Online Data Supplement

Isoniazid-Monoresistance and Rate of Culture Conversion among Confirmed Tuberculosis Patients in the State of Georgia, 2009 – 2014

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Supplemental Table 1. Comparison between clinical TB and culture-confirmed TB patients in the state of Georgia, 2009 – 2014 (N=2049)

Characteristics	Clinical TB[†] N (%) = 863 (42.1) N (%)	Culture-confirmed TB N (%) = 1186 (57.9) N (%)	Total N = 2049 N (%)	P-value[‡]
Age				
15 – 24	87 (10.1)	140 (11.8)	227 (11.1)	0.02*
25 – 44	322 (37.3)	438 (36.9)	760 (37.1)	
45 – 64	296 (34.3)	447 (37.7)	743 (36.3)	
≥ 65	158 (18.3)	161 (13.6)	319 (15.6)	
Gender				
Female	330 (38.2)	347 (29.3)	677 (33.0)	<0.001*
Male	533 (61.8)	839 (70.7)	1372 (67.0)	
Race				
White, Non-Hispanic	122 (14.3)	173 (14.7)	295 (14.6)	0.01*
Black, Non-Hispanic	413 (48.5)	580 (49.3)	993 (48.9)	
Hispanic, all races	131 (15.4)	225 (19.1)	356 (17.6)	
Asian, Non-Hispanic	186 (21.8)	198 (16.8)	384 (18.9)	
Missing	11	10	21	
Foreign Born				
No	440 (51.0)	648 (54.6)	1088 (53.1)	0.10
Yes	423 (49.0)	538 (45.4)	961 (46.9)	
Occupation				
Employed	326 (38.5)	487 (41.6)	813 (40.3)	0.14
Unemployed	322 (38.0)	450 (38.4)	772 (38.2)	
Ineligible for employment	199 (23.5)	235 (20.1)	434 (21.5)	
Missing	16	14	30	
Homelessness				
No	805 (93.7)	1013 (85.5)	1818 (88.9)	<0.001*
Yes	54 (6.3)	172 (14.5)	226 (11.1)	
Missing	4	1	5	
Illicit Drug Use				
No	795 (93.6)	1038 (87.8)	1833 (90.3)	<0.001*
Yes	54 (6.4)	144 (12.2)	198 (9.8)	
Missing	14	4	18	
HIV Status				
Negative	700 (88.4)	980 (86.7)	1680 (87.4)	0.26
Positive	92 (11.6)	151 (13.4)	243 (12.6)	
Missing	71	55	126	
Diabetes Status				
Negative	739 (89.0)	998 (86.7)	1737 (87.7)	0.12
Positive	91 (11.0)	153 (13.3)	244 (12.3)	
Missing	33	35	68	

Abbreviations: HIV – human immunodeficiency virus;
[†]Including patients with missing culture results
[‡]Chi square or Fisher's exact test p-value
*Indicates that the finding is statistically significant at level of confidence of 5% (P-value 0.05)

Supplemental Table 2. Univariate and multivariable models for odds of INH-monoresistant TB among adult patients with pulmonary TB, Georgia, 2009 – 2014 (N=1141)

Models	Odds Ratios (95% Confidence Interval)	P-value	Covariates included in the model

Crude
  HIV Negative
  HIV Positive
	
	1.00
	3.14 (2.04 – 4.76)*
		
		<0.001
			N/A

Model 1
  HIV Negative
  HIV Positive
	
	1.00
	1.46 (0.75 – 2.65)
		
		0.23
			HIV and genotype

Model 2[†]
  HIV Negative
  HIV Positive
	
	1.00
	1.85 (1.08 – 3.13)*
		
		0.02
			Age, gender, race, foreign born, occupation, homelessness, TB history, illicit drug use, HIV status, diabetes, cavitary disease, and miliary disease

Model 3
  HIV Negative
  HIV Positive
	
	1.00
	1.57 (0.75 – 3.13)
		
		0.22
			Age, gender, race, foreign born, occupation, homelessness, TB history, illicit drug use, HIV status, diabetes, cavitary disease, miliary disease, and genotype information

[†]Model reported in manuscript
*Indicates that the finding is statistically significant at level of confidence of 5% (P-value 0.05)

Supplemental Table 3. Multivariable models for cause-specific proportional hazard among adult patients with pulmonary TB, Georgia, 2009 – 2014 (N=1116)

Characteristics	Converted 956/1116[†] (85.7%) N %	Median (IQR)[‡] 30 (13 – 58)	Conventional Cox Proportional Hazards Model		Cause-Specific Hazard Model			
					Culture Conversion		Death	
			aHR[§] (95% CI)	p-value for aHR	aHR[§] (95% CI)	p-value for aHR	aHR[§] (95% CI)	p-value for aHR
INH-monoresistance								
No	826/976 (84.6)	32 (13 – 59)	1.00		1.00		1.00	
Yes	130/140 (92.9)	27 (10 – 51)	1.15 (0.95 – 1.39)	0.16	1.15 (0.95 – 1.40)	0.17	1.40 (0.59 – 3.28)	0.45
Age								
15 – 24	107/131 (81.7)	27 (12 – 50)	1.00		1.00		1.00	
25 – 44	360/412 (87.4)	26 (11 – 53)	0.98 (0.79 – 1.23)	0.89	1.01 (0.81 – 1.26)	0.93	0.40 (0.07 – 2.19)	0.29
45 – 64	376/422 (87.0)	39 (14 – 64)	0.84 (0.67 – 1.05)	0.12	0.80 (0.64 – 1.00)*	0.049	2.80 (0.65 – 12.02)	0.16
≥ 65	122/151 (80.8)	33 (14 – 57)	1.01 (0.77 – 1.32)	0.94	0.90 (0.68 – 1.19)	0.45	6.28 (1.40 – 28.10)*	0.02
Gender								
Female	289/325 (88.9)	29 (13 – 55)	1.00		1.00		1.00	
Male	667/791 (84.3)	32 (13 – 59)	0.93 (0.81 – 1.07)	0.31	0.91 (0.79 – 1.05)	0.18	1.79 (0.85 – 3.77)	0.12
Race								
White, Non-Hispanic	136/159 (85.5)	46 (17 – 81)						
Black, Non-Hispanic	482/556 (86.7)	31 (13 – 56)						
Hispanic, all races	163/208 (78.4)	33 (13 – 56)						
Asian, Non-Hispanic	165/183 (90.2)	25 (10 – 48)						
Foreign born								
No	532/617 (86.2)	35 (13 – 62)						
Yes	424/499 (85.0)	28 (13 – 53)						
Occupation								
Employed	408/454 (89.9)	32 (14 – 58)						
Unemployed	367/424 (86.6)	30 (11 – 56)						
Ineligible for employment, student, retired	176/226 (77.9)	34 (13 – 66)						
Homelessness								
No	813/952 (85.4)	31 (12 – 59)	1.00		1.00		1.00	
Yes	142/163 (87.1)	30 (14 – 55)	1.19 (0.98 – 1.44)	0.08	1.22 (1.00 – 1.48)*	0.049	0.68 (0.29 – 1.62)	0.39
History of								

Characteristics	Converted 956/1116[†] (85.7%) N %	Median (IQR)[‡] 30 (13 – 58)	Conventional Cox Proportional Hazards Model		Cause-Specific Hazard Model			
					Culture Conversion		Death	
			aHR[§] (95% CI)	p-value for aHR	aHR[§] (95% CI)	p-value for aHR	aHR[§] (95% CI)	p-value for aHR
imprisonment								
No	901/1037 (86.9)	32 (13 – 59)						
Yes	51/55 (92.7)	22 (6 – 45)						
Resident of Long Term Care Facility								
No	946/1100 (86.0)	31 (13 – 58)						
Yes	9/15 (60.0)	28 (22 – 33)						
TB History								
No	900/1052 (85.6)	31 (13 – 58)						
Yes	56/64 (87.5)	24 (8 – 60)						
Illicit drug use								
No	834/974 (85.6)	32 (13 – 58)						
Yes	120/138 (87.0)	26 (11 – 58)						
Alcohol abuse								
No	771/902 (85.5)	30 (12 – 58)						
Yes	181/208 (87.0)	33 (15 – 58)						
HIV Status								
Negative	808/925 (87.4)	34 (14 – 59)	1.00		1.00		1.00	
Positive	122/141 (86.5)	18 (8 – 39)	1.23 (1.01 – 1.50)*	0.042	1.14 (0.92 – 1.40)	0.22	4.15 (1.98 – 8.71)*	<0.001
Missing	26/50 (52.0)	30 (10 – 64)						
Diabetes Status								
No	812/940 (86.9)	29 (12 – 56)	1.00		1.00		1.00	
Yes	121/142 (85.2)	51 (27 – 65)	0.88 (0.73 – 1.07)	0.19	0.87 (0.71 – 1.06)	0.16	1.17 (0.56 – 2.48)	0.68
Missing	23/34 (67.7)	25 (2 – 59)						
History of LTBI Prophylaxis								
No	893/1039 (86.0)	30 (13 – 58)						
Yes	40/43 (93.0)	36 (20 – 57)						
Baseline TST								
Negative	202/236 (85.6)	35 (18 – 64)	1.00		1.00		1.00	
Positive	471/523 (90.1)	32 (13 – 58)	1.13 (0.96 – 1.34)	0.15	1.14 (0.96 – 1.36)	0.13	0.58 (0.24 – 1.42)	0.23
Not Done/Missing	283/357 (79.3)	28 (10 – 52)						

Characteristics	Converted 956/1116[†] (85.7%) N %	Median (IQR)[‡] 30 (13 – 58)	Conventional Cox Proportional Hazards Model aHR[§] (95% CI)	p-value for aHR	Cause-Specific Hazard Model — Culture Conversion aHR[§] (95% CI)	p-value for aHR	Cause-Specific Hazard Model — Death aHR[§] (95% CI)	p-value for aHR
Baseline Smear								
Negative	290/348 (83.3)	14 (1 – 38)	1.00		1.00		1.00	
Positive	665/762 (87.3)	39 (19 – 63)	0.65 (0.5 – 0.75)*	<0.001	0.60 (0.52 – 0.69)*	<0.001	1.79 (0.92 – 3.48)	0.09
Baseline CXR Reading								
Normal	60/68 (88.2)	14 (1 – 45)						
Abnormal	848/980 (86.5)	32 (14 – 59)						
Cavitary Disease								
No	566/671 (84.4)	24 (8 – 50)						
Yes	333/370 (90.0)	43 (22 – 65)						
Miliary Disease								
No	868/997 (87.1)	31 (13 – 58)						
Yes	26/32 (81.3)	24 (11 – 58)						
TB Site								
Pulmonary only	870/1016 (85.6)	33 (14 – 59)						
Pulmonary + extrapulmonary	86/100 (86.0)	21 (7 – 46)						
TB Treatment Duration								
≤ 6 months	85/183 (46.5)	28 (14 – 48)						
7-12 months	765/820 (93.3)	30 (12 – 57)						
> 12 months	106/113 (93.8)	39 (19 – 77)						

Abbreviations: IQR – Inter Quartile Range; AHR - Adjusted Hazard Ratio; TB – Tuberculosis; HIV – human immunodeficiency virus; LTBI - Latent Tuberculosis Infection; TST – Tuberculin Skin Test; CXR – Chest X-Ray; INH – Isoniazid;

[†]Patients converted with positive culture at baseline

[‡]Among patients who converted, median time (measured in days) from the initial TB treatment until date of sputum culture conversion

[§]Adjusted hazard ratio after controlling for age, gender, HIV status, diabetes status, TST at baseline, smear status, and INH-monoresistance

*Indicates that the finding is statistically significant at level of confidence of 5% (p-value < 0.05)

Appendix Table 1. Unadjusted and adjusted odds ratios for poor final TB treatment outcome among patients with culture-confirmed TB in the state of Georgia, USA, 2009 – 2014 (N=1087)

Variable	Odds Ratio	
	COR (95% CI)	AOR (95% CI) [†]
INH-monoresistant TB		
No	1.00	1.00
Yes	1.06 (0.59 – 1.80)	1.61 (0.67 – 3.70)
Age		
15 – 24	1.00	1.00
25 – 44	1.10 (0.48 – 2.81)	0.70 (0.24 – 2.21)
45 – 64	2.29 (1.08 – 5.66)*	1.48 (0.54 – 4.51)
≥ 65	5.67 (2.57 – 14.33)*	2.84 (0.95 – 9.27)
Gender		
Female	1.00	1.00
Male	1.58 (1.02 – 2.54)*	1.61 (0.84 – 3.19)
Race/Ethnicity		
White, Non-Hispanic	1.00	
Black, Non-Hispanic	1.28 (0.74 – 2.35)	
Hispanic, all races	1.13 (0.57 – 2.28)	
Asian, Non-Hispanic	0.59 (0.26 – 1.30)	
Foreign born		
No	1.00	
Yes	0.75 (0.51 – 1.11)	
Occupation		
Employed	1.00	
Unemployed	1.93 (1.21 – 3.12)*	
Ineligible for employment, student, retired	2.92 (1.75 – 4.92)*	
Homelessness		
No	1.00	
Yes	1.00 (0.57 – 1.66)	
History of imprisonment		
No	1.00	
Yes	0.33 (0.05 – 1.07)	
Resident of Long Term Care Facility		
No	1.00	
Yes	1.65 (0.25 – 6.36)	
Contact with TB Patient		
No	1.00	
Yes	0.41 (0.17 – 0.84)*	
TB History		
No	1.00	
Yes	0.87 (0.33 – 1.90)	
Illicit drug use		
No	1.00	
Yes	0.93 (0.49 – 1.62)	
Alcohol abuse		
No	1.00	
Yes	1.62 (1.03 – 2.50)*	
HIV Status		

Variable	Odds Ratio	
	COR (95% CI)	AOR (95% CI) [†]
Negative	1.00	1.00
Positive	2.25 (1.37 – 3.60)*	3.80 (1.78 – 8.17)*
Diabetes Status		
No	1.00	
Yes	1.73 (1.04 – 2.80)*	
ESRD		
No	1.00	
Yes	5.18 (1.73 – 14.24)*	
Baseline TST		
Negative	1.00	
Positive	0.40 (0.24 – 0.66)*	
Baseline Smear		
Negative	1.00	1.00
Positive	1.23 (0.81 – 1.91)	2.83 (1.50 – 5.55)*
Baseline CXR Reading		
Normal	1.00	
Abnormal	1.37 (0.63 – 3.62)	
Cavitary Disease		
No	1.00	
Yes	1.01 (0.66 – 1.51)	
Miliary Disease		
No	1.00	
Yes	1.64 (0.55 – 4.04)	
Site of Disease		
Pulmonary	0.38 (0.15 – 1.19)	
Pulmonary + extrapulmonary	0.67 (0.23 – 2.27)	
Extrapulmonary only	1.00	
Treatment Duration		
≤ 6 months	1.00	1.00
7-12 months	0.01 (0.01 – 0.02)*	0.01 (0.01 – 0.02)*
> 12 months	0.02 (0.01 – 0.05)*	0.02 (0.01 – 0.04)*

[†]Model adjusted for INH-monoresistant TB, age, gender, HIV status, smear and TB treatment duration

*Indicates that the finding is statistically significant at level of confidence of 5% (p-value < 0.05)

Appendix Table 2: Covariate selection sensitivity analyses of multivariable hazard models for sputum culture conversion among adult patients with pulmonary TB, Georgia, 2009 – 2014 (N=1116)

Models	Hazard Ratio (95% Confidence Interval)	P-value	Covariates included in the model
Crude 　No INH-monoresistant 　INH-monoresistant	 1.00 1.17 (0.97 – 1.41)	 0.10	N/A
Model 1 　No INH-monoresistant 　INH-monoresistant	 1.00 1.21 (1.00 – 1.46)*	 0.046	Age and gender
Model 2 　No INH-monoresistant 　INH-monoresistant	 1.00 1.17 (0.96 – 1.41)	 0.11	Age, gender, HIV status, and diabetes status
Model 3 　No INH-monoresistant 　INH-monoresistant	 1.00 1.17 (0.97 – 1.41)	 0.11	Age, gender, HIV status, diabetes status, and TST result
Model 4 　No INH-monoresistant 　INH-monoresistant	 1.00 1.14 (0.94 – 1.39)	 0.19	Age, gender, HIV status, diabetes status, TST result, and homelessness
Model 5[†] 　No INH-monoresistant 　INH-monoresistant	 1.00 1.15 (0.94 – 1.39)	 0.17	Age, gender, HIV status, diabetes status, TST result, homelessness, and smear status
Model 6 　No INH-monoresistant 　INH-monoresistant	 1.00 1.08 (0.89 – 1.32)	 0.44	Age, gender, HIV status, diabetes status, TST result, homelessness, and cavitary disease
Model 7 　No INH-monoresistant 　INH-monoresistant	 1.00 1.16 (0.95 – 1.41)	 0.14	Age, gender, race, HIV status, diabetes status, TST result, homelessness, and smear status
Model 8 　No INH-monoresistant 　INH-monoresistant	 1.00 1.15 (0.94 – 1.39)	 0.18	Age, gender, HIV status, diabetes status, TST result, homelessness, history of imprisonment, and smear status
Model 9 　No INH-monoresistant 　INH-monoresistant	 1.00 1.15 (0.94 – 1.40)	 0.17	Age, gender, HIV status, diabetes status, TST result, homelessness, history of imprisonment, alcohol, and smear status
Model 10 　No INH-monoresistant 　INH-monoresistant	 1.00 1.15 (0.94 – 1.40)	0.08	Age, gender, HIV status, diabetes status, TST result, homelessness, history of imprisonment, alcohol, illicit drug use, and smear status

[†]Model used in the manuscript
*Indicates that the finding is statistically significant at level of confidence of 5% (p-value < 0.05)

Appendix Table 3: Effect modification between INH-monoresistant TB and key characteristic of patients with culture-confirmed TB in the state of Georgia, USA, 2009 – 2014 (N=1116)

Interaction Covariates		INH-monoresistant TB	Conversion (%)	Hazard Rate[†] (95% CI)	Adjusted Hazard[‡] Rate (95% CI)
Gender	Female	No	263/299 (88.0)	1.00	1.00
		Yes	26/26 (100.0)	1.22 (0.81 – 1.83)	1.03 (0.67 – 1.57)
	Male	No	563/677 (83.2)	1.00	1.00
		Yes	104/114 (91.2)	1.17 (0.95 – 1.45)	1.14 (0.90 – 1.43)
Race	Other	No	422/505 (83.6)	1.00	1.00
		Yes	50/53 (94.3)	1.10 (0.82 – 1.48)	1.12 (0.82 – 1.53)
	Black	No	402/469 (85.7)	1.00	1.00
		Yes	80/87 (92.0)	1.22 (0.96 – 1.56)	1.18 (0.91 – 1.53)
Foreign Born	No	No	443/520 (85.2)	1.00	1.00
		Yes	89/97 (91.8)	1.21 (0.96 – 1.52)	1.14 (0.89 – 1.47)
	Yes	No	383/456 (84.0)	1.00	1.00
		Yes	41/43 (95.4)	1.25 (0.90 – 1.73)	1.19 (0.86 – 1.67)
TB History	No	No	779/921 (84.6)	1.00	1.00
		Yes	121/131 (12.5)	1.14 (0.94 – 1.38)	1.12 (0.92 – 0.37)
	Yes	No	47/55 (85.5)	1.00	1.00
		Yes	9/9 (100.0)	1.96 (0.92 – 4.17)	1.05 (0.42 – 2.64)
Alcohol	No	No	668/792 (84.3)	1.00	1.00
		Yes	103/110 (93.6)	1.24 (1.01 – 1.53)*	1.18 (0.95 – 1.48)
	Yes	No	154/178 (86.5)	1.00	1.00
		Yes	27/30 (90.0)	0.94 (0.62 – 1.42)	0.88 (0.56 – 1.40)
Homelessness	No	No	741/875 (84.7)	1.00	1.00
		Yes	72/77 (93.5)	1.03 (0.81 – 1.31)	1.04 (0.81 – 1.33)
	Yes	No	84/100 (84.0)	1.00	1.00
		Yes	58/63 (92.1)	1.51 (1.07 – 2.13)*	1.40 (0.94 – 2.10)
HIV	No	No	716/828 (86.5)	1.00	1.00
		Yes	92/97 (94.9)	1.10 (0.89 – 1.37)	1.11 (0.88 – 1.38)
	Yes	No	87/103 (84.5)	1.00	1.00
		Yes	35/38 (92.1)	1.08 (0.73 – 1.60)	1.04 (0.63 – 1.72)
	Missing	No	23/45 (51.1)	1.00	
		Yes	3/5 (60.0)	1.39 (0.41 – 4.73)	
Diabetes	No	No	694/813 (85.4)	1.00	1.00
		Yes	118/127 (92.9)	1.18 (0.97 – 1.43)	1.15 (0.94 – 1.42)
	Yes	No	109/129 (84.5)	1.00	1.00
		Yes	12/13 (92.3)	0.99 (0.53 – 1.85)	1.01 (0.53 – 1.92)
TST	Negative	No	169/199 (84.9)	1.00	1.00
		Yes	33/37 (89.2)	1.29 (0.89 – 1.88)	1.29 (0.86 – 1.96)
	Positive	No	415/464 (89.4)	1.00	1.00
		Yes	56/59 (94.9)	1.28 (0.96 – 1.69)	1.24 (0.92 – 1.67)
Smear	Negative	No	247/303 (81.5)	1.00	1.00
		Yes	43/45 (95.6)	1.40 (1.01 – 1.94)*	1.25 (0.88 – 1.79)
	Positive	No	578/667 (86.7)	1.00	1.00
		Yes	87/95 (91.6)	1.07 (0.86 – 1.34)	0.99 (0.78 – 1.26)

[†]Variables included in the model were INH-monoresistant TB and interaction term
[‡]Model adjusted for age, gender, homelessness, HIV status, DM status, TST result, and smear

result at baseline
*Indicates that the finding is statistically significant at level of confidence of 5% (p-value < 0.05)

Appendix Table 4. Sensitivity analysis of externally adjusted odds ratios for poor TB treatment outcomes and all-cause mortality during TB treatment comparing patients with and without INH-monoresistance (OR_{DX})

P_{Z1}	P_{Z0}	OR_{XZ}	Various OR_{DX} (Poor TB treatment Outcome) OR_{DZ}					Various OR_{DX} (All-cause Mortality) OR_{DZ}				
			1.5	2	3	4	5	1.5	2	3	4	5
0.167	0.038	5.075	0.99	0.94	0.85	0.78	0.73	1.03	0.97	0.88	0.81	0.75
0.072	0.001	77.799	1.02	0.99	0.93	0.87	0.82	1.05	1.02	0.95	0.90	0.85
0.086	0.027	3.450	1.03	1.00	0.95	0.91	0.87	1.06	1.03	0.98	0.94	0.90
0.112	0.037	3.260	1.02	0.99	0.93	0.88	0.84	1.05	1.02	0.96	0.91	0.87
0.155	0.057	3.022	1.01	0.97	0.90	0.85	0.80	1.04	1.00	0.93	0.87	0.83
0.064	0.091	0.685	1.07	1.08	1.11	1.13	1.15	1.10	1.12	1.14	1.16	1.18
0.154	0.020	8.836	0.99	0.93	0.84	0.77	0.71	1.02	0.96	0.87	0.79	0.73
0.160	0.090	1.928	1.02	0.99	0.95	0.91	0.88	1.05	1.02	0.97	0.94	0.90
0.123	0.094	1.347	1.04	1.03	1.01	0.99	0.98	1.08	1.06	1.04	1.02	1.01
0.119	0.066	1.912	1.03	1.01	0.97	0.93	0.91	1.06	1.04	1.00	0.96	0.93
0.046	0.019	2.488	1.04	1.03	1.01	0.98	0.96	1.08	1.06	1.04	1.01	0.99

Note:

P_{Z1}= proportion of TB treatment change among patients with INH-monoresistant TB

P_{Z0}= proportion of TB treatment change among patients with drug-susceptible TB