion P(1), Ray PC(1), Epemolu O(1), Lopez-Román EM(2), López LG(2), Engelhart CA(3), Kim J(3), Pino PA(3), Schnappinger D(3), Read KD(1), Encinas L(2), Bates RH(2), Wyatt PG(1), Green SR(1), Cleghorn LAT(1).

Author information:
(1)Drug Discovery Unit, Division of Biological Chemistry and Drug Discovery, College of Life Sciences, University of Dundee, DD1 5EH Dundee, U.K.
(2)Global Health Medicines R&D, GlaxoSmithKline, Severo Ochoa 2, Tres Cantos, 28760 Madrid, Spain.
(3)Dept. of Microbiology and Immunology, Weill Cornell Medical College, New York, New York 10065, United States.

There is currently a public health crisis due to the rise of multidrug-resistant tuberculosis cases, as well as the rise in the number of deaths from tuberculosis. To achieve the United Nations Sustainable Development Goal of ending the tuberculosis epidemic by 2030, new treatments are urgently required. We previously reported the discovery of 49, a preclinical candidate that acted through inhibition of the Mycobacterium tuberculosis lysyl tRNA synthetase (LysRS). In this report, the full medicinal chemistry program is reviewed from the original hit through to the optimized lead. The work was guided by the first crystal structures of M. tuberculosis LysRS. The physicochemical and pharmacokinetic properties were optimized to afford compounds suitable for evaluation in mouse efficacy models of tuberculosis and with the potential for clinical development.

DOI: 10.1021/acs.jmedchem.5c01331
PMCID: PMC12362622
PMID: 40749104

76. Re-visiting the surgical role in treating chemotherapeutic-resistance pulmonary tuberculosis: Results from a systematic review and meta-analysis.

J Infect Public Health. 2025 Aug 5;18(11):102920. doi: 10.1016/j.jiph.2025.102920. Online ahead of print.

Al-Mourgi M(1), Shams A(2), Al-Morgi MW(3), Al-Morgi Z(4).

Author information:
(1)Department of Surgery, College of Medicine, Taif University, P.O. Box 11099, Taif 21944, Saudi Arabia; Research Center for Health Sciences, Deanship of Graduate Studies and Scientific Research, Taif University, Taif 26432, Saudi Arabia. Electronic address: mourgi@tu.edu.sa.
(2)Department of Pharmacology, College of Medicine, Taif University, P.O. Box 11099, Taif 21944, Saudi Arabia; Research Center for Health Sciences, Deanship of Graduate Studies and Scientific Research, Taif University, Taif 26432, Saudi Arabia; High Altitude Research Center, Taif University, P.O. Box 11099, Taif 21944, Saudi Arabia. Electronic address: a.shams@tu.edu.sa.
(3)Research Center for Health Sciences, Deanship of Graduate Studies and Scientific Research, Taif University, Taif 26432, Saudi Arabia; Department of Infection Control, King Abdulaziz Specialist Hospital, Taif 26521, Saudi Arabia. Electronic address: m.alottaibe@gmail.com.
(4)Research Center for Health Sciences, Deanship of Graduate Studies and Scientific Research, Taif University, Taif 26432, Saudi Arabia; College of Medicine, Taif University, P.O. Box 11099, Taif 21944, Saudi Arabia. Electronic address: zeadcold@gmail.com.

BACKGROUND: The incidence and prevalence of multi-drug-resistant and extensively drug-resistant pulmonary tuberculosis are increasing, posing profound health concerns; therefore, surgical intervention is gaining popularity again. However, the effectiveness of surgical treatment needs to be reassessed. This study attempted to determine the efficacy of surgical treatment and chemotherapy compared to chemotherapy alone among patients with pulmonary tuberculosis.
METHODS: A systematic search and meta-analysis were conducted from inception to June 2025 of the existing databases, including PubMed, EMBASE, Cochrane Central Register of Controlled Trials, and Google Scholar. All double-arm studies available in English published between 2005 and August 2019 were included. Among 618 studies, 468 were selected based on abstract review. Eight out of 468 (8/468) studies were double-arm retrospective cohorts and observational studies, which included 1929 persons who matched the inclusion criteria. To measure the success of the surgical intervention, we used the pooled rate ratio, loss of patient follow-up, and the incidence of mortality using the random effects heterogeneity model.
RESULTS: Overall, there was no statistically significant difference in the treatment success rate (RR=1.24 (0.98-1.56), p = 0.07) and mortality rate (RR=1.82 (0.31-10.63, p = 0.51) between the two groups. Interestingly, the summary rate ratio (RR=0.41 (0.18-0.93), p = 0.03) showed that the surgical group had a considerably lower loss rate to follow-up than the non-surgical group. There was no evidence of heterogeneity amongst the trials (I^2 =0 %, τ^2 =0.00, df=2, p = 0.36).
CONCLUSIONS: The current meta-analysis was the first to use a factor of loss of

follow-up collected from several reports as a predictive tool to assess the effectiveness of surgical participation in treating drug-resistant tuberculosis patients. The rate of patient loss to follow-up in the surgical group suggested that the combination approach of surgery and chemotherapy showed a potential superiority over chemotherapy alone.

DOI: 10.1016/j.jiph.2025.102920
PMID: 40782768

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

77. Effects of missed anti-tuberculosis therapy doses on treatment outcome: a multi-center cohort study.

Lancet Reg Health Am. 2025 Jun 25;48:101162. doi: 10.1016/j.lana.2025.101162. eCollection 2025 Aug.

Ferreira IBB(1)(2), Menezes RC(2)(3)(4), Araújo-Pereira M(2)(3)(4), Rolla VC(5), Kritski AL(6), Cordeiro-Santos M(7)(8), Sterling TR(9), Staats C(9), Amorim G(10), Trajman A(11), Andrade BB(1)(2)(3)(4)(9); RePORT-Brazil Consortium.

Collaborators: Benjamin A, Medeiros Q, Ridolfi F, Gomes-Silva A, Oliveira J, Marine J, Durovni B, Cavalcante S, Rezende A, Bezerra A, Carvalho A, Brito A, Costa A, Spener-Gomes R, Rocha M, Nascimento V, Nogueira B, Andrade A, Silva E.

Author information:
(1)Escola Bahiana de Medicina e Saúde Pública, Pós-graduação em Medicina e Saúde Humana, Salvador, Brazil.
(2)Multinational Organization Network Sponsoring Translational and Epidemiological Research (MONSTER) Institute, Salvador, Brazil.
(3)Laboratório de Pesquisa Clínica e Translacional, Instituto Gonçalo Muniz, Fundação Oswaldo Cruz, Salvador, Brazil.
(4)Curso de Medicina, Faculdade ZARNS, Clariens Educação, Salvador, Brazil.
(5)Laboratório de Pesquisa Clínica em Micobacterioses, Instituto Nacional de Infectologia Evandro Chagas/FIOCRUZ, Rio de Janeiro, Brazil.
(6)Universidade Federal do Rio de Janeiro, Programa Acadêmico de Tuberculose, Rio de Janeiro, Brazil.
(7)Grupo de Pesquisa em Tuberculose, Fundação Medicina Tropical Doutor Heitor

Vieira Dourado, Manaus, Brazil.
(8)Curso de Medicina, Universidade do Estado do Amazonas (UEA), Manaus, Brazil.
(9)Division of Infectious Diseases, Department of Medicine, Vanderbilt University Medical Center, Nashville, TN, USA.
(10)Department of Biostatistics, Vanderbilt University Medical Center, Nashville, USA.
(11)Departamento de Clínica Médica, Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brazil.

BACKGROUND: Tuberculosis (TB) remains a leading cause of infectious disease mortality globally. Although directly observed therapy (DOT) has been widely implemented to improve adherence, nonadherence continues to compromise treatment success rates, especially in real-world settings. Therefore, this study aims to assess the impact of missed doses on TB treatment outcomes.
METHODS: Prospective study that followed adults with drug-sensitive TB for two years after TB treatment initiation at five clinical centers of the RePORT-Brazil cohort between June 2015 and June 2019. Participants not in DOT or followed for less than 30 days were excluded. Nonadherence was defined as the percentage of missed doses relative to the prescribed regimen, monitored daily through DOT. The primary composite outcome comprised treatment failure, disease recurrence, drug resistance, death, or loss to follow-up (LTFU) after 30 days of treatment. Associations were assessed with multivariable logistic regression.
FINDINGS: Among the 578 participants analyzed, 218 (37·7%) experienced unfavorable outcomes. Overall, 23% of participants missed more than 10% of prescribed doses, and this group had an 81·2% likelihood of experiencing unfavorable outcomes, compared to only 21·6% among those with complete adherence. A significant association was observed between the percentage of missed doses and unfavorable outcomes (adjusted OR: 1·11, 95% CI: 1·07-1·14, p-value < 0·0001).
INTERPRETATION: Even minor nonadherence in TB treatment was associated with an increased risk of unfavorable outcomes, highlighting the role of adherence in successful TB care.
FUNDING: Fundação Oswaldo Cruz, Fundação José Silveira, Departamento de Ciência e Tecnologia, US National Institute of Allergy and Infectious Diseases.

DOI: 10.1016/j.lana.2025.101162
PMCID: PMC12246921
PMID: 40657430

Conflict of interest statement: We declare no competing interests.

78. Mycobacterium tuberculosis curli pili reduces oxygen consumption rate of THP-1 macrophages during early infection.

Int J Biochem Cell Biol. 2025 Aug;185:106802. doi: 10.1016/j.biocel.2025.106802. Epub 2025 May 15.

Ashokcoomar S(1), Naidoo TJ(2), Cumming BM(3), Baig Z(4), Truebody B(5), Mackenzie JS(6), Steyn AJC(7), Pillay M(8).

Author information:
(1)Medical Microbiology, School of Laboratory Medicine and Medical Sciences, College of Health Sciences, University of KwaZulu-Natal, 1st floor Doris Duke Medical Research Institute, Congella, Private Bag 7, Durban 4013, South Africa. Electronic address: shineseashokcoomar@gmail.com.
(2)Medical Microbiology, School of Laboratory Medicine and Medical Sciences, College of Health Sciences, University of KwaZulu-Natal, 1st floor Doris Duke Medical Research Institute, Congella, Private Bag 7, Durban 4013, South Africa. Electronic address: tarienjael@gmail.com.
(3)Africa Health Research Institute, Nelson R. Mandela Medical School, 4th floor K-RITH Tower Building, Congella, Private Bag 7, Durban 4013, South Africa. Electronic address: bridgette.cumming@gmail.com.
(4)Africa Health Research Institute, Nelson R. Mandela Medical School, 4th floor K-RITH Tower Building, Congella, Private Bag 7, Durban 4013, South Africa. Electronic address: zainab.baig@ahri.org.
(5)Africa Health Research Institute, Nelson R. Mandela Medical School, 4th floor K-RITH Tower Building, Congella, Private Bag 7, Durban 4013, South Africa. Electronic address: barry.truebody@ahri.org.
(6)Africa Health Research Institute, Nelson R. Mandela Medical School, 4th floor K-RITH Tower Building, Congella, Private Bag 7, Durban 4013, South Africa. Electronic address: jared.mackenzie@ahri.org.
(7)Africa Health Research Institute, Nelson R. Mandela Medical School, 4th floor K-RITH Tower Building, Congella, Private Bag 7, Durban 4013, South Africa. Electronic address: adrie.steyn@ahri.org.
(8)Medical Microbiology, School of Laboratory Medicine and Medical Sciences, College of Health Sciences, University of KwaZulu-Natal, 1st floor Doris Duke Medical Research Institute, Congella, Private Bag 7, Durban 4013, South Africa. Electronic address: pillayc@ukzn.ac.za.

The development of improved anti-tuberculosis (TB) strategies to address drug-resistance and ineffectual TB treatment regimens should focus on interrupting the initial host-pathogen interaction. This study aimed to elucidate the effect of surface-located adhesin, Mycobacterium tuberculosis (Mtb) curli pili (MTP), on the bioenergetic and metabolomic profiles of THP-1 macrophages during initial stages of infection. Differentiated THP-1 macrophages

were infected with wildtype (WT), ∆mtp, or mtp-complemented strains of Mtb. Bioenergetic profiles and metabolic flux were determined and statistical analysis highlighted differences/similarities amongst the THP-1 macrophage groups. The ∆mtp infected THP-1 macrophages mimicked the higher oxygen consumption rate (OCR) for basal respiration, ATP production, maximal respiration and spare respiratory capacity of the uninfected THP-1 macrophages, relative to the WT and mtp-complement infected THP-1 macrophages. The ∆mtp infected THP-1 macrophages displayed the highest compensatory glycolytic rate. Mtb infection caused the redirection of carbon from the tricarboxylic acid cycle to glycolysis, in addition to an increased flux through the pentose phosphate pathway. However, in the ∆mtp infected THP-1 macrophages, the total metabolite abundance was lower, similar to the uninfected THP-1 macrophages. Data indicates that the absence of MTP facilitates prompt clearance of the intracellular pathogen before it establishes a successful infection. This implies that the presence of MTP facilitates the survival of the pathogen during the early stages until infection is established. These findings support the growing evidence that the MTP adhesin is an important virulence factor and interruption of the interaction between pathogen and host, will facilitate swift clearance of the infection by the host.

DOI: 10.1016/j.biocel.2025.106802
PMID: 40381906 [Indexed for MEDLINE]

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

79.Acceptability of a clofazimine tablet in children with rifampicin-resistant TB in three high-burden countries.

IJTLD Open. 2025 Aug 13;2(8):478-485. doi: 10.5588/ijtldopen.25.0309. eCollection 2025 Aug.

Viljoen L(1), Draper HR(1), Castillo-Carandang NT(2)(3), Suryavanshi N(4), Marthinus A(1), Cheong AMA(3), Ocampo JDD(4), Dhumal G(5), Bagchi S(5), Wademan DT(1), Kinikar A(6), Paradkar M(5), Frias MVG 4th(3), Casalme DJO(3), Hesseling AC(1), Garcia-Prats AJ(1)(7), Palmer M(1), Hoddinott G(1)(8).

Author information:
(1)Desmond Tutu TB Centre, Department of Paediatrics and Child Health, Faculty

of Medicine and Health Sciences, Stellenbosch University, Cape Town, South Africa.
(2)Department of Clinical Epidemiology, College of Medicine, University of the Philippines Manila, Philippines.
(3)De La Salle Health Sciences Institute, Dasmariñas City, Cavite, the Philippines.
(4)Program on Social Innovation in Health, National Institutes of Health, University of the Philippines Manila, Philippines.
(5)Byramjee Jeejeebhoy Government Medical College -Johns Hopkins Clinical Research Site, Pune, India.
(6)Department of Paediatrics, Byramjee Jeejeebhoy Government Medical College, Pune, India.
(7)Department of Pediatrics, School of Medicine and Public Health, University of Wisconsin, Madison, Wisconsin, USA.
(8)School of Public Health, Faculty of Medicine and Health, The University of Sydney, Sydney, Australia.

BACKGROUND: Rifampicin-resistant TB (RR-TB) in children is frequently treated with clofazimine (CFZ), widely available as a 100mg gel capsule. This formulation is challenging to administer and is poorly acceptable to children and caregivers. Poor acceptability may negatively impact adherence and treatment outcomes. We describe the acceptability of a novel 50mg CFZ tablet formulation among children in South Africa, India, and the Philippines.
METHODS: Mixed methods assessments were completed in a moxifloxacin and CFZ safety and pharmacokinetics trial in children with RR-TB. Quantitative data were collected from 36 participants at 4 timepoints. A sub-sample of 26 child/caregiver dyads participated in ~4 qualitative interviews. Descriptive statistics and thematic analysis were employed.
FINDINGS: The median age of n=36 participants (South Africa n=20; India n=6; the Philippines n=10) was 4.9 years. The majority (29/36) received a CFZ gel capsule prior to switching to the tablet formulation. The 50mg tablet had better acceptability scores for taste (p=0.035), smell (p=0.035), and ease of swallowing (p=0.02) compared to gel capsules. Participants described the tablet formulation as easier to administer/take without a lingering smell or taste. Limited concerns were noted on staining.
CONCLUSION: The novel 50mg CFZ tablet has better acceptability and should be prioritised for children wherever possible.

DOI: 10.5588/ijtldopen.25.0309
PMCID: PMC12352948
PMID: 40821683

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

80. Negligible clinical impact of subsequent non-tuberculous mycobacteria isolation during MDR/RR-TB treatment: a 9-year retrospective cohort study from Wenzhou, China.

BMC Infect Dis. 2025 Jul 24;25(1):942. doi: 10.1186/s12879-025-11336-0.

Zheng Q(#)(1), Chen Q(#)(2), Zhou W(#)(3), Huang O(3), He G(4).

Author information:
(1)Laboratory of Infectious Diseases, Wenzhou Central Hospital, The Dingli Clinical College of Wenzhou Medical University, Wenzhou, 325000, China.
(2)Department of Radiology, Wenzhou Central Hospital, The Dingli Clinical College of Wenzhou Medical University, Wenzhou, 325000, China.
(3)Department of Infectious Diseases, Wenzhou Central Hospital, The Dingli Clinical College of Wenzhou Medical University, Wenzhou, 325000, China.
(4)Laboratory of Infectious Diseases, Wenzhou Central Hospital, The Dingli Clinical College of Wenzhou Medical University, Wenzhou, 325000, China.
heguiqing@wmu.edu.cn.
(#)Contributed equally

BACKGROUND: The frequency of clinical isolation of non-tuberculous mycobacteria (NTM) in patients with multidrug-resistant or rifampin-resistant tuberculosis (MDR/RR-TB) is increasing, but its relevance remains unclear. This study aimed to assess the frequency of NTM isolation and its clinical relevance in respiratory specimens from MDR/RR-TB patients in Wenzhou, China.
METHODS: Medical records of MDR/RR-TB patients with NTM isolated from 2014 to 2022 were reviewed retrospectively. To establish the clinical relevance, the diagnostic criteria for nontuberculous mycobacterial pulmonary disease (NTM-PD) published by the American Thoracic Society (ATS) and Infectious Diseases Society of America (IDSA) were applied.
RESULTS: Between 2014 and 2022, a total of 922 patients were enrolled, among whom 45 (4.9%) cases yielded NTM isolates, resulting in the isolation of 68 distinct NTM strains. The most prevalent NTM species was M. abscessus, accounting for 36.8% (25/68) of the isolates, followed by M. intracellulare at 22.1% (15/68) and M. avium at 8.8% (6/68). Notably, only five cases (0.54%) met the microbiologic criteria specified in the ATS/IDSA guidelines. Four of these cases received no specific NTM treatment and achieved a favorable prognosis with anti-TB therapy. Remarkably, a single case out of 922 (0.11%) was identified as having concomitant MDR/RR-TB and NTM-PD.
CONCLUSIONS: The clinical relevance of respiratory NTM isolates in patients with MDR/RR-TB is generally low, with the overwhelming majority of these NTM isolates

being either colonizers or contaminants. Consequently, in most cases, those with concomitant NTM isolates do not require specific therapy.

DOI: 10.1186/s12879-025-11336-0
PMCID: PMC12291228
PMID: 40707877 [Indexed for MEDLINE]

Conflict of interest statement: Declarations. Ethics approval and consent to participate: The study was conducted in accordance with the principles outlined in Good Clinical Practice and the Declaration of Helsinki. It was approved by the Ethics Committee of Wenzhou Central Hospital (No. L2024-07-047). Since the study design was retrospective, the requirement for informed consent was waived. Consent for publication: Not applicable. Competing interests: The authors declare no competing interests.

81. A competing risk analysis of predictors of time to lost to follow-up among adults with TB/HIV coinfection in Bahir Dar.

Sci Rep. 2025 Aug 19;15(1):30362. doi: 10.1038/s41598-025-15985-8.

Demelash R(1), Hailu G(2), Abuhay T(2), Addis Z(3), Tega A(4), Nibret D(5), Habtu Y(5).

Author information:
(1)Department of Family Health, Hossana College of Health Sciences, Hossana, Ethiopia. robdemelash@gmail.com.
(2)Department of Epidemiology and Biostatistics, School of Public Health, Bahir Dar University, Bahir Dar, Ethiopia.
(3)Department of Nursing, Hossana College of Health Sciences, Hossana, Ethiopia.
(4)Department of Midwifery, Hossanna College of Health Sciences, Hossanna, Ethiopia.
(5)Department of Family Health, Hossana College of Health Sciences, Hossana, Ethiopia.

Lost to follow-up (LTFU), defined as interrupting anti-TB treatment for ≥ 8 consecutive weeks or missing anti-retroviral therapy (ART) appointments for > 90 days, is a barrier to TB/HIV coinfection management. Poor treatment adherence, a driver of multidrug resistance in TB/HIV, poses critical challenges to case management. Overestimating effect sizes when considering mutually exclusive events, like LTFU from ART and anti-TB treatment, can occur if sources of error are not properly accounted for in competing events. However, studies estimating

the effect sizes of predictors of time to LTFU using competing risk analysis are scarce. Hence, this study aimed to investigate the predictors of time to LTFU among adults with TB/HIV coinfection. We conducted a multicenter facility-based retrospective follow-up study. We randomly selected 471 TB/HIV coinfected adults. Data were extracted using standardised checklists. The LTFUs from ART and anti-TB treatment were events of interest and competing events, respectively, and others were censored. The data were entered into Epi data and then exported to Stata and Rstudio. Statistical differences were tested by Gray's test, and the cumulative incidence of each event was estimated by a cumulative incidence function. Bivariable and multivariable competing risk regression models were fitted, and variables with p values < 0.05 were considered significant predictors. Incidence rates of LTFU for ART and TB treatment were 3.90 and 19.17 per 1000 person-months of observation (PMOs), respectively. The predictors of ART LTFU included rural residence (adjusted subdistribution hazard ratio (SDHR): 3.39), WHO stage IV (SDHR: 2.88), haemoglobin < 11 g/dl (SDHR: 3.56), and opportunistic infections (OIs) (SDHR: 3.65). For TB treatment LTFU, significant predictors were rural residence (SDHR: 0.11), divorced (SDHR: 2.81), widowed (SDHR: 5.92), BMI < 18.5 (SDHR: 0.41), ambulatory functional status (SDHR: 2.59), adverse drug effects (SDHR: 2.87), and poor ART adherence (SDHR: 5.72). Considering errors in competing events, ART LTFU was higher among rural dwellers, individuals with advanced disease, nutritional deficits, or adverse drug effects requiring prioritised, multifaceted interventions. Targeted strategies such as intensified monitoring, adherence counselling, nutritional support, proactive management of drug-related side effects, marital instability, OIs and poor ART adherence should be integrated into the existing ART/TB program to mitigate LTFU.

DOI: 10.1038/s41598-025-15985-8
PMCID: PMC12365281
PMID: 40830417 [Indexed for MEDLINE]

Conflict of interest statement: Declarations. Competing interests: The authors declare no competing interests. Ethical approval and consent to participate: Due to the retrospective nature of the study, the need to obtain the informed consent was waived by the Institutional Review Board (IRB) of the College of Health Sciences of Bahir Dar University approved the study, with study protocol number 730/2023. The IRB performs following the Declaration of Helsinki, the International Conferences on Harmonisation (ICH) Good Clinical Practice, the WHO Operating Guidelines for Ethical Review Committee and the National Guideline for Research Ethics in Ethiopia. The Amhara Public Health Institute (APHI) reviewed the ethical approval protocols and requested that the selected hospitals and health centres provide records of TB/HIV treatment follow-up data to the

authors. Accordingly, the health facilities' patient charts or ART follow-up forms were used. The name of the patient was not included in the checklist. The data of any patient were not used for other purposes other than for the aim of this study.

82. Pyrazolopyridine pyrimidone hybrids as potential DprE1 inhibitors, design, synthesis and biological evaluation as antitubercular agents.

Sci Rep. 2025 Aug 12;15(1):29586. doi: 10.1038/s41598-025-14734-1.

Shah M(1), Patel I(1), Khona P(1), Patel H(1), Yadav MR(2), Nagani A(3)(4).

Author information:
(1)Parul Institute of Pharmacy, Parul University, Vadodara, Gujarat, India.
(2)Research and Development Cell, Parul University, Vadodara, Gujarat, India.
(3)Parul Institute of Pharmacy, Parul University, Vadodara, Gujarat, India. afzal.nagani@gmail.com.
(4)Research and Development Cell, Parul University, Vadodara, Gujarat, India. afzal.nagani@gmail.com.

Tuberculosis (TB) remains a major global health challenge. This study presents the design, synthesis, and evaluation of some novel pyrazolo[3,4-b]pyridine-pyrimidone derivatives targeting Mycobacterium tuberculosis (Mtb). The compounds were assessed for anti-tubercular activity using the Microplate Alamar Blue Assay (MABA) against the Mtb H37Rv strain. Key derivatives (8 and 14) showed significant activity with minimum inhibitory concentration (MIC) values of 3.12 µg/mL, 12.5 µg/mL, respectively, comparable to the standard drugs and are nontoxic at their effective concentration as anti-TB agents. Molecular docking studies demonstrated strong binding interactions with DprE1 and Mtb-DHFR enzymes, suggesting inhibition of these critical proteins. Further computational analyses, including density functional theory (DFT) and molecular dynamics simulations, confirmed the binding stability of the compounds to the target proteins. Overall, these pyrazolo[3,4-b]pyridine-pyrimidone derivatives are potential leads for further development as future therapeutics for treating drug-resistant TB.

DOI: 10.1038/s41598-025-14734-1
PMCID: PMC12343961
PMID: 40797008

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

83. Baeyer-Villiger monooxygenase immobilized on magnetic nanoparticles: reusable biocatalytic system for drug metabolite synthesis.

Int J Biol Macromol. 2025 Aug;319(Pt 3):145588. doi: 10.1016/j.ijbiomac.2025.145588. Epub 2025 Jun 25.

De Angelis M(1), Liyanage USG(1), Marucco AMB(1), Catucci G(1), Schwaminger SP(2), Gilardi G(3), Sadeghi SJ(4).

Author information:
(1)Department of Life Sciences and Systems Biology, University of Torino, via Accademia Albertina 13, 10123 Torino, Italy.
(2)Division of Medicinal Chemistry, Otto Loewi Research Center, Medical University of Graz, Neue Stiftingtalstraße 6, 8010 Graz, Austria; BioTechMed-Graz, Mozartgasse 12, 8010 Graz, Austria.
(3)Department of Life Sciences and Systems Biology, University of Torino, via Accademia Albertina 13, 10123 Torino, Italy; Nanomaterials for Industry and Sustainability Center, University of Torino, via Accademia Albertina 13, 10123 Torino, Italy.
(4)Department of Life Sciences and Systems Biology, University of Torino, via Accademia Albertina 13, 10123 Torino, Italy; Nanomaterials for Industry and Sustainability Center, University of Torino, via Accademia Albertina 13, 10123 Torino, Italy. Electronic address: sheila.sadeghi@unito.it.

Drug metabolites are critical for assessing drug efficacy, pharmacokinetics, and safety. Biocatalysis offers a selective and sustainable route to their synthesis. In this study, a Baeyer-Villiger monooxygenase from Acinetobacter radioresistens (Ar-BVMO) was immobilized onto bare iron oxide nanoparticles (BIONs), producing a reusable biocatalytic system (BVMO@BION) for drug metabolite production. The magnetic properties of BIONs facilitated easy recovery and reuse of the biocatalyst, making the system practical for repeated use. High loading efficiency (0.14 mg enzyme per mg of BIONs) was achieved through histidine-tag-mediated binding. The immobilized enzyme exhibited enhanced thermostability, increasing its melting temperature from 46.3 °C to 54.9 °C, and reduced nanoparticle aggregation. The system demonstrated robust activity for Baeyer-Villiger and S/N-oxidation reactions. Notably, BVMO@BION achieved over 95 % conversion efficiency for the N-oxidation of tozasertib (an anti-cancer drug) across nine reaction cycles (2 h each) over 3 days, while activity recovery values ranged from 81 % to 127 %. For S-oxidation of

ethionamide (an antibiotic used in multidrug-resistant tuberculosis) approximately 26 % conversion was consistently achieved across eight 1-hour cycles. This work demonstrates that BVMO@BION is a robust, magnetically recoverable platform for repeated and selective drug metabolite synthesis, supporting greener and more efficient pharmaceutical development.

DOI: 10.1016/j.ijbiomac.2025.145588
PMID: 40578651 [Indexed for MEDLINE]

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

84. High proportion of tuberculosis recent transmission in rural areas of Northeastern China: a 3-year prospective population-based genotypic and spatial analysis in Hinggan League, China.

Microbiol Spectr. 2025 Aug 5;13(8):e0016925. doi: 10.1128/spectrum.00169-25. Epub 2025 Jul 11.

Ou X(#)(1), Li X(#)(2), Pei S(#)(3), Zhao B(1), Feng L(4), Teng C(1), Lu Y(2), Zhu H(1), Zhou Y(1), Xia H(1), Liu Z(5), Wang X(5), Wang Y(6), Anthony R(7), 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, Beijing, China.
(2)Key Laboratory of Precision Medicine in Diagnosis and Monitoring Research of Zhejiang Province, Hangzhou, Zhejiang, China.
(3)School of Public Health, Peking University, Beijing, China.
(4)Department of Microbiology, Hinggan League Center for Disease Control and Prevention, Ulanhot, China.
(5)Department of Tuberculosis Control and Prevention, Zhejiang Provincial Center for Disease Control and Prevention, Hangzhou, China.
(6)Administration Office, Medical Insurance Service Center of Ulanhot City, Ulanhot, China.
(7)Centre for Infectious Disease Control, National Institute for Public Health and the Environment, Bilthoven, the Netherlands.
(#)Contributed equally

Tuberculosis (TB) remains a significant public health challenge in China, particularly in rural areas like Hinggan League (HL), Inner Mongolia. Understanding the genetic diversity and transmission dynamics of Mycobacterium tuberculosis (MTB) strains is crucial for effective TB control. We conducted a prospective study from 2021 to 2023, sequencing 221 MTB isolates from HL. After quality control, 210 cases were analyzed. The genomic clustering rate was calculated to evaluate the level of recent transmission. Risk factors were identified by logistic regression analysis. Geospatial analysis was conducted with kernel density estimation. The majority of strains belonged to sub-lineage 2.2.1 in lineage 2 (L2), also known as the Beijing family (89.0%, 187/210), while the remainder belonged to lineage 4 (L4). L2 strains showed greater genetic similarity and shorter branch lengths compared with L4 strains. The overall drug resistance rate was 21.9%, with six multidrug-resistant TB (MDR-TB) and five pre-extensively drug resistant TB (pre-XDR-TB) cases identified. Almost half of the strains belonged to putative transmission clusters within 10 SNPs. Logistic regression analysis identified living in Jalaid Banner and being infected by L2 strains as significant risk factors for recent transmission. Spatial analysis identified spatial aggregation of TB cases in the eastern region of HL, with a hotspot for recent transmission in Jalaid Banner. The temporal distribution of TB cases in HL exhibited seasonal fluctuations, with diagnosis rates peaking in the first half of each year, and a notable increase in clustered cases in 2022. This study provides insights into the molecular epidemiology and transmission dynamics of TB in HL. Our results underscore the ongoing problem of TB transmission in rural settings, indicating the need for targeted interventions. These findings are vital for informing TB control strategies in HL and similar settings.IMPORTANCETuberculosis (TB) remains a major public health problem in China. This study provides insights into the molecular epidemiology and transmission dynamics of TB in rural areas (Hinggan League [HL], Inner Mongolia) in China. Nearly half of the enrolled TB cases were attributed to recent transmission, a proportion higher than that observed in other rural areas in China (31.4%), highlighting the significance of recent transmission in driving the TB epidemic in this region. Only 19.6% of all drug-resistant TB (DR-TB) cases were found within putative transmission clusters, indicating a lower proportion compared with the previous studies, which indicated that DR-TB is more associated with the de novo evolution of resistance within patients. Spatial analysis showed that the TB epidemic was concentrated in densely populated areas in eastern HL. The findings identified epidemiological differences within HL, highlighting the importance of targeted interventions and surveillance to control the spread of TB in HL.

DOI: 10.1128/spectrum.00169-25
PMCID: PMC12323342
PMID: 40643231 [Indexed for MEDLINE]

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

85. Development of highly concentrated bedaquiline suspensions for usage as long-acting injectable formulations.

Int J Pharm. 2025 Aug 22:126103. doi: 10.1016/j.ijpharm.2025.126103. Online ahead of print.

Hansen MF(1), Zulbeari N(1), Holm R(2).

Author information:
(1)Department of Physics, Chemistry and Pharmacy, University of Southern Denmark, Campusvej 55, 5230 Odense, Denmark.
(2)Department of Physics, Chemistry and Pharmacy, University of Southern Denmark, Campusvej 55, 5230 Odense, Denmark. Electronic address: reho@sdu.dk.

Tuberculosis (TB) remains a global health problem with an enormous treatment burden and poor treatment adherence, contributing to the emergence of drug resistance. This study investigated the potential of formulating a highly concentrated long-acting injectable (LAI) formulation with bedaquiline fumarate, which could potentially be used as a novel long-term treatment strategy against TB and the prevention of drug resistance. Using wet media milling, micro- and nanosuspensions of bedaquiline fumarate were prepared and evaluated to determine a suitable stabilizer, drug loading capacity, short- and long-term particle size stability, and pharmacokinetic behavior in rats. The stability study revealed a relatively small, but continuous particle size growth over a six-month period when stabilized with 4 % (w/v) polysorbate 20, most pronounced at 40 °C storage. The bedaquiline fumarate salt exhibited superior drug loading capacity compared to the free base form of the compound. When the free base was used in the suspension a viscous paste was obtained at concentrations of 300 mg in 1 mL milling media, whereas the suspensions containing the fumarate salt remained an easy flowing liquid at concentrations as high as 969.5 mg in 1 mL milling media (equivalent to 800 mg free base). Female Spraque-Dawley rats were injected intramuscular with 0.1 mL of one of three formulations, which were identical in composition but differed in particle size distribution. The formulations had mean particle sizes (D50 value) of 0.391 μm, 3.15 μm, 7.80 μm. Particle size displayed a central role in the initial drug release kinetics with smaller particle size profiles yielding higher plasma concentrations. Prolonged plasma concentrations were observed for all three formulations over the 3-months in vivo study. A relatively high sustained plasma concentration of bedaquiline was observed in the animals at the termination of the study suggesting that the prolonged effect continued beyond the investigated three-month period. These

data supported the feasibility of LAI bedaquiline formulations as a treatment option for three months with the potential for an even longer duration. However, further studies are needed to optimize the formulations physical stability.

DOI: 10.1016/j.ijpharm.2025.126103
PMID: 40850505

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

86. ACTG A5409 (RAD-TB): Study protocol for a phase 2 randomized, adaptive, dose-ranging, open-label trial of novel regimens for the treatment of pulmonary Tuberculosis.

Trials. 2025 Aug 15;26(1):291. doi: 10.1186/s13063-025-08973-w.

Harrison LJ(#)(1), Velásquez GE(#)(2)(3), Kempker RR(4), Imperial MZ(2)(5), Nuermberger E(6), Dorman SE(7), Ignatius E(6), Granche J(8), Phillips PPJ(2)(9), Furin J(10), Yang E(2)(5), Foley C(11), Chiambah S(12), Rogers R(12), Van Grack A(13), Roa J(13), Shenje J(14), Nerette S(15), Kanyama C(16), Kyeyune RB(17), Mendoza-Ticona A(18), Murtaugh W(19), Foraida S(20), Goth M(12), Vernon A(12), Dooley KE(#)(21), Savic RM(#)(2)(5).

Author information:
(1)Center for Biostatistics in AIDS Research, Harvard T.H. Chan School of Public Health, Boston, MA, USA. lharriso@sdac.harvard.edu.
(2)UCSF Center for Tuberculosis, University of California, San Francisco, San Francisco, CA, USA.
(3)Division of HIV, Infectious Diseases, and Global Medicine, University of California, San Francisco, San Francisco, CA, USA.
(4)Emory/Georgia Tuberculosis Research Advancement Center, Atlanta, GA, USA.
(5)Department of Bioengineering and Therapeutic Sciences, University of California, San Francisco, San Francisco, CA, USA.
(6)Johns Hopkins University, Baltimore, MD, USA.
(7)Medical University of South Carolina, Charleston, SC, USA.
(8)Center for Biostatistics in AIDS Research, Harvard T.H. Chan School of Public Health, Boston, MA, USA.
(9)Division of Pulmonary and Critical Care Medicine, University of California, San Francisco, San Francisco, CA, USA.

(10)Case Western Reserve University, Cleveland, OH, USA.
(11)Frontier Science Foundation, Amherst, NY, USA.
(12)Division of AIDS (DAIDS), National Institutes of Allergy and Infectious Diseases (NIAID), Rockville, MD, USA.
(13)ACTG Network Coordinating Center, Social and Scientific Systems, DLH Holdings Corp Company, Silver Spring, MD, USA.
(14)South African Tuberculosis Vaccine Initiative (SATVI), Western Province, South Africa.
(15)GHESKIO Institute of Infectious Diseases and Reproductive Health, Port-Au-Prince, Haiti.
(16)UNC Project, Lilongwe, Malawi.
(17)Seattle Children's Research Institute, Washington, USA.
(18)Socios En Salud, Lima, Peru.
(19)ACTG Laboratory Center, UCLA Heath, Los Angeles, CA, USA.
(20)The Global Alliance for TB Drug Development (TB Alliance), New York, USA.
(21)Vanderbilt University Medical Center, Nashville, TN, USA.
(#)Contributed equally

Update of
Res Sq. 2025 Mar 26:rs.3.rs-5931694. doi: 10.21203/rs.3.rs-5931694/v1.

BACKGROUND: The standard of care (SOC) treatment for drug-susceptible pulmonary tuberculosis (DS-TB) consists of isoniazid, rifampicin, pyrazinamide, and ethambutol (HRZE). New treatment regimen options for DS-TB are needed as HRZE is long in duration (6 months), associated with frequent adverse events, unforgiving of adherence lapses, and complicated by rifamycin-based drug-drug interactions. The recent resurgence of TB drug development, particularly in the context of drug-resistant TB, offers promise for additional regimens for persons with DS-TB, provided they are sufficiently effective and well-tolerated. We spotlight wave 1 of the RAD-TB platform trial (ACTG A5409, NCT06192160) that will investigate new chemical entities for the treatment of DS-TB.
METHODS: In wave 1 of the RAD-TB platform, adult participants initiating treatment for DS-TB will be randomized to SOC (HRZE, Arm 1) or one of five experimental arms for the 8-week intensive phase. The experimental treatment arms will consist of a bedaquiline and pretomanid backbone (BPa) in combination with one of three oxazolidinones. Arm 2 will study linezolid (BPaL) at a dose of 600 mg daily, Arms 3A and 3B will study TBI-223 at 1200 mg and 2400 mg daily, respectively, and Arms 4A and 4B will study sutezolid at 800 mg and 1600 mg daily, respectively. The primary efficacy objective is to compare sputum culture time to positivity (TTP) slope over the first 6 weeks of treatment for each experimental treatment arm to SOC. The primary safety objective is to compare new Grade 3 or higher adverse events over the first 8 weeks of treatment for each experimental treatment arm to SOC. After the intensive phase, all participants will receive the standard isoniazid and rifampicin (HR)

continuation phase for 18 weeks. Participants will be followed for 52 weeks after TB treatment initiation to assess long-term outcomes.
DISCUSSION: Wave 1 of the RAD-TB platform aims to identify the optimal oxazolidinone(s), with regard to both efficacy and safety, to combine with the BPa backbone for the treatment of DS-TB. Subsequent waves of this platform trial may add a fourth drug to the regimen, study new diarylquinolines to substitute for bedaquiline, or study novel agents from other TB drug classes.
TRIALS REGISTRATION: ClinicalTrials.gov NCT06192160 . Registered on January 5, 2024.

DOI: 10.1186/s13063-025-08973-w
PMCID: PMC12357366
PMID: 40817073

87. The transmission blocking activity of artemisinin-combination, non-artemisinin, and 8-aminoquinoline antimalarial therapies: A pooled analysis of individual participant data.

PLoS Med. 2025 Aug 14;22(8):e1004683. doi: 10.1371/journal.pmed.1004683. eCollection 2025 Aug.

Vanheer LN(1)(2), Ramjith J(3), Mahamar A(4), Smit MJ(3), Lanke K(3), Roh ME(5), Sanogo K(4), Sinaba Y(4), Niambele SM(4), Diallo M(4), Maguiraga SO(4), Keita S(4), Samake S(4), Youssouf A(4), Diawara H(4), Traore SF(4), Gosling R(6)(7), Brown JM(7), Drakeley C(1)(2), Dicko A(4), Stone W(1)(2), Bousema T(3).

Author information:
(1)Department of Infection Biology, London School of Hygiene & Tropical Medicine, London, United Kingdom.
(2)Malaria Centre, London School of Hygiene & Tropical Medicine, London, United Kingdom.
(3)Department of Medical Microbiology and Radboud Center for Infectious Diseases, Radboud University Medical Center, Nijmegen, the Netherlands.
(4)Malaria Research and Training Centre, Faculty of Pharmacy and Faculty of Medicine and Dentistry, University of Sciences Techniques and Technologies of Bamako, Bamako, Mali.
(5)Institute for Global Health Sciences, University of California, San Francisco, California, United States of America.
(6)Department of Disease Control, London School of Hygiene and Tropical Medicine, London, United Kingdom.
(7)Department of Epidemiology and Biostatistics, University of California, San

Francisco, California, United States of America.

BACKGROUND: Interrupting human-to-mosquito transmission is important for malaria elimination strategies as it can reduce infection burden in communities and slow the spread of drug resistance. Antimalarial medications differ in their efficacy in clearing the transmission stages of Plasmodium falciparum (gametocytes) and in preventing mosquito infection. Here, we present a retrospective combined analysis of six trials conducted at the same study site with highly consistent methodologies that allows for a direct comparison of the gametocytocidal and transmission-blocking activities of 15 different antimalarial regimens or dosing schedules.

METHODS AND FINDINGS: Between January 2013 and January 2023, we conducted six clinical trials evaluating antimalarial treatments with transmission endpoints at the Clinical Research Centre of the Malaria Research and Training Centre of the University of Bamako in Mali. These trials tested Artemisinin-Combination Therapies (ACTs), non-ACT regimens and combinations with 8-aminoquinolines. Participants were males and non-pregnant females, between 5 and 50 years of age, who presented with P. falciparum mono-infection and gametocyte carriage by microscopy. We collected blood samples before and after treatment for thick film microscopy, infectivity assessments by mosquito feeding assays and molecular quantification of gametocytes. To combine direct and indirect effects of treatment groups across studies, we performed a network meta-analysis. This analysis quantified changes in mosquito infection rates and gametocyte densities within treatment groups over time and between treatments. In a pooled analysis of 422 participants, we observed substantial differences between antimalarials in gametocytocidal and transmission-blocking activities. Artemether-lumefantrine (AL) was significantly more potent at reducing mosquito infection rates within 48 h than dihydroartemisinin-piperaquine ($p = 0.0164$) and sulfadoxine-pyrimethamine plus amodiaquine ($p = 0.0451$), while this difference was near-significant for artesunate-amodiaquine ($p = 0.0789$) and pyronaridine-artesunate ($p = 0.0519$). The addition of single low-dose primaquine (SLD PQ) accelerated gametocyte clearance for any ACT and led to a substantially greater reduction in mosquito infection rate within 48 h of treatment for all ACTs except AL, while an SLD of the 8-aminoaquinoline tafenoquine showed a delayed activity, compared to SLD PQ, but was similarly effective. The main limitations of the study include the inclusion of highly infectious individuals, which may not reflect the broader malaria patient population with lower or undetectable gametocyte densities and the small sample sizes in some treatment groups, which resulted in wide confidence intervals and reduced the certainty of effect estimates.

CONCLUSIONS: We found marked differences among ACTs and single low-dose 8-aminoquinoline drugs in their ability and speed to block transmission. The findings from this analysis can support treatment policy decisions for malaria elimination and be integrated into mathematical models to improve the accuracy

of predictions regarding community transmission and the spread of drug resistance under varying treatment guidelines.

DOI: 10.1371/journal.pmed.1004683
PMCID: PMC12352847
PMID: 40811722

Conflict of interest statement: I have read the journal's policy and the authors of this manuscript have the following competing interests: CD is a member of the Malaria Policy Advisory Group (MPAG). TB contributed to a Guideline Development Group of the World Health Organization for recommendations for the final phase of elimination and prevention of re-establishment of malaria.

88.Unpacking bedaquiline heteroresistance: the importance of intermediate profiles for phenotypic drug susceptibility testing.

Antimicrob Agents Chemother. 2025 Aug 6;69(8):e0035625. doi: 10.1128/aac.00356-25. Epub 2025 Jul 21.

Ismail N(#)(1), Sirgel F(#)(1), Omar SV(2), Omar S(1), de Kock M(1), Spies C(1), Folkerts M(3), Theron G(1), Engelthaler D(3), Metcalfe J(#)(4), Warren RM(#)(1).

Author information:
(1)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.
(2)Centre for Tuberculosis, National Institute for Communicable Diseases, Johannesburg, South Africa.
(3)Translational Genomics Research Institute (TGen) North Clinical Laboratory, Flagstaff, Arizona, USA.
(4)University of California-San Francisco, San Francisco, California, USA.
(#)Contributed equally

Update of
bioRxiv. 2025 Mar 10:2025.03.09.642295. doi: 10.1101/2025.03.09.642295.

Phenotypic drug susceptibility testing (pDST) remains a widely used standard for determination of resistance for several drugs for the Mycobacterium tuberculosis

complex. Next-generation sequencing technologies can identify heteroresistant populations at low frequencies, but little is known about the impact of heteroresistance on bedaquiline (BDQ) pDST results. We simulated heteroresistance using in vitro-generated MmpR5 mutants mixed with the progenitor strain at various percentages (1%-20%) and performed pDST using the BACTEC MGIT 960 platform (1 and 2 μg/mL BDQ concentrations) coupled with EpiCenter TB-eXtended individual drug Susceptibility Testing software. Targeted next-generation sequencing was used to quantify the mutant subpopulation in growth control tubes, which were expected to maintain the mutant: wild-type proportion throughout the assay. Growth units of these growth control tubes were also comparable with minor differences in time to positivity between ratio mixtures. Only when intermediate results were considered (i.e., when growth units in a drug-containing tube reach the threshold for resistance but only after a further week of incubation) could BDQ heteroresistance be detected at frequencies of approximately 1% by pDST at a critical concentration of 1 μg/mL. These intermediate results, commonly disregarded during routine testing, could lead to earlier detection of BDQ resistance and may avert adverse clinical outcomes. The ability of pDST, a widely available DST technique, to reveal the presence of BDQ-resistant subpopulations at the phenotypic testing stage could improve resistance determination and potentially reduce time to effective treatment.

DOI: 10.1128/aac.00356-25
PMCID: PMC12326995
PMID: 40689761 [Indexed for MEDLINE]

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

89. A computational approach to mycolic acid biosynthesis disruption in mycobacterium tuberculosis via molluscan metabolites as KasA inhibitors.

Sci Rep. 2025 Jul 29;15(1):27709. doi: 10.1038/s41598-025-13329-0.

Alanzi AR(1), Alsulais FM(2), Alhaidhal BA(2).

Author information:
(1)Department of Pharmacognosy, College of Pharmacy, King Saud University, Riyadh, 11451, Saudi Arabia. aralonazi@ksu.edu.sa.
(2)Department of Pharmacognosy, College of Pharmacy, King Saud University, Riyadh, 11451, Saudi Arabia.

The ongoing global health challenge posed by Mycobacterium tuberculosis, the causative agent of tuberculosis (TB), is exacerbated by the emergence of

drug-resistant strains. This study explores the potential of inhibiting the KasA protein, a key component of the bacterium's type II fatty acid synthase system (FAS-II) involved in mycolic acid biosynthesis. Inhibition of KasA could disrupt the integrity of the mycobacterial cell wall, which is crucial for its survival and virulence. In this study, we screened a library of 730 Molluscan metabolites using molecular docking techniques via the Glide tool, identifying ten compounds with significant binding affinities ranging from - 7.535 to -6.517 kcal/mol. The ADMET profiles of these compounds were evaluated, revealing acceptable toxicity levels for four selected candidates: CMNPD7125, CMNPD22991, CMNPD4542, and CMNPD12265. Additionally, molecular dynamics simulations confirmed the stability of these compounds within the KasA binding pocket, reinforcing their potential as effective inhibitors. This integrated approach combining molecular docking, ADMET analysis, and dynamic simulations advances the search for innovative treatments against drug-resistant TB and supports rational drug design efforts for future anti-tubercular agents.

DOI: 10.1038/s41598-025-13329-0
PMCID: PMC12307626
PMID: 40730846 [Indexed for MEDLINE]

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

90. HIV-1 drug resistance among people living with HIV receiving dolutegravir-based anti-retroviral regimens in Uganda: a national laboratory-based survey using remnant viral load samples, 2022.

J Antimicrob Chemother. 2025 Aug 1;80(8):2126-2134. doi: 10.1093/jac/dkaf180.

Watera C(1), Da Silva JF(2), Namayanja G(3), Asio JN(1), Ssemwanga D(1)(4), Pals S(2), Nabukenya M(5), Raizes E(2), Nanyonjo M(4), Elur B(3), Nazziwa E(3), Sanyu G(1), Ayitewala A(5), Ssali M(6), Katureebe C(6), Balidawa H(6), Zheng DP(2), Zeh C(2), Hackett S(2), Mwangi C(3), Naluguza M(3), Ntale J(3), Katongole Mbidde E(1), Kaleebu P(1)(4).

Author information:
(1)Department of General Virololgy, Uganda Virus Research Institute (UVRI), Entebbe, Uganda.
(2)Division of Global HIV & TB, U.S. Centers for Disease Control and Prevention, Atlanta, USA.
(3)Division of Global HIV & TB, U.S. Centers for Disease Control and Prevention,

Kampala, Uganda.
(4)Sequencing Platform, Medical Research Council (MRC)/UVRI & London School of Hygiene and Tropical Medicine (LSHTM) Uganda Research Unit, Entebbe, Uganda.
(5)Central Public Health Laboratories, Ministry of Health, Kampala, Uganda.
(6)AIDS Control Program, Ministry of Health, Kampala, Uganda.

BACKGROUND AND OBJECTIVES: Uganda adopted dolutegravir as its preferred HIV treatment regimen in the national guidelines for treatment of HIV and AIDS in 2018. We conducted a survey to estimate dolutegravir resistance 4 years post-dolutegravir introduction in routine clinical settings. This was a cross-sectional survey to estimate the prevalence of HIV drug resistance (HIVDR) to dolutegravir among children and adults with viral non-suppression (VNS; ≥1000 copies/mL) receiving dolutegravir-based antiretroviral therapy for at least 9 months.
METHODS: We used remnant specimens from routine viral load monitoring stored at Central Public Health Laboratories during February-April 2022. Genotyping of the protease, reverse transcriptase and integrase regions of the HIV-1 pol gene was done using Thermo Fisher® kits and analysed using the Stanford HIVDR database. Weighted prevalences of HIVDR with 95% confidence intervals (CI) were estimated for adults (≥15 years) and children (0-14 years).
RESULTS: We randomly selected 857 specimens including 457 from adults and 400 from children for HIVDR testing from 3578 eligible specimens collected during February-April 2022. Five hundred and eleven (59.6%) were successfully genotyped in the integrase region. Intermediate- to high-level dolutegravir HIVDR prevalence was 3.9% (CI: 0.7, 7.1) for adults and 6.6% (CI: 3.5, 9.6) for children.
CONCLUSION: HIVDR to dolutegravir was uncommon but present among both children and adults with VNS after 9 months or more of exposure to dolutegravir. Additional longitudinal outcomes data are needed to determine if adherence counselling for patients with VNS on dolutegravir regimens might improve outcomes.

DOI: 10.1093/jac/dkaf180
PMCID: PMC12313458
PMID: 40488412 [Indexed for MEDLINE]

Recent TB News

Urgently scale-up research and innovation to end TB: WHO
https://www.who.int/southeastasia/news/detail/05-08-2025-urgently-scale-up-research-and-innovation-to-end-tb-who
On August 5th 2025, the WHO urgently called for up-scaled research, innovation and collaboration in regards to ending tuberculosis efforts in the WHO South-East Asia Region. This region continues to have half of the global tuberculosis burden, but increasing efforts in both social and scientific innovations are helping this region find new approaches to making positive changes in tuberculosis treatment and management. During this time, WHO organized a three-day virtual workshop consisting of experts, programme managers, researchers, and more, to help strengthen collaboration, preparedness, and other areas related to tuberculosis incidence and outcomes in the region.

New study affirms financial and public health advantages of treating drug-resistant TB with BPaL-Based Regimens in India
https://www.tballiance.org/new-study-affirms-financial-and-public-health-advantages-of-treating-drug-resistant-tb-with-bpal-based-regimens-in-india/
Researchers at the ICMR National Institute for Research in Tuberculosis conducted an economic evaluation study, focused on India, that compared seven short-course treatment regimens to the current standard of care (the 9-11 current standard of care). The outcomes of this study support that BPaL-based regimens both improve health outcomes and are cost-effective. This study supports efforts in shifting to approval of BPaL regimens for treating drug-resistant tuberculosis around the world.