

Supplemental Tables

Table S1a. Characteristics of the 23 studies included in current analysis

First author	Bang 2010 ¹	Brazilian NTP ²	Cattamanchi 2009 ³	Chien 2015 ⁴	Cox 2006 ⁵	Gegia 2012 ⁶	Huyen 2013 ⁷	Jacobson 2011 ⁸
Country	Denmark	Brazil	US (California)	Taiwan	Uzbekistan	Georgia	Vietnam	South Africa
Years of study	2002-07	2012-14	1992-2005	2004-12	2001-02	2007-09	2005-07	2001-09
Concentration used to define H resistance ($\mu\text{m/mL}$)	0.1	0.2	0.2	0.2	0.1	0.2	0.2	0.1
Regimen ^a	Indiv.	Stand.	Stand.	Indiv.	Stand.	Stand.	Stand.	Indiv.
Duration (known vs planned)	Known	Known	Known	Known	Known	Planned	Planned	Known
Age in years (median, IQR)	37 (27; 47)	41 (31; 52)	48 (30; 67)	63 (48; 76)	31 (25; 40)	35 (26; 48)	49 (39; 65)	40 (31; 46)
Sex female, %	35%	30%	38%	25%	30%	23%	25%	44%
HIV positive, % of tested ^b	27%	6%	7%	2%	0%	na	na	27%
Past TB treatment, % ^b	13%	na	36%	12%	53%	14%	16%	80%
Cavity on chest-x ray, % ^b	na	69%	21%	28%	na	na	na	na
Resistance to SM, % ^b	50%	4%	na	na	78%	69%	65%	0%
Total analyzable, N:	71	167	98	242	55	864	204	23
- Success, %	83%	67%	90%	86%	31%	70%	85%	65%
- Failure/relapse, %	4%	15%	1%	4%	49%	9%	9%	22%
- Deaths, %	3%	4%	1%	10%	5%	4%	5%	0
- Loss to follow-up, %	10%	14%	8%	0	15%	17%	1%	13%
N included in analysis:								
- Mortality	64	144	90	242	47	716	201	20
- Success	61	107	55	133	23	686	32	6
- Acquired R resistance	--	--	--	127	11	649	--	6

Notes: a) Regimens were classified as “standardized” if standard regimen was given to all patients; “individualized” if regimens were tailored to individual patients’ characteristics such as prior therapy, or drug susceptibility testing (DST) results; “randomized” if standard regimens were given within a randomized clinical trial.

b) Percentages are of the total for who the information was available. In some sites this information was available for less than 50% of the population

Abbreviations: **H** isoniazid; **Individ.** Individualized; **IQR** Interquartile range; **na:** information in not available for that database or if it is available in less than 10% of the population; **R:** rifampin; **Random.** Randomized; **SM** streptomycin; **Stand.** Standardized.

Table S1a -continued. Characteristics of the 23 studies included in current analysis

First author	Jones-Lopez 2011 ⁹	Kim 2008 ¹⁰	Lee 2016 ¹¹	Munang 2015 ¹²	Netherlands NTP ¹³	New York city ¹⁴	Ohkado 2006 ¹⁵	Park 2016 ¹⁶
Country	Uganda	Korea	Korea	UK	Netherlands	US	Philippines	Korea
Years	2005	2001-05	2005-12	1999-2010	1993-2015	1994-2014	2000	2005-13
Concentration used to define H resistance ($\mu\text{m/mL}$)	0.1	0.2	0.2	0.1	0.2	0.1; 0.2	0.2	0.2
Regimen ^a	Stand.	Stand.	Stand.	Indiv.	Indiv.	Indiv.	Stand.	Indiv.
Duration (known vs planned)	Planned	Planned	Known	Known	Known	Known	Known	Known
Age in years (median, IQR)	na	43 (31; 61)	54 (38; 67)	30 (25; 38)	30 (23; 40)	41 (30; 54)	43 (26; 57)	59 (49; 73)
Sex female, %	na	33%	34%	50%	42%	36%	30%	31%
HIV positive, % on tested ^b	44%	0%	0%	5%	na	24%	na	0%
Past TB treatment, % ^b	100%	36%	30%	na	7%	3%	3%	50%
Cavity on chest-x ray, % ^b	na	41%	24%	15%	na	25%	na	31%
Resistance to SM, % ^b	na	13%	14%	na	na	36%	40%	13%
Total analyzable, N:	34	39	115	41	509	824	33	6
- Success, %	68%	92%	90%	83%	87%	88%	82%	100%
- Failure/relapse, %	9%	8%	10%	5%	0	1%	6%	0
- Deaths, %	18%	0	0	0	2%	6%	3%	0
- Loss to follow-up, %	6%	0	0	12%	11%	5%	9%	0
N included in analysis:								
- Mortality	32	39	115	36	454	778	30	6
- Success	26	13	91	12	15	541	2	5
- Acquired R resistance	26	12	83	12	--	539	--	--

Notes:

a) Regimens were classified as “standardized” if standard regimen was given to all patients; “individualized” if regimens were tailored to individual patients’ characteristics such as prior therapy, or drug susceptibility testing (DST) results; “randomized” if standard regimens were given within a randomized clinical trial.

Abbreviations: H isoniazid; **Individ.** Individualized; **IQR** Interquartile range; **na:** information in not available for that database or if it is available in less than 10% of the population; **R:** rifampin; **SM** streptomycin; **Stand.** Standardized.

Table S1a-continued. Characteristics of the 23 studies included in current analysis

First author	Quy 2003,2006 ^{17,18}	Reves 2014 ¹⁹	Romanowski 2017 ²⁰	Skrachina ²¹	Swaminathan 2010 ²²	Viiklepp ²³	Yoshiyama 2010 ²⁴	Total
Country	Vietnam	US & Canada	Canada	Belarus	India	Estonia	Nepal	--
Years	1998-2000	1999-2004	2002-14	2012-15	2000-05	2008-15	2003-05	1992-2015
Concentration used to define H resistance ($\mu\text{m}/\text{mL}$)	0.2	0.2 or 1.0	0.1	0.1	1.0	0.1	0.25	--
Regimen ^a	Stand.	Stand.	Indiv.	Indiv.	Random.	Indiv.	Stand.	--
Duration (known vs planned)	Planned	Known	Known	Known	Planned	Known	Planned	--
Age in years (median, IQR)	38 (30; 46)	45 (33; 56)	49 (37; 65)	43 (33; 53)	35 (29; 37)	49 (39; 56)	30 (25; 41)	35 (25; 50)
Sex female, %	30%	30%	32%	39%	26%	22%	41%	31%
HIV positive, % of tested ^b	2%	0%	3%	0%	100%	12%	na	13%
Past TB treatment, % ^b	27%	17%	18%	12%	na	7%	100%	16%
Cavity on chest-x ray, % ^b	na	45%	42%	0%	9%	54%	na	32%
Resistance to SM, % ^b	72%	25%	28%	67% ^b	43%	74%	65%	47%
Total analyzable, N:	315	60	121	15	25	42	20	3923
- Success, %	81%	75%	80%	60%	36%	79%	75%	80%
- Failure/relapse, %	9%	3%	1%	20%	48%	2%	10%	6%
- Deaths, %	3%	0	4%	0	8%	14%	0	4%
- Loss to follow-up, %	7%	22%	15%	20%	8%	5%	15%	10%
N included in analysis:								
- Mortality	294	47	103	12	23	40	17	3,550
- Success	101	45	44	11	4	14	17	2,044
- Acquired R resistance	--	--	44	10	3	14	16	1,552

Notes:

a) Regimens were classified as “standardized” if standard regimen was given to all patients; “individualized” if regimens were tailored to individual patients’ characteristics such as prior therapy, or drug susceptibility testing (DST) results; “randomized” if standard regimens were given within a randomized clinical trial.

Abbreviations: H isoniazid; **Individ.** Individualized; **IQR** Interquartile range; **na:** information in not available for that database or if it is available in less than 10% of the population; **R:** rifampin; **SM** streptomycin; **Stand.** Standardized.

Table S1b. Regimens excluded from present analysis –in the 23 included studies. Note: regimens were excluded if they did not correspond to the three study questions.

Regimen	N data sets	N
Regimens excluded from present analysis		817
Any regimens with high-dose isoniazid		139
- High dose H plus R, E, Z		63
- High dose H plus R, E, Z, SM		22
- Containing both FQ and high dose H (+/- SM)		31
- Containing high doses H, group C or D3 drugs ^a +/- FQ +/- any injectables		17
- Other combinations with high dose H		6
Containing WHO Group C or D3 drugs (+/-SM, +/- FQ) (without high dose H)		141
- Ethionamide/prothionamide		69
- Cycloserine/terizidone		36
- Both Ethionamide/prothionamide and Cycloserine/terizidone		19
- Other group C or D3 drugs ^b		17
(H)REZ-Second line injectables (+/- SM)		19
(H)REZ- FQ- Second line injectables (+/- SM)		73
Other regimens containing FQ		240
- (H)RE + FQ (+/- SM)		74
- (H)RZ + FQ (+/-SM)		65
- (H)REZ-SM-FQ		56
- Other combinations		45
Other regimens (RZ, RE, EZ) without FQ or injectables		205
- H, 6R 2Z, SM		108
- H, 6RZ		39
- H, 9RE		37
- Others		21

Notes:

a) Group C or D3 drugs used were Ethionamide/prothionamide or Cycloserine/terizidone or p-aminosalicylic acid (PAS)

b) Group C or D3 drugs used were Clofazimine, Linezolid, p-aminosalicylic acid (PAS), Macrolides, Thioacetazone

Abbreviations: **E:** Ethambutol; **FQ:** fluoroquinolones; **(H)=** isoniazid used in some, but not all regimens. **R :** rifampin (when patients used rifabutin in place of rifampin is specified in the notes); **SM:** Streptomycin; **Z=** pyrazinamide

Table 1Sc: Dosages of drugs used at sites of studies included in the individual patient data meta-analysis on isoniazid-resistant TB.

Author	Drug								
	First line drugs				Fluoroquinolones				Injectable
	H	R	E	Z	Ofloxacin	Levofloxacin	Moxifloxacin	Ciprofloxacin	SM
Bang¹	4-6 mg/kg/day	8-12 mg/kg/day	15-25 mg/kg/day	20-30 mg/kg/day	600 mg/day	not used	400 mg/day	500 mg twice a day	12-18 mg/kg/day
Brazilian NTB²	4-6 mg/kg/day	8-12 mg/kg/day	15-25 mg/kg/day	20-30 mg/kg/day	400mg/kg	According to weight ^a	400 mg/day	Note used	According to weight ^b
Cattamanchi³	4-6 mg/kg/day	8-12 mg/kg/day	15-25 mg/kg/day	20-30 mg/kg/day	not used	750-1000 mg/day	400 mg/day	not used	not used
Chien⁴	4-6 mg/kg/day	8-12 mg/kg/day	15-25 mg/kg/day	20-30 mg/kg/day	not used	750-1000 mg/day	400 mg/day	not used	not used
Cox⁵	4-6 mg/kg/day	8-12 mg/kg/day	15-25 mg/kg/day	20-30 mg/kg/day	not used	not used	not used	not used	12-18 mg/kg/day
Gegia⁶	4-6 mg/kg/day	8-12 mg/kg/day	15-25 mg/kg/day	20-30 mg/kg/day	not used	750-1000 mg/day	400 mg/day	not used	not used
Huyen⁷	4-6 mg/kg/day	8-12 mg/kg/day	15-25 mg/kg/day	20-30 mg/kg/day	not used	not used	not used	not used	12-18 mg/kg/day
Jacobson⁸	4-6 mg/kg/day	8-12 mg/kg/day	15-25 mg/kg/day	20-30 mg/kg/day	not used	not used	not used	not used	12-18 mg/kg/day
Jones-Lopez⁹	4-6 mg/kg/day	8-12 mg/kg/day	15-25 mg/kg/day	20-30 mg/kg/day	not used	not used	not used	not used	12-18 mg/kg/day

Notes:

a) According to weight: 20 kg: 10/mg/kg/day ; 21-35 kg: 250 mg-500 mg/day; 35-50 kg:500-750 mg/day;>50 kg: 750 mg/day.

b) 20 kg: 20 mg/kg/day; 21-35 kg: 500 mg/day ; 36-50 kg: 750-1000 mg /day; >50 kg:1000 mg /day

Table 1Sc (continued): Dosages of drugs used at sites of studies included in the individual patient data meta-analysis on isoniazid-resistant TB.

Author	Drug								
	first line drugs				Fluoroquinolones				Injectable
	H	R	E	Z	Ofloxacin	Levofloxacin	Moxifloxacin	Ciprofloxacin	SM
Kim ¹⁰	4-6 mg/kg/day	8-12 mg/kg/day	15-25 mg/kg/day	20-30 mg/kg/day	400mg bid	750-1000 mg/day	400 mg/day	not used	12-18 mg/kg/day
Lee ¹¹	4-6 mg/kg/day	8-12 mg/kg/day	15-25 mg/kg/day	20-30 mg/kg/day	not used	750-1000 mg/day	400 mg/day	not used	12-18 mg/kg/day
Munang ¹²	4-6 mg/kg/day	8-12 mg/kg/day	15-25 mg/kg/day	20-30 mg/kg/day	not used	not used	400 mg/day	500 -750 mg bid	12-18 mg/kg/day
Netherlands NTB ¹³	4-6 mg/kg/day	8-12 mg/kg/day	15-25 mg/kg/day	20-30 mg/kg/day	not used	not used	400 mg/day	not used	not used
NYC TB ¹⁴	4-6 mg/kg/day	8-12 mg/kg/day	15-25 mg/kg/day	20-30 mg/kg/day	800 mg/day	500-1000 mg/day	400 mg/day	1000-1500 mg/day	12-18 mg/kg/day
Ohkado ¹⁵	4-6 mg/kg/day	8-12 mg/kg/day	15-25 mg/kg/day	20-30 mg/kg/day	not used	not used	not used	not used	12-18 mg/kg/day
Park ¹⁶	4-6 mg/kg/day	8-12 mg/kg/day	15-25 mg/kg/day	20-30 mg/kg/day	not used	750-1000 mg/day	400 mg/day	not used	12-18 mg/kg/day
Quy ^{17,18}	4-6 mg/kg/day	8-12 mg/kg/day	15-25 mg/kg/day	20-30 mg/kg/day	not used	not used	not used	not used	12-18 mg/kg/day
Reves ¹⁹	not used	600 mg, daily for at least 2 weeks then mostly bi-weekly, some thrice weekly	daily for at least 2 weeks then biweekly EMB 40-50 mg/kg and 25-35 mg/kg thrice weekly	daily for at least 2 weeks then biweekly PZA 40-70 mg/kg and 30-40 mg/kg thrice weekly	not used	not used	not used	not used	not used
Romanowski ²⁰	4-6 mg/kg/day	8-12 mg/kg/day	15-25 mg/kg/day	20-30 mg/kg/day	not used	750-1000 mg/day	not used	not used	12-18 mg/kg/day
Skrahina ²¹	4-6 mg/kg/day	8-12 mg/kg/day	max 1600 mg/kg/day	30-30 mg/kg/day	800 mg/day	750-1000 mg/day	400 mg/day	not used	not used

Table 1Sc (continued): Dosages of drugs used at sites of studies included in the individual patient data meta-analysis on isoniazid-resistant TB.

Author	Drug								
	First line drugs				Fluoroquinolones				Injectable
	H	R	E	Z	Ofloxacin	Levofloxacin	Moxifloxacin	Ciprofloxacin	SM
Swaminathan ²²	10 mg/Kg/day	8-12 mg/kg/day	15-25 mg/kg/day	20-30 mg/kg/day	not used	not used	not used	not used	not used
Viiklepp ²³	4-6 mg/kg/day	8-12 mg/kg/day	5-25 mg/kg/day	20-30 mg/kg/day	not used	750-1000 mg/day	400 mg/day	not used	12-18 mg/kg
Yoshiyama ²⁴	4-6 mg/kg/day	8-12 mg/kg/day	15-25 mg/kg/day	20-30 mg/kg/day	not used	not used	not used	not used	12-18 mg/kg

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Table 1Sd: Summary of treatment outcome definitions used in studies included in individual patient data meta-analysis.

Study	Outcome definition				
	Cure	Treatment Completed	Lost to follow-up	Treatment Failure	Treatment Relapse
WHO (Reference Standard)	A patient whose sputum smear or culture was positive at the beginning of the treatment but who was smear- or culture-negative in the last month of treatment and on at least one previous occasion.	A patient who completed treatment but who does not have a negative sputum smear or culture result in the last month of treatment and on at least one previous occasion	A patient whose treatment was interrupted for 2 consecutive months or more.	A patient whose sputum smear or culture is positive at 5 months or later during treatment. Also included in this definition are patients found to harbour a multidrug-resistant (MDR) strain at any point of time during the treatment, whether they are smear-negative or -positive.	Recurrence of bacteriologically confirmed tuberculosis after treatment success (cure or treatment complete).
Bang¹	Same	Same	Same	Patient who is sputum smear positive or culture positive at five months or later during treatment	Same
Brazilian NTB²	Same	Same	Treatment interruption for 30 days or more	Same	Same
Cattamanchi³	Same	Same		Same	Same

Note: "Same" means : as WHO reference definition.

Table 1Sd (continued): Summary of treatment outcome definitions used in studies included in individual patient data meta-analysis.

Study	Outcome definition				
	Cure	Treatment Completed	Lost to follow-up	Treatment Failure	Treatment Relapse
Chien ⁴	Same	Same	Same	Same	Same
Cox ⁵	Same	Same	Same	Same	Same
Gegia ⁶	Same	Same	Same	Same	Same
Huyen ⁷	Same	Same	Same	Any positive sputum or culture at 5 months or later during treatment	Recurrent TB with initial and follow-up M. tuberculosis isolates had identical spoligotypes and VNTR patterns, or if the VNTR patterns differed by "1 locus, and as reinfection if otherwise"
Jacobson ⁸	Same	Same	Same	Same	Not measured
Jones-Lopez ⁹	Treatment completed and one negative culture on solid medium at the end of treatment	Completed 8 months of treatment and free of Tb symptoms at the first post-treatment follow-up visit		Patients culture positive at month 8 OR patients with no culture positive at month 5 and with no culture at month 8 and no confirmation that they were free of TB after the end of treatment	

Note: "Same" means same as WHO reference definition.

Table 1Sd (continued): Summary of treatment outcome definitions used in studies included in individual patient data meta-analysis.

Study	Outcome definition				
	Cure	Treatment Completed	Lost to follow-up	Treatment Failure	Treatment Relapse
Kim ¹⁰	Same	Same	Same	Same	Same
Lee ¹¹	Same	Same	Same	Same	Same
Munang ¹²	Combined with complete (see)	Patients were considered successfully treated if they completed a full course of prescribed treatment and had documented sputum culture conversion (for sputum culture-positive cases) or were discharged by their attending physician.	Same	Treatment failed if a case was smear- or culture- positive at month 5 or later during treatment.	Suspected OR bacteriologically confirmed tuberculosis after treatment success (cure or complete).
Netherlands NTB ¹³	Negative sputum culture result after initial positive culture test.	Same	Same	Same	Not collected
NYC TB ¹⁴	Same	Same	Lost to follow-up, adverse reaction that resulted in the discontinuation of treatment, or refusal of treatment	Positive culture after culture conversion	Treatment was restarted after treatment completion
Ohkado ¹⁵	A sputum smear positive patient who has been completed treatment and is sputum smear negative in the last month of treatment and on at least one previous occasion.	Same	Same	A patient who is sputum smear-positive at five months or later during the treatment OR a sputum smear-negative patient who becomes smear-positive during the treatment.	Same

Note: "Same" means : as WHO reference definition.

Table 1Sd (continued): Summary of treatment outcome definitions used in studies included in individual patient data meta-analysis.

Study	Outcome definition				
	Cure	Treatment Completed	Lost to follow-up	Treatment Failure	Treatment Relapse
Park ¹⁶	Same	Same	Same	Same	Same
Quy ^{17,18}	Same	Same	Same	Positive smear at 5 months of later during treatment	Same
Reves ¹⁹	Same	Same	Same	Treatment failure was suspected for a positive TB culture following 16 calendar weeks of treatment, and relapse was suspected for a positive TB culture within 2 years of treatment completion.	Relapse was suspected for a positive TB culture within 2 years of treatment completion.
Romanowski ²⁰	Same	Same	Same	Same	Same
Skrahina ²¹	Same	same	Same	Same	Same
Swaminathan ²²	All cultures negative in the last 2 months of treatment	Clinical resolution with regression of nodes or radiographic clearance	Same	Same	Same
Viiklepp ²³	Same	Same	Same	Same	Same
Yoshiyama ²⁴	Same	Same	Same	Same	Same

Note: "Same" means : as WHO reference definition

Table S1E: Assessment of Quality of the Included studies

Study	1. Sampling method	2. Outcome measures		3. Participation rate (%)	4. Lost to follow-up rate (%)	5.-8. Completeness of information (%)				Overall Study Quality
		Post-treatment Follow-up >=12mo (%)	Culture confirmed cure			5. Age	6. HIV	7. Cavity	8. AFB	
Bang ¹	census	100	Yes	100	9.0	100	21.6 ^a	6.3	100	High
Brazilian NTP ²	census	0	Yes	100	15.2	100	77.0 ^b	98.4	82.7	High
Cattamanchi ³	census	62	Yes	100	9.5	100	100	97.1	100	High
Chien ⁴	census	21	Yes	100	7.0	99.7	92.1	100	100	High
Cox ⁵	census	100	No	68	14.3	100	100	0	100	Moderate
Gegia ⁶	census	0	No	100	18.6	100	0 ^a	0	96.6	Moderate
Huyen ⁷	census	100	Yes	97.5	1.5	99.5	0 ^a	0	100	High
Jacobson ⁸	census	0	Yes	100	33.8	100	83.8	0	96.0	High
Jones-Lopez ⁹	census	100	Yes	100	5.9	0	100	0	100	High
Kim ¹⁰	census	31	Yes	100	13.0	100	71.8 ^a	100	100	High
Lee ¹¹	census	55	Yes	100	5.9	100	100	100	100	High
Munang ¹²	census	7	Yes	100	10.1	100	100	100	79.8	High
Netherland NTP ¹³	census	0	No	100	10.9	100	9.6 ^a	0	52.2	Low
NYC ¹⁴	census	0	Yes	100	6.2	100	74.6 ^b	84.7	99.4	High
Ohkado ¹⁵	census	0	No	83.3	18.9	100	0 ^a	0	100	Moderate
Park ¹⁶	census	100	Yes	100	0	100	100	100	100	High
Quy ^{17,18}	census	0	No	95.8	6.7	100	100	0	100	Moderate
Reves ¹⁹	RCT	81	Yes	100	4.2	100	100	94.4	88.7	High
Romanowski ²⁰	census	43	Yes	100	8.0	99.5	99.5	96.5	100	High
Skrahina ²¹	census	0	Yes	100	10.3	100	100	100	100	High
Swaminathan ²²	RCT	100	Yes	57.8	7.4	100	100	100	100	High
Viklepp ²³	census	0	Yes	100	7.8	100	97.4	98.3	100	High
Yoshiyama ²⁴	census	100	Yes	100	15.0	100	0 ^a	0	100	High

Notes: a) HIV prevalence is reported to be less than 10% in TB cases in the Country of the study, therefore the reporting on HIV was considered of high quality.

b) HIV prevalence is reported to be less than 1% in the general population in the Country of the study (i.e., low HIV prevalence), therefore the reporting on HIV was considered of high quality.

Definitions used for quality assessment:

Critical criteria:

1. What is the sampling method in the study: census (all patients), random sampling, or convenience sampling? (Must be census or random)

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2. Was end of treatment outcome "cure" confirmed with culture, or were at least 80% of patients with cure/complete outcome followed for at least 1 year for recurrence? (Must be yes to either).

Important criteria

1. Was the participation rate in the study >80%
2. Lost to follow-up rate - defined as : LFU + transferred out (if in DOT or surveillance program, not counted if in tertiary hospital) + unknown outcome. LFU rate must be <=10%.
3. Was age reported in at least 90% of the participants?
4. Was HIV status reported in at least 80% of the participants? (If HIV prevalence is known to be less than 10% in TB cases, or less than 1% in the general population in the country (i.e., low HIV prevalence), this item will be considered acceptable even if HIV status for individuals is not reported)
5. Was cavity reported in at least 80% of the participants?
6. Was AFB reported in at least 80% of the participants?

High quality: Both critical criteria and at least 4 of the 6 important criteria.

Moderate quality: Both critical criteria and 3 of the 6 important criteria OR 1 critical criteria and at least 4 of the 6 important criteria.

Low quality: all remaining.

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Table S2a. Characteristics of 10 studies excluded from current IPD analyses. Note: studies were excluded, after the data was received, if no patients received any of the specific regimens of interest for the three research questions.

First author	BanuRekha 2012 ²⁵	Bonnet 2011 ²⁶	Cegielski ²⁷	Escalante 2001 ²⁸	Garcia-Prats 2016 ²⁹	Gillespie 2014 ³⁰	Glynn 2015 ³¹	Merle 2014 ³²	Swaminathan 2011 ³³	Tabarsi 2009 ³⁴	Total
Country	India	Georgia	US (Texas)	US (Texas)	South Africa	Multiple	Malawi	Multiple	India	Iran	--
Years	2004-06	2003-13	1984-2007	1990-97	2006-12	2013	1986-2015	2007	2006-08	2003-15	1984- 2015
Concentration used to define H resistance ($\mu\text{m}/\text{mL}$)	1-0	0-1	1-0	0-4	0-1	0-1	varied over time	0-2	1-0	0-2	--
Regimen ^a	Random.	Indiv.	Indiv.	Indiv.	Indiv.	Random.	Stand.	Random.	Random.	Indiv.	--
Duration (known vs planned)	Planned	Known	Known	Known	Known	Planned	Known	Planned	Planned	Known	--
Age in years (median, IQR)	32 (27; 39)	43 (32; 52)	46 (29; 60)	39 (25; 49)	4 (2;7)	30 (24; 45)	37 (30; 45)	26 (23; 36)	35 (32; 35)	47 (34; 60)	35 (25; 48)
Sex female, %	27%	18%	24%	22%	58%	34%	37%	27%	40%	32%	34%
HIV positive, % of tested ^b	0%	na	8%	9%	22%	9%	35%	8%	100%	11%	14%
Past TB treatment, % ^b	3%	42%	39%	24%	29%	0%	23%	na	0%	84%	34%
Cavity on chest-x ray, % ^b	na	44%	na	65%	23%	71%	na	45%	na	74%	58%
Resistance to SM, % ^b	na	79%	24%	37%	11% ^b	27%	23%	14%	0%	41% ^c	38%
Analyzable population, N	30	59	43	51	51	127	201	68	5	127	762

Notes:

a) Regimens were classified as “standardized” if a standard regimen was given to all patients; “individualized” if regimens were tailored to individual patients’ characteristics such as prior therapy, or drug susceptibility testing (DST) results; “ randomized” if a standard regimens were given within a randomized clinical trial; b) percentage are on total available information. In some sites this information was available for less than 50% of the population

Abbreviations: **DST:** drug susceptibility test; **H** isoniazid; **Individ.** Individualized; **IQR** Interquartile range; **na:** information in not available for that database or if it is available in less than 10% of the population; **Random.** Randomized; **SM** streptomycin; **Stand.** Standardized.

Table S2b: Regimens used in the 10 excluded studies

Regimen	N
<i>Total patients in the 10 studies</i>	762
(H) REZ	261
- 6(H)R, 2E, 2Z	204
- unknown duration	57
REZ(H)-FQ	105
-4(H)R 2E, 2Z, FQ	46
-unknown duration	59
REZ(H)-SM	30
Other regimens	366
Included high dose isoniazid	35
Included Ethionamide/prothionamide or Cycloserine/Terizidone	66
Included Thioacetazone	63
Included Clofazimine	2
Other combinations of H, R, E, Z (other than HREZ)	11
Other combinations of H, R, E, Z, SM (other than HREZ-SM)	11
Used second line injectables	6
Used FQ and second line injectables	74
Used Other FQ-containing regimens	87
Used combinations of FQ and SM	11

Notes:

Abbreviations: **H:** Isoniazid, **E:** Ethambutol, **FQ:** fluoroquinolones; **SM:** Streptomycin; **R:** Rifampin; **Z:** pyrazinamide.

Table S3: Characteristics of the populations included in analyses of success and acquired rifampin resistance for 6(H)REZ versus >6(H)REZ^a

Type of analysis	Analyses of Success (n=1350)		Analyses of Acquired Rifampin resistance (n=1160)	
	6(H)REZ	>6 (H)REZ	6(H)REZ	>6 (H)REZ
Regimens compared				
Total N^b	262	1088 ^c	168	992 ^c
High Income Country, N(%)	260/262(99)*	397/1088 (36)	166/168 (99)*	338/992(34)
Age (median, IQR)	42 (29; 58)*	37 (27; 50)	43 (30; 61)*	36 (27; 50)
Sex, female, N /tot with info (%)	84/262 (32)	317/1088 (29)	53/168 (32)	286/992 (29)
HIV: positive, N/tot with info (%)	7/221 (3)*	23/295 (8)	5/142 (4)	20/257 (8)
on Antiretroviral therapy, N (% on HIV+)	1/7 (14)	1/23 (4)	0/5 (0)	1/20 (5)
Diabetes, N/tot with info (%)	16/113 (14)	19/99 (19)	5/66 (8)	14/86 (16)
Any Past TB treatment, N/tot with info (%)	44/260 (17)*	116/979 (12)	17/166 (10)	91/888 (11)
Sputum smear positive, N/tot with info (%)	127/252 (50)*	853/1071 (80)	81/166 (49)*	780/976 (80)
Cavity on chest X-ray, N/tot with info (%)	54/237 (23)*	115/366 (31)	27/164 (16)*	103/329 (31)
Poly resistance (resistance to E, Z or SM if used), N/tot with info, %	2/262(1)	3/1088(0)	2/168 (1)	3/992 (0)
Resistance to SM, N/total tested	63/209 (30)*	598/1053 (57)	51/165 (31)*	559/986 (57)
Resistance to E, N/total tested	1/261(0)	3/1086 (0)	1/167 (1)	3/990 (0)
Resistance to Z, N/total tested	1/224 (0.5)	0/325 (0)	1/138 (1)	0/273 (0)
On DOT, N/tot with info(%)	81/162 (50)*	760/842(90)	25/68 (37)*	707/747(95)
Duration in months, median (IQR):				
- Rifampin	6.1 (6.0; 6.5)	9.0 (9.0; 9.0)	6.1 (6.0; 6.5)	9.0 (9.0; 9.0)
- Pyrazinamide	6.1 (6.0; 6.4)	9.0 (9.0; 9.0)	6.1 (6.0; 6.5)	9.0 (9.0; 9.0)

Notes: * p<0. .05 for Chi Squared tests (or Fisher's exact test) for categorical variables, and from T Tests for continuous variables ;

a) Treatment was administered daily for all but 1 study (n=45 subjects) included in this analysis

b) A total of 13 children under 14 years old were treated in population analyzed for success and 9 in analyzed for acquired rifampin resistance;

c) Two patients took rifabutin and rifampin.

Abbreviations: DOT: directly observed therapy; IQR: Inter Quartile Range; E: Ethambutol; (H)= Isoniazid used in some, but not all regimens SM: Streptomycin;

R: Rifampin; Z: pyrazinamide.

Table S4: Characteristics of the population included in analyses of FQ added to ≥ 6 (H)REZ.

Type of analysis	Analyses of Mortality ^b (n=2698)		Analyses of Success (n=1601)		Analyses of Acquired Rifampin resistance (n=1381)	
	≥ 6 (H)REZ FQ	≥ 6 (H)REZ	≥ 6 (H)REZ FQ	≥ 6 (H)REZ	≥ 6 (H)REZ FQ	≥ 6 (H)REZ
Regimens compared						
Total N	524 ^a	2174 ^b	251 ^c	1350 ^d	221 ^c	1160 ^d
High Income Country, N(%)	513 (98)*	1449 (67)	241 (96)*	657 (49)	212 (96)*	504 (43)
Age (median, IQR)^e	48 (34; 63)*	37 (27; 52)	42 (32; 56)*	38 (27; 52)	43 (33; 58)*	37 (27; 51)
Sex, female, N /tot with info (%)	179 (34%)	711 (33%)	82 (33)	401 (30)	72 (33%)	339 (29%)
HIV: positive, N/tot with info (%)	62/428 (14)	106/884 (12)	17/203 (8)	30/516 (6)	14/191 (7%)	25/399 (6%)
on ART, N (% on HIV+)	6/62 (10)	3/106 (3)	0/17 (0)	2/30 (7)	0/14 (0%)	1/25 (4%)
Diabetes, N/tot with info (%)	27/185 (15)	67/385 (17)	8/82 (10)	35/212 (17)	8/80 (10%)	19/152 (13%)
Any Past TB treatment, N/tot with info (%)	57/508 (11)	237/1978 (12)	27/247 (11)	160/1239 (13)	21/217 (10%)	108/1054 (10%)
Sputum smear positive, N/tot with info (%)	286/482 (59)	1412/1997 (71)	154/245 (63)*	980/1323 (74)*	134/215 (62)*	861/1141 (75)
Cavity on chest X-ray, N/tot with info (%)	113/471 (24)	260/959(27)	56/220 (25)	169/603 (28)	54/215 (25%)	130/493 (26%)
Poly resistance (resistance to E, Z or SM if used), N/tot with info, %	38/524 (7)	26/2174 (1)	7/251 (3)*	5/1350 (0.4)*	5/221(2%)*	5/1160 (0%)
Resistance to SM, N/total tested (%)	166/482 (34)	754/1607 (47)	82/236 (35%)*	661/1262 (53%)	70/213 (33%)*	610/1151 (53%)
Resistance to FQ, N/total tested (%)	4/313 (1)	7/497 (1)	3/163 (2%)	3/346 (1%)	1/136 (1%)	3/306 (1%)
on DOT, N/total tested,%	84/246 (34)*	956/1689(57)	31/114 (27)*	841/1004(84)	28/85 (33)*	732/815(90)
Duration in months, median (IQR):						
- Rifampin	9.0 (6.2; 11.0)	9.0 (6.0; 9.0)	9.0 (7.2; 11.2)	9.0(8.3; 9.0)	9.0 (7.7; 11.1)	9.0 (9.0; 9.0)
- Fluoroquinolones	6.6 (3.9; 9.0) ^f	--	6.1 (3.5; 8.4) ^g	--	5.7 (3.3; 8.1)	--
- Pyrazinamide	7.4 (4.1; 9.5)	8.0 (2.1; 9.0)	8.9 (6.8; 10.7)	9.0 (8.1; 9.0)	9.0 (7.0; 10.6)	9.0 (8.9; 9.0)

Notes: * p<0.05 for Chi Squared tests (or Fisher's exact test) for categorical variables, and from T Tests for continuous variables;

a) 19 patients took rifabutin and 26 patients took both rifampin and rifabutin **b)** 13 patients took rifabutin and 17 patients took both rifampin and rifabutin

c) Four patients took both rifampin and rifabutin **d)** Two patients took both rifampin and rifabutin

e) A total of 46 children under 14 years old were included in population analyzed for mortality; 16 in analyzed for success and 11 in analyzed for acquired rifampin resistance;

f) Duration may have been truncated by mortality.

g) Duration of FQ: 104 took FQ for 1-5 months, 137 took FQ for ≥ 6 m; 10 took FQ ≥ 1 m (unknown duration, but at least one month).

Abbreviations: DOT: directly observed therapy; IQR: Inter Quartile Range; E: Ethambutol; FQ: fluoroquinolones; (H)= Isoniazid used in some, but not all regimens; SM: Streptomycin; R: Rifampin; Z: pyrazinamide.

Table S5: Characteristics of the population included in analyses of “FQ with short Z” question (i.e. Six months or more of RE plus 1-3 months of Z plus fluoroquinolone compared to 6 months or more of REZ - with or without isoniazid)

Type of analysis	Analyses of Success (n=1468)		Analyses of Acquired rifampin resistance (n=1273)	
	≥6(H)RE 1-3Z FQ	≥6 (H)REZ	≥(H)6RE 1-3Z FQ	≥6 (H)REZ
Regimens compared				
Total N	118 ^a	1350 ^b	113 ^a	1160 ^b
Age^c (median, IQR)	56 (38; 69)*	38 (27; 52)	56 (38; 68)*	37 (27; 51)
High income countries (N,%)	118 (100)*	657 (49)	113 (100)*	504 (43)
Sex, female, N /tot with info (%)	39/118 (33)	401/1350 (30)	36 (32%)	339 (29%)
HIV: positive, N/tot with info (%)	7/97 (7)	30/516 (6)	7/92 (8%)	26/399 (6%)
On antiretroviral treatment, N (% on HIV+)	3/7 (43)*	2/30 (7)	3/7 (43%)*	1/25 (4%)
Diabetes, N/tot with info (%)	10/51 (20)	35/212 (17)	8/48 (17%)	19/152 (13%)
Any Past TB treatment, N/tot with info (%)	12/109 (11)	160/1239 (13)	10/104 (10%)	108/1054 (10%)
Sputum smear positive, N/tot with info (%)	47/96 (49)*	980/1323 (74)	47/91 (52%)*	861/1141 (75%)
Cavity on chest X-ray, N/tot with info (%)	28/115 (24)	169/603 (28)	27/110 (25%)	130/493 (26%)
Poly resistance (resistance to E, Z or SM if used), N/tot with info, %	15/118 (13)*	5/1350 (0.4)	15/113 (13%)*	5/1160 (0%)
Resistance to SM, N/total tested	37/113 (33%)*	661/1262 (52%)	37/110 (34%)*	610/1151 (53%)
Resistance to FQ, N/total tested	1/66(2%)	3/346 (1%)	1/64 (2%)	3/306 (1%)
on DOT, N/total tested,%	23/60 (38)*	841/1004(84)	21/55 (38%)*	732/815 (90%)
Duration in months, median (IQR):				
- Rifampin	9.6 (8.6; 11.9)	9.0 (8.3; 9.0)	9.5 (8.6; 11.8)	9.0 (9.0; 9.0)
- Fluoroquinolones	7.0 (5.0; 9.5) ^d	--	7.0 (5.0; 9.5)	--
- Pyrazinamide	2.5 (1.9; 3.8)	9.0 (8.1; 9.0)	2.5 (1.9; 3.8)	9.0 (8.9; 9.0)

Notes:

a) Three patients took both rifampin and rifabutin

b) Two patients took both rifampin and rifabutin

c) A total of 13 children under 14 years old were included in population analyzed for success; and 9 in population analyzed for acquired rifampin resistance.

d) Duration of FQ: 31 had 1-5m of FQ; 71 ≥6m and 16 ≥1m (unknown duration, but at least one month).

Abbreviations: DOT: directly observed therapy; IQR: Inter Quartile Range; E : ethambutol; FQ: fluoroquinolones; (H)= isoniazid used in some, but not all

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Table S6. Characteristics of the populations included in Streptomycin-related analyses.

Type of analysis	Analysis of Mortality (n=3,026)		Analysis of Success (n=1,675)		Analysis of Acquired rifampin resistance (n=1,218)	
	(H)REZ SM	(H)REZ	≥6(H)R(E) 1-3Z 1-3SM	≥6 (H)REZ	≥6(H)R(E) 1-3Z 1-3SM	≥6 (H)REZ
Regimens compared						
Total N	763	2263 ^a	325	1350 ^b	58	1160 ^b
Age^c (median, IQR)	42 (32; 52)*	37 (27; 51)	42 (31; 51)	38 (27; 52)	35 (25; 40)*	37 (27; 51)
High Income Countries, N(%)	52/763 (7)	1449/2263 (64)	13 (4)*	657 (49)	2 (3)*	504 (43)
Sex, female, N /tot with info (%)	197/731 (27)*	739 (33)	84/300 (28%)	401/1350 (30)	10/32 (31%)	339 (29%)
HIV: positive, N/tot with info (%)	33/495 (7)*	131/943 (14)	17/238 (7%)	30/516 (6)	12/42 (29%)*	25/399 (6%)
On Antiretroviral treatment, N (% on HIV+)	3/33 (9)	3/131(2)	0/17 (0%)	2/30 (7)	0/12 (0%)	1/25 (4%)
Diabetes, N/tot with info (%)	18/166 (11)	69/413 (17)	13/112 (12%)	35/212 (17)	0/4(0%)	19/152 (13%)
Any Past TB treatment, N/tot with info (%)	235/627 (37)*	238/2033(12)	204/214 (95%)*	160/1239 (13)	55/56 (98%)*	108/1054 (10%)
Sputum smear positive, N/tot with info (%)	705/744 (95)*	1486/2077 (72)	289/312 (93%)*	980/1323 (74)*	56/58 (97%)*	861/1141 (75%)
Cavity disease at chest X-ray, N/tot with info (%)	107/172 (62)*	272/994(27)	76/113 (67%)*	169/603 (28)	2/5 (40%)	130/493 (26%)
Poly resistance (resistance to E, Z or SM if used), N/tot with info, %	378/700 (54)*	36/2263(2)	131/281 (47)*	5/1350 (0.4)*	21/32 (66%)*	5/1160 (0%)
Resistance to SM, N/total tested	375/700 (54)	799/1694 (47)	129/280 (46%)	661/1262 (53%)	20/32 (63%)	610/1151 (53%)
Resistance to E, N/total tested	18/753 (2)*	23/2257 (1)	8/321 (2)*	4/1347 (0)	2/58 (3)*	4/1157 (0)
on DOT, N/tot with info, %	286/346(83)	873/1037(84)	267/325(82)	841/1004(84)	58 (100%)*	732/815 (90%)
Duration in months, median (IQR):						
- Rifampin	6.0 (2.0; 8.0)	9.0 (6.0; 9.0)	8.0 (6.0; 8.0)	9.0 (8.3; 9.0)	8.0 (8.0; 8.0)	9.0 (9.0; 9.0)
- Pyrazinamide	2.0 (2.0; 3.0)	7.4 (2.0; 9.0)	3.0 (2.0; 3.0)	9.0 (8.1; 9.0)	3.0 (3.0; 3.0)	9.0 (8.9; 9.0)

Notes: * p<0.05 for Chi-square test for differences of this characteristic in the two regimens;

a) Thirteen patients took rifabutin, 17 took both rifabutin and rifampin **b)** Two patients took both rifampin and rifabutin

c) A total of 37 children under 14 years old were included in population analyzed for mortality; 13 in analyzed for success and 9 in analyzed for acquired rifampin resistance.

Abbreviations: DOT: directly observed therapy; IQR: Inter Quartile Range; E : Ethambutol; FQ: fluoroquinolones; SM: Streptomycin; R: Rifampin; Z:

Pyrazinamide

Table S7. Results for analyses restricted to high income countries only – success, mortality and acquired rifampin resistance. Note: this analysis is not possible for SM-REZ regimens, because very few patients received this regimen in high-income countries

Outcome and comparison	Regimens:	N datasets included	N of events/N on treatment	N pairs used ^a	from Propensity Score matched Analysis ^b	
					aOR (95% CI)	Risk Difference (per 1,000 treated with 95%CI)
6 (H)REZ vs >6(H)REZ						
Success	6(H)REZ >6(H)REZ	12	252/260 387/397	260	0.7 (0.3; 2.2) 1.0 (reference)	No difference (from 30 fewer to 30 more) reference
Acquired rifampin resistance	6(H)REZ >6(H)REZ	7	1/166 1/338	166	not estimable 1.0 (reference)	No difference (from 120 fewer to 130 more) reference
>=6(H)REZ+FQ vs >=6(H)REZ						
Mortality	REZ FQ REZ	12	25/531 67/1449	513	0.7 (0.4; 1.1) 1.0 (reference)	No difference (from 30 fewer to 30 more) reference
Success	>=6(H)REZ FQ >=6(H)REZ	12	237/241 639/657	238	2.3 (0.7; 7.6) 1.0 (reference)	20 more (from 10 fewer to 50 more) reference
Acquired rifampin resistance	>=6(H)REZ FQ >=6(H)REZ	7	0/212 2/504	210	not estimable 1.0 (reference)	-- reference
>=6(H)RE 1-3Z FQ vs >=6(H)REZ						
Success	>=6(h)RE 1-3Z FQ >=6(H)REZ	12	117/118 639/657	110	4.1 (0.4; 38.6) 1.0 (reference)	30 more (from 30 fewer to 90 more) reference
Acquired rifampin resistance	>=6(h)RE 1-3Z FQ >=6(H)REZ	7	0/113 2/504	105	not estimable 1.0 (reference)	-- reference

Notes:

a) Number of pairs used in propensity score matched analysis.

b) Estimates based on pairs matched for age, sex, HIV, past TB treatment, sputum AFB smear (positive vs negative) and resistance to other drugs besides isoniazid, if used.

Abbreviations: aOR: adjusted odds ratio; CI Confidence interval E: ethambutol; FQ: fluoroquinolones; (H)= isoniazid used in some, but not all regimens. SM: streptomycin; R: rifampin; Z: pyrazinamide.

Table S8. Results for analyses of Streptomycin restricted to low and middle-income countries only - success, mortality and acquired rifampin resistance.

Note: This analysis is possible only for SM-REZ based regimens, as other regimens are taken mostly in high-income countries

Outcome and comparison	Regimens:	N datasets included	N of events/N on treatment	N pairs used ^a	from Propensity Score matched Analysis ^b	
					aOR (95% CI)	Risk Difference (per 1,000 treated with 95%CI)
>=6(H) RE 1-3 Z 2SM vs >=6(H)REZ						
Mortality	(H)REZ SM	11	34/711	703	1.8 (1.0; 3.2)	40 more (from 20 more to 60 more)
	(H) REZ		36/814		1.0 (reference)	reference
Success	>-6(H) RE 1-3 Z 2SM	11	258/312	161	0.7 (0.4; 1.3)	50 fewer (from 120 fewer to 30 more)
	>=6(H)REZ		614/693		1.0 (reference)	reference
Acquired rifampin resistance	>-6(H) RE 1-3 Z 2SM	3	6/56	23	not estimable	--
	>=6(H)REZ		42/656		1.0 (reference)	reference

Notes:

a) Number of pairs used in propensity score matched analysis.

b) Estimates based on pairs matched for age, sex, HIV, past TB treatment, sputum AFB smear (positive vs negative) and resistance to other drugs besides isoniazid, if used.

Abbreviations: aOR: adjusted odds ratio; CI Confidence interval E: ethambutol; FQ: fluoroquinolones; (H)= isoniazid used in some, but not all regimens. SM: streptomycin; R: rifampin; Z: pyrazinamide.

TABLE S9: Comparison of Outcomes in sub-group with cavitation status known, and with cavitation - vs all patients. (Notes: Analysis of patients who did not receive INH not shown because too few patients in sub-sample and the models did not converge; Analysis of acquired drug resistance not shown, because there was zero acquired resistance in one, or both groups in each analysis).

Outcome and comparison	Regimens:	N datasets included	N of events/N on treatment	N pairs used ^a	from Propensity Score matched Analysis ^b	
					aOR (95% CI)	Risk Difference (per 1,000 treated with 95%CI)
Duration of REZ - all patients (with or without isoniazid)						
Success (all patients)	6(H)REZ	15	254/262	262	2.4 (1.0; 5.5)	40 more per 1,000 (from 0 difference to 80 more)
	>6(H)REZ		999/1088		1.0 (reference)	(reference)
Success (in subsample with CXR info - ALL)	6(H)REZ	11	230/237	235	0.4 (0.1; 1.7) ^c	20 fewer per 1,000 (from 60 fewer to 10 more)
	>6(H)REZ		356/366		1.0 (reference)	(reference)
Success (in subsample with cavity)	6(H)REZ	11	49/54	49	0.2 (0, 2.3)	70 fewer per 1,000 (from 220 fewer to 80 more)
	>6(H)REZ		111/115		1.0 (reference)	(reference)
Use of Fluoroquinolones - all patients (with or without isoniazid)						
Mortality (all durations)	(H)REZ FQ	15	25/524	522	0.7 (0.4; 1.1)	20 fewer per 1,000 (from 50 fewer to 0 difference)
	(H)REZ		97/2174		1.0 (reference)	(reference)
Mortality (all durations, in subsample with CXR info ALL)	(H)REZ FQ	12	24/471	470	0.6 (0.4; 1.0)^c	0 difference per 1,000 (from 30 fewer to 30 more)
	(H)REZ		51/959		1.0 (reference)	(reference)
Mortality (all durations, in subsample with cavity)	(H)REZ FQ	12	0/113	108	--- ^d	--- ^d
	(H)REZ		10/260		1.0 (reference)	(reference)
Success	≥6(H)REZ FQ	15	245/251	248	2.8 (1.1 to 7.3)	50 more per 1,000 (from 0 difference to 90 more)
	≥6(H)REZ		1253/1350		1.0 (reference)	(reference)
Success (in subsample with CXR info)	≥6(H)REZ FQ	11	216/220	220	2.0 (0.6 to 6.9) ^c	20 more per 1,000 (from 10 fewer to 50 more)
	≥6(H)REZ		586/603		1.0 (reference)	(reference)
Success (in subsample with cavity)	≥6(H)REZ FQ	11	56/56	55	--- ^d	--- ^d
	≥6(H)REZ		160/169		1.0 (reference)	(reference)

Notes at the end of the table (next page).

Table S9 continuation

Outcome and comparison	Regimens:	N datasets included	N of events/N on treatment	N pairs used ^a	from Propensity Score matched Analysis ^b	
					aOR (95% CI)	Risk Difference (per 1,000 treated with 95%CI)
Use of Fluoroquinolone with 1-3 months PZA - all patients (with or without isoniazid)						
Success (all FQ)	≥(H)6RE 1-3Z FQ ≥6(H)REZ	15	117/118 1253/1350	108	5.2 (0.6 to 46.7) 1.0 (reference)	40 more per 1,000 (from 20 fewer to 90 more) (reference)
Success (all FQ) in subsample with CXR info	≥(H)6RE 1-3Z FQ ≥6(H)REZ	11	114/115 586/603	108	4.1 (0.4 to 38.7) ^c 1.0 (reference)	30 more per 1,000 (from 40 fewer to 10 more) (reference)
Success (all FQ) in subsample with cavity	≥(H)6RE 1-3Z FQ ≥6(H)REZ	11	28/28 160/169	25	... ^d 1.0 (reference)	... ^d (reference)
Use of Streptomycin - all patients (with or without isoniazid)						
Mortality (all durations)	6(H)REZ + SM 6(H)REZ	23	40/763 103/2263	756	0.9 (0.6 to 1.3) 1.0 (reference)	10 fewer per 1,000 (from 30 fewer to 20 more) (reference)
Mortality (in subsample with CXR info)	6(H)REZ + SM 6(H)REZ	13	11/172 54/994	172	1.0 (0.4 to 2.4) ^c 1.0 (reference)	0 difference per 1,000 (from 50 fewer to 60 more) (reference)
Mortality (in subsample with cavity)	6(H)REZ + SM 6(H)REZ	13	5/107 12/272	106	1.3 (0.3, 6.3) 1.0 (reference)	10 more per 1,000 (from 40 fewer to 60 more) (reference)
Success	≥6(H)RE 1-3Z 2SM ≥6(H)REZ	23	271/325 1253/1350	296	0.4 (0.2 to 0.7) 1.0 (reference)	120 fewer per 1,000 (from 190 fewer to 60 fewer) (reference)
Success (in subsample with CXR info)	≥6(H)RE 1-3Z 2SM ≥6(H)REZ	13	94/113 586/603	113	0.1 (0.0 to 0.5)^c 1.0 (reference)	140 fewer per 1,000 (from 220 fewer to 70 fewer) (reference)
Success (in subsample with cavity)	≥6(H)RE 1-3Z 2SM ≥6(H)REZ	13	63/76 160/169	76	0.3 (0.1 to 0.9) 1.0 (reference)	120 fewer per 1,000 (from 230 fewer to 10 fewer) (reference)

Notes:

a) Number of pairs used in propensity score matched analysis.

b) Estimates based on pairs matched for age, sex, HIV status, past TB treatment, sputum AFB smear (positive vs negative) and resistance to other drugs besides isoniazid, if used. Percentage of patents missing information for these variables: past TB treatment: 8%; AFB smear: 2%; HIV 8%, polyresistance, age and sex: 0%. HIV status was missing, but assumed to be negative in 3 studies (n =720 patients) in settings where the prevalence of HIV co-infection rate in patients with active TB was <5% based on WHO surveillance data.

c) Estimates in subsample with CXR info are based on pairs matched also for cavity, in addition to other covariates used (i.e. age, sex, HIV status, past TB treatment, sputum AFB smear (positive vs negative) and resistance to other drugs besides isoniazid, if used.

d) Models did not converge, and/or zero outcomes for one group in this analysis

Abbreviations: aOR: adjusted odds ratio; CI Confidence interval; CXR: Chest-x ray; E: ethambutol; (H)= isoniazid used in some, but not all regimens SM:

TABLE S10. Duration of use of fluoroquinolones and treatment success, or acquired rifampin resistance.

Outcome and comparison	Regimens: FQ Comparator	N datasets included	N of events/N on treatment	N pairs used ^c	from Propensity Score matched Analysis ^d	
					aOR (95% CI)	Risk Difference (per 1,000 treated with 95%CI)
Analyses in all patients (with or without isoniazid)						
Success (All duration of FQ, REZ for ≥6months)	≥6(H)REZ FQ ≥6(H)REZ	15	245/251 1253/1350	248	2.8 (1.1 to 7.3) 1.0 (reference)	50 more per 1,000 (from 0 difference to 90 more) (reference)
Success: in subsample FQ 1- 5months	≥6(H)REZ 1-5FQ ≥6(H)REZ	15	106/108 1253/1350	108	4.2 (0.9 to 20.9) 1.0 (reference)	70 more per 1,000 (from 10 fewer to 150 more) (reference)
Success: in subsample FQ ≥6months	≥6(H)REZ ≥6FQ ≥6(H)REZ	15	129/133 1253/1350	131	2.1 (0.6 to 7.1) 1.0 (reference)	30 more per 1,000 (from 20 fewer to 90 more) (reference)
Acquired rifampin resistance	≥6(H)REZ FQ ≥6(H)REZ	10	1/221 ^b 44/1160 ^b	220	0.1 (0.0 to 1.2) 1.0 (reference)	30 fewer per 1,000 (from 60 fewer to 0 difference) (reference)
Acquired rifampin resistance: in subsample FQ 1-5months	≥6(H)REZ 1-5FQ ≥6(H)REZ	15	0/106 44/1160	-	not estimable 1.0 (reference)	not estimable (reference)
Acquired rifampin resistance: in subsample FQ ≥6months	≥6(H)REZ ≥6FQ ≥6(H)REZ	15	1/107 1253/1350	107	0.2 (0.0 to 2.3) 1.0 (reference)	30 fewer per 1,000 (from 10 fewer to 30 more) (reference)

Notes:

a) Of the 165 treated, 67 received isoniazid for one month or more and 98 did not receive any Isoniazid;

b) Number treated is less than in success analysis because patients with fail/relapse but no acquired drug resistance or with non-rifampin acquired resistances were excluded from this analysis.

c) Number of pairs used in propensity score matched analysis.

d) Estimates based on pairs matched for age, sex, HIV status, past TB treatment, sputum AFB smear(positive vs negative) and resistance to other drugs besides ISONIAZID, if used. Percentage of patents missing information for these variables: past TB treatment: 8%; AFB smear: 8%; HIV 8%, polyresistance, age and sex: 0%. HIV was missing, but assumed to be negative in 3 studies (n=1164 patients) in settings where the prevalence of HIV coinfection rate in patients with active TB was <5%, based on WHO surveillance data.

Abbreviations: aOR: adjusted odds ratio; CI Confidence interval E: ethambutol; (H)= isoniazid used in some, but not all regimens; SM: streptomycin; R: rifampin; Z: pyrazinamide; FQ: fluoroquinolone.

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