Appendix Table A1: Outcome definitions from cohort studies of shorter regimens

No	Study, Ref	Cure	Treatment Completed	Treatment Failure	Lost to follow-up (default)	Relapse
1	Van Deun Aung	Completed treatment without evidence of failure clinically and bacteriologically (negative ≥ 3 occasions over 5 months, and 1 of those taken at the end of treatment) ¹	Full course of treatment completed but incomplete documentation by sputum smears according to the criteria of cure.	•Treatment stopped at ≥6 months due to lack of response, or •Patients reverting to active TB without interruption of treatment with bacteriological evidence, or •Treatment definitively stopped for ≥2 drugs because of side-effects	Interruption of treatment for at least 2 months.	Recurrence clinically and bacteriological positive, and/ confirmed by positive culture on at at least two sputum specimens after cure or treatment completion, unless shown by fingerprinting to represent a different strain from baseline
2	Uzbekistan	 Completed treatment according to programme protocol ≥4 negative cultures from samples collected at least 30 days apart within the final 5 months of treatment 1 positive culture permitted if followed by ≥3 consecutive negative cultures taken at least 30 days apart in the final 3 months of treatment 	An MDR TB patient who has completed treatment according to programme protocol but does not meet the definition for cure because of lack of bacteriological results (i.e. fewer than five cultures were performed in the final months of treatment) or otherwise, completion of treatment with documented bacteriological conversion persisting through the end of treatment, but fewer than five negative cultures.	 No negative culture by the end of month 5 of a prolonged intensive phase, 2 cultures positive during the continuation phase or 1 culture positive during the last 3 months of treatment, Early treatment termination because of poor response or adverse events 	An MDR TB patient who dies for any reason during the course of MDR TB treatment and is not already classified as a treatment failure prior to death.	An MDR TB patient who meets the criteria of cured or completed short course of treatment and at any time during the follow up period (first year after treatment completion) is subsequently diagnosed with at least one sample of bacteriologically positive TB by culture
3	Swaziland	 Completed treatment according to programme protocol ≥5 consecutive negative cultures from samples collected at least 30 days apart 1 positive culture permitted if followed by ≥3 consecutive negative cultures taken at least 30 days apart 	An MDR TB patient who has completed treatment according to programme protocol but does not meet the definition for cure because of lack of bacteriological results (i.e. fewer than five cultures were performed in the final months of treatment) or otherwise, completion of treatment with documented bacteriological conversion persisting through the end of treatment, but fewer than five negative cultures. Treatment completion will only be an outcome for patients that are not able to produce sputum; in case of patients where the lack of bacteriological results is due to other reasons the outcome will be registered as "other" in order to avoid misclassification.	 No negative culture by the end of month 6 of a prolonged intensive phase, Culture positive during the continuation phase: 2 cultures positive (continuation phase) or 1 culture positive (last 3 months), Early treatment termination because of poor response or adverse events 	An MDR TB patient whose treatment was interrupted for two or more consecutive months for any reason without medical approval and not meeting the criteria for failure.	Relapse: An MDR TB patient who meets the criteria of cured or completed short course of treatment and at any time during the follow up period (first year after treatment completion) is subsequently diagnosed with at least one sample of bacteriologically positive MDR TB by culture and DST of the same strain found in initial diagnosis, proven by molecular techniques (Mycobacterium tuberculosis DNA fingerprinting). Re-infection: recurrent disease as defined for a relapse, with a strain showing a molecular pattern different from the initial isolate.
4	Kuaban	 Completed treatment according to the programme's protocol and has ≥5 consecutive negative cultures, each at least 30 days apart 1 positive culture permitted if followed by ≥3 consecutive negative cultures taken at least 30 days apart 	An MDR-TB patient who has completed treatment according to country protocol but does not meet the definition for cure or treatment failure due to lack of bacteriological results (i.e. fewer than five cultures were performed in the final 8 months of therapy).	•Regimen change •Lack of bacteriological response and lack of clinical improvement at 6 months of treatment, or •Bacteriological reversion with concomitant clinical deterioration after initial response occurring after at least 6 months of treatment, or •Adverse drug events	An MDR patient whose treatment was interrupted for two or more consecutive months for any reason without medical approval.	Patient having been declared "cured" or "treatment completed" presenting with a new episode of TB disease (whatever form of TB also instructions where given to declare "relapse" preferentially in bacteriologically confirmed cases)
5	Piubello	•Completed treatment	Treatment completed with	• $\geq 2/5$ cultures	A patient whose	Patient having been declared

¹ Exclude: positive cultures representing different strain from baseline

		and ≥5 consecutive negative cultures collected at least 30 days apart during the last 8 months of treatment, or •1 positive culture without concurrent clinical deterioration, followed by ≥4 consecutive negative cultures (2008-2013) •Treatment completed as recommended by the national policy without evidence of failure, and ≥3 consecutive cultures taken at least 30 days apart are negative after the intensive phase (2014- 2016)	documented bacteriological conversion but not meeting the definition for cure (2008-2013). Treatment completed as recommended by the national policy without evidence of failure BUT no record that three or more consecutive cultures taken at least 30 days apart are negative after the intensive phase (2014-2016).	positive in the final 8 months of treatment, or • 1 of the final 3 cultures positive, or • Treatment stopped definitively due to adverse drug reactions, terminated or permanent regimen change	treatment was interrupted for 2 consecutive months or more	cured or treatment completed with a positive culture during the 24 months follow-up after cure except if molecular tests prove an infection with a different strain from the initial (2008- 2014). Patient having been declared cured or treatment completed with a positive culture during the 12 months follow-up after cure except if molecular tests prove an infection with a different strain from the initial (2015- 2016).
6	Trebucq	•Completed treatment without evidence of failure and ≥3 consecutive negative cultures taken at least 30 days apart	Same as latest WHO definition	• Positive culture after 6 months of treatment (except when preceded by 1 negative and followed by at least 2 negative cultures)	Same as latest WHO definition	Same as latest WHO definition
7	Tajikistan	•Completed treatment as recommended by the national policy without evidence of failure, and •≥3 consecutive negative cultures taken at least 30 days apart after the intensive phase	Treatment completed as recommended by the national policy without evidence of failure BUT no record that 3 or more consecutive cultures taken at least 30 days apart, are negative after the intensive phase.	 Treatment terminated or need for permanent regimen change of ≥2 anti-TB drugs because of: Lack of conversion by the end of intensive phase, or Bacteriological (i.e. culture) reversion in the continuation phase after the conversion to negative, or Evidence of additional acquired resistance to FQ or SL, or Adverse drug reactions 	A patient whose treatment was interrupted for two consecutive months or more.	A DR-TB patient who meets the criteria of cured or completed short course of treatment and at any time within the first year after treatment completion is subsequently diagnosed with at least one sample of bacteriologically positive DR- TB by culture and DST.
8	Kyrgyzstan	 Completed treatment as recommended by the national policy without evidence of failure, and ≥ 3 consecutive negative cultures taken at least 30 days apart after the intensive phase 	Treatment completed as recommended by the national policy without evidence of failure BUT no record that three or more consecutive cultures taken at least 30 days apart are negative after the intensive phase.	Treatment terminated or permanent regimen change of ≥2 anti- TB drugs because of: •Lack of conversion by the end of intensive phase, or •Bacteriological reversion in the continuation phase after conversion to negative, or •Evidence of additional acquired resistance to FQ or SL, or •Adverse drug reactions	A patient whose treatment was interrupted for 2 consecutive months or more (note: this is called lost to follow-up; "default" is not used)	Not defined
9	South Africa	•Completed treatment of ≥9 months •TB culture conversion • ≥3 consecutive	 A patient who has had TB culture conversion Received treatment for a total duration of 9 months or more 	 Patient failed to culture convert by month 4 In final 6 months of 	A patient with Treatment interrupted for: $a. \ge 2$	Not an outcome in the programme

negative TB cultures during continuation phase (at least 30 days apart) •No evidence of clinical deterioration	 Has less than 3 consecutive negative TB Cultures during continuation phase (30 days apart) No evidence of clinical deterioration 	treatment ≥ 2 of 5 cultures are positive, clinical condition deteriorating • Treatment stopped on clinical grounds • ≥ 2 new drugs added because of poor clinical response	consecutive months b. Any reason without medical approval	
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Shorter Regimen Database	Sampling method ^{\dagger}	Info on DST SLI	Info on DST FQN	Participation rate [¶]	Lost to follow-up rate	Outcome definitions ^ø	Info on Age	Info on HIV ^{††}	Info on TB Tx history	Quality
Bangladesh ^{1,2}	Census	93%	93%	100%	7%	Study specific	100%	Not applied	100%	High
Uzbekistan MSF ³	Census	78%	82%	100%	10%	Study specific /WHO 2013	100%	Not applied	100%	Moderate
Swaziland MSF ⁴	Census	53%	55%	100%	0%	Study specific /WHO 2013	100%	100%	23%	Moderate
Cameroon ⁵	Census	79%	79%	100%	2%	Study specific	100%	99%	98%	Moderate
Niger ⁶	Census	98%	97%	100%	2%	Study specific	100%	96%	100%	High
Union 9 country ⁷	Census	58%	59%	98%	5%	Study specific/ WHO 2013	100%	100%	100%	Moderate
*Tajikistan ⁸	Census	82%	82%	100%	6%	WHO 2013	100%	Not applied	6%	High
*Kyrgyzstan ⁹	Convenience	100%	100%	27%	0%	WHO 2013	100%	Not applied	100%	Moderate
*South Africa ¹⁰	Census	0%	0%	20%	12%	WHO 2013	100%	94%	100%	Moderate

Appendix Table A2. Quality assessment of included studies of (a) standardised shorter regimens, and (b) longer regimens. Table A2a.

For methodological details see: Ahmad N, Ahuja SD, Akkerman OW, Alffenaar JW, et al. "Treatment correlates of successful outcomes in pulmonary multidrugresistant tuberculosis: an individual patient data meta-analysis." Lancet 2018; 392 (10150): 821-34. 2018 Sep 1.

* Studies identified through WHO public call for data.

[†]*Census* if all patients treated with shorter regimens at centre or in study provided in database; *Convenience* if neither census or random sample & uncertain on representativeness of the sample of patients provided.

[¶]Participation rate is the number of patients on shorter regimen treatment provided in datasets by investigators divided by the total number of patients treated with the shorter regimen at their centre during the study period, expressed as a percentage.

"All studies received full point for Outcome definitions as they were judged similar to WHO 2013.

^{††}For HIV, quality judged adequate despite low rate of testing in Bangladesh, Uzbekistan, Tajikistan, and Kyrgyzstan, given low HIV prevalence settings.

Each quality criteria counts for 1 point, with the exception of % Lost where 2 points are given if $\leq 10\%$, 1 point if between 10% and 20%, and 0 points if > 20%. **High** = 2 points from critical criteria (Sampling method Census/Random; $\geq 80\%$ of patients with DST on either a fluoroquinolone or second-line injectable) + 5 points from other criteria; **Moderate** = 1 point from critical criteria (Sampling method Census/Random; $\geq 80\%$ of patients with DST on either a fluoroquinolone or second-line injectable) + 5 points from other criteria; or 2 from critical + 4 from other; **Low** = not meeting criteria for High or Moderate.

Appendix Table A2b.

Contact person	Sampling	Info on	Info on	Participation	Lost to	Outcome	Info on	Info on HIV	Info on	Quality
	method	DST-	DST-	rate	follow-	definition	age		TB Tx	
		SLI	FQN		up rate				history	
Ahuja ¹¹	Random	92.4%	92.4%	100%	19.0%	Laserson	100%	80.0%	100%	High
Anderson ¹²	Census	100%	100%	100%	12.4%	Neither	100%	100%	90.5%	High
12						Laserson/WHO				
*Fox ¹³	Census	93.1%	96.6%	100%	3.4%	WHO 2013	100%	100%	100%	High
Bang ¹⁴	Census	96.6%	93.1%	96.7%	17.2%	Laserson	100%	100%	100%	High
Barry/Flood (Calif) ¹⁵	Unclear	98.4%	95.2%	100%	4.8%	WHO 2013	98.4%	100%	100%	Moderate
Bonnet ¹⁶	Census	93.3%	93.3%	100%	41.3%	Laserson	100%	11.5%	98.6%	High
*Rodrigues ¹⁷	Census	87%	85%	100%	10%	Laserson	100%	98%	100%	High
Brode ¹⁸	Census	100%	100%	100%	0.0%	Laserson	100%	100%	100%	High
Cegielski ^{19,20}	Census	92.8%	92.2%	60.1%	19.8%	Laserson	100%	68.3%	98.2%	High
Chan ²¹	Census	100%	100%	100%	26.7%	Laserson	100%	80.0%	100%	High
*endTB ²²	Census	95.2%	95.2%	100%	17.5%	Laserson/WHO	100%	100%	100%	High
Guglielmetti ^{23,24}	Census	100%	100%	100%	11.1%	WHO 2013	100%	100%	100%	High
Isaakidis ^{25,26}	Census	96.7%	95.4%	100%	11.8%	Laserson	100%	100%	98.0%	High
Jarlsberg ²⁷	Census	96.4%	96.4%	100%	3.6%	Laserson	100%	92.9%	100.%	High
Kempker ²⁸	Census	100%	100%	94.9%	32.7%	Laserson	100%	94.7%	100%	High
Koenig ²⁹	Census	96.3%	93.3%	100%	6.1%	Laserson	99.4%	100%	100%	High
Koh ^{30,31}	Census	100%	100%	100%	13.4%	WHO 2013	100%	100%	100%	High
Lange ³²	Census	94.0%	96.7%	100%	20.1%	Laserson	100%	99.5%	98.4%	High
Laniado-Laborin ³³	Census	100%	100%	100%	13.5%	Laserson	100%	100%	100%	High
*Kuksa ³⁴	Census	100%	100%	100%	15%	Laserson	100%	100%	100%	High
*Barkane ³⁵	Census	100%	100%	100%	15.6%	Laserson	100%	100%	100%	High
Leung ^{36,37}	Census	100%	100%	100%	19.9%	Laserson	100%	100%	100%	High
Marks ³⁸	Random	92.3%	91.5%	100%	12.3%	Neither	100%	85.4%	100%	High
						Laserson/WHO				
Migliori ^{39,40}	Census	96.6%	96.6%	Unclear	10.9%	WHO 2013	100%	98.1%	99.3%	High
Migliori ⁴¹	Census	97.0%	100%	Unclear	3.7%	WHO 2013	100%	99.3%	100%	High
Milanov ⁴²	Census	94.0%	94.0%	100%	2.0%	Laserson	100%	100%	100%	High
*Ndjeka ⁴³	Census	100%	100%	100%	18.5%	Laserson/WHO	100%	100%	100%	High
Ndjeka ⁴⁴	Unclear	78.2%	81.2%	Unclear	21.1%	Laserson	100%	95.5%	0.0%	Low
Podewils ⁴⁵	Census	91.0%	91.2%	100%	15.2%	Laserson	100%	55.6%	100%	High
Riekstina/Leimane ⁴⁶	Census	100%	100%	100%	14.7%	Laserson	100%	94.0%	100%	High
*Seo 47	Census	100%	100%	100%	16%	Laserson	100%	100%	100%	High
Shim ^{31,48}	Census	100%	100%	86.4%	8.2%	WHO 2013	100%	40%	100%	High
Smith ⁴⁹	Census	100%	100%	100%	21.5%	Laserson	100%	100%	98.5%	High
TMC207-C208 ^{50,51}	RCT	84.8%	84.8%	82.5%	28.8%	Laserson	100%	100%	100%	High
TMC207-C20952	Census	76.1%	76.1%	93.1%	15.2%	Laserson	100%	96.5%	100%	Moderate
van der Werf53	Census	100%	98.2%	100%	13.4%	Laserson	100%	92.0%	96.4%	High
*Vasilyeva 54	Census	94.4%	94.4%	100%	16%	WHO 2013	100%	100%	100%	High
*Viiklepp ⁵⁵	Census	100%	100%	100%	11.7%	Laserson	100.%	99.7%	100%	High
Yim/Kwak ⁵⁶	Census	100%	100%	100%	4.9%	WHO 2013	100%	100%	100%	High

For methodological details see: Ahmad N, Ahuja SD, Akkerman OW, Alffenaar JW, et al. "Treatment correlates of successful outcomes in pulmonary multidrug-resistant tuberculosis: an individual patient data meta-analysis." Lancet 2018; 392 (10150): 821-34. 2018 Sep 1.

* Studies identified through WHO public call for data.

Appendix Table A3: Associations between drug-susceptibility test results for pyrazinamide (Pza), ethambutol (Emb), and pro/ethionamide (Pto/Eto)

	Emb-R	Emb-S	Total				
Pza-R	459 (74% of Pza-R) (54% of Emb-R)	159 (26% of Pza-R) (32% of Emb-S)	618				
Pza-S	397 (54% of Pza-S) (46% of Emb-R)	344 (46% of Pza-S) (68% of Emb-S)	741				
Total 856		503	Fisher's p-value for table <.001				

Table A3a: Pyrazinamide and ethambutol resistance (R) & susceptibility (S)

Table A3b: Pyrazinamide and pro/ethionamide susceptibility

	Pto/Eto-R	Pto/Eto -S	Total
Pza-R	127 (24% of Pza-R) (51% of Pto/Eto-R)	401 (76% of Pza-R) (43% of Pto/Eto -S)	528
Pza-S	124 (19% of Pza-S) (49% of Pto/Eto -R)	520 (81% of Pza-S) (57% of Pto/Eto -S)	644
Total	251	621	Fisher's p-value for table $= 05$

Table A3c: Ethambutol and pro/ethionamide susceptibility

	Pto/Eto -R	Pto/Eto -S	Total
Emb-R	270 (22% of Emb-R) (68% of Pto/Eto-R)	981 (78% of Emb-R) (63% of Pto/Eto-S)	1251
Emb-S	125 (18% of Emb-S) (32% of Pto/Eto-R)	586 (82% of Emb-R) (37% of Pto/Eto-S)	711
Total	395	1567	Fisher's p-value for table = $\cdot 04$

Table A3d: Correlation between pyrazinamide, ethambutol, and pro/ethionamide resistance in patients tested for all 3

	Emb-R	Pto/Eto -R
Pza-R	ρ = 0·22 p-value <·0001	$\rho = 0.07$ p-value= 0.02
Emb-R		$\rho = 0.04$ p-value=0.16

Appendix Figure A2. Proportion of Failure/Relapse vs. Success, comparing shorter & longer MDR-TB regimens



B) Longer

Study	Events	Total P	roportion	95%–Cl
Δhuia [11]	0	16	0.00	[0 00.0 21]
Anderson [12]	2	16	0.00	[0.00, 0.21]
Fox [13]	0	13	0.00	[0.02, 0.00]
Bang [14]	0	2	0.00	[0.00, 0.20]
Barry [15]	2	28	0.00	[0.00, 0.04]
Diacon [50 51]	1	1	1 00	[0.03, 1.00]
Skrahina [47]	0	1	0.00	[0.00: 0.98]
Bonnet [16]	3	19	0.16	[0.03: 0.40]
Rodrigues[17]	0	7	0.00	[0.00: 0.41]
Brode [18]	0	13	0.00	[0.00: 0.25]
Cegielski [19.20]	9	129	0.07	[0.03: 0.13]
Chan [21]	0	2	0.00	[0.00; 0.84]
endTB [22]	0	5	0.00	[0.00; 0.52]
Guglielmetti [23,24]	0	6	0.00	[0.00; 0.46]
Isaakidis [25,26]	1	11	0.09	[0.00; 0.41]
Pym [52]	0	9	0.00	[0.00; 0.34]
Jarlsberg [27]	0	10	0.00	[0.00; 0.31]
Kempker [28]	3	53 +	0.06	[0.01; 0.16]
Koenig [29]	1	109 +-	0.01	[0.00; 0.05]
Koh [30,31]	0	59 🛏	0.00	[0.00; 0.06]
Lange [32]	0	17	0.00	[0.00; 0.20]
Laniado–Laborin [33]	1	21 🕂	0.05	[0.00; 0.24]
Kuksa [34]	0	7	0.00	[0.00; 0.41]
Chang [36,37]	2	26	0.08	[0.01; 0.25]
Marks [38]	1	37 🕂 —	0.03	[0.00; 0.14]
Tiberi [39,40]	0	43	0.00	[0.00; 0.08]
Borisov [41]	0	8	0.00	[0.00; 0.37]
Milanov [42]	0	21	0.00	[0.00; 0.16]
Ndjeka [44]	0	7	0.00	[0.00; 0.41]
Podewils [45]	2	61 +	0.03	[0.00; 0.11]
Riekstina [46]	0	38	0.00	[0.00; 0.09]
Vasilyeva [54]	2	9	0.22	[0.03; 0.60]
Shim [31,48]	0	2	0.00	[0.00; 0.84]
Smith [49]	4	10	0.40	[0.12; 0.74]
Ndjeka [43]	73	1014 +	0.07	[0.06; 0.09]
van der Werf [53]	0	29	0.00	[0.00; 0.12]
Viiklepp [55]	2	43	0.05	[0.01; 0.16]
Yim [56]	3	24	0.12	[0.03; 0.32]
		1000		
Handom effects model	2 112	1926 ♦	0.03	[0.02; 0.06]
Heterogeneity: $I^{-} = 64\%$, τ	~ = 0.9675	, <i>p</i> = 0.29		
		Proportion Failure/Relapse vs. Succes	S	

Appendix Figure A3. Proportion of Death vs. Success, comparing shorter & longer MDR-TB regimens <u>A) Shorter</u>

Study	Events	Total	Proportion 95%–Cl
Aung, Van Deun (1)	60	877 +	0.07 [0.05; 0.09]
Casas (3)	11	91	0.12 [0.06; 0.21]
DuCros (2)	2	83 +	0.02 [0.00; 0.08]
Kadyrov (8)	0	13	0.00 [0.00; 0.25]
Kuaban (4)	33	346 🕂	0.10 [0.07; 0.13]
Makmudova (7)	0	12	0.00 [0.00; 0.26]
Ndjeka (9)	14	35	0.40 [0.24; 0.58]
Piubello (5)	16	158 🕂	0.10 [0.06; 0.16]
Trebucq (6)	65	750	0.09 [0.07; 0.11]
Random effects model Heterogeneity: $I^2 = 91\%$, τ^2	201 ² = 0.5873	2365 ↔ 3, <i>p</i> < 0.01	0.09 [0.05; 0.15]
		0 0.2 0.4 0.6 0	.8 1



Study	Events Tota	al	Proportion	95%–Cl
Ahuja [11]	1 1	17	0.06	[0.00; 0.29]
Anderson [12]	0 1		0.00	[0.00; 0.23]
Fox [13]	0 1	13	0.00	[0.00; 0.25]
Bang [14]	0	2	0.00	[0.00; 0.84]
Barry [15]	1 2	27	0.04	[0.00; 0.19]
Skrahina [47]	0	1	0.00	[0.00; 0.98]
Bonnet [16]	6 2	22+	0.27	[0.11; 0.50]
Rodrigues[17]	1	8	0.12	[0.00; 0.53]
Brode [18]	1 1	4	0.07	[0.00; 0.34]
Cegielski [19,20]	4 12	24 +	0.03	[0.01; 0.08]
Chan [21]	0	2	0.00	[0.00; 0.84]
endTB [22]	0	5	0.00	[0.00; 0.52]
Guglielmetti [23,24]	0	6	0.00	[0.00; 0.46]
lsaakidis [25,26]	4 1	4	0.29	[0.08; 0.58]
Pym [52]	1 1	10	0.10	[0.00; 0.45]
Jarlsberg [27]	0 1	10	0.00	[0.00; 0.31]
Kempker [28]	35	53	0.06	[0.01; 0.16]
Koenig [29]	14 12	22	0.11	[0.06; 0.19]
Koh [30,31]	05	59	0.00	[0.00; 0.06]
Lange [32]	32	20 + +	0.15	[0.03; 0.38]
Laniado–Laborin [33]	0 2	20	0.00	[0.00; 0.17]
Kuksa [34]	0	7	0.00	[0.00; 0.41]
Chang [36,37]	1 2	25 +	0.04	[0.00; 0.20]
Marks [38]	23	38	0.05	[0.01; 0.18]
Tiberi [39,40]	1 4	14 +	0.02	[0.00; 0.12]
Borisov [41]	0	8	0.00	[0.00; 0.37]
Milanov [42]	7 2	28	0.25	[0.11; 0.45]
Ndjeka [44]	4 1	I1 :	0.36	[0.11; 0.69]
Podewils [45]	66	35 <u>-</u>	0.09	[0.03; 0.19]
Riekstina [46]	34	11 	0.07	[0.02; 0.20]
Vasilyeva [54]	0	7	0.00	[0.00; 0.41]
Shim [31,48]	0	2	0.00	[0.00; 0.84]
Smith [49]	0	6	0.00	[0.00; 0.46]
Ndjeka [43]	199 114	10 +	0.17	[0.15; 0.20]
van der Werf [53]	23	31	0.06	[0.01; 0.21]
Viiklepp [55]	1 4	12 +	0.02	[0.00; 0.13]
Yim [56]	0 2	21	0.00	[0.00; 0.16]
Random effects model Heterogeneity: $I^2 = 72\%$, τ	265 207 ² = 0.8528, <i>p</i> <	79 < 0.01	0.06	[0.04; 0.09]
		U U.2 U.4 U.6 U.8 1 Proportion Death vs Success		
		Toportion Death vs. Success		

Appendix Figure A4. Proportion of Lost vs. Success, Failure, or Relapse comparing shorter & longer MDR-**TB** regimens

A) Shorter



Study Ahuja [11] Anderson [12] Fox [13] Bang [14] Barry [15] Diacon [50,51] Skrahina [47] Bonnet [16] Rodrigues[17] Brode [18] Cegielski [19,20] Chan [21] endTB [22] Guglielmetti [23,24] Isaakidis [25,26] Pym [52] Jarlsberg [27] Kempker [28] Koenig [29] Koh [30,31] Lange [32] Laniado-Laborin [33] Kuksa [34] Burkane [35] Chang [36,37] Marks [38] Tiberi [39,40] Borisov [41] Milanov [42] Ndjeka [44] Podewils [45] Riekstina [46] Vasilyeva [54] Shim [31,48] Smith [49] Ndjeka [43] van der Werf [53] Viiklepp [55] Yim [56]



0.20 [0.06; 0.44] 0.16 [0.03: 0.40] 0.07 [0.00; 0.34] 0.00 [0.00: 0.84] 0.03 [0.00; 0.18] 0.50 [0.01; 0.99] 0.00 [0.00; 0.98] 0.58 [0.42; 0.72] 0.22 [0.03; 0.60] 0.07 [0.00; 0.34] 0.20 [0.14; 0.27] 0.33 [0.01; 0.91] 0.00 [0.00; 0.52] 0.25 [0.03: 0.65] 0.08 [0.00; 0.38] 0.18 [0.02; 0.52] 0.17 [0.02; 0.48] 0.29 [0.19; 0.41] 0.08 [0.04; 0.14] 0.03 [0.00; 0.11] 0.00 [0.00; 0.20] 0.22 [0.09; 0.42] 0.36 [0.11; 0.69] 1.00 [0.03; 1.00] 0.37 [0.22; 0.53] 0.18 [0.08; 0.32] 0.16 [0.07; 0.29] [0.00; 0.37] 0.00 0.05 [0.00; 0.23] 0.42 [0.15; 0.72] 0.19 [0.11; 0.29] [0.10; 0.35] 0.21 0.10 [0.00; 0.45] 0.00 [0.00; 0.84] 0.09 [0.00; 0.41] 0.24 [0.22; 0.27] 0.06 [0.01; 0.21] 0.16 [0.07; 0.29] 0.08 [0.01; 0.25]



0.2 0.4 0.6 0.8 1 Proportion Lost vs. Success

0

Appendix Table A4: Odds ratios for associations of covariates with outcomes, using univariable individual patient-data meta-regression

Covariates	Odds ratio (95%CI)				
	Fail/relapse vs Success	Death vs Success	Loss to follow-up vs Success, Failure, Relapse		
Age (per 1 year older)	1.0 (0.99-1.01)	1.04 (1.03-1.05)	1.0 (0.99-1.01)		
Sex (reference: female)	1.0(0.7-1.3)	1.0(0.8-1.2)	1.5 (1.3-1.8)		
PLWH (reference: HIV negative people)	1.1 (0.8-1.6)	2·8 (2·1-3·6)	1.0 (0.8-1.3)		
Extensive disease (reference: not extensive)	1.4 (0.98-2)	1.1 (0.9-1.4)	1.1 (0.9-1.3)		
Prior treatment with first-line drugs (reference: no prior treatment)	1.0 (0.8-1.4)	1·3 (1·0-1·6)	1.3 (1.04-1.5)		
Pyrazinamide resistance (reference: sensitive to pyrazinamide)	1.6 (0.96-2.7)	$1.4 (0.9 - 2.1)^{\text{F}}$	0.6 (0.4-0.9)		
Prothionamide [*] resistance (reference: sensitive to prothionamide [*])	1.4 (0.7-2.7)	0.8 (0.5-1.3)	1.0(0.7-1.5)		
Ethambutol resistance (reference: sensitive to ethambutol)	2.9 (1.6-5.3)	1.2 (0.9-1.7)	0.8 (0.6-1.1)		

Confidence intervals suggestive of increased odds or risk of failure or relapse are in **bold** red font.

Confidence intervals suggestive of lower odds or risk of failure or relapse are in bold black font.

Data are unadjusted odds ratios (95% CI) from random-effects meta-regression. PLWH: people living with HIV infection.

F: fixed effects model used as random-effects model did not converge.

^{*}Or ethionamide.

Appendix Table A5: Comparison of shorter regimens to longer regimens amongst patients with rifampin or multidrug-resistant tuberculosis confirmed susceptible to fluoroquinolones and additionally resistant to at least two of: pyrazinamide, ethambutol, or prothionamide/ethionamide, using individual patient-data meta-analysis

	Studies Shorter, Longer	Shorter Events/ Total	Longer Events/ Total	Propensity score matched multivariable meta-regression		
				N Pairs	aOR (95%CI)	aRD (95% CI)
Fail/relapse vs Success	7, 27	31/244	13/324	244	5.2 (1.5, 17.6) ^F	0.10 (0.05, 0.15)
Death during first 12 months of treatment vs Success	6, 24	14/227	27/338	227	0.4 (0.1, 1.9)	-0.03 (-0.09, 0.03)
Lost vs Success, Fail/relapse	7, 24	13/257	53/377	257	0.2 (0.0, 1.8)	-0.08 (-0.14, -0.02)

All models adjust for age, sex, HIV status, previous treatment with first-line tuberculosis medications, and extensiveness of disease. Results were adjusted as described in the Methods. aOR: adjusted odds ratio; aRD: adjusted risk difference.

F: fixed effects model used as random-effects model did not converge.

Appendix Table A6: Characteristics of patients included in the comparison of moxifloxacin- or levofloxacinbased shorter regimens with longer regimens composed per 2018 World Health Organization guidelines including either bedaquiline or linezolid

	Shorter, n=1004	Longer, n=162
Baseline characteristics	1004	162
Mean Age (standard deviation)	35.5 (12.8)	39.2 (13.2)
Male Sex	594 (59·2%)	96 (59.3%)
People living with HIV	204 (20.4%)	93 (57.4%)
Antiretroviral treatment	175 (90.2%)	93 (100%)
Extensive disease	834 (83.1%)	131 (80.9%)
Previous Treatment with First Line Drugs	780 (82.5%)	73 (45.9%)
High Income Country	0 (0%)	12 (7.4%)
Upper Middle Income Country	41 (4.1%)	149 (92%)
Low Middle or Low Income Country	963 (95.9%)	1 (0.6%)
Pyrazinamide-resistant tuberculosis	226 (59%)	17 (77.3%)
Ethambutol-resistant tuberculosis	224 (67.3%)	18 (78.3%)
Ethionamide/Prothionamide-resistant tuberculosis	156 (50.2%)	13 (61.9%)
Total number of drugs in regimen, median (IQR)	7	7 (6-8)*
WHO 2018 Group A Drugs in regimen		
Moxifloxacin or levofloxacin	1004 (100%)	162 (100%)
Bedaquiline	0	151(93.2%)
Linezolid	0	144(88.9%)
WHO 2018 Group B Drugs in regimen		
Cycloserine	0	16(9.9%)
Clofazimine	1004 (100%)	122(75.3%)

Restricted to patients with tuberculosis confirmed susceptible to fluoroquinolones.

*This is the number of drugs given for > 1 month, not all of which may have been given concomitantly.

Appendix Table A7A. Sensitivity Analysis: Comparison of shorter regimens to longer regimens amongst patients with rifampin-resistant and isoniazid-susceptible tuberculosis, rifampin-resistant tuberculosis with unmeasured DST for isoniazid, or multidrug-resistant tuberculosis, using individual patient-data meta-analysis

	Studies	Shorter Longer		Propensity score matched multivariable meta-regression		
	Longer	Longer Total	Total	N Pairs	aOR (95%CI)	aRD (95% CI)
(A) Including patients with INH-susceptible, RR-TB						
Fail/relapse vs Success	9, 38	123/2478	115/1953	1953	1.5 (0.8, 3.0)	0.02 (-0.01, 0.04)
Death vs Success	9, 37	225/2580	268/2106	2106	1.2 (0.96, 1.5)	0.02 (-0.01, 0.05)
Lost vs Success, Fail/relapse	9, 39	149/2627	533/2486	2486	0.2(0.2, 0.3)	-0.15 (-0.17, -0.13)

All models adjust for age, sex, HIV status, previous treatment with first-line tuberculosis medications, and extensiveness of disease. Results were adjusted as described in the Methods. aOR: adjusted odds ratio; aRD: adjusted risk difference.

Appendix Table A7B. Sensitivity Analysis: Comparison of shorter regimens to longer regimens amongst patients with rifampin- or multidrug-resistant
tuberculosis confirmed resistant to fluoroquinolones, using individual patient-data meta-analysis

	Studies Shorter Longer Shorter Evented		Longer Events/	Propensity score matched multivariable meta-regression			
	Longer Total	Total	N Pairs	aOR (95%CI)	aRD (95% CI)		
(B) Fluoroquinolone-resistant							
Fail/relapse vs Success	4, 15	39/103	10/130	103	15.0 (2.8, 80.6)	0.33 (0.22, 0.44)	
Death vs Success	4, 16	8/72	14/134	72	2.1 (0.3, 17.0)	0.04 (-0.08, 0.15)	
Lost vs Success, Fail/relapse	4, 17	8/111	37/167	111	0.3(0.1, 1.4)	-0.11 (-0.25, 0.03)	

All models adjust for age, sex, HIV status, previous treatment with first-line tuberculosis medications, and extensiveness of disease. Results were adjusted as described in the Methods. aOR: adjusted odds ratio; aRD: adjusted risk difference.

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