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Title: Outcomes for multidrug-resistant tuberculosis patients with and without resistance to fluoroquinolones and second-line injectable drugs: A meta-analysis of individual patient data

Dr. G.B. 8678 Migliori giovannibattista.migliori@fsm.it MD ¹, Dr. S. 8685 Ahuja shama.d.ahuja@gmail.com ², Dr. D. 8686 Ashkin David_Ashkin@doh.state.fl.us ³, Dr. M. 8733 Avendano Monica.Avendano@westpark.org ⁴, Dr. R. 8735 Banerjee Banerjee.ritu@mayo.edu ⁵, Dr. M. 8740 Bauer melissaebauer@gmail.com ⁶, Dr. J. 8759 Bayona Jaime.n.bayona@dartmouth.edu ⁷, Dr. M. 8788 Becerra mercedes.c.becerra@gmail.com ⁸, Dr. A. 8799 Benedetti andrea.benedetti@mcgill.ca ⁶, Dr. M. 8805 Burgos mburgos@salud.unm.edu ⁹, Dr. R. 8806 Centis rosella.centis@fsm.it ¹, Dr. E.D. 8807 Chan chane@njhealth.org ¹⁰, Dr. C.-Y. 8808 Chiang cychiang@theunion.org ^{11,12}, Dr. H. 8813 Cox hcox@burnet.edu.au ¹³, Dr. L. 8829 D'Ambrosio lia.dambrosio@fsm.it ¹, Dr. K. 8833 DeRiemer kderiemer@ucdavis.edu ¹⁴, Dr. N.H. 8835 Dung bshuydung@yahoo.com ¹⁵, Dr. D. 8846 Enarson denarson@theunion.org ¹¹, Dr. K. 8849 Flanagan katie.flanagan@dhhs.tas.gov.au ¹⁶, Dr. J. 8854 Flood Jennifer.Flood@cdph.ca.gov ¹⁷, Dr. M.L. 8856 Garcia-Garcia garcigarm@gmail.com ¹⁸, Dr. N. 8858 Gandhi neelgandhi@alumni.williams.edu ¹⁹, Dr. R. 8859 Granich granichr@who.int ²⁰, Dr. M.G. 8861 Hollm-Delgado mghollm@gmail.com ⁶, Dr. T.H. 8862 Holtz tkh3@th.cdc.gov ²¹, Dr. M. 8864 Iseman IsemanM@NJHealth.org ²², Dr. L. 8866 Jarlsberg JarlsbergL@medsfgh.ucsf.edu ²³, Dr. S. 8869 Keshavjee salmaan.keshavjee@gmail.com ⁸, Dr. H.R. 8873 Kim slowly7@kcch.re.kr ²⁴, Dr. W.-J. 8883 Koh wonjung.koh@gmail.com ²⁵, Dr. J. 8902 Lancaster joey.lancaster@mrc.ac.za ²⁶, Dr. C. 8905 Lange clange@fz-borstel.de ²⁷, Dr. W.C.M. 8906 de Lange w.c.m.de.lange@cvr.umcg.nl ²⁸, Dr. V. 8909 Leimane vaira.leimane@lic.gov.lv ²⁹, Dr. C.C. 8923 Leung cc_leung@dh.gov.hk ³⁰, Dr. J. 8924 Li jli3@health.nyc.gov ³¹, Dr. S. 8940 Mishustin sergeymish@inbox.ru ³², Dr. C. 8942 Mitnick carole_mitnick@hms.harvard.edu ⁸, Dr. M. 8944 Narita masa.narita@kingcounty.gov ³³, Dr. P. 8946 O'Riordan phillyoriordan@yahoo.co.uk ³⁴, Dr. M. 8948 Pai madhukar.pai@mcgill.ca ⁶, Dr. D. 8949 Palmero djpalmero@intramed.net ³⁵, Dr. S.K. 8950 Park pulmo116@nmh.go.kr ³⁶, Dr. G. 8951 Pasvol g.pasvol@imperial.ac.uk ³⁷, Dr. J. 8952 Pena jmpena.hulp@salud.madrid.org ³⁸, Dr. C. 8953 Pérez-Guzmán carperguz1@hotmail.com ³⁹, Dr. M. 8954 Quelapio mameldquelapio@gmail.com ⁴⁰, Dr. A. 8961 Ponce-de-Leon alf.poncedeleon@gmail.com ⁴¹, Dr. V. 8984 Riekstina Vija.Riekstina@lic.gov.lv ²⁹, Dr. J. 9079 Robert jerome.robert0@upmc.fr ⁴², Dr. S. 9084 Royce sarahroycemd@gmail.com ⁴³, Dr. H.S. 9085 Schaaf hss@sun.ac.za ⁴⁴, Dr. K.J. 9089 Seung kjseung@gmail.com ⁴⁵, Dr. L. 9090 Shah lena.shah@mail.mcgill.ca ⁶, Dr. T.S. 9091 Shim shimts@amc.seoul.kr ⁴⁶, Dr. S.S. 9102 Shin SSHIN@PARTNERS.ORG ⁴⁷, Dr. Y. 9104 Shiraishi yujishi@mvp.biglobe.ne.jp ⁴⁸, Dr. J. 9115 Sifuentes-Osornio jsifuentesosornio@gmail.com ⁴¹, Dr. G. 9120 Sotgiu gsothgiu@uniss.it ⁴⁹, Dr. M.J. 9121 Strand strandm@njhealth.org ⁵⁰, Dr. P. 9122 Tabarsi payamtabarsi@yahoo.com ⁵¹, Dr. T.E. 9123 Tupasi tetupasi@tdf.org.ph ⁴⁰, Dr. R. 9136 van Altena

R.van.Altena@cvr.umcg.nl²⁸, Dr. M. 9139 Van der Walt vdwalt@mrc.ac.za²⁶, Dr. T.S. 9141 Van der Werf t.s.van.der.werf@int.umcg.nl²⁸, Dr. M.H. 9147 Vargas mhvargas@yahoo.com.mx⁵², Dr. P. 9154 Viiklepp piret.viiklepp@tai.ee⁵³, Dr. J. 9155 Westenhause Janice.Westenhause@cdph.ca.gov¹⁷, Dr. W.W. 9156 Yew yewww@ha.org.hk⁵⁴, Dr. J.J. 9157 Yim yimjj@snu.ac.kr²⁴ and Dr. D. 9160 Menzies dick.menzies@mcgill.ca⁶.¹ WHO Collaborating Centre for TB and Lung Diseases, Fondazione S. Maugeri, Care and Research Institute, Tradate, Italy ;² Bureau of Tuberculosis Control, New York City Department of Health and Mental Hygiene, Long Island City, United States ;³ Florida Department of Health, A.G. Holley Hospital, Lantana, United States ;⁴ Tuberculosis Service, West Park Healthcare Centre, Toronto, Canada ;⁵ Pediatric Infectious Diseases, Mayo Clinic, Rochester, United States ;⁶ Montreal Chest Institute, McGill University, Montreal, Canada ;⁷ Global Health Programs and Practice, The Dartmouth Center for Health Care Delivery Science, Hanover, United States ;⁸ Department of Global Health & Social Medicine, Harvard Medical School, Boston, United States ;⁹ Department of Internal Medicine, Division of Infectious Diseases, University of New Mexico, Albuquerque, United States ;¹⁰ Pulmonary Department, Denver Veterans Affairs Medical Center; National Jewish Health, Denver, United States ;¹¹ International Union Against Tuberculosis and Lung Disease, Paris, France ;¹² Department of Internal Medicine, Wan Fang Hospital, School of Medicine, Taipei Medical University, Taipei City, Taiwan ;¹³ Médecins Sans Frontières, Cape Town, South Africa ;¹⁴ UC Davis School of Medicine, Davis, United States ;¹⁵ Pham Ngoc Thach Hospital for Tuberculosis and Lung Diseases, Ho Chi Minh City, Viet Nam ;¹⁶ Launceston General Hospital, Tasmania, Australia ;¹⁷ Tuberculosis Control Branch, Division of Communicable Disease Control, Center for Infectious Diseases, California Department of Public Health, Richmond, United States ;¹⁸ Instituto Nacional de Salud Pública (INSP), Cuernavaca, Mexico ;¹⁹ Divisions of General Internal Medicine, Infectious Diseases, and Epidemiology, Albert Einstein College of Medicine, Division of General Internal Medicine, Montefiore Medical Center, Bronx, United States ;²⁰ Antiretroviral Treatment and HIV Care, Department of HIV/AIDS, World Health Organization, Geneva, Switzerland ;²¹ HIV/STD Research Program, Thailand MOPH & US CDC Collaboration, Centers for Disease Control and Prevention, Atlanta, United States ;²² Division of Mycobacterial and Respiratory Infections, Department of Medicine, National Jewish Health, Denver, United States ;²³ Division of Pulmonary and Critical Care Medicine, San Francisco General Hospital, University of California, San Francisco, United States ;²⁴ Department of Internal Medicine, Korea Cancer Center Hospital, Seoul, Korea ;²⁵ Division of Pulmonary and Critical Care Medicine, Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea ;²⁶ Tuberculosis Epidemiology and Intervention Research Unit, South African Medical Research Council, Pretoria, South Africa ;²⁷ Clinical Infectious Diseases and Center for Clinical Studies, Medical Clinic, Tuberculosis Center, Borstel, Germany ;²⁸ Department of Pulmonary Diseases & Tuberculosis, University Medical Center, Groningen, Netherlands ;²⁹ s/a Infectology Center of Latvia, Clinic of Tuberculosis and Lung Diseases, Upeslejas, Latvia ;³⁰ Department of Health, Tuberculosis and Chest Service, Hong Kong, China ;³¹ New York City Department of Health and Mental Hygiene, NYC, United States ;³² Tomsk Oblast Tuberculosis Dispensary, Tomsk, Russian Federation ;³³ Division of Pulmonary and Critical Care, University of Washington, Seattle, United States ;³⁴ City Road Medical Centre, London, United Kingdom ;³⁵ Pulmonology Division, Hospital F. J. Muñiz, Buenos Aires, Argentina ;³⁶ National Masan Tuberculosis Hospital, Masan City, Korea ;³⁷ Dept of Infection & Tropical Medicine, Imperial College London, London, United Kingdom ;³⁸ Servicio de Medicina Interna, Hospital Universitario La Paz, Universidad Autonoma Madrid, Madrid, Spain ;³⁹ Instituto de Salud del Estado de Aguascalientes, and Unidad de Medicina Ambulatoria Aguascalientes, Instituto Mexicano del Seguro Social, Aguascalientes, Mexico ;⁴⁰ Tropical Disease Foundation, Makati, Philippines ;⁴¹ Instituto Nacional de Ciencias Médicas y de Nutrición “Salvador Zubirán”, Mexico D.F,

Mexico ; ⁴² Bactériologie-Hygiène - UPMC PARIS 6 - Site Pitié-Salpêtrière, Paris, France ; ⁴³ Global Health Sciences, University of California, San Francisco, United States ; ⁴⁴ Desmond Tutu TB Centre, Department of Paediatrics and Child Health, Faculty of Health Sciences, Stellenbosch University, Tygerberg, South Africa ; ⁴⁵ Brigham and Women's Hospital, Boston, United States ; ⁴⁶ Division of Pulmonary and Critical Care Medicine, University of Ulsan College of Medicine, Asan Medical Center, Seoul, Korea ; ⁴⁷ Division of Global Health Equity, Division of Infectious Diseases, Brigham and Women's Hospital, Boston, United States ; ⁴⁸ Section of Chest Surgery, Fukujuji Hospital, JATA, Tokyo, Japan ; ⁴⁹ Epidemiology and Medical Statistics Unit, Department of Biomedical Sciences, University of Sassari, Italy ; ⁵⁰ Division of Biostatistics and Bioinformatics, National Jewish Health, Denver, United States ; ⁵¹ Mycobacteriology Research Center, NRITLD, Shaheed Beheshti Medical University, Tehran, Islamic Republic of Iran ; ⁵² Instituto Nacional de Enfermedades Respiratorias, and Unidad de Investigación Médica en Enfermedades Respiratorias, Instituto Mexicano del Seguro Social., México DF, Mexico ; ⁵³ Estonian Tuberculosis Registry, National Institute for Health Development, Tallinn, Estonia and ⁵⁴ Grantham Hospital, Hong Kong, China .

Body: Poor treatment outcomes have been reported for tuberculosis (TB) patients harbouring strains resistant to isoniazid and rifampicin (multidrug resistance or MDR-TB), fluoroquinolones and/or second-line injectable drugs. We undertook a meta-analysis for response to treatment using individual data for MDR-TB patients whose strains had additional resistance to fluoroquinolones (MDR-TB+FQ), second-line injectables (MDR-TB+Inj) or both (extensive drug resistance; XDR-TB) including demographic and clinical details, treatment regimens, and outcomes. 26 centres provided data for 424 MDR-TB+FQ, 1129 MDR-TB+Inj, 405 XDR-TB, and 4776 other MDR-TB patients susceptible to FQ and Inj. Success was lower in MDR-TB+FQ (adjusted OR=0.6 [95%CL 0.5-0.7]) and XDR-TB patients (0.4 [0.3-0.6]) than in those with MDR-TB+Inj (0.8 [0.7-0.9]) and those with MDR-TB and no additional resistance (reference). No single drug was significantly associated with treatment success in MDR-TB+FQ and XDR-TB patients. In XDR-TB patients, success was highest if at least 6 drugs were used in the intensive phase (4.9 [1.4-16.6]) and 4 in the continuation phase (6.1[1.4-26.3]). Study results suggest that regimens of a similar duration to those recommended in MDR-TB patients but containing more drugs achieve better results in XDR-TB patients. As all data in the analysis were from observational studies, bias may be substantial and better quality evidence will be needed to guide the optimization of regimens.