***Supplementary Table 1*:** Distribution of allele and genotype frequencies in the included studies

***MTHFR* 677C>T polymorphism**								
				Allele frequencies, n (%)		**Genotype frequencies, n (%)**		
Author	**Population**	**Disease status**	**Study size**	**C**	**T**	**CC**	**CT**	**TT**
Kowa, 2000[1]	women+men	controls	261	340 (65)	182 (35)	104 (39.8)	132 (50.6)	25 (9.6)
		any migraine	74	77 (52)	71 (48)	18 (24.3)	41 (55.4)	15 (20.3)
		MA	22	16 (36)	28 (64)	3 (13.6)	10 (45.5)	9 (40.9)
		MO	52	61 (59)	43 (41)	15 (28.8)	31 (59.6)	6 (11.5)
Kara, 2003[2]	women+men	controls	136	203 (74.6)	69 (25.4)	69 (50.7)	65 (47.8)	2 (1.5)
		any migraine	93	121 (65.1)	65 (34.9)	36 (38.7)	49 (52.7)	8 (8.6)
		MA	23	34 (73.9)	12 (26.1)	12 (52.2)	10 (43.5)	1 (4.3)
		MO	70	87 (62.1)	53 (37.9)	24 (34.3)	39 (55.7)	7 (10.0)
Lea, 2004[3]	women+men	controls	269	363 (67)	175 (33)	117 (43)	129 (48)	23 (9)
		any migraine	268	333 (62)	203 (38)	104 (39)	125 (46)	39 (15)
		MA	168	200 (60)	136 (40)	64 (38)	72 (43)	32 (19)
		MO	100	133 (66)	67 (34)	40 (40)	53 (53)	7 (7)
Oterino, 2005[4]	women+men	controls	237	302 (63.7)	172 (36.3)	94 (39.7)	114 (48.1)	29 (12.2)
		any migraine	329	431 (65.5)	227 (34.5)	142 (43.2)	147 (44.7)	40 (12.2)
		MA	138	164 (59.4)	112 (40.6)	52 (37.7)	60 (43.5)	26 (18.8)
		MO	191	267 (69.9)	115 (30.1)	90 (47.1)	87 (45.5)	14 (7.3)
Scher, 2006[5]	women+men	controls	1212	1661 (68.5)	763 (31.5)	567 (47)	527 (43)	118 (10)
		any migraine	413	548 (66.3)	278 (33.7)	181 (43.9)	186 (45.0)	46 (11.1)
		MA	187	230 (61.5)	144 (38.5)	72 (39)	86 (46)	29 (16)
		MO	226	318 (70.4)	134 (29.6)	109 (48)	100 (44)	17 (8)
Todt, 2006[6]	women+men	controls	625	802 (64.2)	448 (35.8)	251 (40.2)	300 (48)	74 (11.8)
		MA	656	879 (67)	433 (33)	300 (45.7)	279 (42.5)	77 (11.7)
Kaunisto, 2006[7]	women+men	controls	900	1368 (76)	432 (24)	522 (58)	324 (36)	54 (6)
		MA	898	1374 (76)	422 (24)	521 (58)	332 (37)	45 (5)
Bottini, 2006[8]	women+men	controls	66	81 (61.4)	51 (38.6)	24 (29.7)	33 (50)	9 (13.6)
		any migraine	45	49 (54.4)	41 (45.6)	16 (35.6)	17 (37.8)	12 (26.7)
		MA	33	35 (53)	31 (47)	11 (33.3)	13 (39.4)	9 (27.3)
		MO	12	14 (58)	10 (42)	5 (41.7)	4 (33.3)	3 (25)
de Tommaso, 2007[9]	women+men	controls	97	119 (61.35)	75 (38.65)	36 (37.1)	47 (48.5)	14 (14.3)
		any migraine	105	111 (52.86)	99 (47.14)	33 (31.4)	45 (42.9)	27 (25.7)

Pezzini, 2007[10]	women+men	controls	105	133 (63.3)	77 (36.7)	41 (39.0)	51 (48.6)	13 (12.4)
		any migraine	206	240 (58.3)	172 (41.7)	75 (36.4)	90 (43.7)	41 (19.9)
		MA	100	107 (53.5)	93 (46.5)	33 (33)	41 (41)	26 (26)
		MO	106	133 (62.7)	79 (37.3)	42 (39.6)	49 (46.2)	15 (14.2)
Schürks, 2008[11]	women	controls	20424	27285 (67)	13563 (33)	9173 (44.9)	8939 (43.8)	2312 (11.3)
		any migraine	4577	6178 (67)	2976 (33)	2070 (45.2)	2038 (44.5)	469 (10.3)
		MA	1275	1749 (69)	801 (31)	591 (46.3)	567 (44.5)	117 (9.2)
		MO	1951	2590 (66)	1312 (34)	855 (43.8)	880 (45.1)	216 (11.1)
Ferro, 2008[12]	women+men	controls	96	117 (61)	75 (39)	35 (36)	47 (49)	14 (15)
		any migraine	186	249 (67)	123 (33)	79 (42)	91 (49)	16 (9)
		MA	78	110 (71)	46 (29)	37 (47)	36 (46)	5 (6)
		MO	108	139 (64)	77 (36)	42 (39)	55 (51)	11 (10)
Joshi, 2009[13]	women+men	controls	150	255 (85.5)	45 (15.5)	108 (72.0)	39 (26.0)	3 (2.0)
		any migraine	150	254 (84.7)	46 (15.3)	104 (69.3)	46 (30.7)	0 (0.0)
		MA	67	113 (84.3)	21 (15.7)	46 (69.9)	21 (30.1)	0 (0.0)
		MO	83	141 (85.0)	25 (15.0)	58 (70.2)	25 (29.8)	0 (0.0)
	women	controls	100	169 (84.5)	31 (15.5)	72 (72.0)	25 (25.0)	3 (3.0)
		any migraine	100	166 (83.0)	34 (17.0)	66 (66.0)	34 (34.0)	0 (0.0)
	men	controls	50	86 (86.0)	14 (14.0)	36 (72.0)	14 (28.0)	0 (0.0)
		any migraine	50	88 (88.0)	12 (12.0)	38 (76.0)	12 (24.0)	0 (0.0)

ACE D/I polymorphism								
				Allele frequencies, n (%)		Genotype frequencies, n (%)		
Author	**Population**	**Disease status**	**Study size**	**D**	**I**	**DD**	**DI**	**II**
Paterna, 2000[14]	women+men	controls	201	251 (62.4)	151 (37.6)	75 (37.32)	101 (50.24)	25 (12.43)
		MO	302	421 (69.7)	183 (30.3)	146 (48.34)	129 (42.71)	27 (8.94)
Cakmak, 2003[15]	women+men	controls	231	275 (59.53)	187 (40.47)	88 (38.1)	99 (42.8)	44 (19)
		any migraine	200	237 (59.25)	163 (40.75)	77 (38.5)	83 (41.5)	40 (20)
	women	controls	78	99 (63.41)	57 (36.58)	31 (39.7)	34 (43.6)	13 (16.7)
		any migraine	174	204 (58.62)	144 (41.37)	65 (37.4)	74 (42.5)	35 (20.1)
	men	controls	153	179 (58.49)	127 (41.5)	57 (37.2)	65 (42.5)	31 (20.3)
		any migraine	26	33 (63.46)	19 (36.53)	12 (46.2)	9 (34.6)	5 (19.2)
Lin, 2005[16]	women+men	controls	200	153 (38.3)	247 (61.8)	34 (17.0)	85 (42.5)	81 (40.5)
		any migraine	240	175 (36.5)	305 (63.5)	40 (16.7)	95 (39.6)	105 (43.7)
	women	controls	141	107 (37.9)	175 (62.1)	23 (16.3)	61 (43.3)	57 (40.4)
		any migraine	169	134 (39.6)	204 (60.4)	35 (20.7)	64 (37.9)	70 (41.4)
	men	controls	59	46 (39.0)	72 (61.0)	11 (18.6)	24 (40.7)	24 (40.7)
		any migraine	71	41 (28.9)	101 (71.1)	5 (7.0)	31 (43.7)	35 (49.3)
Kowa, 2005[17]	women+men	controls	248	176 (35)	320 (65)	31 (12)	114 (46)	103 (42)
		any migraine	176	152 (43.2)	200 (56.8)	33 (18.8)	86 (48.8)	57 (32.4)
		MA	54	54 (50)	54 (50)	14 (26)	26 (48)	14 (26)
		MO	122	98 (40)	146 (60)	19 (16)	60 (49)	43 (35)
Lea, 2005[18]	women+men	controls	244	274 (56)	214 (44)	76 (31)	122 (50)	46 (19)
		any migraine	250	296 (59)	204 (41)	77 (31)	142 (57)	31 (12)
		MA	151	181 (60)	121 (40)	48 (32)	85 (56)	18 (12)
		MO	99	115 (58)	83 (42)	29 (29)	57 (58)	13 (13)
Kara, 2007[19]	women+men	controls	210	252 (60)	168 (40)	81 (38.5)	90 (42.9)	39 (18.6)
		any migraine	180	239 (66.39)	121 (33.61)	72 (40)	95 (52.8)	13 (7.2)
		MA	59	79 (66.95)	39 (33.05)	25 (42.4)	29 (49.1)	5 (8.5)
		MO	109	144 (66.06)	74 (33.94)	43 (39.5)	58 (53.2)	8 (7.3)
Tronvik, 2008[20]	women+men	controls	403	388 (48.1)	418 (51.9)	92 (26.6)	204 (50.6)	107 (22.8)
		any migraine	347	342 (49.3)	352 (50.7)	78 (22.5)	186 (53.6)	83 (23.9)
		MA	155	155 (50)	155 (50)	34 (21.9)	87 (56.1)	34 (21.9)
		MO	187	182 (48.7)	192 (51.3)	43 (23.0)	96 (51.3)	48 (25.7)
Schürks, 2009[21]	women	controls	20423	21365 (52)	19481 (48)	5996 (29.4)	9373 (45.9)	5054 (24.7)
		any migraine	4577	4806 (53)	4348 (47)	1331 (29.1)	2144 (46.8)	1102 (24.1)
		MA	1275	1346 (53)	1204 (47)	370 (29.0)	606 (47.5)	299 (23.5)
		MO	1951	2085 (53)	1817 (47)	584 (29.9)	917 (47.0)	450 (23.1)
Joshi, 2009[13]	women+men	controls	150	104 (34.7)	196 (65.3)	12 (8.0)	78 (52.0)	60 (40.0)
		any migraine	150	114 (38.0)	186 (62.0)	18 (12.0)	78 (52.0)	54 (36.0)

		MA	67	58 (43.3)	76 (56.7)	11 (16.4)	36 (53.7)	20 (29.9)
		MO	83	56 (33.7)	110 (66.3)	7 (8.4)	42 (50.6)	34 (41.0)
	women	controls	100	62 (31.0)	138 (69.0)	5 (5.0)	52 (52.0)	43 (43.0)
		any migraine	100	76 (38.0)	124 (62.0)	10 (10.0)	56 (56.0)	34 (34.0)
		MA	51	42 (41.2)	60 (58.8)	7 (13.7)	28 (54.9)	16 (31.4)
		MO	49	34 (34.7)	64 (65.3)	3 (6.12)	28 (57.14)	18 (36.74)
	men	controls	50	42 (42.0)	58 (58.0)	8 (16.0)	26 (52.0)	16 (32.0)
		any migraine	50	38 (38.0)	62 (62.0)	8 (16.0)	22 (44.0)	20 (40.0)
		MA	16	16 (50.0)	16 (50.0)	4 (25.0)	8 (50.0)	4 (25.0)
		MO	34	22 (32.4)	46 (67.6)	4 (11.8)	14 (41.2)	16 (47.0)

MA: migraine with aura; MO: migraine without aura

1. Kowa H, Yasui K, Takeshima T, Urakami K, Sakai F, Nakashima K. The homozygous C677T mutation in the methylenetetrahydrofolate reductase gene is a genetic risk factor for migraine. *Am J Med Genet*. 2000;96:762-764.
2. Kara I, Sazci A, Ergul E, Kaya G, Kilic G. Association of the C677T and A1298C polymorphisms in the 5,10 methylenetetrahydrofolate reductase gene in patients with migraine risk. *Brain Res Mol Brain Res*. 2003;111:84-90.
3. Lea RA, Ovcaric M, Sundholm J, MacMillan J, Griffiths LR. The methylenetetrahydrofolate reductase gene variant C677T influences susceptibility to migraine with aura. *BMC Med*. 2004;2:3.
4. Oterino A, Valle N, Pascual J*, et al.* Thymidylate synthase promoter tandem repeat and MTHFD1 R653Q polymorphisms modulate the risk for migraine conferred by the MTHFR T677 allele. *Brain Res Mol Brain Res*. 2005;139:163-168.
5. Scher AI, Terwindt GM, Verschuren WM*, et al.* Migraine and MTHFR C677T genotype in a population-based sample. *Ann Neurol*. 2006;59:372-375.
6. Todt U, Freudenberg J, Goebel I*, et al.* MTHFR C677T polymorphism and migraine with aura. *Ann Neurol*. 2006;60:621-622; author reply 622-623.
7. Kaunisto MA, Kallela M, Hamalainen E*, et al.* Testing of variants of the MTHFR and ESR1 genes in 1798 Finnish individuals fails to confirm the association with migraine with aura. *Cephalalgia*. 2006;26:1462-1472.
8. Bottini F, Celle ME, Calevo MG*, et al.* Metabolic and genetic risk factors for migraine in children. *Cephalalgia*. 2006;26:731-737.
9. de Tommaso M, Difruscolo O, Sardaro M*, et al.* Influence of MTHFR genotype on contingent negative variation and MRI abnormalities in migraine. *Headache*. 2007;47:253-265.
10. Pezzini A, Grassi M, Del Zotto E*, et al.* Migraine mediates the influence of C677T MTHFR genotypes on ischemic stroke risk with a stroke-subtype effect. *Stroke*. 2007;38:3145-3151.
11. Schürks M, Zee RY, Buring JE, Kurth T. Interrelationships among the MTHFR 677C>T polymorphism, migraine, and cardiovascular disease. *Neurology*. 2008;71:505-513.
12. Ferro A, Castro MJ, Lemos C*, et al.* The C677T polymorphism in MTHFR is not associated with migraine in Portugal. *Dis Markers*. 2008;25:107-113.
13. Joshi G, Pradhan S, Mittal B. Role of the ACE ID and MTHFR C677T polymorphisms in genetic susceptibility of migraine in a north Indian population. *J Neurol Sci*. 2009;277:133-137.
14. Paterna S, Di Pasquale P, D'Angelo A*, et al.* Angiotensin-converting enzyme gene deletion polymorphism determines an increase in frequency of migraine attacks in patients suffering from migraine without aura. *Eur Neurol*. 2000;43:133-136.
15. Cakmak EA, Cataloluk O, Yoldas T*, et al.* Migraine and angiotensin-converting enzyme association in Turkish patients. *Pain Clinic*. 2003;15:473-477.
16. Lin JJ, Wang PJ, Chen CH, Yueh KC, Lin SZ, Harn HJ. Homozygous deletion genotype of angiotensin converting enzyme confers protection against migraine in man. *Acta Neurol Taiwan*. 2005;14:120-125.

17. Kowa H, Fusayasu E, Ijiri T*, et al.* Association of the insertion/deletion polymorphism of the angiotensin I-converting enzyme gene in patients of migraine with aura. *Neurosci Lett*. 2005;374:129-131.
18. Lea RA, Ovcaric M, Sundholm J, Solyom L, Macmillan J, Griffiths LR. Genetic variants of angiotensin converting enzyme and methylenetetrahydrofolate reductase may act in combination to increase migraine susceptibility. *Brain Res Mol Brain Res*. 2005;136:112-117.
19. Kara I, Ozkok E, Aydin M*, et al.* Combined effects of ACE and MMP-3 polymorphisms on migraine development. *Cephalalgia*. 2007;27:235-243.
20. Tronvik E, Stovner LJ, Bovim G*, et al.* Angiotensin-converting enzyme gene insertion/deletion polymorphism in migraine patients. *BMC Neurol*. 2008;8:4.
21. Schürks M, Zee RYL, Buring JE, Kurth T. ACE D/I Polymorphism, Migraine, and Cardiovascular Disease in Women. *Neurology*. 2009;72:650-656.

Supplementary Table 2: Hardy-Weinberg Equilibrium and odds ratios (95% confidence intervals) for the included studies

***MTHFR* 677C>T polymorphism**										
					Additive model		**Dominant model**		**Recessive model**	
Author	**Population**	**Disease status**	**Study size**	**HWE**	**OR (95% CI)**	**P value**	**OR (95% CI)**	**P value**	**OR (95% CI)**	**P value**
Kowa, 2000[1]	women+men	controls	261	0.0755	Referent	----	Referent	----	Referent	----
		any migraine	74	----	1.852 (1.24-2.767)	0.0026	2.061 (1.147-3.703)	0.0156	2.40 (1.191-4.837)	0.0143
		MA	22	----	3.796 (1.881-7.659)	0.0002	4.195 (1.211-14.535)	0.0237	6.535 (2.541-16.808)	<0.0001
		MO	52	----	1.376 (0.864-2.193)	0.1788	1.634 (0.854-3.127)	0.1382	1.231 (0.478-3.169)	0.6661
Kara, 2003[2]	women+men	controls	136	0.0019	Referent	----	Referent	----	Referent	----
		any migraine	93	----	1.797 (1.125-2.872)	0.0142	1.631 (0.954-2.786)	0.0737	6.306 (1.308-30.405)	0.0218
		MA	23	----	1.051 (0.462-2.390)	0.9053	0.944 (0.390-2.286)	0.8984	3.046 (0.265-35.027)	0.3715
		MO	70	----	2.161 (1.284-3.636)	0.0037	1.974 (1.086-3.586)	0.0257	7.442 (1.503-36.844)	0.0139
Lea, 2004[3]	women+men	controls	269	0.1626	Referent	----	Referent	----	Referent	----
		any migraine	268	----	1.277 (0.988-1.651)	0.0623	1.214 (0.860-1.712)	0.2703	1.821 (1.055-3.144)	0.0313
		MA	168	----	1.415 (1.063-1.884)	0.0173	1.251 (0.844-1.854)	0.2653	2.516 (1.416-4.473)	0.0017
		MO	100	----	1.051 (0.728-1.518)	0.79	1.155 (0.724-1.842)	0.5464	0.805 (0.334-1.939)	0.6288
Oterino, 2005[4]	women+men	controls	237	0.581	Referent	----	Referent	----	Referent	----
		any migraine	329	----	0.924 (0.721-1.184)	0.5324	0.866 (0.616-1.216)	0.405	0.993 (0.596-1.653)	0.9776
		MA	138	----	1.196 (0.883-1.620)	0.2464	1.087 (0.706-1.674)	0.7044	1.665 (0.935-2.965)	0.0833
		MO	191	----	0.743 (0.552-1.001)	0.051	0.738 (0.502-1.084)	0.1217	0.567 (0.291-1.107)	0.0966
Scher, 2006[5]	women+men	controls	1212	0.8373	Referent	----	Referent	----	Referent	----
		any migraine	413	----	1.105 (0.934-1.308)	0.2447	1.127 (0.90-1.411)	0.298	1.162 (0.810-1.667)	0.4143
		MA	187	----	1.364 (1.088-1.710)	0.0071	1.404 (1.024-1.925)	0.035	1.702 (1.097-2.640)	0.0177
		MO	226	----	0.916 (0.734-1.143)	0.437	0.944 (0.710-1.254)	0.6889	0.754 (0.444-1.281)	0.2965
Todt, 2006[6]	women+men	controls	625	0.2944	Referent	----	Referent	----	Referent	----
		MA	656	----	0.882 (0.749-1.038)	0.131	0.796 (0.638-0.994)	0.0442	0.99 (0.705-1.391)	0.9548
Kaunisto, 2006[7]	women+men	controls	900	0.7093	Referent	----	Referent	----	Referent	----
		MA	898	----	0.972 (0.833-1.135)	0.7219	0.999 (0.829-1.205)	0.9939	0.827 (0.551-1.242)	0.3599
Bottini, 2006[8]	women+men	controls	66	0.8002	Referent	----	Referent	----	Referent	----

		any migraine	45	----	1.305 (0.77-2.212)	0.3225	1.036 (0.470-2.282)	0.9307	2.303 (0.878-6.043)	0.0901
		MA	33	----	1.39 (0.771-2.506)	0.274	1.143 (0.474-2.757)	0.7663	2.375 (0.840-6.718)	0.103
		MO	12	----	1.134 (0.469-2.742)	0.7802	0.80 (0.229-2.799)	0.7269	2.111 (0.479-9.309)	0.3236
de Tommaso, 2007[9]	women+men	controls	97	1	Referent	----	Referent	----	Referent	----
		any migraine	105	----	1.386 (0.942-2.039)	0.098	1.288 (0.719-2.306)	0.3951	2.052 (1.003-4.198)	0.049
Pezzini, 2007[10]	women+men	controls	105	0.8293	Referent	----	Referent	----	Referent	----
		any migraine	206	----	1.225 (0.877-1.711)	0.2347	1.119 (0.690-1.816)	0.649	1.758 (0.896-3.448)	0.1009
		MA	100	----	1.464 (0.995-2.152)	0.0529	1.301 (0.734-2.305)	0.3679	2.486 (1.195-5.173)	0.0148
		MO	106	----	1.026 (0.689-1.529)	0.898	0.976 (0.562-1.696)	0.9319	1.166 (0.525-2.588)	0.7054
Schürks, 2008[11]	women	controls	20424	0.0626	Referent	----	Referent	----	Referent	----
		any migraine	4577	----	0.969 (0.924-1.017)	0.206	0.987 (0.926-1.053)	0.7001	0.894 (0.805-0.993)	0.037
		MA	1275	----	0.922 (0.846-1.005)	0.0636	0.944 (0.842-1.057)	0.316	0.792 (0.651-0.962)	0.0188
		MO	1951	----	1.019 (0.951-1.092)	0.5956	1.045 (0.952-1.148)	0.3554	0.975 (0.841-1.131)	0.7422
Ferro, 2008[12]	women+men	controls	96	0.8319	Referent	----	Referent	----	Referent	----
		any migraine	186	----	0.754 (0.516-1.10)	0.143	0.777 (0.468-1.291)	0.3299	0.551 (0.257-1.184)	0.1266
		MA	78	----	0.634 (0.397-1.014)	0.0574	0.636 (0.346-1.168)	0.1446	0.401 (0.138-1.168)	0.0939
		MO	108	----	0.855 (0.563-1.298)	0.4609	0.902 (0.511-1.591)	0.7211	0.664 (0.286-1.543)	0.3414
Joshi, 2009[13]	women+men	controls	150	1	Referent	----	Referent	----	Referent	----
		any migraine	150	----	1.029 (0.643-1.648)	0.9045	1.137 (0.692-1.870)	0.6123	----	----
		MA	67	----	1.057 (0.589-1.898)	0.8518	1.174 (0.627-2.198)	0.6164	----	----
		MO	83	----	1.005 (0.579-1.745)	0.9855	1.108 (0.615-1.997)	0.7321	----	----
	women	controls	100	0.7006	Referent	----	Referent	----	Referent	----
		any migraine	100	----	1.128 (0.647-1.966)	0.6714	1.325 (0.726-2.417)	0.3595	----	----
	men	controls	50	0.5639	Referent	----	Referent	----	Referent	----
		any migraine	50	----	0.812 (0.332-1.989)	0.6492	0.812 (0.332-1.989)	0.6492	----	----
***ACE* D/I polymorphism**										
					Additive model		**Dominant model**		**Recessive model**	
Author	**Population**	**Disease status**	**Study size**	**HWE**	**OR (95% CI)**	**P value**	**OR (95% CI)**	**P value**	**OR (95% CI)**	**P value**
Paterna, 2000[14]	women+men	controls	201	0.37	Referent	----	Referent	----	Referent	----
		MO	302	----	0.714 (0.543-0.938)	0.0154	0.636 (0.442-0.915)	0.0149	0.691 (0.389-1.230)	0.2088
Cakmak, 2003[15]	women+men	controls	231	0.1033	Referent	----	Referent	----	Referent	----
		any migraine	200	----	1.01 (0.781-1.306)	0.9386	0.983 (0.666-1.451)	0.9313	1.063 (0.659-1.713)	0.8032
	women	controls	78	0.4752	Referent	----	Referent	----	Referent	----
		any migraine	174	----	1.116 (0.773-1.611)	0.5585	1.106 (0.640-1.913)	0.7183	1.259 (0.624-2.539)	0.5199
	men	controls	153	0.1349	Referent	----	Referent	----	Referent	----
		any migraine	26	----	0.833 (0.471-1.473)	0.5296	0.693 (0.300-1.601)	0.3903	0.937 (0.327-2.683)	0.9035
Lin, 2005[16]	women+men	controls	200	0.1764	Referent	----	Referent	----	Referent	----

		any migraine	240	----	1.07 (0.827-1.386)	0.6057	1.024 (0.620-1.691)	0.9258	1.143 (0.781-1.672)	0.4921
	women	controls	141	0.3741	Referent	----	Referent	----	Referent	----
		any migraine	169	----	0.94 (0.694-1.272)	0.6871	0.746 (0.417-1.335)	0.3238	1.042 (0.661-1.642)	0.8593
	men	controls	59	0.2802	Referent	----	Referent	----	Referent	----
		any migraine	71	----	1.547 (0.926-2.586)	0.0959	3.024 (0.986-9.275)	0.0529	1.418 (0.706-2.848)	0.3265
Kowa, 2005[17]	women+men	controls	248	1	Referent	----	Referent	----	Referent	----
		any migraine	176	----	0.724 (0.546-0.959)	0.0243	0.619 (0.363-1.056)	0.0782	0.674 (0.450-1.010)	0.0561
		MA	54	----	0.551 (0.361-0.843)	0.006	0.408 (0.200-0.835)	0.0141	0.493 (0.255-0.952)	0.0353
		MO	122	----	0.818 (0.595-1.123)	0.214	0.774 (0.418-1.436)	0.417	0.766 (0.489-1.201)	0.2453
Lea, 2005[18]	women+men	controls	244	0.8953	Referent	----	Referent	----	Referent	----
		any migraine	250	----	0.871 (0.668-1.136)	0.3086	1.016 (0.694-1.488)	0.9334	0.609 (0.372-0.999)	0.0495
		MA	151	----	0.845 (0.624-1.145)	0.2777	0.971 (0.627-1.502)	0.8938	0.583 (0.324-1.049)	0.0716
		MO	99	----	0.919 (0.651-1.298)	0.6325	1.092 (0.655-1.820)	0.7356	0.651 (0.334-1.266)	0.2059
Kara, 2007[19]	women+men	controls	210	0.1129	Referent	----	Referent	----	Referent	----
		any migraine	180	----	0.755 (0.561-1.017)	0.0641	0.942 (0.627-1.416)	0.7732	0.341 (0.176-0.662)	0.0015
		MA	59	----	0.753 (0.495-1.146)	0.1858	0.854 (0.475-1.535)	0.5977	0.406 (0.152-1.082)	0.0714
		MO	109	----	0.773 (0.550-1.087)	0.1389	0.964 (0.600-1.548)	0.8786	0.347 (0.156-0.773)	0.0095
Tronvik, 2008[20]	women+men	controls	403	0.8522	Referent	----	Referent	----	Referent	----
		any migraine	347	----	0.954 (0.775-1.173)	0.6528	1.020 (0.724-1.438)	0.9091	0.870 (0.624-1.211)	0.4089
		MA	155	----	0.925 (0.708-1.209)	0.5689	1.052 (0.674-1.644)	0.8223	0.777 (0.501-1.207)	0.2619
		MO	187	----	0.979 (0.764-1.254)	0.8656	0.991 (0.656-1.496)	0.9644	0.955 (0.643-1.419)	0.8214
Schürks, 2009[21]	women	controls	20423	<0.0001	Referent	----	Referent	----	Referent	----
		any migraine	4577	----	0.993 (0.950-1.037)	0.7444	1.014 (0.945-1.088)	0.7084	0.965 (0.895-1.040)	0.3447
		MA	1275	----	0.982 (0.909-1.061)	0.6517	1.017 (0.897-1.151)	0.7968	0.932 (0.815-1.065)	0.2979
		MO	1951	----	0.959 (0.900-1.022)	0.1943	0.973 (0.879-1.077)	0.5931	0.912 (0.817-1.018)	0.0995
Joshi, 2009[13]	women+men	controls	150	0.0687	Referent	----	Referent	----	Referent	----
		any migraine	150	----	0.819 (0.572-1.172)	0.275	0.638 (0.296-1.375)	0.2511	0.844 (0.529-1.346)	0.4759
		MA	67	----	0.633 (0.401-0.998)	0.0492	0.443 (0.185-1.062)	0.068	0.638 (0.344-1.183)	0.1538
		MO	83	----	1.014 (0.657-1.566)	0.95	0.944 (0.357-2.498)	0.9072	1.041 (0.603-1.797)	0.8857
	women	controls	100	0.038	Referent	----	Referent	----	Referent	----
		any migraine	100	----	0.678 (0.425-1.081)	0.1026	0.474 (0.156-1.440)	0.1877	0.683 (0.385-1.211)	0.1917
		MA	51	----	0.578 (0.329-1.013)	0.0557	0.331 (0.099-1.101)	0.0713	0.606 (0.297-1.235)	0.1678
		MO	49	----	0.803 (0.446-1.447)	0.4659	0.807 (0.185-3.524)	0.7756	0.770 (0.381-1.554)	0.4655
	men	controls	50	0.7747	Referent	----	Referent	----	Referent	----
		any migraine	50	----	1.182 (0.670-2.085)	0.5642	1.000 (0.343-2.913)	1	1.417 (0.624-3.218)	0.4054
		MA	16	----	0.712 (0.312-1.623)	0.4188	0.571 (0.147-2.228)	0.4203	0.708 (0.197-2.543)	0.597
		MO	34	----	1.526 (0.791-2.945)	0.2074	1.429 (0.394-5.181)	0.5874	1.889 (0.769-4.637)	0.1652

HWE: Hardy-Weinberg Equilibrium p-value from exact test; MA: migraine with aura; MO: migraine without aura

1. Kowa H, Yasui K, Takeshima T, Urakami K, Sakai F, Nakashima K. The homozygous C677T mutation in the methylenetetrahydrofolate reductase gene is a genetic risk factor for migraine. *Am J Med Genet*. 2000;96:762-764.
2. Kara I, Sazci A, Ergul E, Kaya G, Kilic G. Association of the C677T and A1298C polymorphisms in the 5,10 methylenetetrahydrofolate reductase gene in patients with migraine risk. *Brain Res Mol Brain Res*. 2003;111:84-90.
3. Lea RA, Ovcaric M, Sundholm J, MacMillan J, Griffiths LR. The methylenetetrahydrofolate reductase gene variant C677T influences susceptibility to migraine with aura. *BMC Med*. 2004;2:3.
4. Oterino A, Valle N, Pascual J*, et al.* Thymidylate synthase promoter tandem repeat and MTHFD1 R653Q polymorphisms modulate the risk for migraine conferred by the MTHFR T677 allele. *Brain Res Mol Brain Res*. 2005;139:163-168.
5. Scher AI, Terwindt GM, Verschuren WM*, et al.* Migraine and MTHFR C677T genotype in a population-based sample. *Ann Neurol*. 2006;59:372-375.
6. Todt U, Freudenberg J, Goebel I*, et al.* MTHFR C677T polymorphism and migraine with aura. *Ann Neurol*. 2006;60:621-622; author reply 622-623.
7. Kaunisto MA, Kallela M, Hamalainen E*, et al.* Testing of variants of the MTHFR and ESR1 genes in 1798 Finnish individuals fails to confirm the association with migraine with aura. *Cephalalgia*. 2006;26:1462-1472.
8. Bottini F, Celle ME, Calevo MG*, et al.* Metabolic and genetic risk factors for migraine in children. *Cephalalgia*. 2006;26:731-737.
9. de Tommaso M, Difruscolo O, Sardaro M*, et al.* Influence of MTHFR genotype on contingent negative variation and MRI abnormalities in migraine. *Headache*. 2007;47:253-265.
10. Pezzini A, Grassi M, Del Zotto E*, et al.* Migraine mediates the influence of C677T MTHFR genotypes on ischemic stroke risk with a stroke-subtype effect. *Stroke*. 2007;38:3145-3151.
11. Schürks M, Zee RY, Buring JE, Kurth T. Interrelationships among the MTHFR 677C>T polymorphism, migraine, and cardiovascular disease. *Neurology*. 2008;71:505-513.
12. Ferro A, Castro MJ, Lemos C*, et al.* The C677T polymorphism in MTHFR is not associated with migraine in Portugal. *Dis Markers*. 2008;25:107-113.
13. Joshi G, Pradhan S, Mittal B. Role of the ACE ID and MTHFR C677T polymorphisms in genetic susceptibility of migraine in a north Indian population. *J Neurol Sci*. 2009;277:133-137.
14. Paterna S, Di Pasquale P, D'Angelo A*, et al.* Angiotensin-converting enzyme gene deletion polymorphism determines an increase in frequency of migraine attacks in patients suffering from migraine without aura. *Eur Neurol*. 2000;43:133-136.
15. Cakmak EA, Cataloluk O, Yoldas T*, et al.* Migraine and angiotensin-converting enzyme association in Turkish patients. *Pain Clinic*. 2003;15:473-477.
16. Lin JJ, Wang PJ, Chen CH, Yueh KC, Lin SZ, Harn HJ. Homozygous deletion genotype of angiotensin converting enzyme confers protection against migraine in man. *Acta Neurol Taiwan*. 2005;14:120-125.
17. Kowa H, Fusayasu E, Ijiri T*, et al.* Association of the insertion/deletion polymorphism of the angiotensin I-converting enzyme gene in patients of migraine with aura. *Neurosci Lett*. 2005;374:129-131.
18. Lea RA, Ovcaric M, Sundholm J, Solyom L, Macmillan J, Griffiths LR. Genetic variants of angiotensin converting enzyme and methylenetetrahydrofolate reductase may act in combination to increase migraine susceptibility. *Brain Res Mol Brain Res*. 2005;136:112-117.
19. Kara I, Ozkok E, Aydin M*, et al.* Combined effects of ACE and MMP-3 polymorphisms on migraine development. *Cephalalgia*. 2007;27:235-243.
20. Tronvik E, Stovner LJ, Bovim G*, et al.* Angiotensin-converting enzyme gene insertion/deletion polymorphism in migraine patients. *BMC Neurol*. 2008;8:4.
21. Schürks M, Zee RYL, Buring JE, Kurth T. ACE D/I Polymorphism, Migraine, and Cardiovascular Disease in Women. *Neurology*. 2009;72:650-656.