Supplementary data

S1 Table. Completed MOOSE (Meta-analysis Of Observational Studies in Epidemiology) checklist

Item No	Recommendation	Reported on Page No
Reporting of background should include		
1	Problem definition	5-6
2	Hypothesis statement (Objectives)	6
3	Description of study outcome(s)	6
4	Type of exposure or intervention used	NA
5	Type of study designs used	7
6	Study population	7
Reporting of search strategy should include		
7	Qualifications of searchers (eg, librarians and investigators)	NA
8	Search strategy, including time period included in the synthesis and key words	7 S2 Table
9	Effort to include all available studies, including contact with authors	7
10	Databases and registries searched	7
11	Search software used, name and version, including special features used (eg, explosion)	7
12	Use of hand searching (eg, reference lists of obtained articles)	7
13	List of citations located and those excluded, including justification	Fig 1
14	Method of addressing articles published in languages other than English	7
15	Method of handling abstracts and unpublished studies	7, Fig 1
16	Description of any contact with authors	-
Reporting of methods should include		
17	Description of relevance or appropriateness of studies assembled for assessing the hypothesis to be tested	NA
18	Rationale for the selection and coding of data (eg, sound clinical principles or convenience)	7
19	Documentation of how data were classified and coded (eg, multiple raters, blinding and interrater reliability)	6
20	Assessment of confounding (eg, comparability of cases and controls in studies where appropriate)	NA
21	Assessment of study quality, including blinding of quality assessors, stratification or regression on possible predictors of study results	Table 1, S3 Table
22	Assessment of heterogeneity	9
23	Description of statistical methods (eg, complete description of fixed or random effects models, justification of whether the chosen models account for predictors of study results, dose-response models, or cumulative meta-analysis) in sufficient detail to be replicated	8-9
24	Provision of appropriate tables and graphics	Table 1-2, Fig 1-4

Reporting of results should include		
25	Graphic summarizing individual study estimates and overall estimate	Fig 2-4
26	Table giving descriptive information for each study included	Table 1
27	Results of sensitivity testing (eg, subgroup analysis)	13-14, S9-11 Table
28	Indication of statistical uncertainty of findings	-

S2 Table. Search strategies

Electronic database	Search strategies
PubMed	((((((((((("glutathione S transferase") OR GST)) OR ("glutathione S-transferase T1" [Supplementary Concept] OR "glutathione S-transferase M1" [Supplementary Concept])) AND Humans[Mesh] AND English[lang])) OR ((("SLCO1B1 protein, human" [Supplementary Concept]) OR "solute carrier organic anion transporter") AND Humans[Mesh] AND English[lang])) OR ("isoniazid acetyltransferase" [Supplementary Concept]OR "ArylamineN-Acetyltransferase"[Mesh] OR "NAT2 protein, human" [Supplementary Concept])) OR "Cytochrome P-450 CYP2E1"[Mesh]) OR drug metaboli#er*) OR "Genetic Predisposition to Disease"[Mesh]) AND (("Drug-Induced Liver Injury"[Mesh] OR "Drug-Induced Liver Injury, Chronic"[Mesh]))) AND ((("AntitubercularAgents"[Mesh]) OR tuberculosis OR antituberculo*)) Filters: Humans; English
EMBASE	'solute carrier organic anion transporter 1b1'/expOR 'solute carrier organic anion transporter 1b1' OR 'multidrug resistance protein 1'/expOR 'multidrug resistance protein 1' OR 'organic anion transporter'/expOR 'organic anion transporter' AND [humans]/limAND [english]/limOR slco1b1 OR 'drug transporter gene*' OR abcb1 AND ('hepatitis'/expOR hepatitis OR 'liver toxicity'/expOR ('drug induced' AND ('liver'/expOR liver) AND ('toxicity'/expOR toxicity)) OR 'toxic hepatitis'/expOR 'hepatotoxicity'/expOR hepatotoxicity) AND ('tuberculostaticagent'/expOR 'tuberculostaticagent' OR antituberculosisOR 'isoni*' OR 'rifampi*') AND [humans]/limAND [english]/lim
Web of Science	(((((("Glutathione S transferase") OR GST) OR GSTT1) OR GSTM1) OR (((NAT2) OR "arylaminN acetyltransferase") OR N acetyltransferase*) OR ((drug metaboli?er*) OR (drug metabli?ingenzyme*)) OR (("Cytochrome 2E1") OR "CYP 2E1") OR (("The solute carrier organic anion transporter family member 1B1") OR SLCO1B1) OR (genotyp* OR acetylator*) OR (gene* susceptibilit*) OR (*polymorphism*)) AND ((drug NEAR/3 liver) OR (hepatotoxi*) OR (drug induced liver injury) OR (hepatitis)) AND ((rifampi*) OR (isoni*) OR (antituberculosis) OR ("antitubercul* agent* "))
Cochrane Reviews	[AntitubercularAgents] explode all trees AND [Drug-Induced Liver Injury] explode all trees AND ([Cytochrome P-450 CYP2E1] explode all trees OR nat2 OR "N acetyltrasferase" "glutathione S transferase" OR GST OR GSTM1 OR GSTT1 "Solute carrier organic anion transporter" OR SLCO1B1)(Limitation : Trials)

S3 Table. Study quality assessment

Studies	Scientific design	Definite inclusion of study population[a]	Explicit information on study population[a]	Explicit diagnostic criteria on ATDILI[a]	Genetic detection method[a]	Correct statistical analysis[a]	Logical discussion of study bias[a]
Feng, 2014 [1]	1	1	1	1	1	1	0
Kim, 2009 [2]	1	1	1	1	1	1	1
Singh, 2014 [3]	1	1	1	1	1	1	1
Tang, 2013 [4]	1	1	1	1	1	1	1
Ben Mahmoud, 2012 [5]	1	1	1	1	1	1	1
Bozok Cetintas, 2008 [6]	1	1	1	1	1	0	1
Higuchi, 2007 [7]	1	1	1	1	1	1	1
Ho, 2013 [8]	1	1	1	1	1	1	0
Huang, 2002 [9]	1	1	1	1	1	1	1
Khalili, 2011 [10]	1	1	1	1	1	1	0
Leiro-Fernandez, 2011 [11]	1	1	1	1	1	1	1
Lv, 2012 [12]	1	1	1	1	1	1	1
Ng, 2014 [13]	1	1	1	1	1	1	1
Ohno, 2000 [14]	1	1	1	1	1	1	1
Possuelo, 2008 [15]	1	1	1	1	1	1	1
Rana, 2012 [16]	1	1	1	1	1	1	1
Shimizu, 2006 [17]	1	1	1	1	1	1	0
Yuliwulandari, 2016 [18]	1	1	1	1	1	1	1
Wattanapokayakit, 2016 [19]	1	1	1	1	1	1	1
Chatterjee, 2010 [20]	1	1	1	1	1	1	1
Gupta, 2013 [21]	1	1	1	1	1	1	1
Huang, 2007 [22]	1	1	1	1	1	1	0
Kim, 2010 [23]	1	1	1	1	1	1	1
Leiro, 2008 [24]	1	1	1	1	1	1	1
Liu, 2014 [25]	1	1	1	1	1	1	1
Monteiro, 2012 [26]	1	1	1	1	1	1	1
Rana, 2013 [27]	1	1	1	1	1	1	0
Roy, 2001 [28]	1	1	1	1	1	1	1
Chen, 2015 [29]	1	1	1	1	1	1	1
Kim, 2012 [30]	1	1	1	1	1	1	1
Li, 2012 [31]	1	1	1	1	1	1	1
An, 2012 [32]	1	1	1	1	1	1	1
Bose, 2011 [33]	1	1	1	1	1	1	1

Chamorro, 2013 [34]	1	1	1	1	1	1	1
Cho, 2007 [35]	1	1	1	1	1	1	1
Gupta, 2013 [36]	1	1	1	1	1	1	1
Huang, 2003 [37]	1	1	1	1	1	1	1
Lee, 2010 [38]	1	1	1	1	1	1	1
Mishra, 2013 [39]	1	1	1	1	1	1	1
Santos, 2013 [40]	1	1	1	1	1	1	1
Vuilleumier, 2006 [41]	1	1	1	1	1	1	1
Yamada, 2009 [42]	1	1	1	1	1	1	1
Zaverucha-do-Valle, 2014 [43]	1	1	1	1	1	1	0
Sharma, 2014 [44]	1	1	1	1	1	1	1
Wang, 2010 [45]	1	1	1	1	1	1	1
Tang, 2012 [46]	1	1	1	1	1	1	1
Yimer, 2011 [47]	1	1	1	1	1	1	0
Brito, 2014 [48]	1	1	1	1	1	1	1
Forestiero, 2013 [49]	1	1	1	1	1	1	0
Rana, 2014 [50]	1	1	1	1	1	1	0
Singla, 2014 [51]	1	1	1	1	1	1	1
Sotsuka, 2011 [52]	1	1	1	1	1	1	1
Teixeira, 2011 [53]	1	1	1	1	1	1	1
Xiang, 2014 [54]	1	1	1	1	1	1	1

Abbreviation: ATDILI, anti-tuberculosis drug-induced liver injury

[a] 0 indicates ‘not mentioned’ in the study; 1 indicates ‘sufficient information provided’ in the study

S4 Table. Genotype distribution and the genotyping method used for the *CYP2E1* genetic polymorphisms in the included studies (n = 26)

Study	*Rsa*I/*Pst*I genotype (n = 24)				*Dra*I genotype (n = 6)				Genotyping method
	Case (number of individuals [%])		Control (number of individuals [%])		Case (number of individuals [%])		Control (number of individuals [%])		
	C1/C1	C1/C2 + C2/C2	C1/C1	C1/C2 + C2/C2	D/D	D/C + C/C	D/D	D/C + C/C	
An [32]	72 (71.3)	29 (28.7)	64 (59.8)	43 (40.2)	NA	NA	NA	NA	Sequencing
Bose [33]	NA	NA	NA	NA	4 (9.8)	37 (90.2)	32 (18.1)	145 (81.9)	PCR-RFLP
Brito [48]	13 (86.7)	2 (13.3)	195 (84.8)	35 (15.2)	12 (80.0)	3 (20.0)	179 (76.8)	54 (23.2)	PCR-RFLP
Chamorro [34]	30 (63.8)	17 (36.2)	83 (64.8)	45 (35.2)	NA	NA	NA	NA	PCR-RFLP
Cho [35]	10 (55.6)	8 (44.4)	65 (57.0)	49 (43.0)	NA	NA	NA	NA	Sequencing
Feng [1]	142 (82.1)	31 (17.9)	90 (52.0)	83 (48.0)	NA	NA	NA	NA	Sequencing
Forestiero [49]	53 (89.8)	6 (10.2)	30 (75.0)	10 (25.0)	NA	NA	NA	NA	PCR-RFLP
Gupta [36]	49 (98.0)	1 (2.0)	156 (94.5)	9 (5.5)	33 (66.0)	17 (34.0)	107 (64.9)	58 (35.1)	PCR-RFLP
Huang [37]	37 (75.5)	12 (24.5)	148 (55.0)	121 (45.0)	NA	NA	NA	NA	PCR-RFLP

Kim [2]	54 (81.8)	12 (18.2)	97 (63.4)	56 (36.6)	NA	NA	NA	NA	SNP stream
Lee [55]	26 (57.8)	19 (42.2)	55 (57.9)	40 (42.1)	NA	NA	NA	NA	Taqman
Mishra [39]	31 (93.9)	2 (6.1)	168 (97.1)	5 (2.9)	NA	NA	NA	NA	PCR-RFLP
Rana [56]	28 (50.9)	27 (49.1)	150 (61.2)	95 (38.8)	NA	NA	NA	NA	PCR-RFLP
Santos [57]	15 (83.3)	3 (16.7)	173 (75.6)	56 (24.4)	15 (83.3)	3 (16.7)	166 (72.8)	62 (27.2)	Taqman
Sharma [44]	81 (77.1)	24 (22.9)	139 (75.1)	46 (24.9)	NA	NA	NA	NA	PCR-RFLP
Singh [3]	42 (84.0)	8 (16.0)	77 (56.6)	59 (43.4)	NA	NA	NA	NA	PCR-RFLP
Singla [51]	15 (88.0)	2 (12.0)	375 (96.0)	16 (4.0)	NA	NA	NA	NA	PCR-RFLP
Sotsuka [52]	11 (55.0)	9 (45.0)	60 (65.2)	32 (34.8)	9 (45.0)	11 (55.0)	45 (48.9)	47 (51.1)	PCR-RFLP
Tang [46]	NA	NA	NA	NA	47 (52.8)	42 (47.2)	204 (57.3)	152 (42.7)	PCR-RFLP
Tang [4]	56 (62.9)	33 (37.1)	225 (63.2)	131 (36.8)	NA	NA	NA	NA	Taqman
Teixeira [53]	23 (88.5)	3 (11.5)	128 (90.8)	13 (9.2)	NA	NA	NA	NA	PCR-RFLP
Vuilleumier [41]	7 (87.5)	1 (12.5)	58 (92.1)	5 (7.9)	NA	NA	NA	NA	PCR-RFLP

Wang [45]	82 (78.8)	22 (21.2)	71 (64.0)	40 (36.0)	NA	NA	NA	NA	PCR-RFLP
Xiang [54]	58 (82.9)	12 (17.1)	1264 (79.0)	336 (21.0)	NA	NA	NA	NA	PCR/ligase detection reaction assays
Yamada [42]	17 (73.9)	6 (26.1)	107 (72.8)	40 (27.2)	NA	NA	NA	NA	PCR-RFLP
Zaverucha-do-Valle [43]	48 (94.1)	3 (5.9)	74 (94.9)	4 (5.1)	NA	NA	NA	NA	PCR-RFLP

Abbreviations: ***NA***, not available; ***PCR***, polymerase chain reaction; ***RFLP***, restriction fragment length polymorphism; ***SNP***, single nucleotide polymorphism

S5 Table. Genotype distribution and the genotyping method used for the *NAT2* genetic polymorphism in the included studies (n = 35)

Study	Case (number of individuals [%])		Control (number of individuals [%])		Genotyping method
	Slow acetylator	Intermediate and fast acetylator	Slow acetylator	Intermediate and fast acetylator	
An [32]	40 (39.6)	61 (60.4)	13 (12.1)	94 (87.9)	Sequencing
Ben Mahmoud [5]	11 (78.5)	3 (21.5)	22 (42.4)	30 (57.6)	PCR-RFLP
Bose [33]	29 (70.7)	12 (29.3)	79 (44.6)	98 (55.4)	PCR-RFLP
Bozok Cetintas [6]	23 (76.7)	7 (23.3)	19 (27.1)	51 (72.9)	PCR
Brito [48]	9 (60.0)	6 (40.0)	56 (24.3)	174 (75.7)	PCR-RFLP
Chamorro [34]	28 (58.7)	19 (41.3)	48 (37.5)	80 (62.5)	PCR-RFLP
Cho [35]	7 (38.9)	11 (61.1)	12 (10.5)	102 (89.5)	Sequencing
Forestiero [49]	28 (47.4)	31 (52.6)	13 (32.5)	27 (67.5)	PCR-RFLP
Gupta [36]	28 (56.0)	22 (44.0)	63 (38.2)	102 (61.8)	PCR-RFLP
Higuchi [7]	6 (33.3)	12 (66.7)	4 (4.9)	78 (95.1)	PCR-RFLP
Ho [8]	12 (63.2)	7 (36.8)	67 (20.4)	262 (79.6)	Sequenom MassARRAY

Huang [9]	14 (42.4)	19 (57.6)	39 (20.4)	152 (79.6)	PCR-RFLP
Huang [37]	19 (38.8)	30 (61.2)	58 (21.6)	211 (78.4)	PCR-RFLP
Khalili [10]	9 (64.3)	5 (35.7)	5 (13.9)	31 (86.1)	PCR-RFLP
Lee [38]	21 (46.7)	24 (53.3)	20 (21.1)	75 (78.9)	Taqman
Leiro-Fernandez [11]	36 (72.0)	14 (28.0)	44 (65.7)	23 (34.3)	PCR-RFLP
Lv [58]	18 (20.2)	71 (79.8)	74 (20.8)	282 (79.2)	PCR-RFLP
Mishra [39]	23 (70.0)	10 (30.0)	73 (42.0)	100 (58.0)	PCR-RFLP
Ng [13]	22 (84.6)	4 (15.4)	57 (56.4)	44 (43.6)	PCR-RFLP
Ohno [14]	7 (50.0)	7 (50.0)	0 (0.0)	63 (100.0)	PCR-RFLP
Possuelo [15]	9 (64.3)	5 (35.7)	60 (25.0)	180 (75.0)	Sequencing
Rana [16]	19 (38.0)	31 (62.0)	30 (14.9)	171 (85.1)	PCR-RFLP
Rana [50]	21 (38.2)	34 (61.8)	36 (14.7)	209 (85.3)	PCR-RFLP
Santos [40]	11 (61.1)	7 (38.9)	75 (29.8)	177 (70.2)	Sequencing
Shimizu [17]	4 (40.0)	6 (60.0)	1 (3.1)	31 (96.9)	PCR-RFLP
Singla [51]	15 (88.2)	2 (11.8)	213 (54.5)	178 (45.5)	PCR-RFLP

Sotsuka [52]	8 (15.4)	44 (84.6)	5 (5.4)	87 (94.6)	PCR-RFLP
Teixeira [53]	18 (75.0)	6 (25.0)	64 (51.2)	61 (48.8)	Sequencing
Vuilleumier [41]	3 (37.5)	5 (62.5)	8 (12.7)	55 (87.3)	PCR-RFLP
Wattanapokayakit [19]	38 (71.7)	15 (28.3)	15 (17.7)	70 (82.3)	Sequencing
Xiang [54]	28 (31.5)	61 (68.5)	501 (23.2)	1654 (76.8)	PCR/ligase detection reaction assays
Yamada [42]	14 (60.9)	9 (39.1)	64 (43.5)	83 (56.5)	Sequencing
Yimer [47]	31 (75.6)	10 (24.4)	107 (66.9)	53 (33.1)	Taqman
Yuliwulandari [18]	32 (64.0)	18 (36.0)	65 (34.0)	126 (66.0)	Sequencing
Zaverucha-do-Valle [43]	37 (71.2)	15 (28.8)	36 (45.6)	43 (54.4)	Sequencing

Abbreviations: ***NA***, not available; ***PCR***, polymerase chain reaction; ***RFLP***, restriction fragment length polymorphism

S6 Table. Genotype distribution and the genotyping method used for the *GST* genetic polymorphisms in the included studies (n = 19)

Study	*GSTM1* genotype (n = 19)				*GSTT1* genotype (n = 17)				*GSTM1/GSTT1* genotype (n = 11)				Genotyping method
	Case (number of individuals [%])		Control (number of individuals [%])		Case (number of individuals [%])		Control (number of individuals [%])		Case (number of individuals [%])		Control (number of individuals [%])		
	Null	Non-null	Null	Non-null	Null	Non-null	Null	Non-null	Dual-null	One-/non-null	Dual-null	One-/non-null	
Brito [48]	6 (40.0)	9 (60.0)	99 (43.0)	131 (57.0)	2 (13.3)	13 (86.7)	28 (12.2)	202 (87.8)	1 (6.7)	14 (93.3)	12 (5.2)	218 (94.8)	PCR
Chatterjee [20]	25 (49.0)	26 (51.0)	49 (49.0)	51 (51.0)	3 (5.9)	48 (94.1)	3 (3.0)	97 (97.0)	3 (5.9)	48 (94.1)	11 (11.0)	89 (89.0)	Multiplex PCR
Forestiero [49]	25 (42.4)	34 (57.6)	21 (52.5)	19 (47.5)	10 (17.0)	49 (83.0)	8 (20.0)	32 (80.0)	4 (6.8)	55 (93.2)	5 (12.5)	35 (87.5)	Multiplex PCR
Gupta [21]	21 (42.0)	29 (58.0)	61 (24.8)	185 (75.2)	11 (22.0)	39 (78.0)	30 (12.2)	216 (87.8)	5 (10.0)	45 (90.0)	4 (1.6)	242 (98.4)	Multiplex PCR
Huang [22]	42 (66.7)	21 (33.3)	29 (46.0)	34 (54.0)	24 (38.1)	39 (61.9)	25 (39.7)	38 (60.3)	NA	NA	NA	NA	Multiplex PCR
Kim [23]	26 (45.6)	31 (54.4)	104 (54.7)	86 (45.3)	34 (59.6)	23 (40.4)	103 (54.2)	87 (45.8)	17 (29.8)	40 (70.2)	56 (29.6)	133 (70.4)	PCR
Leiro [24]	12 (34.3)	23 (65.7)	25 (41.7)	35 (58.3)	17 (48.6)	18 (51.4)	16 (26.7)	44 (73.3)	7 (20.0)	28 (80.0)	6 (10.0)	54 (90.0)	PCR
Liu [25]	14 (70.0)	6 (30.0)	96 (67.1)	47 (32.9)	13 (65.0)	7 (35.0)	97 (67.8)	46 (32.2)	NA	NA	NA	NA	Multiplex PCR

Monteiro [26]	21 (35.6)	38 (64.4)	34 (28.8)	84 (71.2)	11 (18.7)	48 (81.3)	28 (23.8)	90 (76.2)	NA	NA	NA	NA	PCR
Rana [27]	10 (41.6)	20 (58.4)	37 (18.5)	183 (81.5)	6 (25.0)	24 (75.0)	68 (33.8)	152 (66.2)	9 (37.5)	21 (62.5)	96 (47.7)	124 (52.3)	PCR
Rana [16]	19 (34.5)	36 (65.5)	42 (17.1)	203 (82.9)	14 (25.5)	41 (74.5)	81 (33.1)	164 (66.9)	22 (40.0)	33 (60.0)	122 (49.8)	123 (50.2)	PCR
Roy [28]	17 (52.0)	15 (48.0)	8 (24.0)	25 (76.0)	5 (15.0)	28 (85.0)	1 (3.0)	32 (97.0)	NA	NA	NA	NA	PCR
Sharma [44]	42 (40.0)	63 (60.0)	68 (36.7)	117 (63.3)	NA	NA	NA	NA	NA	NA	NA	NA	PCR
Singla [51]	10 (59.0)	7 (41.0)	165 (42.0)	226 (58.0)	8 (47.0)	9 (53.0)	102 (26.0)	289 (74.0)	5 (29.0)	12 (71.0)	32 (8.0)	359 (92.0)	Multiplex PCR
Sotsuka [52]	12 (60.0)	8 (40.0)	50 (54.3)	42 (45.7)	7 (35.0)	13 (65.0)	40 (43.5)	52 (56.5)	NA	NA	NA	NA	PCR
Tang [46]	55 (61.8)	34 (38.2)	203 (57.0)	153 (43.0)	40 (44.9)	49 (55.1)	164 (46.1)	192 (53.9)	22 (24.7)	67 (75.3)	94 (26.4)	262 (73.6)	Multiplex PCR
Teixeira [53]	11 (42.3)	15 (57.7)	61 (43.3)	80 (56.7)	4 (15.4)	22 (84.6)	27 (19.2)	114 (80.8)	NA	NA	NA	NA	Multiplex PCR
Wang [45]	63 (60.6)	41 (39.4)	54 (48.6)	57 (51.4)	NA	NA	NA	NA	NA	NA	NA	NA	PCR
Xiang [54]	41 (46.1)	48 (53.9)	925 (42.9)	1230 (57.1)	18 (20.2)	71 (79.8)	477 (22.1)	1678 (77.9)	7 (9.3)	68 (90.7)	283 (16.5)	1427 (83.5)	PCR

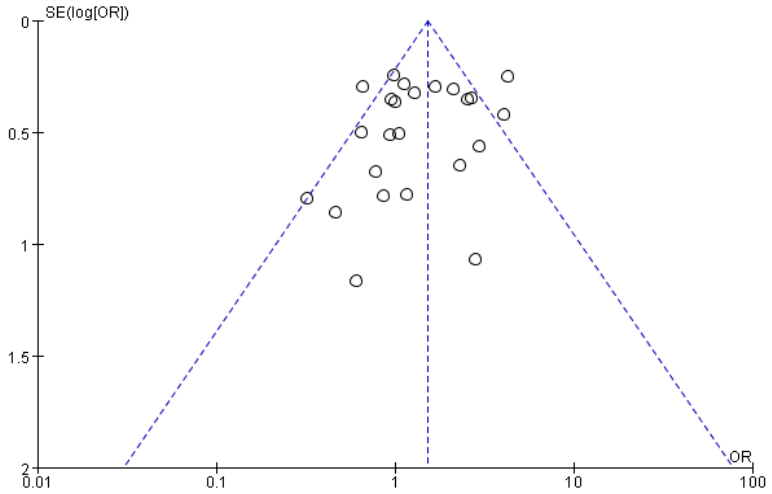
Abbreviations: ***NA***, not available; ***PCR***, polymerase chain reaction

S7 Table. Genotype distribution and the genotyping method used for the *SLCO1B1* genetic polymorphisms in the included studies (n = 4)

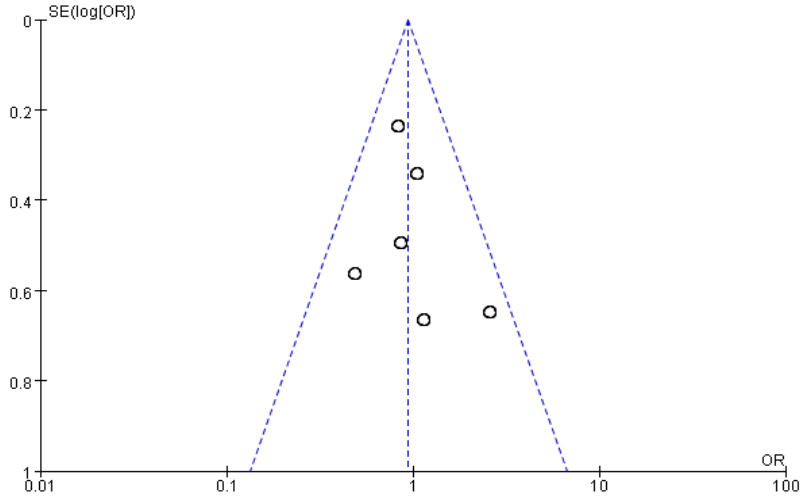
Study	*SLCO1B1* 388A>G (rs2306283)						*SLCO1B1* 521T>C (rs4149056)						Genotyping method
	Case (number of individuals [%])			Control (number of individuals [%])			Case (number of individuals [%])			Control (number of individuals [%])			
	AA	**AG**	**GG**	**AA**	**AG**	**GG**	**TT**	**CT**	**CC**	**TT**	**CT**	**CC**	
Chen [29]	8 (9.0)	34 (38.2)	47 (52.8)	33 (7.5)	164 (37.1)	245 (55.4)	72 (80.9)	15 (16.9)	2 (2.2)	351 (79.6)	87 (19.7)	3 (0.7)	Taqman
Kim [30]	6 (9.2)	26 (40.0)	33 (50.8)	11 (7.1)	60 (38.5)	85 (54.5)	46 (69.7)	20 (30.3)	0 (0.0)	113 (72.4)	40 (25.6)	3 (1.9)	SNPstream
Li [31]	11 (9.3)	38 (32.2)	69 (58.5)	12 (7.7)	48 (31.0)	95 (61.3)	83 (70.3)	34 (28.8)	1 (0.8)	136 (87.7)	18 (11.6)	1 (0.7)	PCR direct sequencing
Yimer [47]	9 (22.0)	17 (41.5)	15 (36.6)	20 (12.5)	87 (54.4)	53 (33.1)	27 (65.9)	13 (31.7)	1 (2.4)	107 (66.9)	49 (30.6)	4 (2.5)	Taqman

Abbreviations: ***PCR***, polymerase chain reaction; ***SNP***, single nucleotide polymorphism

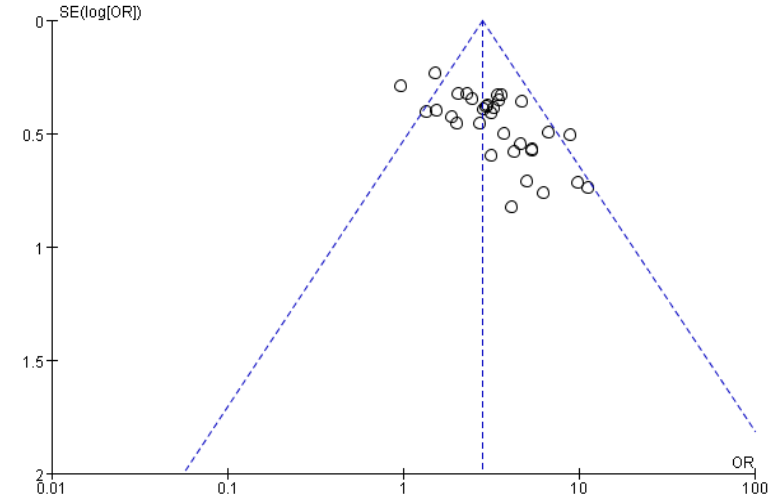
(A) *CYP2E1 Rsa*I/*Pst*I polymorphism



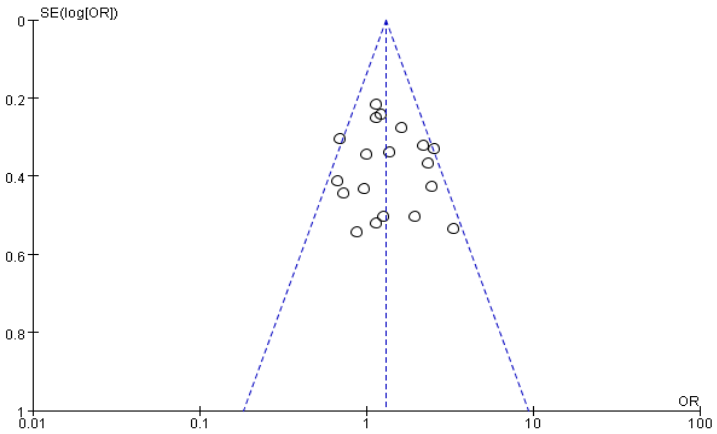
(B) *CYP2E1 Dra*I polymorphism



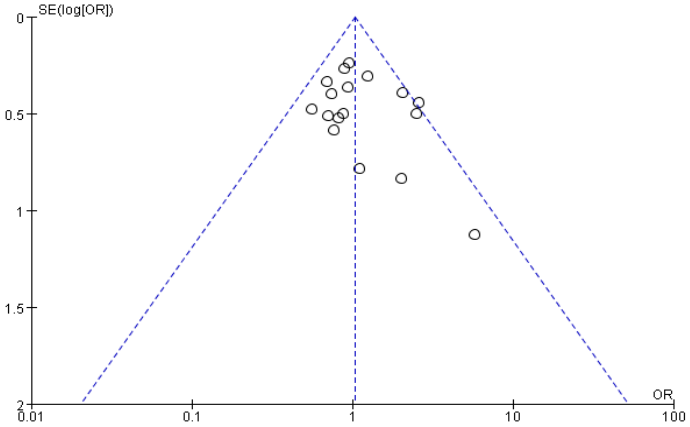
(C) *NAT2* polymorphism



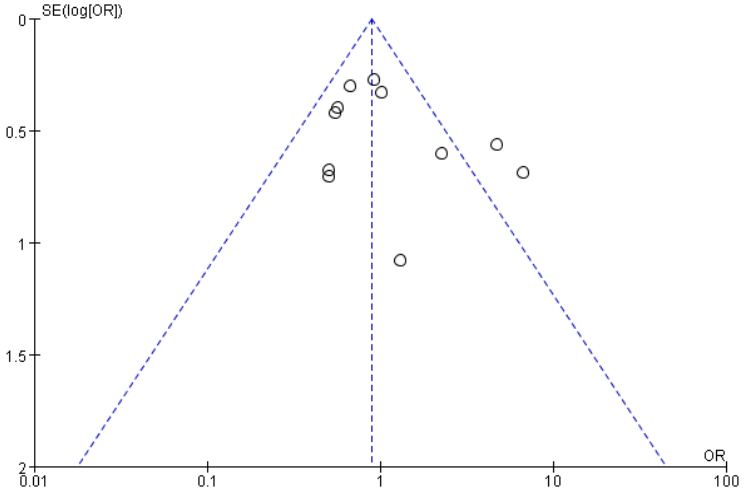
(D) *GSTM1* polymorphism



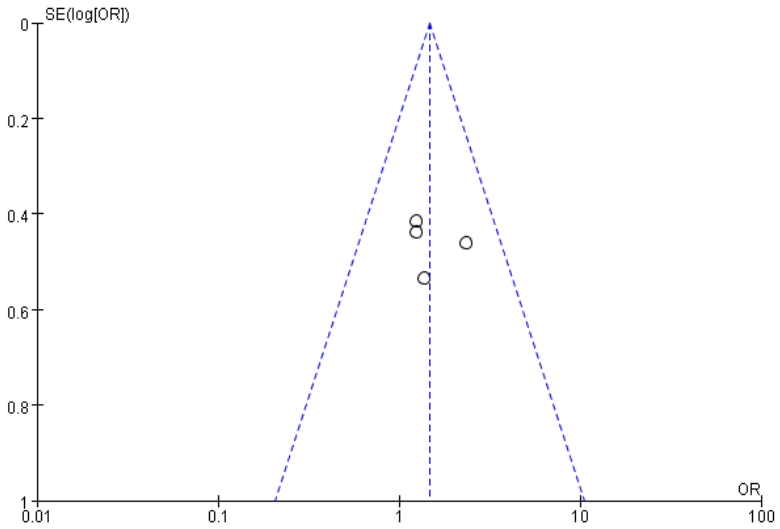
(E) *GSTT1* polymorphism



(F) *GSTT1/M1* polymorphism



(G) *SLCO1B1 388A>G* and *521T>C* polymorphism



S8 Figure. Funnel plots to evaluate publication bias for the *CYP2E1, NAT2, GST,* and *SLCO1B1* polymorphisms associated with the risk of anti-tuberculosis drug-induced liver injury. (A) C*YP2E1 Rsa*I*/Pst*I polymorphism, (B) *CYP2E1 Dra*I polymorphism, (C) *NAT2* polymorphism, (D) *GSTM1* polymorphism, (E) *GSTT1* polymorphism, (F) *GSTT1/M1* polymorphism, and (G) *SLCO1B1* 388A>G and 521T>C polymorphism.

S9 Table. Subgroup analysis for the association between *CYP2E1* polymorphisms and the risk of anti-tuberculosis drug-induced liver injury based on ethnicity, anti-tuberculosis drug regimen, and study design

Polymorphic gene	Subgroup		Number of studies	Case/ control (n)	Test of association		Model of meta-analysis	Test of heterogeneity	
					OR [95% CI]	P value[a]		I^2 ,%	P value[b]
*CYP2E1 Rsa*I/*Pst*I (c1/c1 vs. c1/c2 + c2/c2)	Total		24	1293/5450	1.39 [1.06, 1.83]	0.02	Random	60	<0.0001
	Ethnicity	East Asian	10	736/3076	1.62 [1.12, 2.36]	0.01	Random	69	0.0006
		Indian	6	310/1295	1.08 [0.52, 2.25]	0.85	Random	70	0.005
		South American	6	216/869	1.30 [0.83, 2.03]	0.25	Fixed	0	0.49
		Others	2	31/210	0.98 [0.39, 2.45]	0.96	Fixed	0	0.66
	Anti-TB drug regimen	INH alone	2	31/210	0.98 [0.39, 2.45]	0.96	Fixed	0	0.66
		Combination	21	1212/5104	1.35 [1.01, 1.79]	<0.00001	Random	61	0.0002
	Study design	Cohort	11	564/3120	1.32 [0.94, 1.87]	0.11	Random	50	0.03
		Case-control	12	729/2330	1.42 [0.93, 2.16]	0.10	Random	65	0.0006
*CYP2E1 Dra*I[c] (D/D vs. D/C + C/C)	Total		6	233/1272	0.93 [0.68, 1.27]	0.64	Fixed	0	0.51
	Ethnicity	East Asian	2	109/448	0.84 [0.55, 1.28]	0.41	Fixed	0	0.96
		Indian	2	91/342	0.83 [0.48, 1.45]	0.51	Fixed	27	0.24
		South American	2	33/482	1.80 [0.73, 4.45]	0.20	Fixed	0	0.37
	Study design	Cohort	2	56/407	0.68 [0.31, 1.50]	0.33	Fixed	0	0.33
		Case-control	4	177/865	0.99 [0.70, 1.38]	0.94	Fixed	0	0.42

Abbreviations: ***CI***, confidence interval; ***CYP2E1***, cytochrome P450 2E1; ***INH***, isoniazid; ***OR***, odds ratio; ***TB***, tuberculosis

[a] P value from Z test

[b] P value from Cochran's Q test based on chi-square statistic

[c] Subgroup analysis based on anti-TB drug regimen could not be performed due to insufficient information provided.

S10 Table. Subgroup analysis for the association between *NAT2* polymorphism and the risk of anti-tuberculosis drug-induced liver injury based on ethnicity, anti-tuberculosis drug regimen, and study design

Polymorphic gene	Subgroup		Number of studies	Case/ control (n)	Test of association		Model of meta-analysis	Test of heterogeneity	
					OR [95% CI]	P value[a]		I^2,%	P value[b]
NAT2 (Slow acetylator vs. fast and intermediate acetylator)	Total		35	1323/7319	3.30 [2.65, 4.11]	<0.00001	Random	47	0.002
	Ethnicity	East Asian	13	590/3970	4.00 [2.42, 6.60]	<0.00001	Random	77	<0.00001
		Indian	6	246/1352	3.07 [2.26, 4.16]	<0.00001	Fixed	0	0.74
		West Asian	2	44/106	9.51 [4.19, 21.61]	<0.00001	Fixed	0	0.79
		South American	7	231/1110	2.94 [2.11, 4.08]	<0.00001	Fixed	0	0.75
		African	2	55/212	2.08 [1.06, 4.10]	0.03	Fixed	52	0.15
		Others	5	157/569	2.56 [1.72, 3.79]	<0.00001	Fixed	15	0.32
	Anti-TB drug regimen	INH alone	2	31/210	2.32 [1.05, 5.13]	0.04	Fixed	0	0.45
		Combination	32	1256/6954	3.37 [2.67, 4.25]	<0.00001	Random	56	<0.0001
	Study design	Cohort	18	673/4850	2.82 [2.35, 3.40]	<0.00001	Fixed	40	0.04
		Case-control	17	650/2469	3.53 [2.42, 5.16]	<0.00001	Random	65	0.0001

Abbreviations: ***CI***, confidence interval; ***INH***, isoniazid; ***NAT2***, N-acetyltransferase 2; ***OR***, odds ratio; ***TB***, tuberculosis

[a] P value from Z test

[b] P value from Cochran's Q test based on chi-square statistic

S11 Table. Subgroup analysis for the association between *GST* polymorphisms and the risk of anti-tuberculosis drug-induced liver injury based on ethnicity, anti-tuberculosis drug regimen, and study design

Polymorphic gene	Subgroup		Number of studies	Case/ control (n)	Test of association		Model of meta-analysis	Test of heterogeneity	
					OR [95% CI]	P value[a]		I^2 ,%	P value[b]
GSTM1[c] (null vs. non-null)	Total		19	977/5119	1.30 [1.12, 1.52]	0.0007	Fixed	33	0.08
	Ethnicity	East Asian	7	442/3110	1.23 [0.99, 1.54]	0.06	Fixed	23	0.25
		Indian	7	341/1420	1.68 [1.30, 2.19]	<0.0001	Fixed	36	0.15
		Brazilian	4	159/529	0.98 [0.66, 1.47]	0.94	Fixed	0	0.60
	Study design	Cohort	8	462/3439	1.41 [1.04, 1.93]	0.03	Random	44	0.08
		Case-control	11	515/1680	1.25 [1.01, 1.55]	0.20	Fixed	29	0.17
GSTT1[c] (null vs. non-null)	Total		17	768/4823	1.03 [0.85, 1.25]	0.76	Fixed	16	0.26
	Ethnicity	East Asian	6	338/2999	0.96 [0.74, 1.24]	0.75	Fixed	0	0.94
		Indian	6	236/1235	1.37 [0.72, 2.59]	0.33	Random	57	0.04
		Brazilian	4	159/529	0.80 [0.47, 1.33]	0.39	Fixed	0	0.97
	Study design	Cohort	8	408/3354	0.89 [0.67, 1.19]	0.44	Fixed	3	0.41
		Case-control	9	360/1469	1.16 [0.90, 1.50]	0.26	Fixed	24	0.23
GSTM1/GSTT1[c] (dual-null vs. one-/non-null)	Total		11	547/4233	1.05 [0.67, 1.62]	0.84	Random	59	0.006
	Ethnicity	East Asian	3	235/2701	0.83 [0.58, 1.20]	0.33	Fixed	0	0.49
		Indian	5	203/1202	1.33 [0.50, 3.53]	0.56	Random	80	0.0005
		Brazilian	2	74/270	0.67 [0.20, 2.18]	0.50	Fixed	0	0.47
	Study design	Cohort	6	298/3136	0.85 [0.45, 1.61]	0.62	Random	58	0.04
		Case-control	5	249/1097	1.31 [0.71, 2.43]	0.39	Random	59	0.04

Abbreviations: ***CI***, confidence interval; ***GSTM1***, glutathione S-transferase Mu 1; ***GSTT1***, glutathione S-transferase Theta 1; ***OR***, odds ratio

[a] P value from Z test

[b] P value from Cochran's Q test based on chi-square statistic

[c] Subgroup analysis based on anti-tuberculosis drug regimen could not be performed due to insufficient information provided

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