

Supplementary File 8

In order to assess the impact of any documented treatment non-adherence on the regimen-outcomes relationship, thrice weekly treatment was swapped for an adherence variable within the multivariable model. Evidence for effect modification between regimen and adherence was not detected. The inclusion of this variable did not have an appreciable impact on the effect estimate for treatment regimen (0.90 [0.50-1.63], 0.73; Supplementary File 8 Table 1). When individuals with any drug resistance pattern were included in the model the effect estimate also remained largely unaltered (0.98 [0.55-1.76], 0.94; Supplementary File 8 Table 2).

After finding a potential association between drug resistance and site of disease with the use of Fqs (Supplementary File 4 Table 2), *post hoc* these variables were also included the main multivariable model. No discernible difference in the odds of a negative outcome between the two regimens was detected (0.96 [0.51-1.83], 0.91).

Table 1: Sensitivity analysis- multivariable logistic regression of treatment regimen as a predictor of negative outcomes (adherence included)

Multivariable logistic regression of treatment regimen as a predictor of negative regimen-specific outcomes in patients without additional drug resistance, unless to streptomycin, adjusted for all variables in the table. Sensitivity analysis adjusting for adherence to treatment instead of thrice weekly dosing. Model contains 453 patients. CI- confidence interval, E- ethambutol, Fq- fluoroquinolones, H- isoniazid, m- months, M- moxifloxacin, OR- odds ratio, p- p-value, Rf- rifamycin, TB- tuberculosis, Z- pyrazinamide

Exposure variables		OR [95% CI], p-value
Regimen	[H]RfZE	p=0.73
	[H]RfZE-Fq/M	0.90 [0.50-1.63]
Adherence issues or treatment gaps	No or unknown	p=0.22
	Not severe or of unknown severity	2.02 [0.90-4.52]
	Severe	0.82 [0.31-2.17]
Phenotype	Highly resistant	p=0.32
	Resistant	0.62 [0.17-2.28]
	Borderline, sensitive or results not logged	2.01 [0.71-5.68]
	Missing	
Sex	Male	p=0.14
	Female	1.52 [0.87-2.65]
Age (years)	18-37	
	Per 20 year increase	1.08 [0.71-1.66]
Ethnic group	White	0.38 [0.14-1.00]
	Black African	0.34 [0.09-1.36]
	Black Other	0.52 [0.23-1.19]
	Indian subcontinent	1.02 [0.42-2.48]
	Other	
Previous TB diagnosis	No	2.70 [0.67-10.78]
	Yes	p=0.73

Table 2: Sensitivity analysis- multivariable logistic regression of treatment regimen as a predictor of negative outcomes (all patterns of drug resistance included)

Multivariable logistic regression of treatment regimen as a predictor of negative regimen-specific outcomes, adjusted for all variables in the table (including the presence of additional drug resistance). Sensitivity analysis including all individuals, regardless of drug resistance status. Model contains 459 patients. CI- confidence interval, E- ethambutol, Fq- fluoroquinolones, H- isoniazid, m- months, M- moxifloxacin, OR- odds ratio, p- p-value, Rf- rifamycin, TB- tuberculosis, Z- pyrazinamide

Exposure variables		OR [95% CI], p-value
Regimen	[H]RfZE	p=0.94
	[H]RfZE-Fq/M	0.98 [0.55-1.76]
Thrice weekly dosing	More frequent	p=0.01
	Thrice weekly	3.09 [1.31-7.33]
Phenotype	Highly resistant	p=0.68
	Resistant	0.62 [0.19-2.02]
	Borderline, sensitive or results not logged	1.17 [0.39-3.49]
Sex	Male	p=0.00
	Female	2.25 [1.28-3.95]
Age (years)	18-37	p=0.71
	Per 20 year increase	1.09 [0.70-1.69]
Ethnic group	White	p=0.08
	Black African	0.36 [0.13-0.97]
	Black Other	0.32 [0.09-1.17]
	Indian subcontinent	0.57 [0.24-1.35]
	Other	0.99 [0.39-2.52]
Previous TB diagnosis	No	p=0.03
	Yes	4.54 [1.22-16.83]
Any additional drug resistance	Absent	p=0.59
	Present	1.19 [0.64-2.21]