

## SUPPLEMENTAL MATERIALS

**Table S1:** The observed maximum concentrations of TB drugs by HbA1c% categories, crude and adjusted models

Cmax	Geometric Mean	GMR (95% CI)	p-value	Adj mean diff	p-value
<b>RMP</b>					
Both visits	3.57 (3.00 4.24)	Ref		Ref	
<5	3.51 (2.85 4.35)	.99 (.75 1.29)	.921	.93 (.70 1.24)	.639
5-6.5	3.92 (3.17 4.86)	1.10 (.84 1.43)	.482	1.00 (.72 1.40)	.982
>6.5					
Visit 1					
<5	4.54 (3.64 5.65)	Ref		Ref	
5-6.5	3.32 (2.49 4.43)	.73 (.51 1.05)	.086	1.03 (.78 1.36)	.836
>6.5	4.01 (3.06 5.25)	.88 (.63 1.25)	.475	.77 (.53 1.13)	.180
Visit 2					
<5	2.78 (2.14 3.61)	Ref		Ref	
5-6.5	3.76 (2.72 5.18)	1.35 (.90 2.04)	.147	1.26 (.81 1.95)	.309
>6.5	3.83 (2.69 5.44)	1.38 (.89 2.12)	.146	1.08 (.62 1.91)	.777
<b>INH</b>					
Both visits	7.58 (6.59 8.72)	Ref		Ref	
<5	7.40 (6.10 8.97)	.97 (.76 1.25)	.831	.96 (.75 1.24)	.781
5-6.5	6.63 (5.54 7.95)	.88 (.69 1.11)	.272	.87 (.64 1.17)	.357
>6.5					
Visit 1					
<5	7.87 (6.71 9.22)	Ref		Ref	
5-6.5	6.88 (5.19 9.11)	.76 (.57 1.02)	.407	.89 (.64 0.24)	.487
>6.5	6.00 (4.67 7.72)	.76 (.57 1.02)	.071	.84 (.60 1.19)	.324
Visit 2					
<5	7.29 (5.76 9.23)	Ref		Ref	
5-6.5	8.02 (6.12 10.50)	1.10 (.77 1.57)	.595	1.06 (.74 1.52)	.757
>6.5	7.54 (5.80 9.79)	1.03 (.73 1.46)	.849	.87 (.54 1.41)	.568
<b>PZA</b>					
Visit 1					
<5	31.43 (26.41	Ref		Ref	
5-6.5	37.41)	.95 (.71 1.29)	.751	1.02 (.71 1.46)	.910
>6.5	29.95 (23.36	.67 (.49 .89)	.006	1.22 (.74 2.01)	.430
	38.40)				
	20.74 (16.23				
	26.49)				

\*adjusted for age sex weight and baseline bacterial burden

**Table S2:** Exposure-response relationships between TB drugs and time to culture conversion, crude and adjusted model overall and crude model by diabetes status

	HR (95%CI)	p-value	Adj HR	p-value
DM	1.08 (.83 1.42)	.566	1.34 (.91 1.97)	.132
Age	.99 (.98 1.00)	.228	.98 (.97 .996)	.010
Sex	1.53 (1.14 2.06)	.004	1.75 (1.25 2.45)	.001
weight	1.00 (.99 1.01)	.840	1.01 (.995 1.02)	.231
Baseline Bacterial load	1.42 (1.20 1.68)	<.001	1.40 (1.18 1.66)	<.001
RMP	1.00 (.98 1.03)	.790	1.03 (1.00 1.05)	.049
INH	1.01 (.98 1.04)	.540	1.03 (.99 1.06)	.105
PZA	.99 (.98 .999)	.030	.99 (.97 .996)	.006
<b>No Diabetes</b>			<b>Diabetes</b>	
	Crude HR(95%CI)	p-value	Crude HR(95%CI)	p-value
Age	.98 (.97 .996)	.013	1.00 (.98 1.02)	.998
Sex	1.55 (1.07 2.24)	.022	1.62 (.99 2.64)	.055
weight	1.00 (.98 1.02)	.912	.998 (.98 1.02)	.858
Baseline Bacterial load	1.47 (1.16 1.88)	.002	1.35 (1.07 1.69)	.012
RMP	.97 (.92 1.02)	.222	1.03 (.998 1.06)	.070
INH	.99 (.95 1.02)	.451	1.05 (1.01 1.09)	.011
PZA	.99 (.98 1.01)	.275	.98 (.96 .996)	.018

**Table S3.A:** The proportion of patients with culture conversion to negative at week 8 and week 12, by diabetes status and HbA1c categories

% culture negative	Week 8 (7-9) N=209	p-value	Week 12(11-13) N=124	p-value
Diabetes				
No	(101)82.79%	.831	(69)93.24%	.794
Yes	(73)83.91%		(46)92%	
Hb1c				
<5.6	(80)84.21%	.571	(52)94.55%	.670
5.6 -6.5	(45)78.95%		(35)89.74%	
>6.5	(49)85.96%		(28)93.33%	
Hba1c				
<6.5	(122)84.14%	.606	(85)93.41%	.636
>6.5	(52)81.25%		(30)90.91%	

**Table S3.B:** The odds ratio of patients with culture conversion to negative in crude and adjusted model, by diabetes status

	<b>OR (95%CI)</b>	<b>p-value</b>	<b>Adj OR</b>	<b>p-value</b>
DM	1.08 (.52 2.28)	.831	1.54 (.59 4.04)	.381
Age	.98 (.95 1.01)	.120	.96 (.93 .999)	.044
Sex	2.47 (1.02 5.98)	.046	3.44 (1.25 9.45)	.016
Weight	1.012 (.98 1.04)	.392	1.03 (.99 1.07)	.144
Baseline bacterial load	1.77 (1.18 2.67)	.006	1.74 (1.14 2.65)	.011
RMP	1.02 (.95 1.12)	.541	1.08 (.97 1.20)	.175
INH	1.02 (.96 1.09)	.501	1.07 (.98 1.16)	.127
PZA	.98 (.96 1.01)	.143	.97 (.94 1.00)	.069
<b>No Diabetes</b>				
Age	.96 (.92 .996)	.033	.97 (.93 1.03)	.170
Sex	2.90 (.98 8.55)	.054	4.87 (1.50 15.85)	.008
Weight	1.02 (.97 1.07)	.503	1.07 (.99 1.16)	.09
Baseline bacterial load	1.54 (.96 2.45)	.072	1.50 (.93 2.42)	.097
RMP	1.01 (.87 1.17)	.909	1.07 (.90 1.26)	.445
INH	1.01 (.91 1.12)	.824	1.07 (.96 1.03)	.248
PZA	.99 (.96 1.02)	.507	.99 (.96 1.03)	.615
<b>Diabetes</b>				
Age	.99 (.93 1.04)	.615	.94 (.88 1.00)	.069
Sex	2 (.4 9.89)	.395	5.03 (.89 28.42)	.067
Weight	1.01 (.98 1.04)	.543	1.02 (.97 1.07)	.387
Baseline bacterial load	2.35 (1.02 5.40)	.045	2.72 (.91 8.16)	.074
RMP	1.04 (.96 1.12)	.360	1.09 (.97 1.23)	.132
INH	1.03 (.95 1.13)	.435	1.07 (.94 1.22)	.320
PZA	.98 (.94 1.01)	.185	.94 (.89 .99)	.017

**Table S4.A:** The incidence rate ratio of treatment failure, crude and adjusted model, by diabetes status

**Failure: overall analysis, stratified by diabetic status (over four months)**

N=23	IRR (95% CI)	p-value	Adj IRR (95% CI)	p-value
DM	.76 (.34 1.69)	.501	1.05 (.42 2.59)	.920
Age	.998 (.97 1.03)	.915	.99 (.95 1.02)	.537
Sex	1.08 (.49 2.38)	.858	.92 (.38 2.20)	.846
weight	.99 (.95 1.04)	.750	1.01 (.97 1.06)	.509
Baseline Bacterial load	.70 (.46 1.07)	.104	.66 (.42 1.06)	.088
RMP	.997 (.93 1.07)	.926	.96 (.89 1.04)	.331
INH	1.04 (.98 1.11)	.171	1.03 (.97 1.09)	.282
PZA	1.02 (.999 1.05)	.058	1.02 (1.0 1.05)	.049
<b>No Diabetes (n=15)</b>				
Age	.998 (.95 1.05)	.922	.96 (.90 1.03)	.295
Sex	.99 (.38 2.55)	.976	.66 (.24 1.85)	.435
weight	.98 (.93 1.04)	.535	.997 (.94 1.06)	.924
Baseline Bacterial load	.98 (.60 1.60)	.936	.997 (.59 1.68)	.990
RMP	1.04 (.95 1.14)	.393	.99 (.90 1.09)	.837
INH	1.05 (.96 1.16)	.278	1.00 (.93 1.08)	.905
PZA	1.03 (.995 1.06)	.096	1.03 (.999 1.06)	.058
<b>Diabetes (n=8)</b>				
Age	1.02 (.99 1.06)	.187	1.05 (.98 1.12)	.183
Sex	1.12 (.25 5.05)	.879	.57 (.06 5.53)	.630
weight	1.01 (.95 1.07)	.752	1.02 (.96 1.09)	.493
Baseline Bacterial load	.30 (.16 .53)	<.001	.21 (.10 .48)	<.001
RMP	.93 (.81 1.07)	.301	.91 (.70 1.18)	.492
INH	1.03 (.96 1.10)	.426	1.12 (1.03 1.21)	.006
PZA	1.02 (.98 1.06)	.401	1.03 (.97 1.10)	.344

**Table S4.B:** The incidence rate ratio of failure, crude and adjusted model, among patients with HbA1c% values above 8%

**Failure if HbA1c $\geq$ 8 (n=5)**

	IRR (95% CI)	p-value	Adj IRR (95% CI)	p-value
Age	.999 (.94 1.06)	.968	1.04 (.93 1.16)	.499
Sex	1.05 (.13 8.24)	.966	.30 (.01 17.021)	.558
weight	.96 (.91 1.01)	.124	.99 (.95 1.03)	.613
Baseline Bacterial load	.36 (.18 .72)	.004	.22 (.05 .90)	.035
RMP	.91 (.73 1.14)	.413	.70 (.40 1.22)	.205
INH	1.07 (.99 1.15)	.097	1.18 (.98 1.41)	.078
PZA	1.08 (1.04 1.12)	<.001	1.12 (.99 1.27)	.075

**Table S4.C:** The incidence rate ratio of treatment relapse, crude and adjusted model, by diabetes status

**Relapse:**

N=28/218	IRR (95% CI)	p-value	Adj IRR (95% CI)	p-value
DM	1.02 (.49 2.10)	.967	1.31 (.45 3.85)	.618
Age	.99 (.97 1.02)	.592	.99 (.95 1.03)	.569
Sex	.97 (.45 2.09)	.944	.93 (.40 2.15)	.860
weight	.99 (.96 1.02)	.497	.99 (.96 1.03)	.752
Baseline Bacterial load	.71 (.49 1.05)	.087	.68 (.44 1.04)	.076
RMP	.99 (.92 1.06)	.733	.98 (.91 1.06)	.558
INH	1.03 (.97 1.08)	.369	1.02 (.96 1.09)	.499
PZA	1.01 (.99 1.04)	.329	1.01 (.98 1.05)	.498
<b>No Diabetes (n=16)</b>				
Age	1.02 (.98 1.05)	.326	1.01 (.97 1.05)	.782
Sex	1.18 (.45 3.06)	.736	1.49 (.51 4.35)	.470
weight	.99 (.92 1.07)	.863	1.03 (.96 1.10)	.472
Baseline Bacterial load	.64 (.37 1.09)	.102	1.53 (.30 .93)	.027
RMP	1.01 (.92 1.10)	.906	.96 (.87 1.07)	.466
INH	1.11 (1.03 1.20)	.007	1.14 (1.03 1.27)	.012
PZA	1.02 (.98 1.06)	.433	1.00 (.96 1.05)	.832
<b>Diabetes (n=12)</b>				
Age	.96 (.91 1.01)	.111	.96 (.90 1.02)	.190
Sex	.66 (.15 2.90)	.582	1.00 (.20 4.96)	.999
weight	.98 (.94 1.02)	.325	.97 (.93 1.01)	.184

Baseline Bacterial load	.83 (.50 1.40)	.492	.83 (.49 1.39)	.471
RMP	.98 (.88 1.09)	.654	1.00 (.90 1.12)	.987
INH	.95 (.87 1.04)	.241	.86 (.76 .97)	.016
PZA	1.01 (.97 1.05)	.606	1.02 (.98 1.07)	.356

**Table S4.D:** The incidence rate ratio of overall-cause death, crude and adjusted model, by diabetes status

**Death:**

N=14	IRR (95% CI)	p-value	Adj IRR (95% CI)	p-value
DM	.87 (.28 2.69)	.814	.87 (.19 3.93)	.862
Age	1.01(.97 1.05)	.620	1.02 (.98 1.06)	.339
Sex	.37 (.08 1.65)	.192	.34 (.04 2.56)	.293
weight	.97 (.92 1.03)	.310	.96 (.87 1.07)	.481
Baseline Bacterial load	.61 (.35 1.07)	.083	.69 (.96 1.14)	.170
RMP	1.06 (.98 1.14)	.158	1.04 (.96 1.14)	.357
INH	1.03 (.91 1.15)	.676	1.03 (.88 1.21)	.724
PZA	1.01(.96 1.06)	.740	1.00 (.95 1.06)	.945
<b>No Diabetes (n=8)</b>				
Age	1.01 (.96 1.06)	.675	.999 (.94 1.06)	.968
Sex	.21 (.03 1.70)	.143	.21 (.01 4.69)	.322
weight	.99 (.90 1.10)	.918	1.03 (.82 1.29)	.784
Baseline Bacterial load	.70 (.36 1.36)	.293	.92 (.45 1.89)	.815
RMP	1.16 (1.04 1.29)	.007	1.18 (.99 1.40)	.062
INH	1.04 (.88 1.23)	.650	.96 (.78 1.16)	.667
PZA	1.03 (.95 1.11)	.497	1.04 (.92 1.17)	.523
<b>Diabetes (n=6)</b>				
Age	1.04 (.95 1.12)	.412	1.04 (.97 1.11)	.267
Sex	.86 (.10 7.65)	.890	.54 (.02 12.18)	.695
weight	.94 (.85 1.05)	.271	.94 (.83 1.08)	.382
Baseline Bacterial load	.47 (.17 1.31)	.150	.48 (.17 1.34)	.161
RMP	.95 (.78 1.16)	.624	.94 (.83 1.07)	.372
INH	1.01 (.84 1.21)	.923	1.05 (.78 1.41)	.737
PZA	.99 (.92 1.06)	.734	.99 (.90 1.08)	.800

**Table S4.F:** The odds ratio of overall unfavorable effects (failure, relapse or death), crude and adjusted model, by diabetes status

**Overall unfavorable events: (failure or relapse or death)**

N=61	OR (95% CI)	p-value	*Adj OR	p-value
DM	1.06 (.59 1.92)	.836	1.43 (.62 3.27)	.403
Age	1.00 (.98 1.02)	.884	.99 (.96 1.02)	.554
Sex	1.00 (.54 1.86)	.999	.88 (.42 1.83)	.727
weight	.99 (.96 1.02)	.416	.99 (.96 1.03)	.747
Baseline Bacterial load	.66 (.48 .91)	.011	.66 (.47 .93)	.017
RMP	1.00 (.95 1.06)	.977	.99 (.92 1.06)	.716
INH	1.03 (.98 1.08)	.319	1.03 (.97 1.09)	.404
PZA	1.01 (.99 1.04)	.181	1.01 (.99 1.04)	.405
<b>No Diabetes (n=35)</b>				
Age	1.01 (.97 1.04)	.697	.99 (.95 1.03)	.512
Sex	1.02 (.47 2.24)	.952	1.06 (.41 2.75)	.900
weight	.99 (.94 1.04)	.679	1.02 (.96 1.08)	.593
Baseline Bacterial load	.71 (.46 1.10)	.125	.96 (.43 1.11)	.126
RMP	1.07 (.98 1.16)	.122	1.03 (.97 1.17)	.615
INH	1.08 (1.00 1.16)	.049	1.07 (.97 1.05)	.177
PZA	1.02 (.99 1.05)	.206	1.01 (.98 1.05)	.580
<b>Diabetes (n=26)</b>				
Age	.99 (.95 1.04)	.739	.99 (.95 1.04)	.832
Sex	1.01 (.35 2.92)	.991	.81 (.21 3.10)	.763
weight	.98 (.94 1.02)	.368	.98 (.93 1.03)	.345
Baseline Bacterial load	.45 (.27 .85)	.012	.49 (.28 .88)	.016
RMP	.94 (.85 1.04)	.226	.96 (.87 1.05)	.365
INH	.97 (.91 1.05)	.483	.97 (.87 1.07)	.526
PZA	1.01 (.98 1.04)	.560	1.01 (.97 1.06)	.498

\*adjusted for age sex weight baseline bacterial load



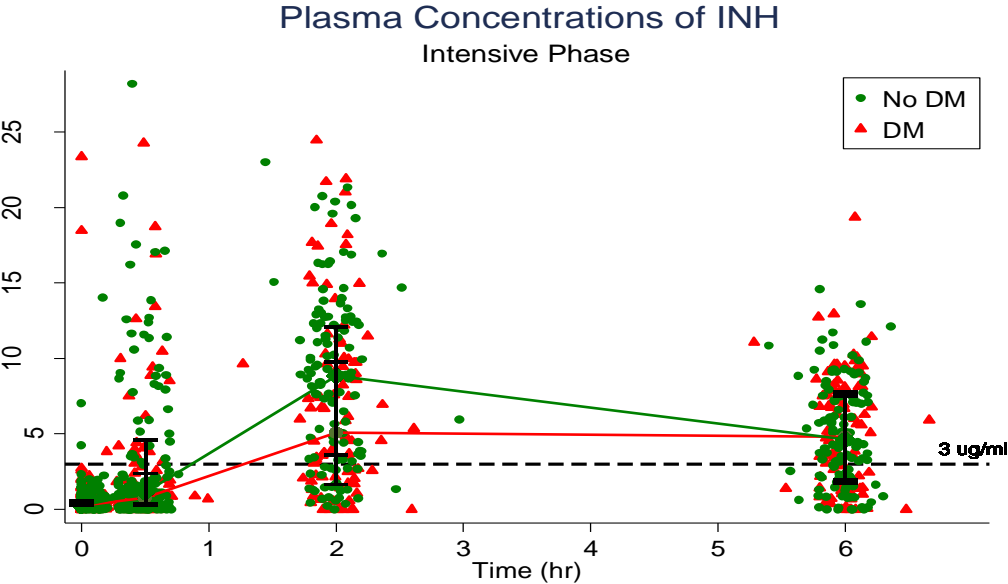
**Table S5.A:** Overall unfavorable effects by drug concentration above or below the therapeutic target

	N(%)	OR	95% CI	p-value
<b>PZA</b>				
Below the TTC	20 (19.42%)	1.92	1.03 3.59	.041
Above the TTC	37 (31.62%)			
<b>INH</b>				
Below the TTC	8 (22.86%)	1.18	.50 2.75	.707
Above the TTC	53 (25.85%)			
<b>RMP</b>				
Below the TTC	46 (23.96%)	1.44	.72 2.89	.302
Above the TTC	15 (31.25%)			

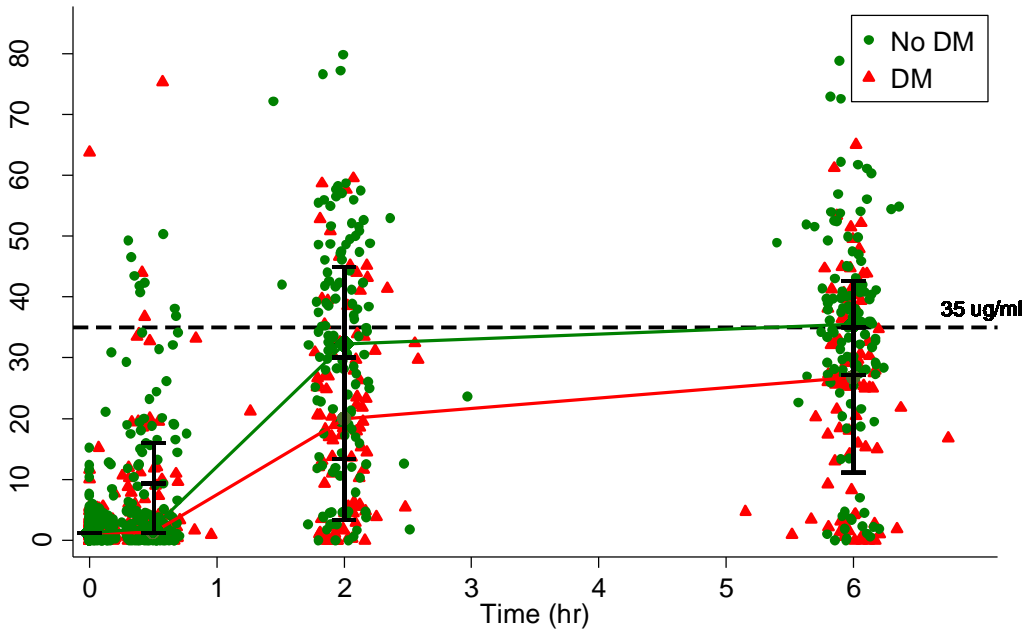
**Table S5.B:** Overall unfavorable effects by HbA1c values above or below 8%

	HbA1c<8%				HbA1c>=8%			
	N(%)	OR	95% CI	p-value	N(%)	OR	95% CI	p-value
<b>PZA</b>								
Below the TTC	16(26.23%)	1.34	.66- 2.74	.421	4(9.52%)	3.8	.93 - 15.57	.064
Above the TTC	31(32.29%)				6(28.57%)			
<b>INH</b>								
Below the TTC	7(33.33%)	.81	.31- 2.16	.681	1(7.14%)	2.66	.30- 23.36	.378
Above the TTC	44(28.95%)				9(16.98%)			
<b>RMP</b>								
Below the TTC	39(28.47%)	1.26	.57- 2.76	.570	7(12.93%)	2.29	.49- 10.66	.293
Above the TTC	12(33.33%)				3(25%)			

**Figure S1.** Concentration-time profiles of rifampicin (Panel A), isoniazid (Panel B), and pyrazinamide (Panel C) during the intensive phase of TB treatment.



### Plasma Concentrations of PZA Intensive Phase



### Plasma Concentrations of RMP Intensive Phase

