

Table S1. Characteristics of studies for *MTHFR* 677 and 1298 loci distributions (70 papers).

First Author (Reference number)	Year	Ethnicity- Country	MTHFR 677									MTHFR 1298				Quality Score			
			Cases, Type, n (%)				Controls, source (s), n (%)					Cases, n (%)			Controls, n (%)				
			Type	CC	CT	TT	S	CC	CT	TT	HWE	AA	AC	CC	AA		AC	CC	HWE
<b>Australia</b>																			
Kaiser (16)	2001	Caucasian- Australia	1	71 (45.5)	66 (42.3)	19 (12.2)	1	37 (46.8)	31 (39.2)	11 (13.9)	Yes	NA				18 (5, 9, 4)			
Kaiser (17)	2000	Caucasian- Australia	1	65 (44.2)	68 (46.3)	14 (9.5)	1	46 (42.2)	49 (45.0)	14 (12.8)	Yes	53 (36.0)	81 (55.2)	13 (8.8)	44 (40.4)	53 (48.6)	12 (11.0)	No	20 (5, 9, 6)
<b>Europe</b>																			
Hiltunen (18)	2009	Caucasian- Finland	1	150 (42.7)	84 (45.7)	14 (11.6)	1	380 (56.3)	263 (39.0)	32 (04.7)	Yes	NA				26 (8, 12, 6)			
Jääskeläinen (19)	2006	Caucasian- Finland	1	78 (55.1)	43 (36.2)	12 (8.7)	1	64 (70.1)	42 (25.4)	6 (4.5)	Yes	NA				23 (7, 10, 6)			
Laivuori (20)	2000	Caucasian- Finland	1	64 (46.3)	45 (43.3)	4 (10.4)	1	56 (47.3)	40 (43.3)	7 (9.4)	Yes	NA				23 (6, 10, 7)			
Mislanova (21)	2011	Caucasian- Slovak	1	12 (42.8)	11 (39.3)	5 (17.8)	1	21 (52.5)	17 (42.5)	2 (5.0)	Yes	NA				22 (6, 10, 6)			
Nagy (22)	2007	Caucasian- Hungary	1, 4	71 (43.3)	68 (41.5)	25 (15.2)	1	32 (43.8)	35 (47.9)	6 (8.2)	Yes	NA				24 (7, 11, 6)			
			1	49 (48.5)	43 (42.5)	9 (8.9)	NA												
			4	22 (34.9)	25 (39.6)	16 (25.4)	NA												
Rigó, Jr. (23)	2000	Caucasian- Hungary	1	46 (38.3)	66 (55)	8 (6.7)	1	42 (41.6)	53 (52.5)	6 (5.9)	No	NA				18 (6, 7, 5)			
Procházka (24)	2003	Caucasian- Czech	1	24 (63.1)	12 (31.6)	2 (5.3)	1	40 (80)	10 (20)	0 (0)	Yes	NA				21 (5, 10, 6)			
Stonek (25)	2007	Caucasian- Austria	1	9 (36.0)	14 (56.0)	2 (8.0)	1	669 (48.0)	573 (41.0)	155 (11.0)	Yes	NA				24 (7, 10, 7)			
Grandone (26)	1997	Caucasian- Italy	1	25 (26.6)	41 (43.6)	28 (29.8)	1	41 (31.8)	64 (49.6)	24 (18.6)	Yes	NA				22 (6, 10, 6)			
Muetze (27)	2008	Caucasian- Germany	4	30 (42.3)	34 (47.9)	7 (9.9)	1	35 (44.3)	29 (36.7)	15 (19.0)	Yes	NA				21 (6, 9, 6)			

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			Cases, Type, n (%)				Controls, source (s), n (%)					Cases, n (%)			Controls, n (%)				
			Type	CC	CT	TT	S	CC	CT	TT	HWE	AA	AC	CC	AA	AC	CC	HWE	
Europe																			
Prasmusinto (28)	2002	Caucasian - Germany	1	7 (46.7)	7 (46.7)	1 (6.7)	1	12 (35.3)	15 (44.1)	7 (20.6)	Yes	NA						24 (6, 11, 7)	
		Caucasian - Croatia	1	11 (44.0)	12 (48.0)	2 (7.6)	1	18 (47.3)	15 (39.5)	5 (13.2)	Yes								
		South Asia - Indonesia	1	34 (83.0)	6 (14.6)	1 (2.4)	1	22 (81.5)	5 (18.5)	0 (0.0)	Yes								
Lykke (29)	2012	Caucasian - Denmark	1, 4	113 (43.1)	118 (45.0)	31 (11.8)	1	906 (49.2)	793 (43.1)	143 (7.8)	Yes	NA						24 (7, 10, 7)	
Demaat (30)	2004	Caucasian - Netherland	1	78 (46.8)	59 (37.6)	20 (12.7)	1	63 (40.1)	75 (47.8)	19 (12.1)	Yes	NA						22 (5, 11, 6)	
Lachmeijer (31)	2001	Caucasian - Netherland	1, 4	22 (37.9)	21 (44.7)	4 (8.5)	1	58 (48.3)	51 (42.5)	11 (9.2)	Yes	18 (38.3)	22 (46.8)	7 (14.9)	45 (37.5)	64 (53.3)	11 (9.2)	Yes	20 (6, 8, 6)
Zusterzeel (14)	2000	Caucasian - Netherland	1, 4	72 (43.0)	74 (44.0)	21 (13.0)	1	205 (51.0)	162 (40.0)	36 (9.0)	Yes	91 (52.0)	68 (39.0)	17 (10.0)	179 (44.0)	186 (46.0)	38 (9.0)	Yes	23 (7, 10, 6)
			1	32 (42.0)	33 (43.0)	11 (14.0)			NA										
			4	40 (44.0)	41 (45.0)	10 (11.0)			NA										
Morrison (15)	2002	Caucasian - Scotland	3	284 (40.2)	347 (49.1)	76 (10.7)	1	81 (49.4)	66 (40.2)	17 (10.4)	Yes	NA						20 (5, 9, 6)	
			1	169 (41.8)	193 (47.7)	42 (10.4)			NA										
			2	115 (37.9)	154 (50.8)	34 (11.2)			NA										
O'Shaughnessy (32)	1999	Caucasian- UK	1	138 (48.8)	114 (40.3)	31 (11.0)	1	51 (51.0)	37 (37.0)	12 (12.0)	Yes	NA						20 (7, 7, 6)	
Murphy (33)	2000	Caucasian - Ireland	1	5 (45.4)	3 (27.3)	3 (27.3)	1	214 (39.6)	270 (50.0)	56 (10.4)	No	NA						20 (3, 11, 6)	
Pertegal (34)	2016	Caucasian - Spain	1	16 (30.2)	24 (45.3)	13 (24.5)	1	31 (43.1)	29 (40.3)	12 (16.7)	Yes	NA						23 (6, 10, 7)	
Also-Rallo (35)	2005	Caucasian- Spain	1	11 (25.6)	24 (55.8)	8 (18.6)	1	38 (30.8)	57 (46.7)	27 (22.5)	Yes	24 (54.6)	19 (43.6)	0 (0.0)	70 (57.3)	41 (33.6)	11 (9.1)	Yes	24 (7, 11, 6)

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			Cases, Type, n (%)				Controls, source (s), n (%)					Cases, n (%)			Controls, n (%)				
			Type	CC	CT	TT	S	CC	CT	TT	HWE	AA	AC	CC	AA		AC	CC	HWE
<b>North America</b>																			
Powers (36)	2003	Caucasian - USA	1	14 (51.9)	0 (0.0)	13 (48.1)	1	15 (50.0)	0 (0.0)	15 (50.0)	No	NA				19 (5, 8, 6)			
Kim (37)	2001	Caucasian - USA	1, 4 4	131 10 (46.6) (47.6)	117 9 (41.6) (42.9)	33 2 (11.7) (9.5)	2	167 (46.4)	152 (42.2)	41 (11.4)	Yes NA	NA				25 (7, 11, 7)			
Livingstone (38)	2001	Caucasian - USA	1	66 (60.0)	34 (31.0)	10 (9.0)	1	61 (64.2)	27 (28.4)	7 (7.4)	Yes	NA				23 (7, 9, 7)			
Powers (39)	1999	Caucasian - USA	3 1 2	46 35 (37.4) (35.5) (47.0)	58 49 (47.2) (49.5) (38.3)	19 15 (15.4) (15.0) (14.7)	1	54 (47.4)	46 (40.4)	14 (12.2)	Yes NA NA	NA				22 (7, 9, 6)			
<b>Hispanic</b>																			
Vazquez-Alaniz (40)	2014	Mestizo - Mexican	3 1 2	59 37 (31.4) (32.7) (29.3)	91 57 (48.4) (50.5) (45.4)	38 19 (20.2) (16.8) (25.3)	1	54 (28.0)	97 (50.0)	43 (22.0)	Yes NA NA	NA				23 (7, 10, 6)			
Coral-Vázquez (41)	2013	Mestizo – Mexican	1	38 (16.5)	109 (47.4)	83 (36.1)	1	71 (20.2)	166 (47.2)	115 (32.7)	Yes	NA				22 (6, 9, 7)			
Rojas (42)	2010	Mestizo – Mexican	1	8 (28.5)	9 (32.1)	11 (39.2)	1	12 (29.2)	19 (46.3)	10 (24.3)	Yes	NA				20 (4, 10, 6)			
Canto (43)	2008	Mestizo – Mexican	1	36 (28.8)	66 (52.8)	23 (18.4)	1	61 (22.2)	131 (47.8)	82 (29.9)	Yes	NA				23 (6, 10, 7)			
Dávalos (44)	2005	Mestizo – Mexican	1	13 (39.4)	14 (42.4)	6 (18.2)	1	24 (38.7)	27 (43.5)	11 (17.7)	Yes	NA				21 (7, 9, 5)			
Pérez-Mutul (45)	2004	Mestizo - Mexican	1	33 (22.0)	66 (45.0)	49 (33.0)	1	36 (20.0)	80 (45.0)	61 (35.0)	Yes	NA				20 (6, 8, 6)			
Perales Dávila (46)	2001	Mestizo- Mexican	1	3 (23.1)	5 (38.5)	5 (38.5)	1	8 (53.3)	4 (26.6)	3 (20.0)	Yes	NA				20 (4, 10, 6)			

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			Cases, Type, n (%)				Controls, source (s), n (%)					Cases, n (%)			Controls, n (%)				
			Type	CC	CT	TT	S	CC	CT	TT	HWE	AA	AC	CC	AA	AC	CC	HWE	
South American																			
Dusse (47)	2007	Mixed- Brazil	1	16 (53.3)	12 (40.0)	2 (6.7)	1	46 (53.5)	31 (37.3)	6 (7.2)	Yes	NA					20 (6, 10, 4)		
Dalmáz (48)	2006	Mixed- Brazil	1	31 (41.3)	27 (36.0)	17 (22.7)	1	76 (52.4)	51 (35.2)	18 (12.4)	Yes	NA					20 (6, 8, 6)		
Chedraui (49)	2014	Mixed - Ecuador	1	59 (39.3)	73 (48.7)	18 (12.0)	1	47 (31.3)	91 (60.7)	12 (8.0)	No	100 (66.7)	27 (18.0)	23 (15.3)	110 (73.3)	39 (26.0)	1 (0.7)	Yes	20 (6, 9, 5)
Williams (50)	2004	Mixed- Peru	1	37 (29.6)	61 (48.8)	25 (20.0)	1	62 (34.6)	85 (47.5)	30 (16.8)	Yes	NA					24 (6, 11, 7)		
East Asia																			
Yoshida (51)	2008	East Asian- Japan	1	17 (32.7)	17 (32.7)	18 (34.6)	1	48 (42.5)	54 (47.8)	11 (9.7)	Yes	NA					20 (5, 9, 6)		
Watanabe (52)	2001	East Asian- Japan	1	40 (30.0)	59 (44.0)	34 (26.0)	1	89 (40.0)	103 (46.0)	32 (14.0)	Yes	NA					15* (5, 6, 4)		
Kobashi (53)	2000	East Asian- Japan	3	37 (36.6)	52 (51.5)	12 (11.9)	1	83 (38.6)	99 (46.0)	33 (15.3)	Yes	NA					21 (6, 9, 6)		
			1	25 (34.2)	40 (54.8)	8 (11.0)	NA												
			2	12 (42.9)	12 (42.9)	4 (14.2)	NA												
Sohda (54)	1997	East Asian- Japan	1	19 (28.0)	32 (48.0)	16 (24.0)	1	38 (39.0)	49 (50.0)	11 (11.0)	Yes	NA					16* (5, 7, 4)		
Su (55)	2011	East Asian- China	1	32 (59.2)	11 (20.4)	11 (20.4)	1	331 (64.5)	154 (30.0)	28 (5.5)	Yes	NA					22 (6, 10, 6)		
Zhong (56)	2010	East Asian- China	3	33 (36.0)	44 (46.9)	16 (17.0)	1	26 (64.7)	8 (20.6)	6 (14.7)	No	NA					22 (7, 10, 5)		
Shen (57)	2009	East Asian- China	3	20 (25.0)	42 (52.5)	18 (22.5)	1	30 (50.0)	21 (35.0)	9 (15.0)	Yes	NA					21 (6, 10, 5)		
			1	12 (19.7)	35 (57.4)	14 (23.0)	NA												
			2	8 (42.1)	7 (36.8)	4 (21.1)	NA												

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			Cases, Type, n (%)				Controls, source (s), n (%)					Cases, n (%)			Controls, n (%)				
			Type	CC	CT	TT	S	CC	CT	TT	HWE	AA	AC	CC	AA	AC	CC	HWE	
<b>East Asia</b>																			
Ding (58)	2008	East Asian- China	2	20 (21.8)	37 (40.2)	35 (38.0)	1	18 (20.2)	55 (61.8)	16 (18.0)	No	NA				19 (4, 9, 6)			
Wang (59)	2008	East Asian- China	1	6 (14.3)	19 (45.2)	17 (40.5)	1	13 (20.3)	40 (62.5)	11 (17.2)	No	NA				21 (5, 11, 5)			
Zhang (60)	2007	East Asian- China	1	12 (22.7)	21 (39.6)	20 (37.7)	1	10 (20.4)	30 (61.2)	9 (18.4)	Yes	NA				22 (6, 10, 6)			
Wang (61)	2006	East Asian- China	3	26 (48.1)	22 (40.7)	6 (11.1)	1	89 (71.2)	27 (21.6)	9 (7.2)	No	NA				19 (3, 10, 6)			
Tian (62)	2005	East Asian- China	3	34 (55.7)	20 (32.7)	7 (11.5)	1	40 (71.5)	12 (21.4)	4 (7.1)	No	NA				23 (7, 11, 5)			
			1	22 (56.9)	12 (30.8)	5 (12.8)					NA								
			2	12 (54.5)	8 (36.4)	2 (9.1)					NA								
Niu (63)	2004	East Asian- China	1, 4	6 (8.2)	45 (61.6)	22 (30.2)	1	12 (16.2)	43 (58.1)	19 (25.7)	Yes	NA				20 (5, 10, 5)			
Wang (64)	2004	East Asian- China	3	53 (53.5)	31 (31.3)	15 (15.2)	1	25 (46.3)	24 (44.4)	5 (9.3)	Yes	NA				20 (5, 9, 6)			
Fu (65)	2003	East Asian- China	2	24 (23.5)	53 (52.0)	25 (24.5)	1	46 (46.0)	40 (40.0)	14 (14.0)	Yes	NA				18 (4, 10, 4)			
Wei (66)	2001	East Asian- China	2	23 (54.7)	13 (31.0)	6 (14.3)	1	20 (55.6)	11 (30.5)	5 (13.9)	Yes	NA				22 (6, 11, 5)			
Li (67)	2000	East Asian- China	1	9 (16.0)	30 (53.0)	18 (31.0)	2	44 (37.0)	58 (49.0)	18 (15.0)	Yes	NA				17 (4, 8, 5)			
Liao (68)	2005	East Asian- China	2		NA		1		NA			31 (57.4)	20 (37.0)	3 (5.6)	60 (60.0)	36 (36.0)	4 (4.0)	Yes	22 (7, 10, 5)
<b>South Asia</b>																			
Kaur (69)	2013	South Asian- India	1	122 (84.1)	19 (13.1)	4 (2.8)	1	463 (78.1)	109 (18.4)	21 (3.5)	No	NA				20 (5, 9, 6)			
Aggarwal (70)	2011	South Asian- India	1	160 (80.0)	33 (16.5)	7 (3.5)	1	134 (67.0)	58 (29.0)	8 (4.0)	Yes	NA				24 (7, 10, 7)			
Dissanayake (71)	2012	South Asian- Sri Lanka	1	136 (77.7)	36 (20.6)	3 (1.7)	1	142 (83.0)	27 (15.8)	2 (1.2)	Yes	71 (41.0)	89 (51.4)	13 (7.5)	76 (44.4)	83 (48.5)	12 (7.0)	Yes	22 (6, 10, 6)

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			Cases, type, n (%)				Controls, source (s), n (%)					Cases, n (%)			Controls, n (%)					
			Type	CC	CT	TT	S	CC	CT	TT	HWE	AA	AC	CC	AA	AC	CC	HWE		
<b>Middle Eastern</b>																				
Salimi (72)	2015	Mid-Eastern- Iran	1	124 (64.6)	60 (31.2)	8 (4.2)	1	136 (69.4)	51 (26.0)	9 (4.6)	Yes	124 (64.6)	58 (30.2)	10 (5.2)	146 (74.5)	43 (22.0)	7 (3.5)	Yes	24 (7, 11, 6)	
Rahimi (73)	2013	Mid-Eastern- Iran	1	110 (55.6)	72 (36.4)	16 (8.1)	1	52 (51.5)	45 (44.6)	4 (4.0)	Yes	NA						20 (7, 7, 6)		
Saravani (74)	2011	Mid-Eastern- Iran	1	82 (77.0)	23 (22.0)	1 (1.0)	1	78 (73.0)	21 (19.5)	8 (7.5)	No	NA								
Deveer (75)	2013	Mid-Eastern- Turkey	1	29 (58.0)	16 (32.0)	5 (10.0)	1	26 (52.0)	18 (36.0)	6 (12.0)	Yes	28 (36.0)	25 (50.0)	7 (14.0)	20 (40.0)	26 (52.0)	4 (8.0)	Yes	19 (5, 9, 5)	
Dogan (76)	2011	Mid-Eastern- Turkey	4	16 (47.1)	15 (44.1)	3 (8.8)	1	17 (68.0)	7 (28.0)	1 (4.0)	Yes	NA						22 (6, 10, 6)		
Demir (77)	2006	Mid-Eastern- Turkey	2	31 (34.4)	49 (54.5)	10 (11.1)	1	43 (42.2)	47 (46.1)	12 (11.8)	Yes	NA						20 (6, 8, 6)		
Yilmaz (78)	2004	Caucasian- Turkey	1	29 (45.3)	28 (43.8)	7 (10.9)	1	24 (51.1)	17 (36.2)	6 (12.7)	Yes	NA						20 (6, 8, 6)		
<b>Africa</b>																				
Ibrahim (79)	2012	Mid-Eastern- Egypt	1	9 (20.5)	20 (45.4)	15 (34.1)	1	16 (36.4)	28 (63.6)	0 (0.0)	No	NA						22 (5, 11, 6)		
Klai (80)	2012	African- Tunisia	1	22 (40.9)	20 (54.6)	2 (4.6)	2	61 (61.0)	39 (39.0)	0 (0.0)	No	40 (90.9)	0 (0.0)	4 (9.1)	93 (93.0)	7 (7.0)	0 (0.0)	Yes	21 (5, 10, 6)	
Rajkovic (81)	2000	African- Zimbabwe	1	142 (83.0)	28 (16.4)	1 (0.6)	1	151 (82.5)	32 (17.5)	0 (0.0)	Yes	NA						23 (7, 10, 6)		
Pergoraro (82)	2004	African- South Africa	3	298 (85.4)	50 (14.3)	1 (0.3)	1	298 (88.0)	38 (11.0)	2 (1.0)	Yes	265 (75.9)	80 (22.9)	4 (0.2)	263 (78.0)	67 (20.0)	8 (2.0)	Yes	22 (7, 9, 6)	
			1	232 (86.0)	38 (14.0)	1 (0.0)	NA					213 (79.0)	55 (20.0)	3 (1.0)	NA					
			2	66 (85.0)	12 (15.0)	0 (0.0)	NA					52 (67.0)	25 (32.0)	1 (1.0)	NA					
Chikosi (83)	1999	African- South Africa	1	86 (82.9)	18 (17.1)	1 (1.0)	1	97 (88.2)	13 (11.8)	0 (0.0)	Yes	NA						16 (6, 6, 4)		

Type (Type of hypertensive disorders in pregnancy): 1 = preeclampsia, and eclampsia, 2 = gestational hypertension, 3 = mixed (include 1 & 2), and 4= hemolysis, elevated liver enzymes and low platelet count (HELLP) syndrome,

S (Sources of controls): 1 = healthy pregnancy, 2 = healthy female adults, 3= healthy general people

HWE (Hardy Weinberg Equilibrium) [updated from the original report based on our calculations using the formula available at http://www.koonec.com/k-blog/2010/06/20/hardy-weinberg-equilibrium-calculator](http://www.koonec.com/k-blog/2010/06/20/hardy-weinberg-equilibrium-calculator).

Quality score ranges: 0 - 28 (external validity, 0 – 9; Internal Validity, 0 – 12; report quality, 0 -7). NA: Not available. \*: Brief Report.

## Reference List of Studies included in the Meta-analysis

### 12 Meta-analysis Papers

1. Wang X-m, Wu H-y, Qiu X-j. Methylenetetrahydrofolate reductase (MTHFR) gene C677T polymorphism and risk of preeclampsia: an updated meta-analysis based on 51 studies. *Arch Med Res* 2013;44:159-68.
2. Xia X-p, Chang W-w, Cao Y-x. Meta-analysis of the methylenetetrahydrofolate reductase C677T polymorphism and susceptibility to pre-eclampsia. *Hypertens Res* 2012;35:1129-34.
3. Lin J, August P. Genetic thrombophilias and preeclampsia: a meta-analysis. *Obstet Gynecol* 2005;105:182-92.
4. Li X, Luo YL, Zhang QH, Mao C, Wang XW, Liu S et al. Methylenetetrahydrofolate reductase gene C677T, A1298C polymorphisms and pre-eclampsia risk: a meta-analysis. *Mol Biol Rep* 2014;41:5435-48.
5. Kosmas IP, Tatsioni A, Ioannidis JP. Association of C677T polymorphism in the methylenetetrahydrofolate reductase gene with hypertension in pregnancy and pre-eclampsia: a meta-analysis. *J Hypertens* 2004;22:1655–62.
6. Yang B, Fan S, Zhi X, Li Y, Liu Y, Wang D et al. Associations of MTHFR gene polymorphisms with hypertension and hypertension in pregnancy: a meta-analysis from 114 studies with 15411 cases and 21970 controls. *PLoS One* 2014;9:e87497.
7. Reilly R, McNulty H, Pentieva K, Strain JJ, Ward M. MTHFR 677TT genotype and disease risk: is there a modulating role for B-vitamins? *Proc Nutr Soc* 2014;73:47-56.
8. Niu W, You Y, Qi Y. Strong association of methylenetetrahydrofolate reductase gene C677T polymorphism with hypertension and hypertension-in-pregnancy in Chinese: a meta-analysis. *J Hum Hypertens* 2012;26:259-67.
9. Qian X, Lu Z, Tan M, Liu H, Lu D. A meta-analysis of association between C677T polymorphism in the methylenetetrahydrofolate reductase gene and hypertension. *Eur J Hum Genet* 2007;15:1239-45.
10. Wu X, Yang K, Tang X, Sa Y, Zhou R, Liu J et al. Folate metabolism gene polymorphisms MTHFR C677T and A1298C and risk for preeclampsia: a meta-analysis. *J Assist Reprod Genet* 2015;32:797-805.
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Table S2a. Differences on risk ratio and odds ratio for *MTHFR C677T* polymorphism in hypertensive disorders in pregnancy (71 studies).

Genotype (number of studies)	Case N=8064 n (%)	Control N=13232 n (%)	Ratio Type	Test of Heterogeneity			Statistical Model	Test of Association	
				Q	p	I <sup>2</sup>		Relative risk Ratio (95% CI)	p
TT (71)	1087 (13.48)	1410 (10.66)	Risk	107.30	.0028	34.8%	Random	1.28 (1.15 - 1.43)	<.0001
			Odds	108.06	.0024	35.2%	Random	1.34 (1.17 - 1.53)	<.0001
CT (71)	3142 (38.96)	5166 (39.04)	Risk	103.13	.0049	33.1%	Random	1.01 (0.96 - 1.06)	.7256
			Odds	106.52	.0025	35.2%	Random	1.02 (0.93 - 1.11)	.7059
CC (71)	3835 (47.56)	6656 (50.30)	Risk	120.18	.0002	41.8%	Random	0.94 (0.90 - 0.98)	.0017
			Odds	109.86	.0017	36.3%	Random	0.85 (0.78 - 0.93)	.0004
TT +CT (71)	4229 (52.44)	6576 (49.70)	Risk	106.43	.0033	34.2%	Random	1.07 (1.03 - 1.11)	.0002
			Odds	109.86	.0017	36.3%	Random	1.17 (1.07 - 1.28)	.0004
CC+CT (71)	6977 (86.52)	11822 (89.34)	Risk	185.55	<.0001	62.3%	Random	0.98 (0.96 - 0.99)	.0023
			Odds	108.06	.0024	35.2%	Random	0.75 (0.66 - 0.85)	<.0001

Table S2b. Differences on risk ratio and odds ratio for *MTHFR A1298C* polymorphism in hypertensive disorders in pregnancy (11 studies).

Genotype (number of studies)	Case N=1425 n (%)	Control N=1859 n (%)	Ratio Type	Test of Heterogeneity			Statistical Model	Test of Association	
				Q	p	I <sup>2</sup>		Relative risk Ratio (95% CI)	p
CC (11)	101 ( 7.08)	108( 5.81)	Risk	19.83	.0309	49.6%	Random	1.30 (0.82 - 2.07)	.2586
			Odds	20.62	.0239	51.5%	Random	1.35 (0.81 - 2.25)	.244
AC (11)	489 (34.27)	645 (34.70)	Risk	14.81	.1393	32.5%	Fixed	1.01 (0.92 - 1.11)	.8107
			Odds	15.04	.1307	33.5%	Fixed	1.02 (0.87 - 1.19)	.8384
AA (11)	835 (58.51)	1106 (59.49)	Risk	7.97	.6321	0%	Fixed	0.96 (0.91 - 1.02)	.1671
			Odds	8.64	.5666	0%	Fixed	0.90 (0.77 - 1.05)	.181
CC +AC (11)	590 (41.35)	753 (40.51)	Risk	9.12	.5206	0%	Fixed	1.06 (0.97 - 1.15)	.1965
			Odds	8.58	.5726	0%	Fixed	1.11 (0.95 - 1.29)	.2074
AA+AC (11)	1324 (92.78)	1751 (94.19)	Risk	43.53	<.0001	77.0%	Random	0.98 (0.94 - 1.02)	.2826
			Odds	20.48	.025	51.2%	Random	0.73 (0.44 - 1.20)	.2122

Table S3. Pooled meta-analysis: *MTHFR A1298C* polymorphism and risk of hypertensive disorders in pregnancy (11 studies).

Genotype (number of studies	Case N=1425 n (%)	Control N=1859 n (%)	Test of Heterogeneity			Statistical Model	Test of Association	
			Q	<i>p</i>	I <sup>2</sup> (%)		Relative risk (95% CI)	<i>p</i>
CC (11)	101 (7.09)	108 (5.81)	19.81	.0311	49.5	Random	1.31 (0.82 – 2.07)	.2558
Caucasian (4)	37 (8.96)	72 (9.55)	3.73	.2926	19.5	Fixed	0.92 (0.62 – 1.35)	.6603
South American (1)	23(15.33)	1 (0.67)	-	-	-	-	-	-
Asian# (2)	16 (6.99)	16 (5.90)	0.10	.7565	0	Fixed	1.13 (0.58 – 2.21)	.7192
Middle East (2)	17 (7.02)	11 (4.47)	0.06	.8116	0	Fixed	1.57 (0.75 – 3.26)	.2311
African (2)	8 (2.04)	8 (1.83)	5.88	.0153	83.0	Random	2.18 (0.08 – 62.07)	.6485
AC (11)	489 (34.31)	645 (34.70)	14.87	.1367	32.8	Fixed	1.01 (0.92 – 1.11)	.7807
Caucasian (4)	190 (46.00)	344 (45.62)	5.77	.1200	48	Fixed	0.97 (0.84 – 1.11)	.6167
South American (1)	27 (18.00)	39 (26.00)	-	-	-	-	-	.2538
Asian# (2)	109 (47.60)	119 (43.91)	0.01	.9035	0	Fixed	1.05 (0.87 – 1.27)	.5987
Middle East (2)	83 (34.30)	69 (28.05)	1.96	.1619	48.9	Fixed	1.22 (0.94 – 1.58)	.1337
African (2)	80 (20.36)	74 (16.89)	2.02	.1556	50.4	Fixed	1.09 (0.82 – 1.45)	.5690
AA (11)	835 (58.60)	1106 (59.49)	7.97	.6383	0	Fixed	0.96 (0.91 – 1.02)	.1773
Caucasian (4)	186 (45.04)	338 (44.83)	2.52	.4707	0	Fixed	1.05 (0.92 – 1.20)	.4363
South American (1)	100 (66.67)	110 (73.33)	-	-	-	-	-	-
Asian# (2)	102 (44.54)	136 (50.18)	0.04	.8499	0	Fixed	0.94 (0.78 – 1.13)	.4816
Middle East (2)	142 (56.68)	166 (67.48)	0.02	.8849	0	Fixed	0.87 (0.76 – 0.99)	.0404
African (2)	305 (77.61)	356 (81.28)	0.00	.9788	0	Fixed	0.98 (0.91 – 1.05)	.5004
CC+AC	590 (41.35)	753 (40.51)	9.15	.5182	0	Fixed	1.06 (0.97 – 1.15)	.1815
AA+AC	1324 (92.78)	1751 (94.19)	42.93	<.0001	76.7	Random	0.98 (0.94 – 1.02)	.3086
<b>Subgroups</b>								
<b>CC Risk &gt; 1 (7 countries)</b>	886 (62.18)	1290 (69.39)						
CC (8)	84 (9.46)	77 (5.97)	14.41	.0444	51.4	Random	1.69 (0.99 – 2.88)	.0540
AC (8)	309 (34.80)	484 (37.52)	10.74	.1502	34.8	Fixed	0.95 (0.85 – 1.06)	.3563
AA (8)	493 (55.52)	729 (56.51)	7.62	.3675	8.1	Fixed	0.96 (0.89 – 1.03)	.2845
CC+AC (8)	393 (44.36)	561 (43.49)	8.98	.2541	22.1	Fixed	1.05 (0.95 – 1.16)	.3091
AA+AC (8)	802 (90.52)	1113 (86.28)	17.52	.0143	60.1	Random	0.95 (0.92 – 0.99)	.0258
<b>CC risk &lt; 1 (3 countries)</b>	539 (37.82)	569 (30.61)						
CC (3)	17 (3.15)	31 (5.45)	2.26	.3232	11.5	Fixed	0.55 (0.29 – 1.02)	.0569
AC (3)	180 (33.40)	161 (28.30)	0.37	.8308	0	Fixed	1.17 (0.98 – 1.39)	.0769
AA(3)	342 (63.45)	377 (66.26)	0.32	.8529	0	Fixed	0.96 (0.89 – 1.05)	.3779
CC+AC (3)	197 (36.55)	192 (33.74)	0.04	.9826	0	Fixed	1.07 (0.92 – 1.25)	.3789
AA+AC (3)	522 (96.85)	538 (94.55)	6.29	.0431	68.2	Random	1.04 (0.99 – 1.10)	.1502

Note:

1. #: Asia include East and South Asia

2. CC risk > 1 (7 countries): Netherland (2 studies), Ecuador, China, Sri Lanka, Iran, Turkey, and Tunisia

3. CC risk < 1 (3 countries): Australia, Spain, and South Africa



Table S4a. Pooled meta-analysis: *MTHFR C677T polymorphism* and risks of hypertensive disorders in pregnancy (HDP) per HDP types. (71 studies)

Genotype (number of studies)	Case N= 8064 n (%)	Control N= 13232 n (%)	Test of Heterogeneity			Statistical Model	Test of Association	
			Q	p	I <sup>2</sup> (%)		Relative risk ratio (95% CI)	p
<b>TT (71)</b>	1087 (13.48)	1410 (10.66)	107.30	.0028	34.8	Random	1.28 (1.15 – 1.43)	<.0001
<b>PE (57)</b>	799 (13.61)	1221 (10.58)	94.98	.0009	41.0	Random	1.29 (1.13 – 1.47)	.0001
Caucasian (25)	330 (11.71)	669 (9.75)	25.02	.4046	4.1	Fixed	1.15 (1.00 – 1.32)	.0473
Hispanic (6)	177 (30.68)	282 (30.62)	9.09	.1057	45.0	Fixed	0.98 (0.83 – 1.15)	.7838
South American (4)	62 (16.40)	66 (11.89)	1.47	.6891	0	Fixed	1.40 (1.01 – 1.93)	.0405
East Asian (8)	156 (29.38)	139 (11.08)	10.89	.1433	35.7	Fixed	2.06 (1.68 – 2.53)	<.0001
South Asian (4)	15 (2.67)	31 (3.13)	0.73	.8654	0	Fixed	0.94 (0.49 – 1.81)	.8606
Middle East (6)	40 (6.21)	34 (6.46)	6.35	.2734	21.3	Fixed	0.92 (0.58 – 1.46)	.7254
African (4)	19 (5.22)	0	1.92	.5901	0	Fixed	11.38 (2.73 – 47.55)	.0009
<b>GH (4)</b>	80 (23.81)	47 (14.37)	2.44	.4872	0	Fixed	1.65 (1.20 – 2.29)	.0023
East Asian (3)	66 (27.97)	35 (15.56)	1.38	.5015	0	Fixed	1.81 (1.26 – 2.60)	.0014
Middle East (1)	14 (14.00)	12 (11.76)	-	-	-	-	-	-
<b>Mix (10)</b>	208 (11.21)	142 (10.44)	5.00	.8344	0	Fixed	1.08 (0.87 – 1.33)	.4837
Caucasian (2)	95 (11.45)	31 (11.15)	0.22	.6412	0	Fixed	1.11 (0.75 – 1.65)	.5927
Hispanic (1)	38 (20.21)	43 (22.16)	-	-	-	-	-	-
East Asian (6)	74 (15.16)	66 (12.00)	3.21	.6683	0	Fixed	1.20 (0.86 – 1.68)	.2845
African (1)	1 (0.29)	2 (0.59)	-	-	-	-	-	-
<b>CT (71)</b>	3142 (38.96)	5166 (39.04)	103.13	.0049	33.1	Random	1.01 (0.96 – 1.06)	.7256
<b>PE (57)</b>	2229 (37.95)	4575 (39.63)	61.38	.258	10.4	Fixed	0.98 (0.93 – 1.02)	.2461
Caucasian (25)	1159 (41.13)	2889 (42.11)	19.57	.6674	0	Fixed	1.01 (0.95 – 1.07)	.8459
Hispanic (6)	269 (46.62)	427 (46.36)	2.53	.7712	0	Fixed	1.01 (0.91 – 1.13)	.8015
South American (4)	173 (45.77)	258 (46.49)	3.24	.3558	7.5	Fixed	0.94 (0.81 – 1.08)	.3468
East Asian (8)	234 (44.07)	531 (42.31)	10.00	.1887	30.0	Fixed	0.88 (0.78 – 0.99)	.0354
South Asian (4)	94 (16.76)	199 (20.08)	7.74	.0516	61.3	Fixed	0.77 (0.61 – 0.98)	.0335
Middle East (6)	214 (33.23)	159 (30.23)	5.59	.3481	10.6	Fixed	1.05 (0.88 – 1.24)	.5985
African (4)	86 (23.63)	112 (25.63)	4.63	.2006	35.3	Fixed	1.00 (0.79 – 1.26)	.9787
<b>GH (4)</b>	156 (46.43)	153 (46.79)	11.79	.0081	74.6	Random	0.99 (0.70 – 1.41)	.9751
East Asian (3)	103 (43.64)	106 (47.11)	10.23	.006	80.4	Random	0.94 (0.57 – 1.56)	.8131
Middle East (1)	53 (53.00)	47 (46.08)	-	-	-	-	-	-
<b>Mix (10)</b>	757 (40.81)	438 (32.21)	20.39	.0157	55.9	Random	1.22 (1.04 – 1.43)	.0162
Caucasian (2)	405 (48.80)	112 (40.29)	0.06	.8129	0	Fixed	1.20 (1.02 – 1.42)	.0281
Hispanic (1)	91 (48.80)	97 (50.00)	-	-	-	-	-	-
East Asian (6)	211 (43.24)	191 (34.73)	16.19	.0063	69.1	Random	1.35 (0.98 – 1.86)	.0621
African (1)	50 (14.33)	38 (11.24)	-	-	-	-	-	-
<b>CC (71)</b>	3835 (47.56)	6656 (50.30)	120.18	.0002	41.8	Random	0.94 (0.90 – 0.98)	.0017
<b>PE (57)</b>	2845 (48.44)	5749 (49.80)	72.50	.0682	22.8	Fixed	0.96 (0.93 – 0.99)	.0313
Caucasian (25)	1329 (47.16)	3302 (48.13)	18.46	.7803	0	Fixed	0.96 (0.91 – 1.02)	.1639
Hispanic (6)	131 (22.70)	212 (23.02)	5.66	.3409	11.6	Fixed	1.00 (0.83 – 1.21)	.996
South American (4)	143 (37.83)	231 (41.62)	4.85	.1833	38.1	Fixed	0.96 (0.81 – 1.13)	.6263
East Asian (8)	141 (26.55)	585 (46.61)	7.39	.3897	5.2	Fixed	0.76 (0.65 – 0.88)	.0004
South Asian (4)	452 (80.57)	761 (76.79)	9.64	.0219	68.9	Random	1.06 (0.95 – 1.17)	.3296
Middle East (6)	390 (60.56)	333 (63.31)	5.29	.3818	5.4	Fixed	0.99 (0.90 – 1.08)	.7435
African (4)	259 (71.15)	325 (74.37)	4.99	.1724	39.9	Fixed	0.93 (0.86 – 1.00)	.0864
<b>GH (4)</b>	100 (29.76)	127 (38.84)	6.67	.0831	55.0	Fixed	0.76 (0.62 – 0.94)	.0106
East Asian (3)	67 (28.39)	84 (37.33)	6.70	.0351	70.1	Random	0.80 (0.50 – 1.29)	.3628
Middle East (1)	33 (33.00)	43 (42.16)	-	-	-	-	-	-
<b>Mix (10)</b>	890 (47.98)	780 (57.35)	33.60	.0001	73.2	Random	0.83 (0.71 – 0.96)	.0102
Caucasian (2)	330 (39.76)	135 (48.56)	0.03	.8672	0	Fixed	0.81 (0.69 – 0.94)	.0062
Hispanic (1)	59 (31.38)	54 (27.84)	-	-	-	-	-	-
East Asian (6)	203 (41.60)	293 (53.27)	15.01	.0103	66.0%	Random	0.75 (0.59 – 0.95)	.0159
African (1)	298 (85.39)	298 (88.17)	-	-	-	-	-	-
<b>TT+CT (71)</b>	4229 (52.44)	6576 (49.70)	106.46	.0033	34.2	Random	1.07 (1.03 – 1.11)	.0002

<b>PE (57)</b>	2845 (48.44)	5749 (49.80)	67.96	.1313	17.6	Fixed	1.04 (1.00 – 1.07)	.0287
Caucasian (25)	1489 (52.84)	3558 (51.87)	18.67	.7694	0	Fixed	1.03 (0.99 – 1.08)	.1559
Hispanic (6)	446 (77.30)	709 (76.98)	5.78	.3285	13.5	Fixed	1.00 (0.94 – 1.06)	.9961
South American (4)	235 (62.17)	324 (58.38)	5.38	.146	44.2	Fixed	1.03 (0.93 – 1.14)	.6174
East Asian (8)	390 (73.45)	670 (53.39)	6.35	.4993	0	Fixed	1.15 (1.07 – 1.23)	.0001
South Asian (4)	109 (19.43)	230 (23.21)	7.93	.0475	62.2	Random	0.83 (0.56 – 1.22)	.3382
Middle East (6)	254 (39.44)	193 (36.69)	4.96	.4211	0	Fixed	1.02 (0.89 – 1.19)	.743
African (4)	105 (28.85)	112 (25.63)	1.56	.6695	0	Fixed	1.20 (0.98 – 1.48)	.0801
<b>GH (4)</b>	236 (70.24)	200 (61.16)	8.35	.0393	64.1	Random	1.14 (0.94 – 1.38)	.1749
East Asian (3)	169 (71.61)	141 (62.67)	8.30	.0158	75.9	Random	1.14 (0.85 – 1.52)	.3868
Middle East (1)	67 (67.00)	59 (57.84)	-	-	-	-	-	-
<b>Mix (10)</b>	965 (52.02)	580 (42.65)	27.82	.001	67.6	Random	1.21 (1.05 – 1.26)	<.0001
Caucasian (2)	500 (60.24)	143 (51.44)	0.00	.9652	0	Fixed	1.18 (1.04 – 1.35)	.0116
Hispanic (1)	129 (68.62)	140 (72.16)	-	-	-	-	-	-
East Asian (6)	285 (58.40)	257 (46.73)	18.19	.0027	72.5	Random	1.34 (1.04 – 1.72)	.0251
African (1)	51 (14.61)	40 (11.83)	-	-	-	-	-	-
<b>CC+CT (71)</b>	6977 (86.52)	11822 (89.34)	185.18	<.0001	62.3	Random	0.98 (0.96 – 0.99)	.0023
<b>PE (57)</b>	5074 (86.40)	10324 (89.42)	128.50	<.0001	56.4	Random	0.97 (0.96 – 0.98)	<.0001
Caucasian (25)	2488 (88.29)	6191 (90.25)	24.83	.415	3.3	Fixed	0.98 (0.97 – 1.00)	.0552
Hispanic (6)	400 (69.32)	639 (69.38)	9.92	.0776	49.6	Fixed	1.01 (0.94 – 1.08)	.7806
South American (4)	316 (83.60)	489 (88.11)	2.25	.5215	0	Fixed	0.95 (0.90 – 0.99)	.0475
East Asian (8)	375 (70.62)	1116 (88.92)	5.61	.5854	0	Fixed	0.83 (0.78 – 0.88)	<.0001
South Asian (4)	546 (97.33)	960 (96.87)	0.78	.8549	0	Fixed	1.00 (0.98 – 1.02)	.8334
Middle East (6)	604 (93.79)	492 (93.54)	8.34	.1383	40.1	Fixed	1.01 (0.98 – 1.04)	.7176
African (4)	345 (94.78)	437 (100.0)	56.03	<.0001	94.6	Random	0.94 (0.87 – 1.02)	.1506
<b>GH (4)</b>	256 (29.76)	280 (85.63)	7.27	.0635	58.8	Fixed	0.89 (0.83 – 0.96)	.002
East Asian (3)	170 (76.19)	190 (84.44)	4.66	.0975	57.0	Fixed	0.85 (0.77 – 0.94)	.0012
Middle East (1)	86 (86.00)	90 (88.24)	-	-	-	-	-	-
<b>Mix (10)</b>	1647 (88.79)	1218 (89.56)	10.35	.3229	13.0	Fixed	0.99 (0.97 – 1.02)	.4767
Caucasian (2)	735 (88.55)	247 (88.85)	0.30	.5846	0	Fixed	0.99 (0.94 – 1.04)	.5888
Hispanic (1)	150 (79.79)	151 (77.84)	-	-	-	-	-	-
East Asian (6)	414 (84.84)	484 (88.00)	3.37	.6436	0	Fixed	0.97 (0.93 – 1.02)	.2698
African (1)	348 (99.71)	336 (99.41)	-	-	-	-	-	-

PE: pre-eclampsia, eclampsia and HELLP syndrome; GH: gestational hypertension; Mix: combined PE and GH

Table S4b. Pooled meta-analysis: *MTHFR A1298C polymorphism* and risk of hypertensive disorders in pregnancy (HDP) per HDP types. (11 studies)

Genotype (number of studies)	Case N=1425 n (%)	Control N=1859 n (%)	Test of Heterogeneity			Statistical Model	Test of Association	
			Q	p	I <sup>2</sup>		Relative risk ratio (95% CI)	p
<b>CC (11)</b>	101 (7.09)	108 (5.81)	19.83	.0309	49.6%	Random	1.30 (0.82 – 2.07)	.2586
<b>PE (9)</b>	94 (9.18)	96 (6.76)	17.61	.0244	54.6%	Random	1.45 (0.87 – 2.45)	.1576
Caucasian (4)	37 (8.96)	72 (9.55)	3.73	.2926	19.5%	Fixed	0.92 (0.62 – 1.35)	.6603
South American (1)	23 (15.33)	1 (0.67)	-	-	-	-	-	-
South Asian (1)	13 (7.51)	12 (7.02)	-	-	-	-	-	-
Middle East (2)	17 (7.02)	11 (4.47)	0.06	.8116	0%	Fixed	1.57 (0.75 – 3.26)	.2311
African (1)	4 (9.09)	0 (0.00)	-	-	-	-	-	-
<b>GH</b> East Asian (1)	3(5.56)	4 (4.00)	-	-	-	-	-	-
<b>Mix</b> African (1)	4 (1.18)	8 (2.37)	-	-	-	-	-	-
<b>AC (11)</b>	489 (34.31)	645 (34.70)	14.81	.1393	32.5%	Fixed	1.01 (0.92 – 1.11)	.8107
<b>PE (9)</b>	389 (37.99)	542 (38.14)	14.01	.0816	42.9%	Fixed	0.99 (0.89 – 1.10)	.8137
Caucasian (4)	190 (46.00)	344 (45.62)	5.77	.1232	48.0%	Fixed	0.97 (0.84 – 1.11)	.6167
South American (1)	27 (18.00)	39 (26.00)	-	-	-	-	-	-
South Asian (1)	89 (51.45)	83 (48.54)	-	-	-	-	-	-
Middle East (2)	83 (34.30)	69 (28.05)	1.96	.1619	48.9%	Fixed	1.22 (0.94 – 1.58)	.1337
African (1)	0 (0.00)	7 (7.00)	-	-	-	-	-	-
<b>GH</b> East Asian (1)	20 (37.04)	36 (36.00)	-	-	-	-	-	-
<b>Mix</b> African (1)	80 (22.92)	67 (19.82)	-	-	-	-	-	-
<b>AA (11)</b>	835 (58.60)	1106 (59.49)	7.97	.6321	0%	Fixed	0.96 (0.91 – 1.02)	.1671
<b>PE (9)</b>	539 (52.64)	783 (55.10)	7.77	.4564	0%	Fixed	0.96 (0.89 – 1.03)	.225
Caucasian (4)	186 (45.04)	338 (44.83)	2.53	.4707	0%	Fixed	1.05 (0.92 – 1.20)	.4363
South American (1)	100 (66.76)	110 (73.33)	-	-	-	-	-	-
South Asian (1)	71 (41.04)	76 (44.44)	-	-	-	-	-	-
Middle East (2)	142 (58.68)	166 (67.48)	0.02	.8849	0%	Fixed	0.87 (0.76 – 0.99)	.0404
African (1)	40 (90.91)	93 (93.00)	-	-	-	-	-	-
<b>GH</b> East Asian (1)	31 (57.40)	60 (60.00)	-	-	-	-	-	-
<b>Mix</b> African (1)	265 (75.93)	263 (77.81)	-	-	-	-	-	-
<b>CC+AC (11)</b>	590 (41.35)	753 (40.51)	9.12	.5206	0%	Fixed	1.06 (0.97 – 1.15)	.1965
<b>PE (9)</b>	483 (47.26)	638 (44.90)	9.04	.3388	11.5%	Fixed	1.05 (0.97 – 1.15)	.2459
Caucasian (4)	227 (54.96)	416 (55.17)	2.66	.4478	0%	Fixed	0.96 (0.85 – 1.07)	.4504
South American (1)	50 (33.33)	40 (26.67)	-	-	-	-	-	-
South Asian (1)	102 (58.96)	95 (55.56)	-	-	-	-	-	-
Middle East (2)	100 (41.32)	80 (32.52)	1.55	.2135	0%	Fixed	1.27 (1.01 – 1.59)	.0403
African (1)	4 (9.09)	7 (7.00)	-	-	-	-	-	-
<b>GH</b> East Asian (1)	23 (42.59)	40 (40.00)	-	-	-	-	-	-
<b>Mix</b> African (1)	84 (24.07)	75 (22.19)	-	-	-	-	-	-
<b>AA+AC (11)</b>	1324 (92.78)	1751 (94.19)	43.53	<.0001	77.0%	Random	0.98 (0.94 – 1.02)	.2826
<b>PE (9)</b>	928 (90.80)	1325 (93.24)	31.88	<.0001	74.9%	Random	0.97 (0.93 – 1.02)	.2493
Caucasian (4)	376 (91.04)	682 (90.45)	7.07	.0695	57.6%	Fixed	1.01 (0.97 – 1.05)	.6944
South American (1)	127 (84.67)	149 (99.33)	-	-	-	-	-	-
South Asian (1)	160 (92.49)	159 (92.98)	-	-	-	-	-	-
Middle East (2)	225 (92.98)	235 (95.53)	0.53	.4669	0%	Fixed	0.97 (0.93 – 1.02)	.2279
African (1)	40 (90.91)	100 (100)	-	-	-	-	-	-
<b>GH</b> East Asian (1)	51 (94.44)	96 (96.00)	-	-	-	-	-	-
<b>Mix</b> African (1)	345 (98.85)	330 (97.63)	-	-	-	-	-	-

PE: pre-eclampsia, eclampsia and HELLP syndrome; GH: gestational hypertension; Mix: combined PE and GH

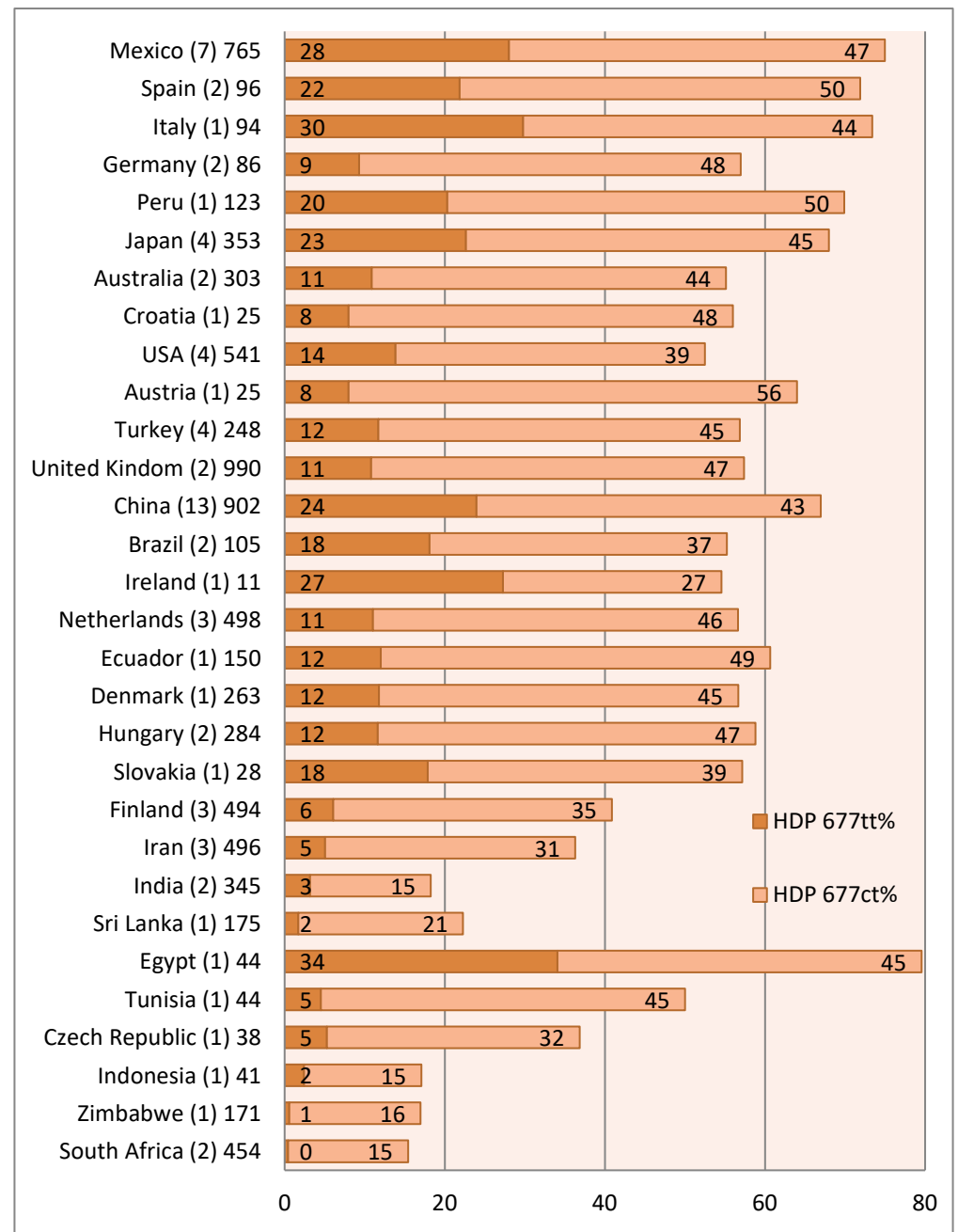
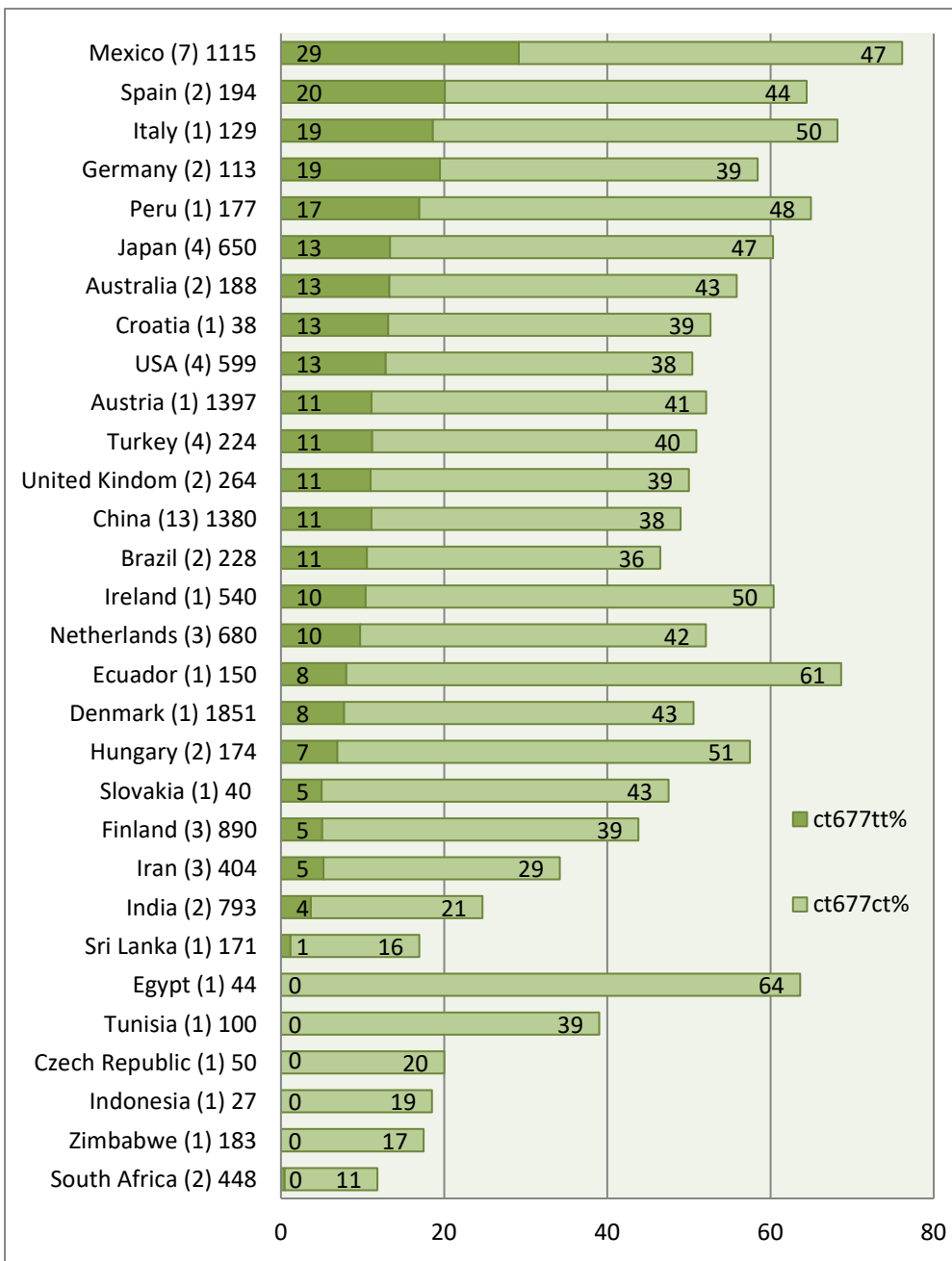


Figure S1a. The percentage of *MTHFR* 677 CT and TT polymorphisms per control and hypertensive disorders in pregnancy (HDP) case groups.

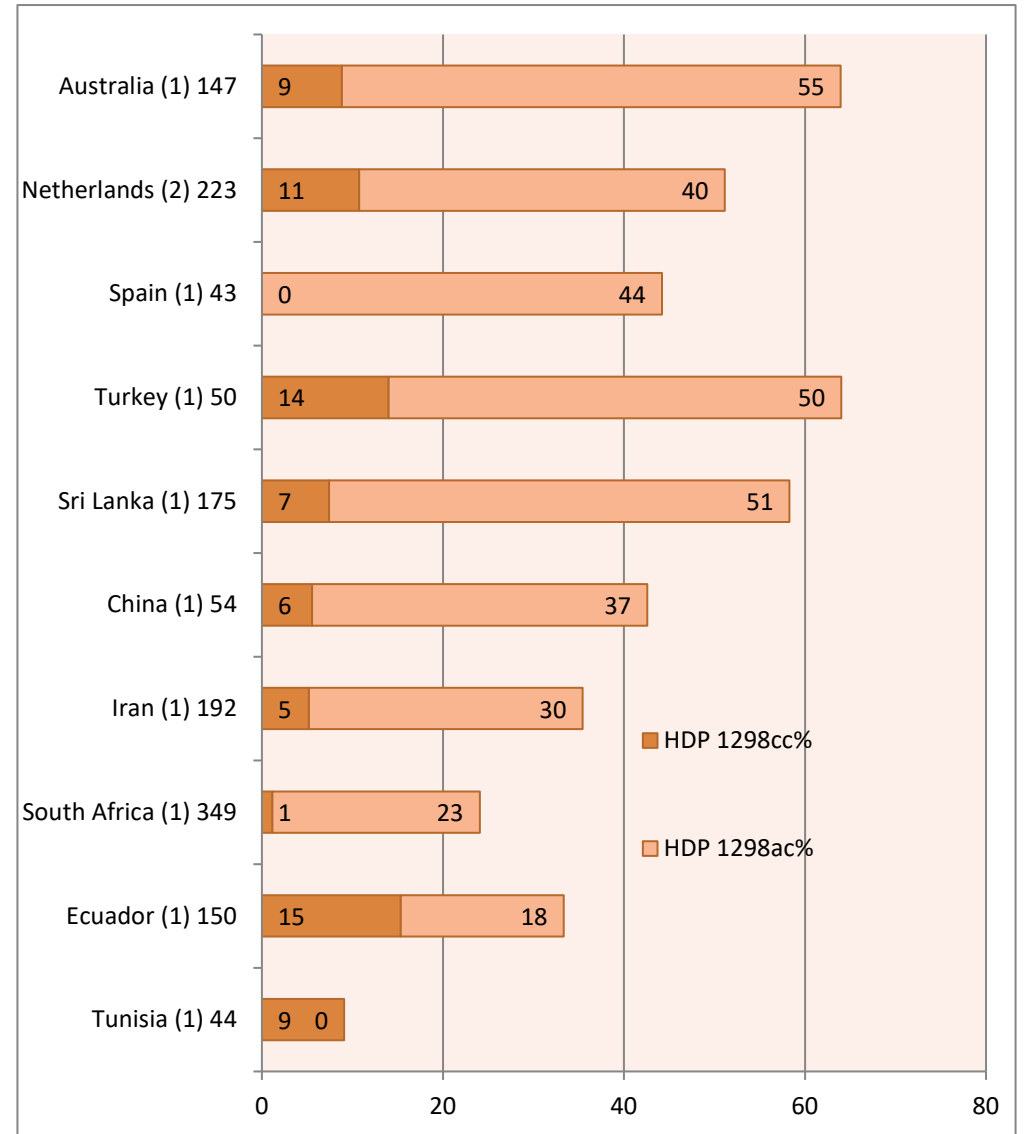
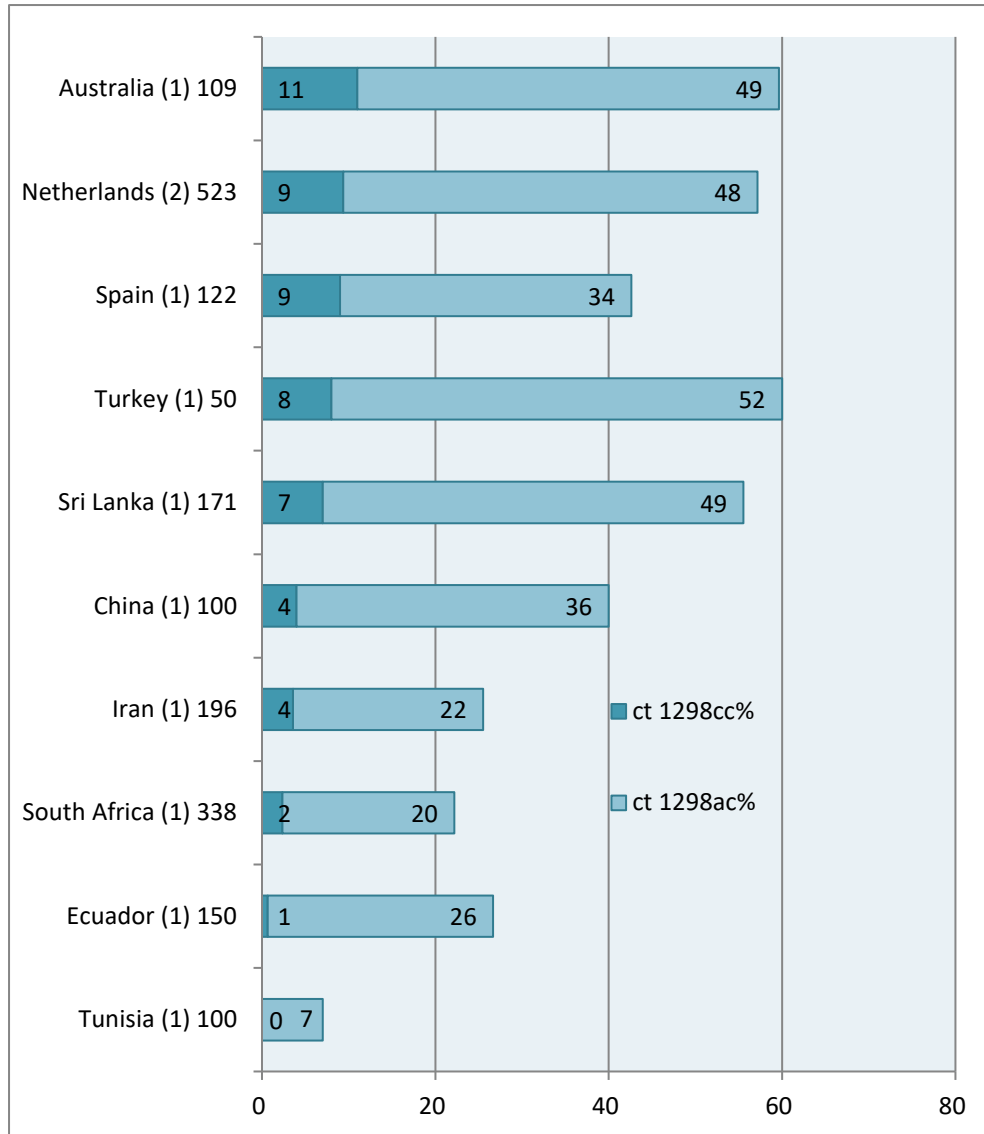


Figure S1b. The percentage of *MTHFR* 1298 AC and CC polymorphisms per control and hypertensive disorders in pregnancy (HDP) case groups.

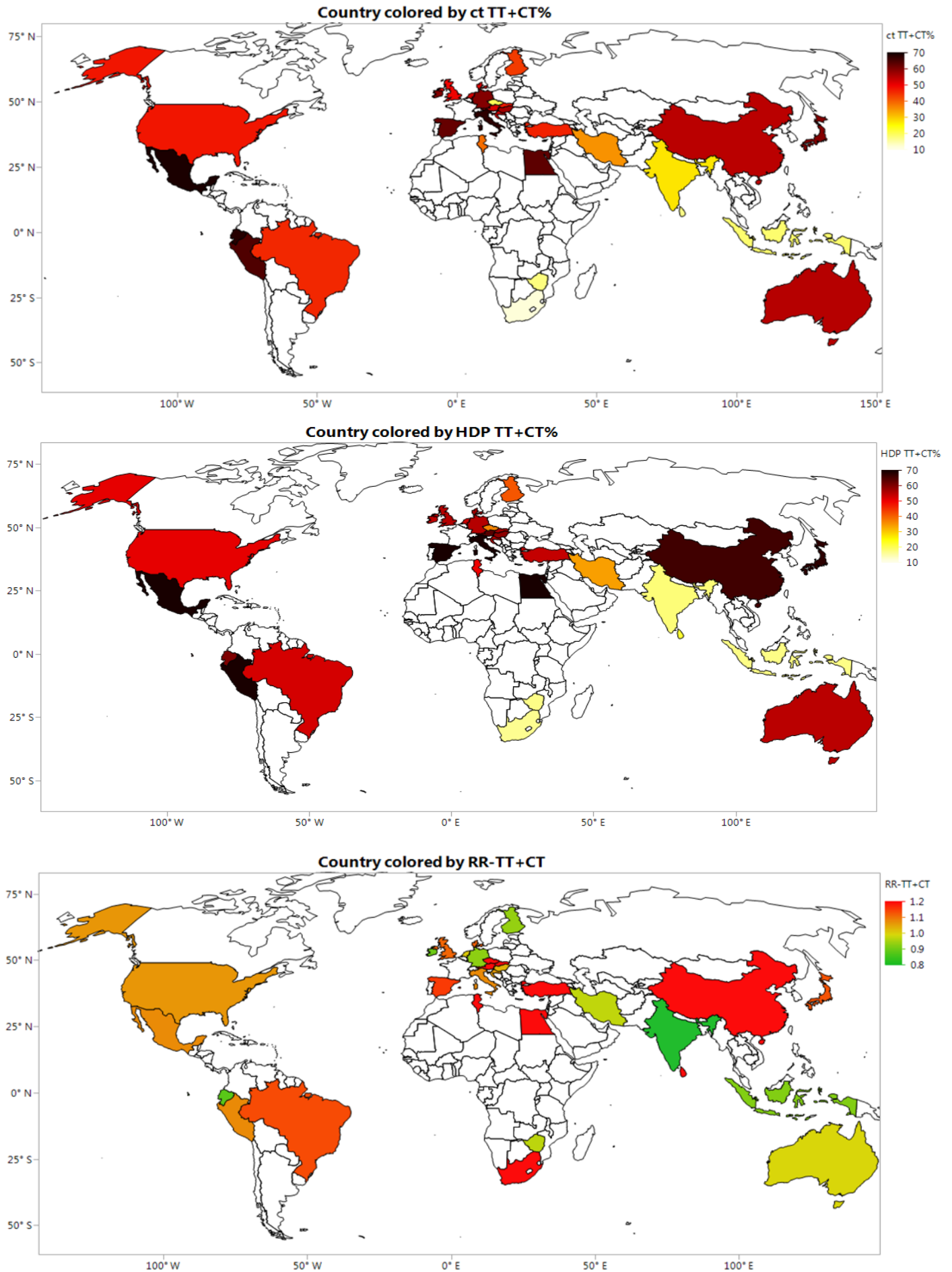


Figure S2a. Geographic information maps for % *MTHFR* 677 *TT* plus *CT* polymorphism per control and hypertensive disorders in pregnancy (HDP) groups, and HDP risks.

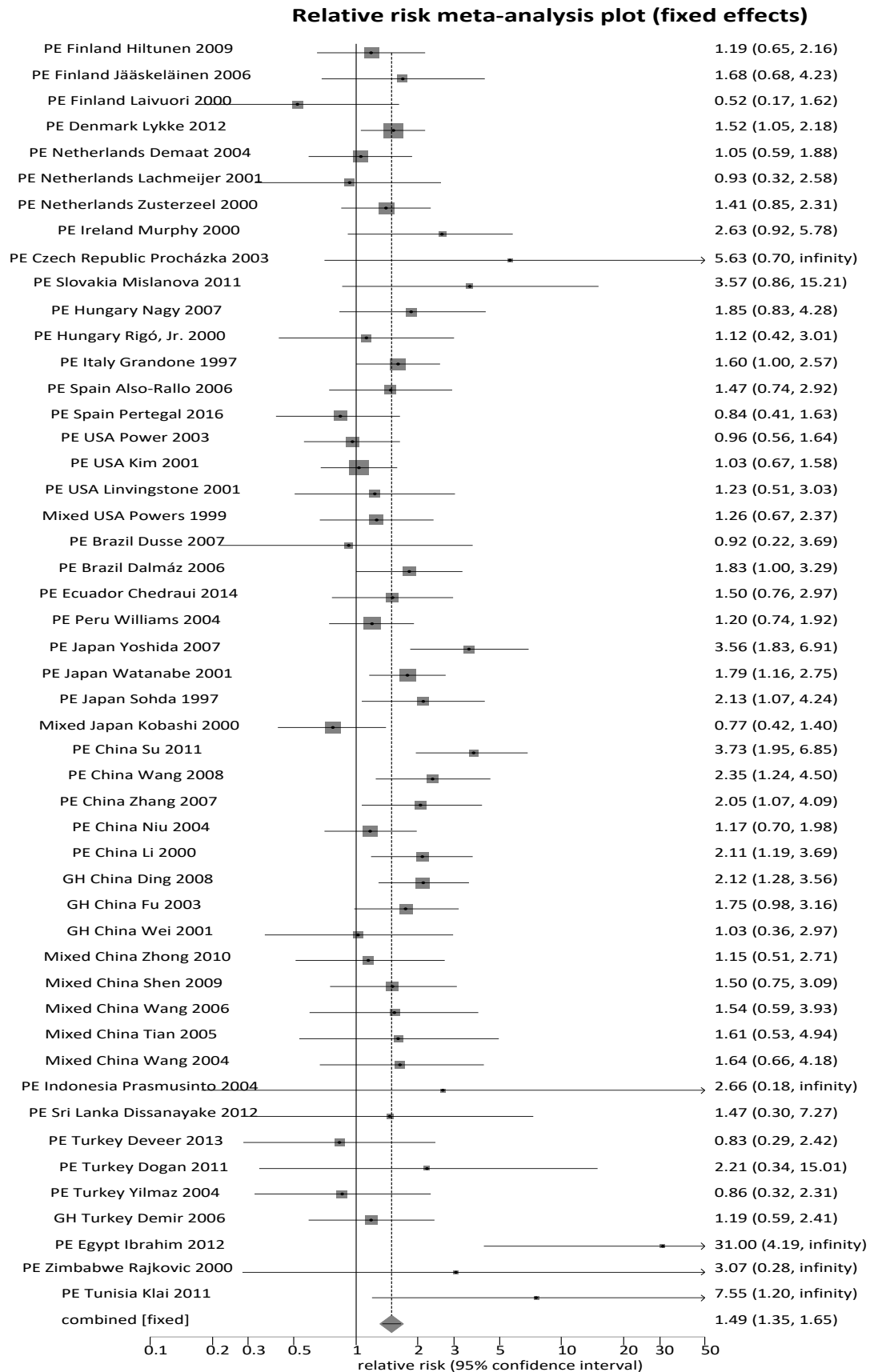


Figure S3a. Forest plot for *MTHFR C677T* with types of hypertensive disorders in pregnancy for countries of *TT* risk > 1.

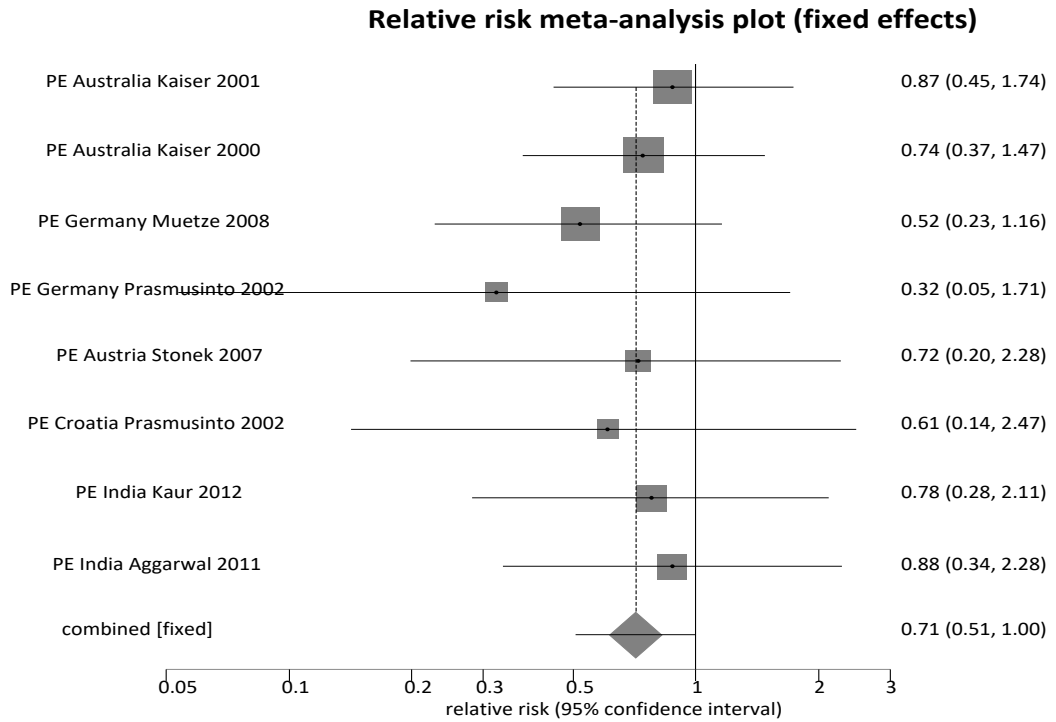


Figure S3b. Forest plot for *MTHFR C677T* with types of hypertensive disorders in pregnancy for countries of *TT* risk < 1.

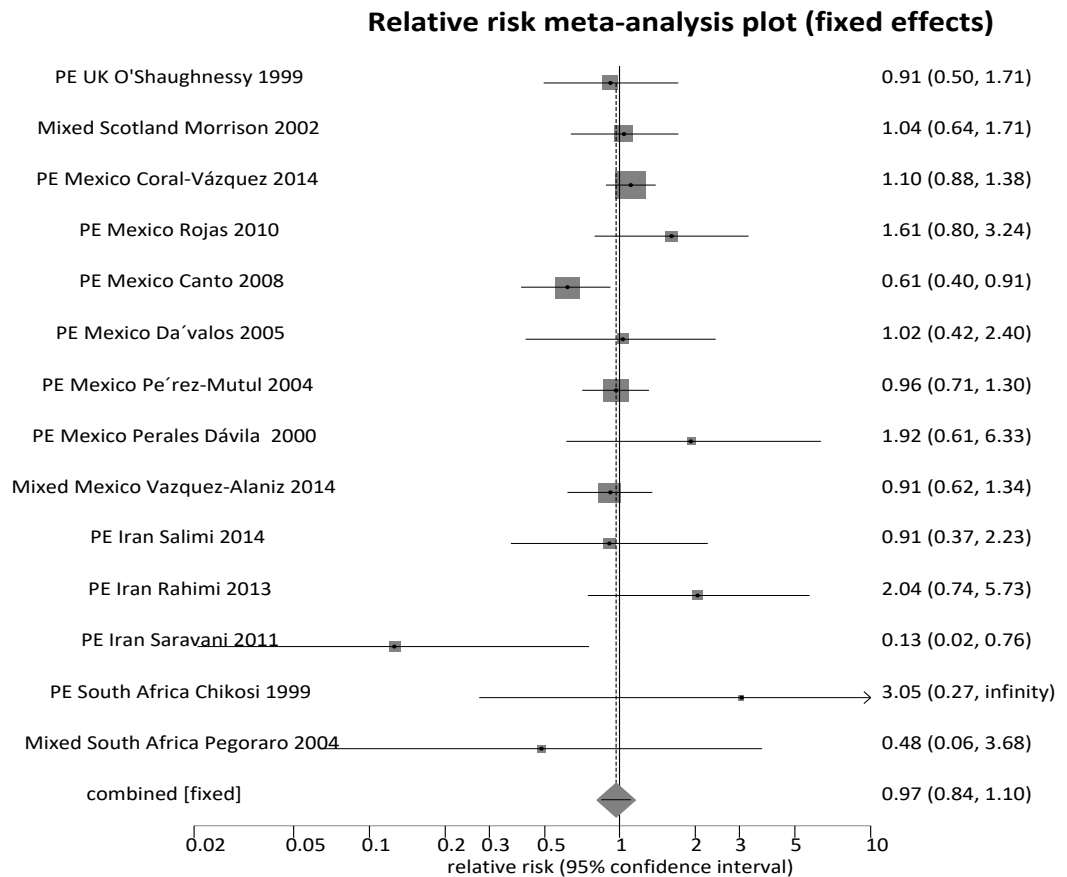


Figure S3c. Forest plot for *MTHFR C677T* with types of hypertensive disorders in pregnancy for countries of *TT* risk ~ 1.



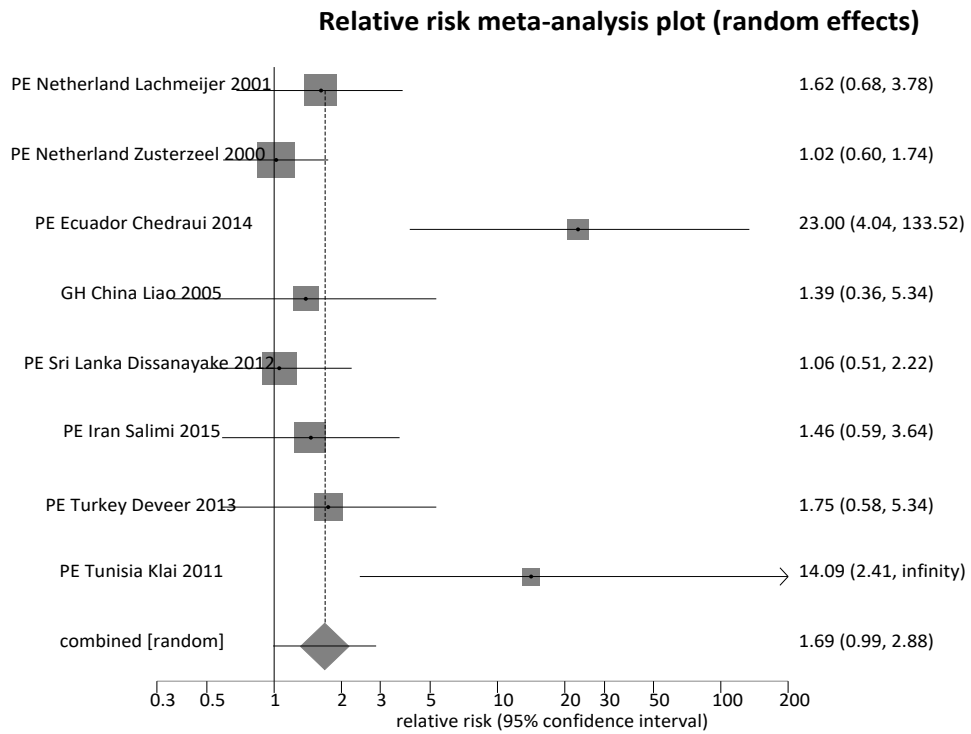


Figure S4a. Forest plot for *MTHFR A1298C* with types of hypertensive disorders in pregnancy for countries of CC risk > 1.

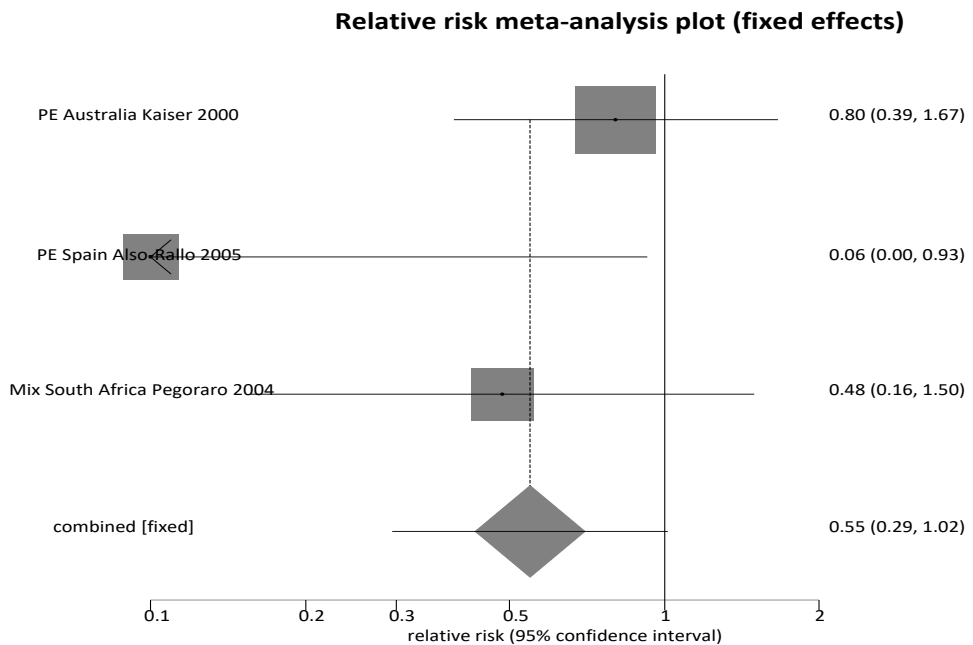


Figure S4b. Forest plot for *MTHFR A1298C* with types of hypertensive disorders in pregnancy for countries of CC risk < 1.

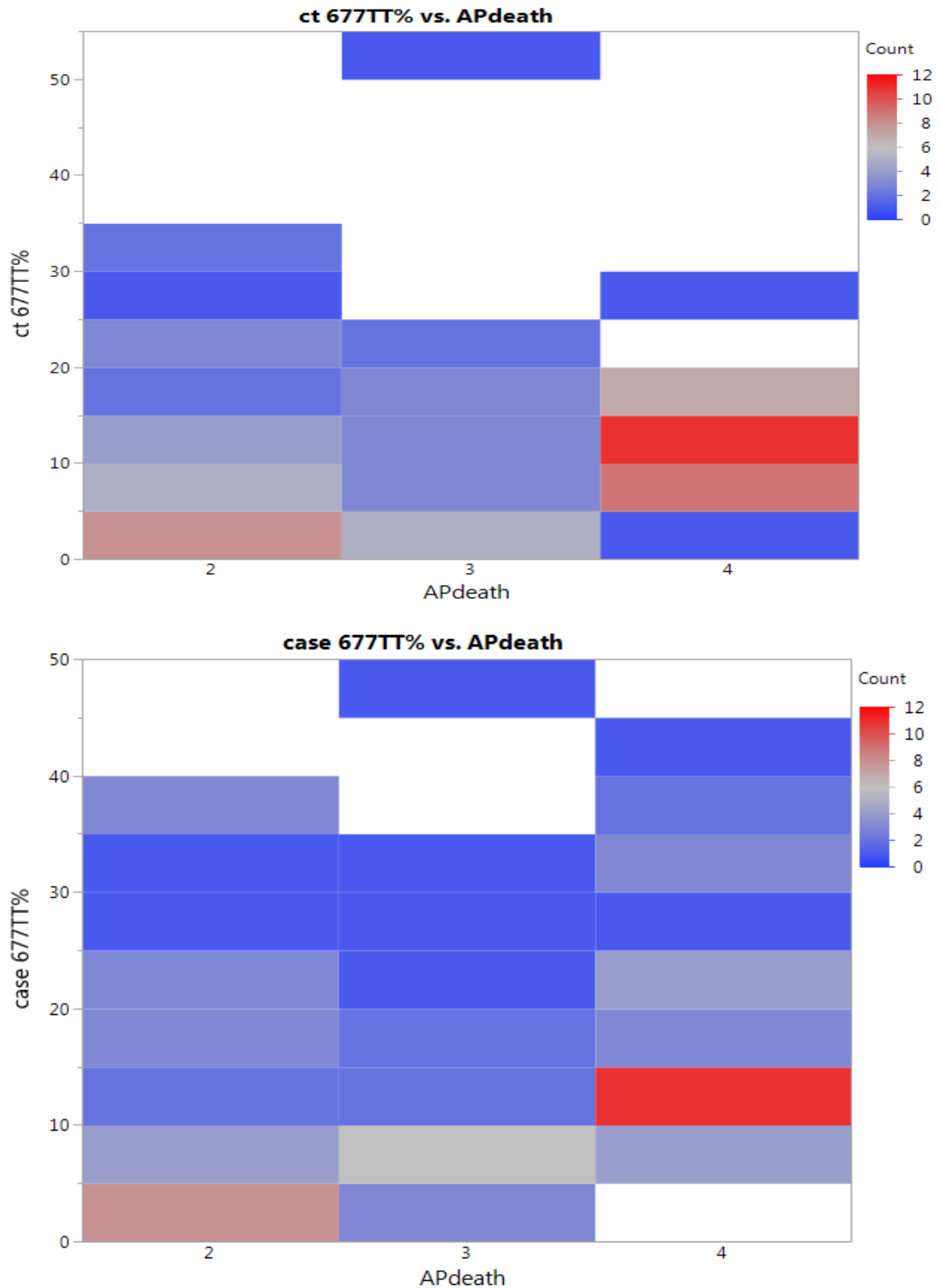


Figure S5a. Heat maps of *MTHFR* 677 homozygous *TT* genotypes for control and case groups in association with the rate of deaths from air pollution.

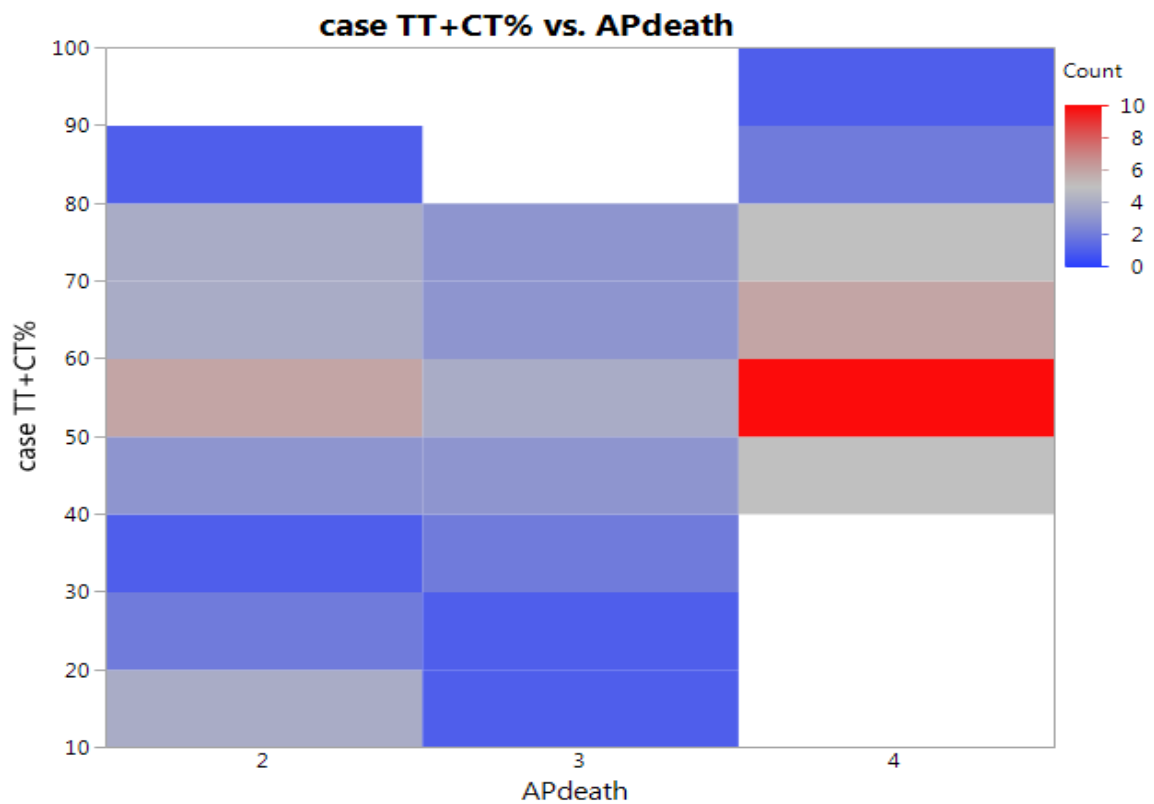
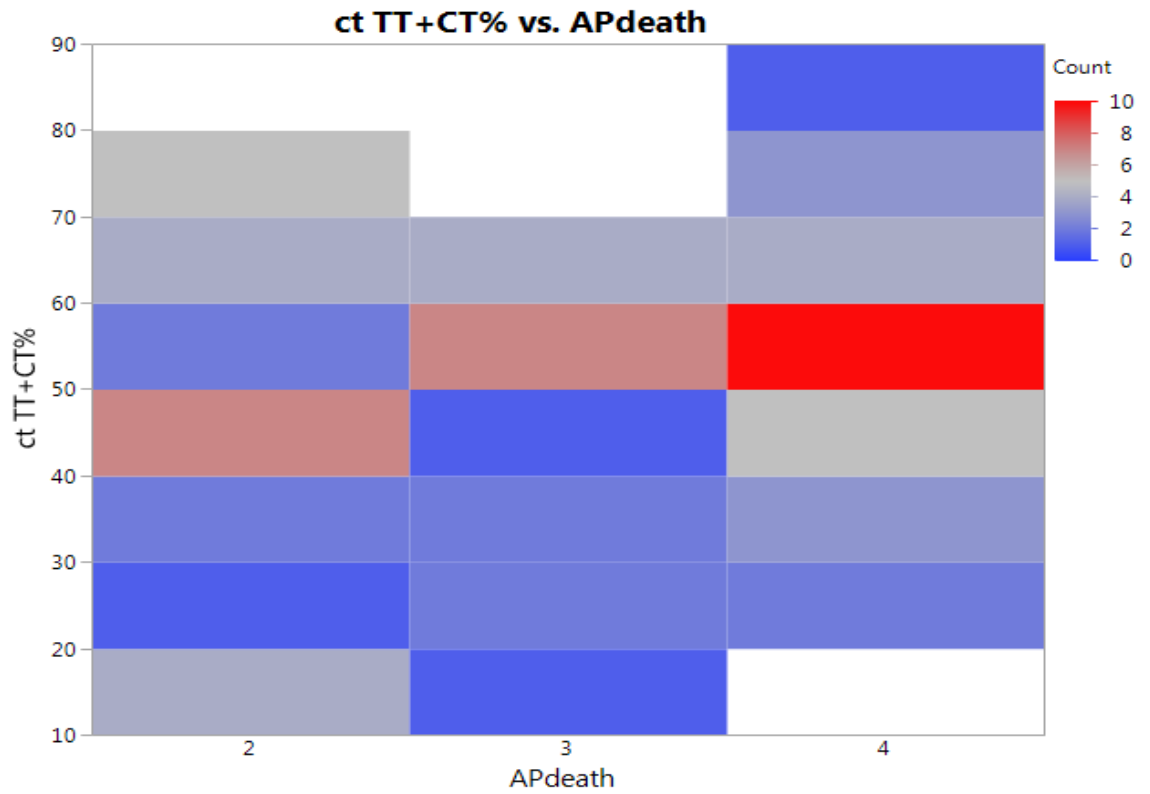


Figure S5b. Heat maps of *MTHFR* 677 *TT* plus *CT* genotypes for control and case groups in association with the rate of deaths from air pollution.