

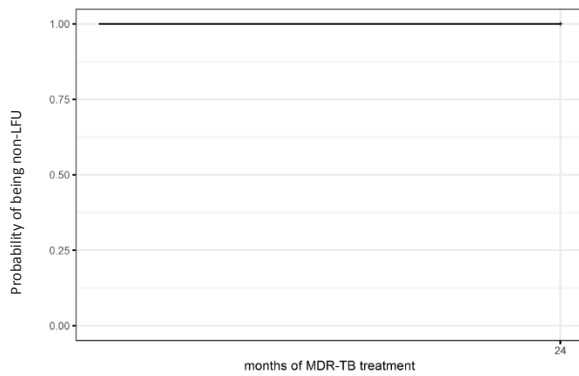
Supplementary Appendices

Analysis of loss to follow up in 4,099 multidrug-resistant pulmonary tuberculosis patients

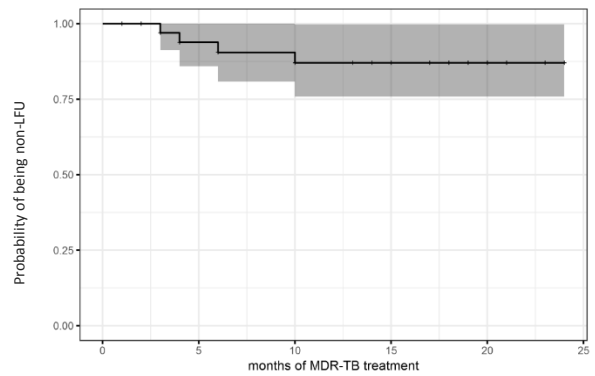
Ian F. Walker, Oumin Shi, Joseph Hicks, Helen Elsey, Xiaolin Wei, Dick Menzies, Zhiyi Lan, Dennis Falzon, Giovanni Battista Migliori, Carlos Pérez-Guzmán, Mario H. Vargas, Lourdes García-García, José Sifuentes Osornio, Alfredo Ponce-De-León, Martie van der Walt and James N. Newell

Kaplan-Meier plots of individual cohorts (shaded areas are confidence intervals)

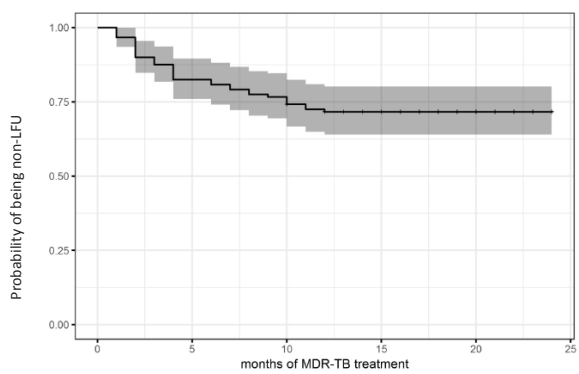
Cohort i – Canada (n=70)



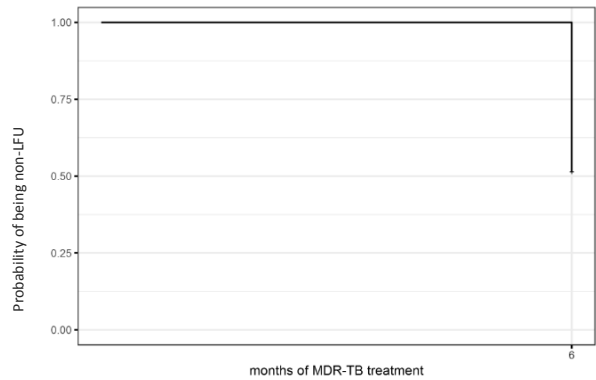
Cohort ii – USA (n=35)



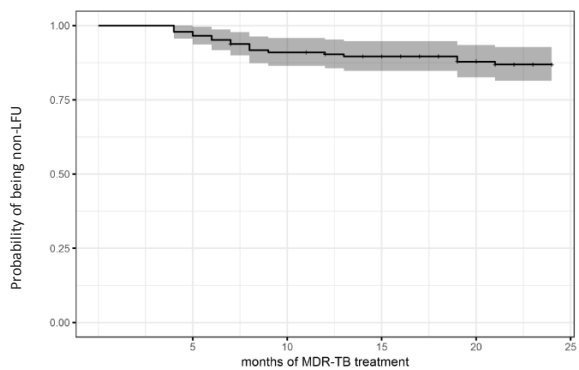
Cohort iii – Taiwan (n=120)



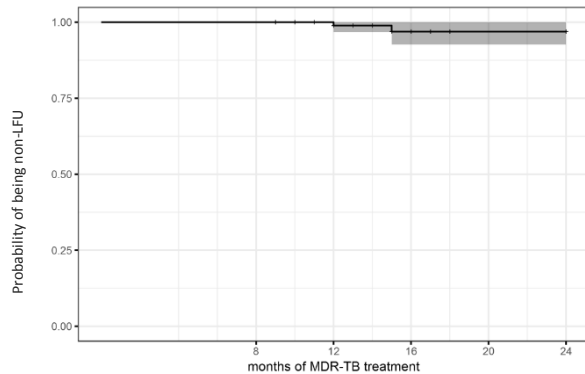
Cohort iv – Mexico (n=35)



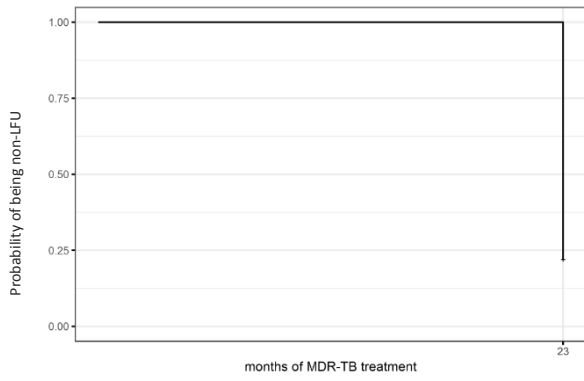
Cohort v - South Korea (n=145)



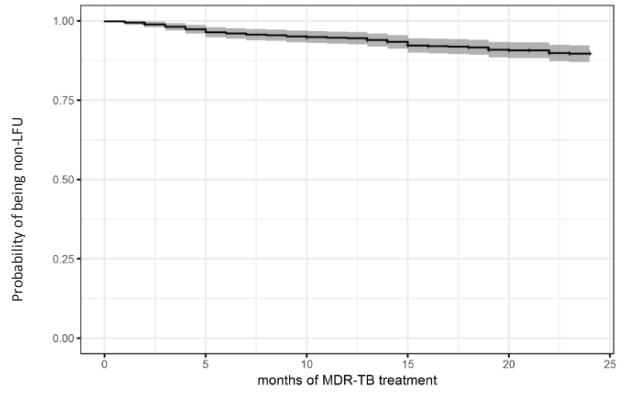
Cohort vi – Hong Kong (n=96)



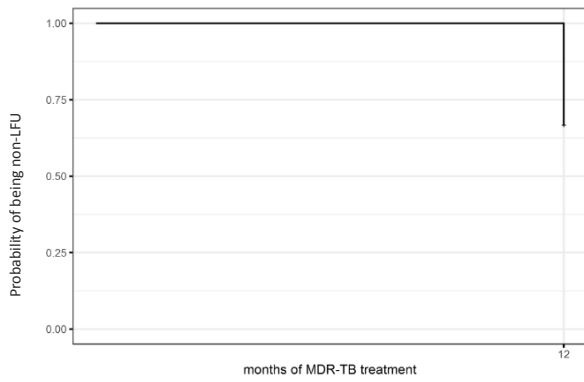
Cohort vii - Italy (n=82)



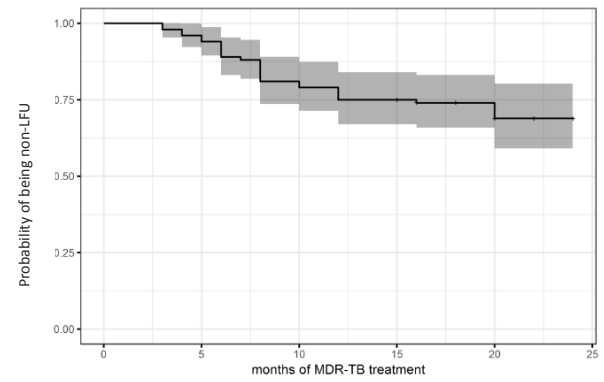
Cohort viii - Peru (n=529)



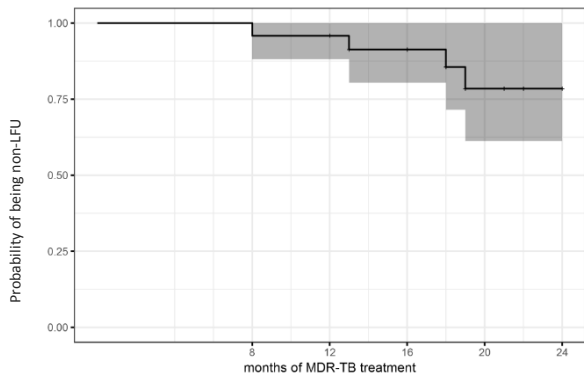
Cohort ix - Mexico (n=33)



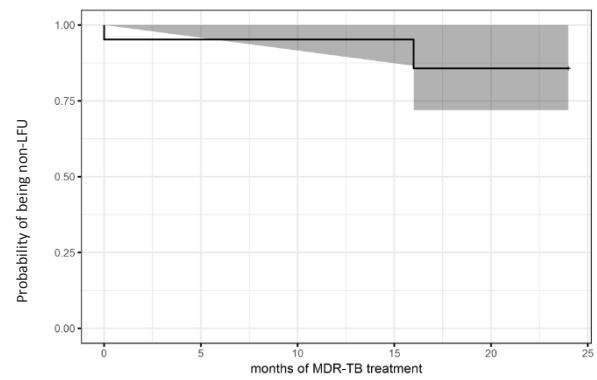
Cohort x - Argentina (n=100)



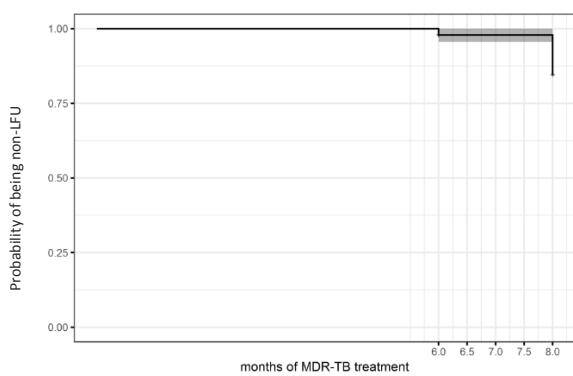
Cohort xi - UK (n=24)



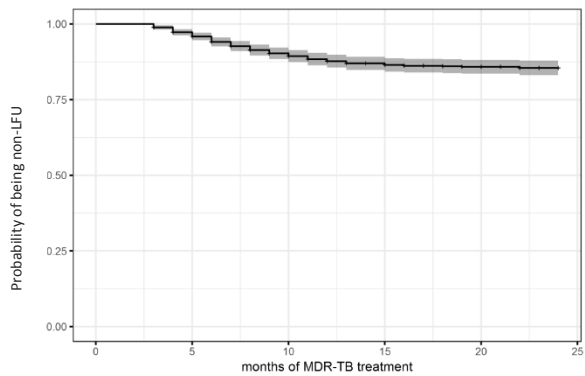
Cohort xii - Spain (n=21)



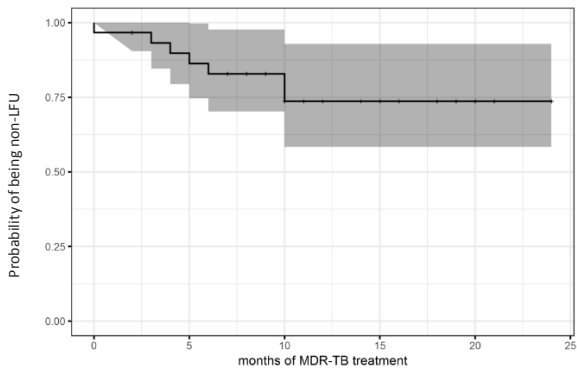
Cohort xiii - Vietnam (n=144)



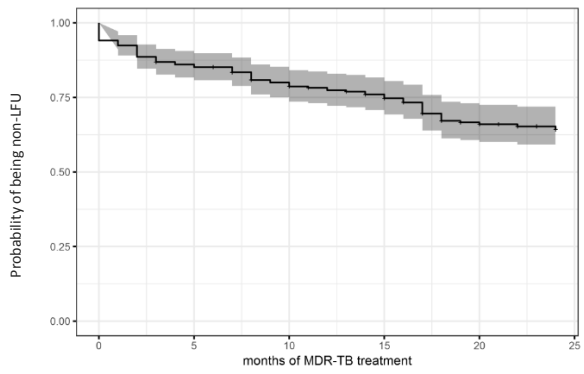
Cohort xiv - Latvia (n=949)



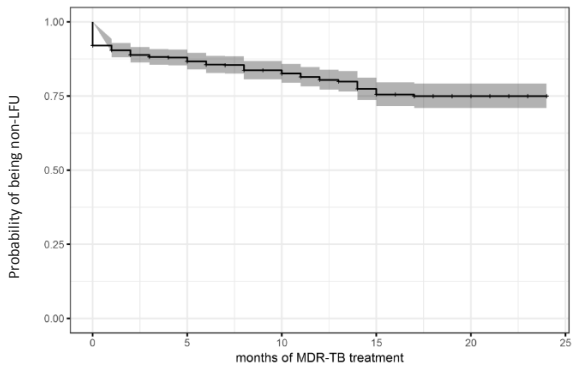
Cohort xv - France (n=30)



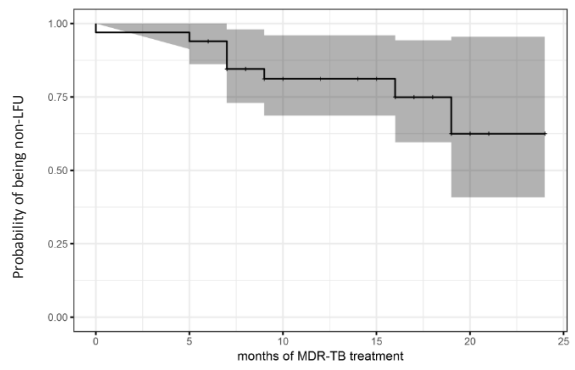
Cohort xvi - USA (n=236)



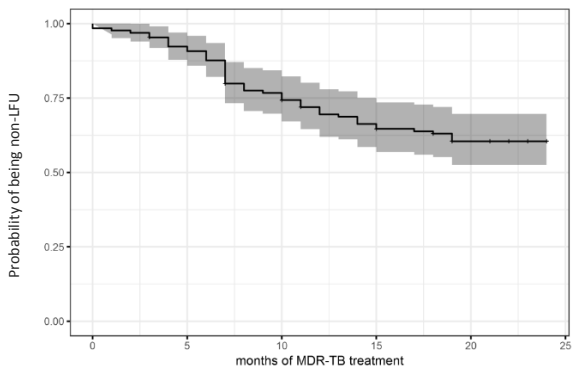
Cohort xvii - Russian Federation (n=577)



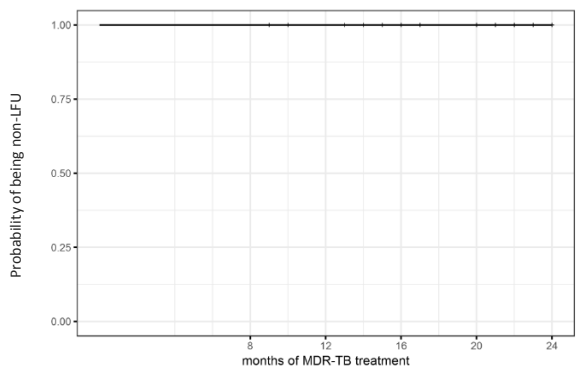
Cohort xviii - South Africa (n=33)



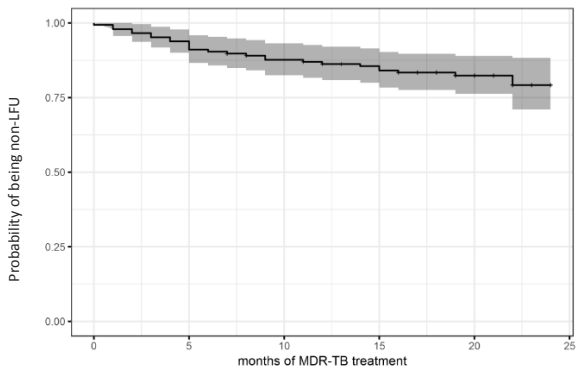
Cohort xix - South Korea (n=130)



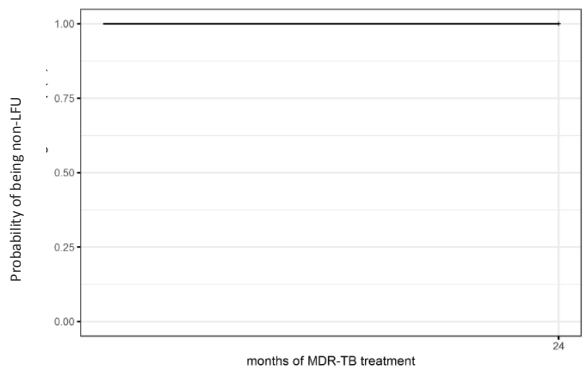
Cohort xx - Japan (n=59)



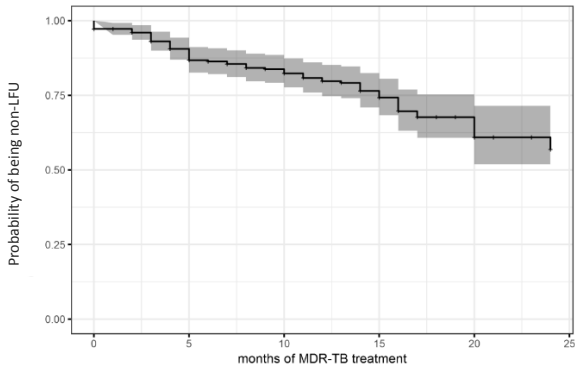
Cohort xxi - Philippines (n=146)



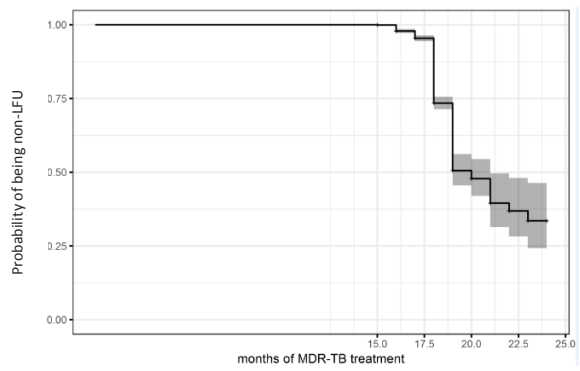
Cohort xxii - Iran (n=35)



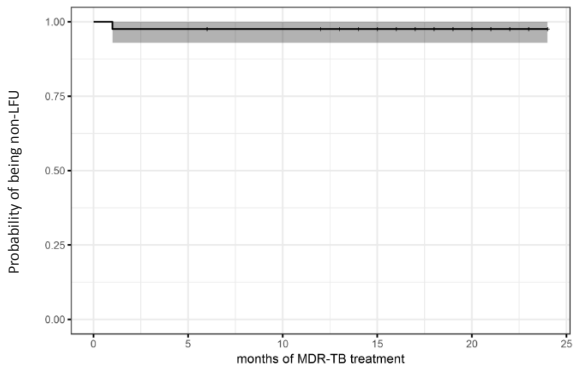
Cohort xxiii – Estonia (n=253)



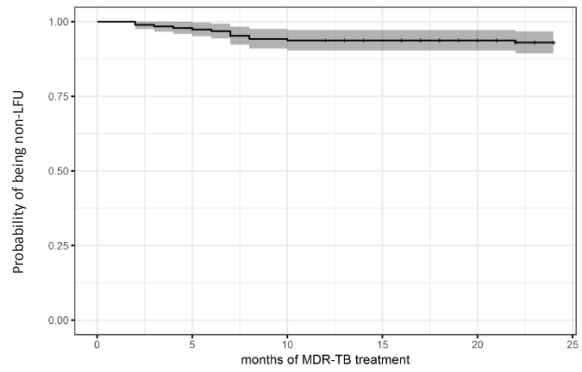
Cohort xxiv – South Africa (n=1,789)



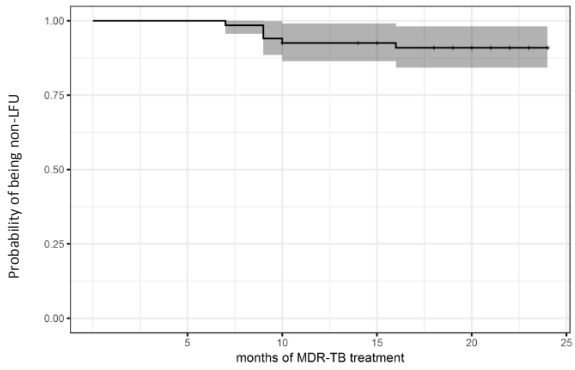
Cohort xxv – The Netherlands (n=41)



Cohort xxvi – South Korea (n=191)



Cohort xxvii – Uzbekistan (n=67)



Individual Cohort Studies Included in this Meta-analysis study

First Author	Years of Study Cohort	Location	Total number of subjects with MDR-TB	Reference
<i>Avendaño</i>	1986-1999	Canada (Toronto)	72	Avendano M, Goldstein RS (2000) Multidrug-resistant tuberculosis: long term follow-up of 40 non-HIV-infected patients. <i>Can Respir J</i> 7: 383–389.
<i>Burgos</i>	1983-2000	USA (San Francisco)	45	Burgos M, Gonzalez LC, Paz EA, Gournis E, Paz A, et al. (2005) Treatment of multidrug-resistant tuberculosis in San Francisco: an outpatient-based approach. <i>Clin Infect Dis</i> 40: 968–975.
<i>Chan</i>	1984-1998	USA (Colorado)	194	Iseman MD, Madsen L, Goble M, Pomerantz M (1990) Surgical intervention in the treatment of pulmonary disease caused by drug-resistant mycobacterium tuberculosis. <i>Am Rev Respir Dis</i> 141: 623–625. Chan ED, Laurel V, Strand MJ, Chan JF, Huynh MLN, et al. (2004) Treatment and outcome analysis of 205 patients with multidrug-resistant tuberculosis. <i>Am J Respir Crit Care Med</i> 169: 1103–1109.
<i>Chiang</i>	1992-1996	Taiwan (Taipei)	125	Chiang CY, Enarson DA, Yu MC, Bai KJ, Huang RM, et al. (2006) Outcome of pulmonary multidrug-resistant tuberculosis: a 6-yr follow-up study. <i>Eur Respir J</i> 28: 980–985.
Cox	2003-2005	Uzbekistan	77	Cox HS, Stobdan K, Allamuratova S, Sizaire V, Tigay ZN, et al. (2007) Multidrug-resistant tuberculosis treatment outcomes in Karakalpakstan, Uzbekistan: treatment complexity and XDR-TB among treatment failures. <i>PLoS One</i> 2: e1126. doi:10.1371/journal.pone.0001126.
<i>De Riemer</i>	1994-2009	Mexico (Veracruz)	47	DeRiemer K, Garcia-Garcia L, Bodadilla-del-Valle M, Palacinós-Martinez M, Martínez-Gamboa A, et al. (2005) Does DOTS work in populations with drug resistant tuberculosis? <i>Lancet</i> 365: 1239–1345.

<i>Escudero</i>	1998-2000	Spain (Madrid)	18	Escudero E, Pena JM, Alvarez-Sala R, Vazquez JJ, Ortega A (2006) Multidrug resistant tuberculosis without HIV infection: success with individualised therapy. <i>Int J Tuberc Lung Dis</i> 10: 409–414.
<i>Geerligs</i>	1987-1988, 1998-2008	The Netherlands	43	Geerligs WA, van Altena R, delange WCM, van Soolingen D, van der Werf TS (2000) Multidrug-resistant tuberculosis: long-term treatment outcome in the Netherlands. <i>Int J Tuberc Lung Dis</i> 4: 758–764.
<i>Granich/ Banerjee</i>	1994-2006	USA (California)	100	Granich RM, Oh P, Lewis B, Porco TC, Flood J (2005) Multidrug resistance among persons with tuberculosis in California, 1994–2003. <i>JAMA</i> 293: 2732– 2739. Banerjee R, Allen J, Westenhouse J, Oh P, Elms W, et al. (2008) Extensively drug-resistant tuberculosis in California, 1993–2006. <i>Clin Infect Dis</i> 47: 450– 457.
<i>DH Kim</i>	2000-2002	South Korea (Seoul)	1288	Kim DH, Kim HJ, Park SK, Kong S, Kim YS, et al. (2008) Treatment outcomes and long-term survival in patients with extensively drug-resistant tuberculosis. <i>Am J Respir Crit Care Med</i> 178: 1075–1082.
<i>HR Kim</i>	1980-2007	South Korea (Seoul)	182	Kim HR, Hwang SS, Kim HJ, Lee SM, Yoo CG, et al. (2007) Impact of extensive drug resistance on treatment outcomes in non-HIV-infected patients with multidrug-resistant tuberculosis. <i>Clin Infect Dis</i> 45: 1290–1295.
<i>Kwon</i>	1995-2005	South Korea (Seoul)	129	Kwon YS, Kim YH, Suh GY, Chung M, Kim H, et al. (2008) Treatment outcomes for HIV-uninfected patients with multidrug-resistant and extensively drug-resistant tuberculosis. <i>Clin Infect Dis</i> 47: 496–502.
<i>Leimane/Holtz/Riekstina</i>	2000-2004	Latvia (Stopinu Novads)	945	Riekstina V, Leimane V, Holtz TH, Leimans J, Wells CD (2007) Treatment outcome cohort analysis in an integrated DOTS and DOTS-Plus TB program in Latvia. <i>Int J Tuberc Lung Dis</i> 11: 585–587. Leimane V, Riekstina V, Holtz TH, Zarovska E, Skripconoka V, et al. (2005) Clinical outcome of individualised treatment of multi-drug resistant tuberculosis in Latvia: a retrospective cohort study. <i>Lancet</i> 386: 318–326. Holtz TH, Stenberg M, Kammerer S, Laserson KF, Riekstina V, et

				al. (2006) Time to sputum culture conversion in multidrug-resistant tuberculosis: predictors and relationship to treatment outcome. <i>Ann Intern Med</i> 144: 650–659.
<i>Lockman</i>	2000-2002	Estonia (All centres)	218	Lockman S, Kruuner A, Binkin N, Levina K, Wang YC, et al. (2001) Clinical outcomes of Estonian patients with primary multidrug-resistant versus drug-susceptible tuberculosis. <i>Clin Infect Dis</i> 32: 373–80
<i>Masjedi</i>	2002-2006	Iran	27	Masjedi MR, Tabarsi P, Chitsaz P, Baghaei P, Miraeidi M, et al. (2008) Outcome of treatment of MDR-TB patients with standardised regimens, Iran, 2002–2006. <i>Int J Tuberc Lung Dis</i> 12: 750–755.
<i>Mitnick</i>	1996-2002	Peru (Lima)	654	Mitnick C, Bayona J, Palacios E, Shin SS, Furin J, et al. (2003) Community based therapy for multidrug-resistant tuberculosis in Lima, Peru. <i>N Engl J Med</i> 348: 119–128. Mitnick C, Shin SS, Seung KJ, Rich ML, Atwood SS, et al. (2010) Comprehensive treatment of extensively drug-resistant tuberculosis. <i>N Engl J Med</i> 359: 563–574.
<i>Munsiff/Li</i>	1992-1997	USA (New York)	671	Munsiff SS, Ahuja SD, Li J, Driver CR (2006) Public-private collaboration for multidrug-resistant tuberculosis control in New York city. <i>Int J Tuberc Lung Dis</i> 10: 639–648. Li J, Burzynski JN, Lee YA, Berg D, Driver CR, et al. (2004) Use of therapeutic drug monitoring for multidrug-resistant tuberculosis patients. <i>Chest</i> 126: 1770–1776.
<i>Narita</i>	1993-1997	USA (Florida)	66	Narita M, Alonso P, Lizardo M, Hollender E, Pitchenik A, et al. (2001) Treatment experience of multidrug-resistant tuberculosis in Florida, 1994–1997. <i>Chest</i> 120: 343–348
<i>O’Riordan</i>	1982-2004	UK (London)	28	O’Riordan P, Schwab U, Logan S, Cooke G, Wilkinson RJ, et al. (2008) Rapid molecular detection of rifampicin resistance facilitates early diagnosis and treatment of multidrug-resistant tuberculosis: case control study. <i>PLoS One</i> 3: e3173. doi:10.1371/journal.pone.0003173
<i>Palmero</i>	1996-1999	Argentina (Buenos Aires)	112	Palmero DJ, Ambroggi M, Brea A, De Lucas M, Fulgenzi A, et al. (2004) Treatment and follow-up of HIV-negative multidrug-resistant tuberculosis patients in an infectious diseases reference

				hospital, Buenos Aires, Argentina. Int J Tuberc Lung Dis 8: 778–784
<i>Park</i>	1998-2002	South Korea (Masan)	131	Park SK, Lee WC, Lee DH, Mitnick CD, Han L, et al. (2004) Self-administered, standardized regimens for multidrug-resistant tuberculosis in South Korea. Int J Tuberc Lung Dis 8: 361–368
<i>Perez-Guzman</i>	1994-1995	Mexico	33	Pe´rez-Guzma´n C, Vargas MH, Martinez-Rossier LA, Torres-Cruz A, Villarreal-Velarde H (2002) Results of a 12-month regimen for drug-resistant pulmonary tuberculosis. Int J Tuberc Lung Dis 6: 1102–1109
<i>Quy</i>	1998-2000	Vietnam (Ho Chi Minh City)	157	Quy HT, Cobelens FGJ, Lan NTN, Buu TN, Lambregts CSB, et al. (2006) Treatment outcomes by drug resistance and HIV status among tuberculosis patients in Ho Chi Minh City, Vietnam. Int J Tuberc Lung Dis 10: 45–51.
<i>Schaaf</i>	1998-2002	South Africa (Western Cape, Capetown Metropole, West Coast)	36	Schaaf HS, Shean K, Donald PR (2003) Culture confirmed multidrug resistant tuberculosis: diagnostic delay, clinical features, and outcome. Arch Dis Child 88:1106–1111
<i>Shin</i>	2000-2004	Russian Federation (Tomsk)	535	Shin SS, Pasechnikov AD, Gelmanova IY, Peremitin GG, Strelis AK, et al. (2006) Treatment outcomes in an integrated civilian and prison MDR-TB treatment program in Russia. Int J Tuberc Lung Dis 10: 402–408
<i>Shiraishi</i>	2000-2007	Japan (Tokyo)	61	Shiraishi Y, Nakalima Y, Katsuragi N, Kurai M, Takahashi N (2004) Resectional surgery combined with chemotherapy remains the treatment of choice for multidrug-resistant tuberculosis. J Thorac Cardiovasc Surg 128: 523–528.
<i>Tupasi</i>	1999-2003	Philippines	159	Tupasi TE, Quelapio MID, Orillaza RB, Alcantara C, Mira NRC, et al. (2003) DOTS-Plus for multidrug-resistant tuberculosis in the Philippines: global assistance urgently needed. Tuberculosis 83: 52–58. Tupasi TE, Gupta R, Quelapio MID, Orillaza RB, Mira NR, et al. (2006) Feasibility and cost-effectiveness of treating multidrug

				resistant tuberculosis: a cohort study in the Philippines. PLoS Med 3: e352. doi:10.1371/journal.pmed.0030352
<i>Uffredi</i>	1998-1999	France (Paris)	41	Uffredi ML, Truffot-Pernot C, Dautzenberg B, Renard M, Jarlier V, et al. (2007) An intervention programme for the management of multidrug-resistant tuberculosis in France. Intl J Antimicrob Agents 29: 434–439.
<i>Yew</i>	1990-1997	Hong Kong	99	Yew WW, Chan CK, Leung CC, Chau CH, Tam CM, et al. (2003) Comparative roles of levofloxacin and ofloxacin in the treatment of multidrug resistant tuberculosis. Chest 124: 1476–1481. Yew WW, Chan CK, Chau CH, Tam CM, Leung CC, et al. (2000) Outcomes of patients with multidrug-resistant pulmonary tuberculosis treated with ofloxacin/levofloxacin-containing regimens. Chest 117: 744–751

Individual studies excluded from our analysis

First Author	Years of Study Cohort	Location	Total number of subjects with MDR-TB	Reference
<i>Holtz</i>	2000-2004	South Africa (All centres)	2174	Holtz TH, Lancaster J, Laserson KF, Wells CD, Thorpe L, et al. (2006) Risk factors associated with default from multidrug-resistant tuberculosis treatment, South Africa, 1999–2001. Int J Tuberc Lung Dis 10: 649–655
<i>Migliori</i>	2001-2004	Italy	82	Migliori GB, Espinal M, Danilova ID, Punga VV, Grzemska M, et al. (2002) Frequency of recurrence among MDR-TB cases ‘successfully’ treated with standardised short-course chemotherapy. Int J Tuberc Lung Dis 6: 858–864. Migliori GB, Besozzi G, Girardi E, Kliiman K, Lange C, et al. (2007) Clinical and operational value of the extensively drug-resistant tuberculosis definition. Eur Respir J 30: 623–626.

<i>Van Deun</i>	1997-2010	Bangladesh	607	Van Deun A, Salim MAH, Das APK, Bastian I, Portaels F (2004) Results of a standardised regimen for multidrug-resistant tuberculosis in Bangladesh. <i>Int J Tuberc Lung Dis</i> 8: 560–567. Van Deun A, Maug AKJ, Salim MAH, Das PK, Sarker MR, et al. (2010) Short, highly effective and inexpensive standardized treatment of multidrug-resistant tuberculosis. <i>Am J Respir Crit Care Med</i> 182: 684–692.
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