

**Table e1. Description of migraine cohorts included in the current study.**

| Study                            | Cases/<br>Controls    | Migraine<br>% | Female<br>% of<br>cases | Female<br>% of<br>control<br>s | Ethnicity                           | Migraine definition  | Control definition  | Ref study<br>PMID                  |
|----------------------------------|-----------------------|---------------|-------------------------|--------------------------------|-------------------------------------|--|---|------------------------------------|
| <b>ALSPAC</b>                    | 3134/5103             | 38.0          | 100.0                   | 100.0                          | European, British                   | Self-reported migraine, current or prior   | No migraine or use of migraine medications; Pop.                      | 22507742                           |
| <b>Australia<br/>ATM<br/>ERF</b> | 1683/2383<br>330/1216 | 41.4<br>21.3  | 72.3<br>75.5            | 48.6<br>50.6                   | European descent<br>European, Dutch | Modified ICHD-II criteria, current migraine<br>Full ICHD-II criteria, current migraine | Pop.<br>No migraine   | 20303062,<br>18676988<br>20071666  |
| <b>Finnish MA</b>                | 1032/3513             | 22.7          | 80.2                    | 52.6                           | European, Finnish                   | ICHD-II  |   | 11509082;<br>20802479              |
| MA cases                         | 1032/0                |               |                         |                                |                                     |  |   |                                    |
| Health 2000                      | 0/1862                |               |                         |                                |                                     |  | Mig-free  | 20532202                           |
| Helsinki Birth Cohort            | 0/1651                |               |                         |                                |                                     |  | Pop.  | 16251536                           |
| <b>FinnTwin</b>                  | 189/580               | 28.5          | 63.5                    | 46.0                           | European, Finnish                   | Self-reported migraine, current or prior   | No migraine, use of migraine medication or severe recurrent headaches | 12537859,<br>12537860,<br>20953688 |
| <b>German MA</b>                 | 997/1105              | 47.4          | 81.1                    | 60.8                           |                                     |  |   |                                    |
| MA cases                         | 997/0                 |               |                         |                                | European, German                    | ICHD-II  |   | 20802479                           |
| PopGen                           | 0/661                 |               |                         |                                | European, German                    |  | Pop.  | 16490960                           |
| Illumina<br>iControlDB           | 0/444                 |               |                         |                                | MDS-filtered<br>Caucasian           |  | Pop.  | -                                  |
| <b>German MO</b>                 | 1208/2564             | 32.0          | 87.0                    | 55.1                           | European, German                    | ICHD-II  |   | 22683712                           |
| MO cases                         | 1208/0                |               |                         |                                |                                     |  |   |                                    |
| GSK                              | 0/861                 |               |                         |                                |                                     |  | Pop.  | 19107115                           |
| KORA                             | 0/834                 |               |                         |                                |                                     |  | Pop.  | 16032514                           |
| MPIPSYKL                         | 0/489                 |               |                         |                                |                                     |  | Pop.  | -                                  |
| HNR                              | 0/380                 |               |                         |                                |                                     |  | Pop.  | 12177636                           |
| <b>HUNT</b>                      | 1608/1097             | 59.4          | 74.9                    | 75.0                           | European,<br>Norwegian              | Self-reported migraine or fulfilling Modified  | No migraine; Pop.   | 10999674                           |

|                      |            |      |       |       |                   |   |  |                       |
|----------------------|------------|------|-------|-------|-------------------|---|--|-----------------------|
| <b>LUMINA MA</b>     | 820/4774   | 14.7 | 82.2  | 58.6  | European, Dutch   | ICHD-II criteria, current migraine  |  |                       |
| MA cases             | 820/0      |      |       |       |                   | ICHD-II   |  | 21914734;<br>20802479 |
| Rotterdam I          | 0/4774     |      |       |       |                   |   | Pop.                                     | 21877163              |
| <b>LUMINA MO</b>     | 1118/2016  | 35.7 | 85.8  | 54.2  | European, Dutch   |   |  |                       |
| MO cases             | 1118/0     |      |       |       |                   | ICHD-II   |  | 21914734;<br>22683712 |
| Rotterdam II         | 0/2016     |      |       |       |                   |   | Pop.                                     | 21877163              |
| <b>NTR</b>           | 265/2128   | 11.1 | 85.3  | 55.2  | European, Dutch   | Modified ICHD-II criteria, current migraine   | No migraine or severe recurrent headache | 17254420,<br>16611468 |
| <b>NESDA</b>         | 17/132     | 11.4 | 82.4  | 56.1  | European, Dutch   | Modified ICHD-II criteria, current migraine   | No migraine or severe recurrent headache | 18763692,<br>20713558 |
| <b>NFBC</b>          | 757/4399   | 14.7 | 76.5  | 48.2  | European, Finnish | Self-reported migraine, current or prior  | No migraine                              | 4911003               |
| <b>Rotterdam III</b> | 351/1647   | 17.6 | 77.5  | 51.2  | European, Dutch   | Modified ICHD-II criteria, current migraine   | No migraine                              | 21877163              |
| <b>TWINS UK</b>      | 972/3837   | 20.2 | 96.2  | 89.8  | European, British | Self-reported migraine or fulfilling Modified ICHD-II criteria, current or prior migraine | No migraine                              | 22253318              |
| <b>WGHS</b>          | 5122/18108 | 22.0 | 100.0 | 100.0 | European descent  | Self-reported migraine or fulfilling Modified ICHD-II criteria, current or prior migraine | No migraine                              | 18263651              |
| <b>Young Finns</b>   | 378/2065   | 15.5 | 79.6  | 49.3  | European, Finnish | Full ICHD-II criteria, current migraine   | No migraine                              | 18263651              |

The indented rows describe studies that were combined together to generate the set named on the first line of the set.

Where more than one control definition was used, control groups are listed in decreasing size.

ICHD-II = cases fulfill the International Classification of Headache Disorders, 2nd edition definition for current or past migraine; Pop. = Unscreened population-matched population-based sample; Mig-free = migraine-free population-matched population-based sample; PMID = PubMed ID; MA = migraine with aura; MO = migraine without aura.

**Table e2. Description of coronary artery disease cohorts included in the current study.**

| Study             | Cases/<br>Controls | Myocardial<br>infarction<br>% | Female<br>% of<br>cases | Female<br>% of<br>controls | M (SD) Age<br>cases/controls | CAD definition   | Control definition                         | Ref study<br>PMID |
|-------------------|--------------------|-------------------------------|-------------------------|----------------------------|------------------------------|--|--|-------------------|
| <b>ADVANCE</b>    | 278/312            | 50.4                          | 57.9                    | 59.0                       | 45.8 (6.2)/<br>45.3 (5.7)    | Clinical non fatal CAD<br>men ≤45 yrs, women ≤55<br>yrs) including AMI<br>(enzymes), typical angina<br>with ≥1 artery with >50%<br>stenosis, positive non<br>invasive test, or PCI or<br>CABG  | No history of clinical CAD,<br>CVA, or PAD | 18443000          |
| <b>CADomics</b>   | 2078/2952          | 58.3                          | 21.9                    | 50.5                       | 60.8 (10.1)/<br>55.3 (10.8)  | CAD: >50% stenosis in 1<br>major coronary artery<br>and/or MI based on ECG<br>and enzyme   | Population sample with no<br>history of MI | -                 |
| <b>CHARGE</b>     | 2287/22024         | 48.0                          | 33.4                    | 59.6                       | 28.1 (7.4)/<br>27.5 (8.0)    | CHD: definite or probably<br>MI, PTCA or CABG, or<br>ECG MI  | None of the conditions that<br>define CAD  | 20031568          |
| <b>deCODE CAD</b> | 6640/27611         | 54.7                          | 36.3                    | 61.9                       | 74.8 (11.8)/<br>53.7 (21.5)  | MI: MONICA criteria<br>(<75 yrs) or discharge<br>diagnosis of MI; CAD:<br>PCI or participation in<br>CVD genetics program<br>with self-report or CABG<br>or PCI, or discharge<br>diagnosis of angina<br>pectoris, MI or chronic<br>heart disease | Population sample                          | 17478679          |
| <b>GERMIFS I</b>  | 884/1604           | 100.0                         | 49.4                    | 50.8                       | 50.2 (7.8)/<br>27.7 (4.5)*   | MI (<65 yrs) with >1 1 <sup>st</sup><br>degree sibling with severe<br>CAD (PTCA; MI; CABG)   | Population sample                          | 17634449          |
| <b>GERMIFS II</b> | 1222/1287          | 100.0                         | 33.1                    | 48.3                       | 51.4 (7.5)/<br>51.2 (11.9)*  | MI (<60 yrs); 59.4% with<br>family history of CAD  | Population sample                          | 19198612          |
| <b>LURIC/</b>     | 652/213            | 71.9                          | 20.3                    | 46.0                       | 61.0 (11.8)/                 | Symptoms of angina   | No coronary lesions or                     | 11258203          |

|                                |           |       |      |      |                            |   |   |                       |
|--------------------------------|-----------|-------|------|------|----------------------------|---|---|-----------------------|
| <b>AtheroRemo 1</b>            |           |       |      |      | 58.3 (12.1)                | pectoris, NSTEMI, STEMI, or >50% coronary stenosis                                      | minor stenoses (<20%)                                   |                       |
| <b>LURIC/<br/>AtheroRemo 2</b> | 486/296   | 79.0  | 23.4 | 48.6 | 63.7 (9.4)/<br>56.4 (12.7) | Symptoms of angina pectoris, NSTEMI, STEMI, or >50% coronary stenosis                   | No coronary lesions or minor stenoses (<20%)            | 11258203              |
| <b>MedStar</b>                 | 874/447†  | 48.1  | 33.0 | 54.6 | 48.9 (6.4)/<br>59.7 (8.9)  | Angiography (≥1 coronary vessel with >50% stenosis); ≤55 for males and ≤60 for females. | Angiography normal, >45 yrs                             | 21239051              |
| <b>MIGen</b>                   | 1274/1407 | 100.0 | 37.2 | 39.9 | 42.4 (6.6)/<br>43.0 (7.8)* | MI (men <50 yrs / women <60 yrs)  | Hospital-based, community based, or nested case-control | 19198609              |
| <b>OHGS1</b>                   | 1542/1455 | 61.6  | 24.1 | 48.0 | 48.7 (7.3)/<br>75.9 (5.0)  | Angiographic (>50% stenosis)  | Asymptomatic  | 19371834              |
| <b>PennCATH</b>                | 933/468†  | 50.3  | 23.7 | 51.9 | 52.7 (7.6)/<br>61.7 (9.6)  | Angiography (≥1 coronary vessel with >50% stenosis); ≤60 for males and ≤65 for females. | Angiography normal, men >40 yrs / women >45 yrs         | 19198609;<br>17258089 |
| <b>WTCCC‡</b>                  | 1926/2938 | 71.5  | 20.7 | 50.0 | 49.8 (7.7)/‡               | Validated MI, CABG, PTCA or angina with positive non-invasive testing <66 yrs           | Unselected  | 17554300              |

M(SD) = mean (standard deviation); AMI = acute myocardial infarction; CABG = coronary artery bypass surgery; CAD = coronary artery disease; CVA = cerebrovascular accident; CHD = coronary heart disease; ECG = electrocardiogram; MI = myocardial infarction; NSTEMI = Non-ST-Elevated Myocardial Infarction; PTCA = percutaneous transluminal coronary angioplasty; STEMI = ST segment elevation myocardial infarction; PAD = peripheral artery disease; PCI = percutaneous coronary intervention; \*for cases age at diagnosis; for controls age at recruitment

†Cases: Angiographic CAD (>50% stenosis in at least 1 vessel); controls: Angiography normal or <10% stenosis in all vessels.

‡WTCC controls comprised of an equal number of subjects from the 1958 Birth Cohort and from the National Blood Service (NBS) Donors. The latter were recruited in equal 10 years age bands from 11 to 70 years of age. Additional phenotypes are not available for these controls.

**Table e3. List of independent SNPs ( $r^2 < 0.05$ ) with nominal association ( $p < 0.01$ ) to both CAD and migraine.**

| SNP        | Chr | Position* | CAD P value | Migraine P value | Direction of effect† | Nearest gene§               |
|------------|-----|-----------|-------------|------------------|----------------------|-----------------------------|
| rs13208321 | 6   | 96967075  | 2.53E-03    | 1.41E-10         | +                    | FUT9, UFL1                  |
| rs11759769 | 6   | 97171933  | 1.49E-03    | 1.71E-10         | +                    | FHL5                        |
| rs9349379  | 6   | 13011943  | 8.97E-08    | 5.88E-09         | +                    | PHACTR1                     |
| rs11000137 | 10  | 53351800  | 2.31E-03    | 7.99E-07         | +                    | PRKG1                       |
| rs7905968  | 10  | 105125309 | 9.00E-03    | 3.65E-06         | -                    | TAF5                        |
| rs9490306  | 6   | 121858578 | 1.53E-03    | 4.80E-06         | +                    | GJA1, HSF2                  |
| rs1890185  | 10  | 104738708 | 1.92E-03    | 5.58E-06         | +                    | CNNM2                       |
| rs7920251  | 10  | 104940187 | 2.60E-03    | 1.25E-05         | -                    | NT5C2                       |
| rs10456100 | 6   | 39291448  | 5.16E-04    | 2.37E-05         | +                    | KCNK5                       |
| rs11986252 | 8   | 138699854 | 8.35E-03    | 2.49E-05         | -                    | LOC101927915,<br>FAM135B    |
| rs11079844 | 17  | 44383333  | 7.30E-06    | 3.06E-05         | +                    | SNF8, GIP                   |
| rs1234221  | 10  | 89606459  | 6.96E-03    | 5.07E-05         | -                    | CFL1P1, KLLN                |
| rs12181638 | 6   | 121855958 | 1.36E-03    | 6.29E-05         | +                    | GJA1, HSF2                  |
| rs17453089 | 1   | 231224476 | 9.93E-03    | 1.03E-04         | +                    | PCNXL2                      |
| rs9992598  | 4   | 20208689  | 9.65E-03    | 1.05E-04         | -                    | SLIT2                       |
| rs3010671  | 9   | 80267958  | 9.86E-03    | 1.52E-04         | +                    | PSAT1, LOC101927450         |
| rs10859876 | 12  | 94282757  | 9.59E-03    | 2.06E-04         | +                    | MIR3685, METAP2             |
| rs2015278  | 12  | 67154556  | 5.20E-03    | 2.07E-04         | -                    | LOC100507195, RAP1B         |
| rs6469372  | 8   | 89443032  | 1.84E-03    | 2.35E-04         | -                    | MMP16, RIPK2                |
| rs10794612 | 10  | 124501636 | 1.93E-03    | 2.36E-04         | +                    | C10orf120, DMBT1P1          |
| rs7136874  | 12  | 110598041 | 2.49E-03    | 2.49E-04         | -                    | BRAP                        |
| rs12951376 | 17  | 17693534  | 2.30E-04    | 2.56E-04         | +                    | TOM1L2                      |
| rs12917651 | 16  | 74024197  | 1.55E-03    | 2.64E-04         | -                    | CFDP1                       |
| rs7908000  | 10  | 69689901  | 7.87E-03    | 3.03E-04         | -                    | ATOH7, PBLD                 |
| rs7304572  | 12  | 111009456 | 1.52E-03    | 3.09E-04         | -                    | NAA25                       |
| rs9856543  | 3   | 106074814 | 6.52E-03    | 3.55E-04         | -                    | NONE, ALCAM                 |
| rs7302763  | 12  | 110311952 | 6.18E-04    | 3.56E-04         | -                    | FAM109A, SH2B3              |
| rs11066322 | 12  | 111406912 | 2.64E-03    | 3.91E-04         | +                    | PTPN11                      |
| rs17015634 | 2   | 78855471  | 5.12E-03    | 4.14E-04         | +                    | LOC101927967, REG3G         |
| rs1889277  | 6   | 72386917  | 3.26E-04    | 4.15E-04         | -                    | LINC00472, RIMS1            |
| rs4302641  | 6   | 71124890  | 6.54E-03    | 4.23E-04         | +                    | COL9A1, LOC101928353        |
| rs4783386  | 16  | 21139552  | 6.60E-03    | 4.58E-04         | -                    | ZP2, ANKS4B                 |
| rs7749094  | 6   | 159767271 | 4.50E-03    | 5.52E-04         | +                    | LOC102724053, SOD2          |
| rs17043141 | 12  | 76149365  | 6.63E-04    | 6.78E-04         | +                    | E2F7, NAV3                  |
| rs17801974 | 5   | 150617527 | 3.84E-03    | 7.16E-04         | -                    | GM2A                        |
| rs10096696 | 8   | 4027418   | 8.90E-03    | 7.38E-04         | +                    | CSMD1                       |
| rs13270676 | 8   | 74490846  | 7.59E-03    | 7.79E-04         | -                    | LOC101926926, STAU2-<br>AS1 |
| rs12423041 | 12  | 110809229 | 4.55E-03    | 8.54E-04         | -                    | MAPKAPK5                    |
| rs10109848 | 8   | 58007616  | 1.59E-03    | 8.89E-04         | -                    | LINC00968, IMPAD1           |

Table e3 (continued)

| SNP        | Chr | Position* | CAD P value | Migraine P value | Direction of effect† | Nearest gene§          |
|------------|-----|-----------|-------------|------------------|----------------------|------------------------|
| rs7920106  | 10  | 7393139   | 4.89E-03    | 9.05E-04         | -                    | SFMBT2                 |
| rs2664283  | 10  | 75296379  | 1.03E-03    | 1.05E-03         | -                    | CAMK2G                 |
| rs7818729  | 8   | 127474852 | 6.48E-03    | 1.05E-03         | -                    | LOC101927657, FAM84B   |
| rs16906779 | 9   | 119959632 | 7.33E-03    | 1.07E-03         | -                    | TLR4, BRINP1           |
| rs4925138  | 17  | 17933518  | 5.21E-03    | 1.07E-03         | +                    | DRG2                   |
| rs7947345  | 11  | 74031875  | 3.34E-03    | 1.09E-03         | -                    | POLD3                  |
| rs12540319 | 7   | 27463119  | 8.58E-03    | 1.11E-03         | -                    | EVX1-AS, HIBADH        |
| rs1815519  | 1   | 100857130 | 5.81E-03    | 1.19E-03         | +                    | GPR88, LINC01349       |
| rs10828092 | 10  | 20962552  | 2.80E-03    | 1.21E-03         | +                    | MIR4675, NEBL          |
| rs7311376  | 12  | 109089942 | 1.78E-03    | 1.22E-03         | +                    | IFT81                  |
| rs11191841 | 10  | 105629601 | 6.12E-03    | 1.27E-03         | +                    | OBFC1                  |
| rs3729702  | 10  | 74900641  | 6.24E-03    | 1.44E-03         | -                    | PPP3CB                 |
| rs2511439  | 11  | 67610611  | 5.95E-03    | 1.48E-03         | -                    | CHKA                   |
| rs765467   | 6   | 72181890  | 2.06E-07    | 1.50E-03         | -                    | LINC00472              |
| rs11195781 | 10  | 113743177 | 2.88E-03    | 1.55E-03         | -                    | ADRA2A, GPAM           |
| rs17465651 | 1   | 38191083  | 2.80E-04    | 1.62E-03         | +                    | INPP5B, SF3A3          |
| rs2365261  | 1   | 61810709  | 1.40E-03    | 1.80E-03         | +                    | NFIA, MGC34796         |
| rs2039623  | 13  | 39637964  | 7.78E-03    | 1.85E-03         | +                    | COG6, LINC00332        |
| rs10916649 | 1   | 222835688 | 3.44E-04    | 1.97E-03         | -                    | WDR26, CNIH3           |
| rs7963504  | 12  | 109391263 | 2.28E-03    | 1.98E-03         | -                    | FAM216A                |
| rs7773293  | 6   | 114070787 | 4.61E-04    | 1.98E-03         | -                    | LOC101927686           |
| rs2476601  | 1   | 114179091 | 7.33E-04    | 2.05E-03         | -                    | PTPN22                 |
| rs8014986  | 14  | 99205471  | 3.02E-05    | 2.20E-03         | +                    | HHIPL1                 |
| rs11120900 | 1   | 7300767   | 9.35E-03    | 2.20E-03         | -                    | CAMTA1                 |
| rs10520569 | 15  | 82520393  | 3.65E-03    | 2.21E-03         | -                    | ADAMTSL3, EFTUD1P1     |
| rs838717   | 2   | 233961183 | 2.49E-03    | 2.24E-03         | -                    | DGKD                   |
| rs488624   | 9   | 27205792  | 5.40E-03    | 2.49E-03         | +                    | TEK                    |
| rs10786736 | 10  | 104839106 | 4.08E-05    | 2.54E-03         | -                    | NT5C2                  |
| rs13200037 | 6   | 13038738  | 7.96E-04    | 2.56E-03         | +                    | PHACTR1                |
| rs1427461  | 4   | 83460158  | 1.15E-03    | 2.71E-03         | -                    | RASGEF1B, HNRNPD       |
| rs2929282  | 15  | 42033223  | 3.07E-03    | 2.84E-03         | -                    | FRMD5                  |
| rs1516133  | 2   | 188590478 | 5.48E-03    | 2.91E-03         | -                    | TFPI, GULP1            |
| rs3904265  | 11  | 50316695  | 6.04E-03    | 2.94E-03         | -                    | LOC441601, LOC646813   |
| rs12941722 | 17  | 19292774  | 3.97E-03    | 2.97E-03         | -                    | RNF112, SLC47A1        |
| rs12450679 | 17  | 8297718   | 3.30E-04    | 3.01E-03         | +                    | NDEL1                  |
| rs2929275  | 15  | 42046189  | 4.25E-03    | 3.05E-03         | +                    | FRMD5                  |
| rs10518874 | 15  | 34446099  | 7.81E-03    | 3.06E-03         | -                    | MIR4510, C15orf41      |
| rs7501148  | 16  | 71875058  | 3.88E-04    | 3.24E-03         | +                    | C16orf47, LOC100506172 |
| rs17476034 | 11  | 50056843  | 8.67E-04    | 3.31E-03         | +                    | OR4C12, LOC441601      |
| rs9579648  | 13  | 30225032  | 2.09E-03    | 3.37E-03         | +                    | ALOX5AP                |
| rs10945970 | 6   | 164617709 | 2.33E-03    | 3.51E-03         | -                    | QKI, C6orf118          |

Table e3 (continued)

| SNP        | Chr | Position* | CAD P value | Migraine P value | Direction of effect† | Nearest gene§                 |
|------------|-----|-----------|-------------|------------------|----------------------|-------------------------------|
| rs11639989 | 16  | 9682661   | 4.39E-03    | 3.55E-03         | +                    | MIR7641-2, GRIN2A             |
| rs13263450 | 8   | 89643491  | 1.17E-03    | 3.59E-03         | +                    | MMP16, LOC101929709           |
| rs1316410  | 1   | 228952429 | 2.04E-03    | 3.71E-03         | +                    | CAPN9                         |
| rs7108904  | 11  | 51334382  | 3.71E-03    | 3.81E-03         | -                    | OR4A5, OR4C46                 |
| rs12636192 | 3   | 151015598 | 3.50E-03    | 3.96E-03         | -                    | RNF13                         |
| rs4026627  | 1   | 210924971 | 6.32E-03    | 4.05E-03         | +                    | FAM71A, BATF3                 |
| rs8188911  | 11  | 50727590  | 2.09E-03    | 4.25E-03         | +                    | LOC646813, OR4A5              |
| rs2280134  | 11  | 3638095   | 3.05E-04    | 4.32E-03         | -                    | ART1                          |
| rs10763976 | 10  | 34604298  | 1.14E-03    | 4.43E-03         | -                    | PARD3                         |
| rs827782   | 5   | 169766421 | 6.40E-03    | 4.51E-03         | +                    | CTD-2270F17.1                 |
| rs7029433  | 9   | 83423900  | 3.25E-03    | 4.54E-03         | +                    | TLE1                          |
| rs10902284 | 11  | 51078592  | 2.09E-03    | 4.63E-03         | +                    | LOC646813, OR4A5              |
| rs13231    | 6   | 161059847 | 2.35E-04    | 4.87E-03         | +                    | PLG                           |
| rs1508063  | 2   | 72957384  | 2.09E-03    | 4.91E-03         | +                    | EXOC6B, SPR                   |
| rs1108927  | 1   | 34105854  | 4.78E-03    | 4.93E-03         | +                    | CSMD2                         |
| rs1826907  | 4   | 100520149 | 6.07E-04    | 4.94E-03         | +                    | ADH1C, ADH7                   |
| rs7281595  | 21  | 42389601  | 8.35E-03    | 4.96E-03         | +                    | UMODL1                        |
| rs6069057  | 20  | 36240223  | 2.58E-03    | 5.10E-03         | +                    | TGM2, KIAA1755                |
| rs11187393 | 10  | 95097418  | 1.14E-03    | 5.12E-03         | -                    | MYOF                          |
| rs2925174  | 5   | 114680083 | 4.24E-03    | 5.29E-03         | -                    | CCDC112, FEM1C                |
| rs1556581  | 1   | 43544777  | 6.15E-03    | 5.33E-03         | -                    | TIE1                          |
| rs346522   | 19  | 48954385  | 4.99E-04    | 5.43E-03         | +                    | SMG9, KCNN4                   |
| rs2068414  | 11  | 49658664  | 5.19E-03    | 5.59E-03         | +                    | LOC440040                     |
| rs4692549  | 4   | 26194979  | 3.23E-03    | 5.61E-03         | +                    | TBC1D19                       |
| rs924765   | 8   | 134917078 | 4.34E-03    | 5.78E-03         | -                    | LOC101927798,<br>LOC101927822 |
| rs12083075 | 1   | 167377625 | 6.38E-03    | 5.83E-03         | +                    | NME7                          |
| rs1230666  | 1   | 113974933 | 5.54E-04    | 5.91E-03         | -                    | MAGI3                         |
| rs2300435  | 10  | 124242269 | 7.44E-03    | 5.92E-03         | +                    | HTRA1                         |
| rs196569   | 7   | 36270857  | 6.60E-03    | 5.99E-03         | -                    | EEPDI                         |
| rs1442243  | 7   | 52615087  | 1.74E-03    | 6.09E-03         | -                    | COBL, POM121L12               |
| rs17605951 | 16  | 70855143  | 8.10E-03    | 6.16E-03         | -                    | PMFBP1, ZFH3                  |
| rs4479352  | 18  | 60066408  | 9.59E-03    | 6.23E-03         | +                    | LINC01538, LOC284294          |
| rs11569557 | 19  | 6631510   | 9.11E-03    | 6.29E-03         | +                    | C3                            |
| rs371100   | 4   | 171708106 | 5.66E-03    | 6.51E-03         | -                    | LOC101928223,<br>LOC100506122 |
| rs693720   | 11  | 77570200  | 5.70E-03    | 6.74E-03         | +                    | KCTD21                        |
| rs12130112 | 1   | 37979629  | 7.46E-03    | 6.76E-03         | -                    | EPHA10                        |
| rs2478516  | 1   | 228935275 | 5.62E-03    | 7.03E-03         | +                    | AGT, CAPN9                    |
| rs5768001  | 22  | 46576776  | 4.77E-04    | 7.06E-03         | -                    | LOC284930                     |
| rs11929794 | 4   | 180109117 | 8.22E-03    | 7.62E-03         | -                    | LINC01098, NONE               |

Table e3 (continued)

| SNP        | Chr | Position* | CAD P value | Migraine P value | Direction of effect† | Nearest gene§        |
|------------|-----|-----------|-------------|------------------|----------------------|----------------------|
| rs17278009 | 2   | 55539888  | 5.32E-04    | 7.64E-03         | +                    | CCDC88A, CFAP36      |
| rs12989712 | 2   | 201814536 | 4.48E-03    | 7.67E-03         | -                    | CASP8                |
| rs6694531  | 1   | 148950136 | 1.52E-04    | 7.79E-03         | -                    | HORMAD1              |
| rs6920844  | 6   | 42653616  | 4.24E-03    | 7.83E-03         | -                    | UBR2                 |
| rs7662464  | 4   | 155905830 | 2.03E-03    | 7.94E-03         | -                    | LRAT, RBM46          |
| rs17193778 | 3   | 1797161   | 4.38E-04    | 7.98E-03         | -                    | CNTN6, CNTN4         |
| rs2042549  | 2   | 169238400 | 4.26E-04    | 8.09E-03         | -                    | CERS6                |
| rs12073872 | 1   | 170817021 | 3.49E-03    | 8.17E-03         | +                    | SUCO                 |
| rs6832419  | 4   | 40096367  | 2.90E-03    | 8.25E-03         | -                    | CHRNA9, RBM47        |
| rs7310409  | 12  | 119909244 | 4.15E-06    | 8.44E-03         | +                    | HNF1A                |
| rs7990504  | 13  | 41498003  | 3.03E-04    | 8.46E-03         | -                    | VWA8-AS1, DGKH       |
| rs12275064 | 11  | 49109173  | 8.06E-05    | 8.47E-03         | +                    | TRIM64C, FOLH1       |
| rs10137574 | 14  | 99232677  | 1.35E-03    | 8.70E-03         | -                    | CYP46A1              |
| rs6139515  | 20  | 4595512   | 5.14E-03    | 8.70E-03         | -                    | ADRA1D, PRNP         |
| rs11941167 | 4   | 43817331  | 1.84E-03    | 8.92E-03         | -                    | GRXCR1, KCTD8        |
| rs10490445 | 2   | 37470988  | 7.95E-03    | 8.96E-03         | +                    | QPCT, CDC42EP3       |
| rs17642516 | 6   | 148858197 | 4.93E-03    | 9.05E-03         | +                    | SASH1                |
| rs293974   | 11  | 26546702  | 6.79E-03    | 9.11E-03         | +                    | ANO3, MUC15          |
| rs550517   | 5   | 31421693  | 8.42E-03    | 9.14E-03         | -                    | CDH6, DROSHA         |
| rs7096797  | 10  | 43640310  | 1.50E-03    | 9.27E-03         | +                    | HNRNPA3P1, LINC00619 |
| rs11694529 | 2   | 49114653  | 8.52E-03    | 9.34E-03         | +                    | FSHR                 |
| rs934287   | 2   | 203416552 | 3.93E-08    | 9.49E-03         | +                    | ICA1L                |
| rs2160847  | 2   | 211309361 | 5.96E-03    | 9.54E-03         | -                    | CPS1, ERBB4          |
| rs10050682 | 5   | 133358825 | 9.98E-03    | 9.71E-03         | +                    | VDAC1                |
| rs7095475  | 10  | 106197923 | 4.84E-03    | 9.75E-03         | -                    | CFAP58               |
| rs12898704 | 15  | 72048036  | 1.79E-03    | 9.87E-03         | +                    | LOXL1, STOML1        |
| rs10142643 | 14  | 29490756  | 8.58E-03    | 9.92E-03         | -                    | PRKD1, G2E3          |

CAD = coronary artery disease. \*Positions refer to build NCBI36/hg18. †SNPs with the same effect direction for association to CAD and migraine are marked as plus (+), opposing effect direction are marked as minus (-). §RefSeq genes. For intergenic SNPs the nearest gene on either side is listed. The list is sorted by increasing *P* value for association to migraine.



**Table e4. Association between coronary artery disease polygenic risk score and the presence of migraine.**

|                          | <b>CAD risk<br/>SNP set*</b> | <b>OR</b> | <b>Standard<br/>error</b> | <b>R<sup>2</sup><br/>explained†</b> | <b>P value</b> |
|--------------------------|------------------------------|-----------|---------------------------|-------------------------------------|----------------|
| All migraine             | Weak                         | 1.000     | 0.0005                    | 1.93E-06                            | 8.56E-01       |
|                          | Moderate                     | 0.997     | 0.0012                    | 4.27E-04                            | 6.89E-03       |
|                          | Strong                       | 0.997     | 0.0017                    | 1.76E-04                            | 8.28E-02       |
| Migraine<br>without aura | Weak                         | 1.000     | 0.0007                    | 5.88E-05                            | 5.11E-01       |
|                          | Moderate                     | 0.994     | 0.0017                    | 1.96E-03                            | 1.48E-04       |
|                          | Strong                       | 0.992     | 0.0023                    | 1.64E-03                            | 5.13E-04       |
| Migraine with<br>aura    | Weak                         | 1.000     | 0.0007                    | 1.95E-05                            | 6.74E-01       |
|                          | Moderate                     | 1.000     | 0.0018                    | 5.17E-08                            | 9.83E-01       |
|                          | Strong                       | 1.003     | 0.0024                    | 1.37E-04                            | 2.64E-01       |

CAD = coronary artery disease.

\*Weak – *P* value <1.0E-02; Moderate – *P* value <1.0E-04; Strong – *P* value <5.0E-08.

†Difference in Nagelkerke's pseudo R<sup>2</sup> between model including and model not including CAD polygenic risk score.

The CAD risk SNP sets were based on SNPs with weak ( $P < 1 \times 10^{-2}$ ), moderate ( $P < 1 \times 10^{-4}$ ) or strong ( $P < 5 \times 10^{-8}$ ) association to CAD in the CAD study.

Analyses were corrected for gender, and for dummy-coded covariates representing the individual migraine cohorts.

**Table e5. Details of lead SNPs for coronary artery disease and migraine at each overlapping locus identified by Cross-Phenotype Spatial Mapping (CPSM).**

| Locus no. | Chr band |                   | SNP        | Position*   | CAD <i>P</i> value† | Migraine <i>P</i> value† | Migraine                     | Migraine                  | Direction of effect‡ | Nearest gene§          |
|-----------|----------|-------------------|------------|-------------|---------------------|--------------------------|------------------------------|---------------------------|----------------------|------------------------|
|           |          |                   |            |             |                     |                          | without aura <i>P</i> value† | with aura <i>P</i> value† |                      |                        |
| 1         | 6p24     | Lead CAD SNP      | rs4714955  | 13,011,421  | <b>9.80E-11</b>     | 5.04E-07                 | <b>2.68E-09</b>              | 3.43E-01                  | +---                 | <i>PHACTR1</i>         |
|           |          | Lead migraine SNP | rs9349379  | 13,011,943  | 8.97E-08            | <b>5.88E-09</b>          | <b>2.52E-10</b>              | 2.36E-01                  | +---                 | <i>PHACTR1</i>         |
| 2         | 17q21    | Lead CAD SNP      | rs46522    | 44,343,596  | 2.58E-07            | 1.24E-04                 | 6.93E-03                     | 8.10E-02                  | +---                 | <i>UBE2Z</i>           |
|           |          | Lead migraine SNP | rs11079844 | 44,383,333  | 7.30E-06            | 3.06E-05                 | 8.30E-03                     | 1.57E-02                  | +---                 | <i>SNF8, GIP</i>       |
| 3         | 6q16     | Lead CAD SNP      | rs2064947  | 97,159,475  | 6.40E-04            | 2.46E-07                 | <b>5.47E-11</b>              | 2.78E-02                  | +---                 | <i>FHL5</i>            |
|           |          | Lead migraine SNP | rs13208321 | 96,967,075  | 2.53E-03            | <b>1.41E-10</b>          | <b>1.35E-12</b>              | 7.40E-04                  | +---                 | <i>FUT9, UFL1</i>      |
| 4         | 12q24    | Lead CAD SNP      | rs2238151  | 110,696,216 | 2.43E-07            | 7.29E-03                 | 2.34E-03                     | 3.95E-01                  | +---                 | <i>ALDH2</i>           |
|           |          | Lead migraine SNP | rs7136874  | 110,598,041 | 2.49E-03            | 2.49E-04                 | 1.26E-03                     | 1.05E-01                  | +---                 | <i>BRAP</i>            |
| 5         | 17p11    | Lead CAD SNP      | rs6502622  | 17,775,416  | 7.61E-06            | 3.03E-03                 | 4.88E-03                     | 5.31E-01                  | ++++                 | <i>TOMIL2</i>          |
|           |          | Lead migraine SNP | rs12951376 | 17,693,534  | 2.30E-04            | 2.56E-04                 | 1.23E-01                     | 8.55E-02                  | ++++                 | <i>TOMIL2</i>          |
| 6         | 16q23    | Lead CAD SNP      | rs4888422  | 74,028,077  | 6.88E-05            | 9.55E-04                 | 7.38E-02                     | 2.59E-02                  | +---                 | <i>CFDP1, TMEM170A</i> |
|           |          | Lead migraine SNP | rs12917651 | 74,024,197  | 1.55E-03            | 2.64E-04                 | 2.07E-02                     | 6.13E-02                  | +---                 | <i>CFDP1</i>           |
| 7         | 10q24    | Lead CAD SNP      | rs10786736 | 104,839,106 | 4.08E-05            | 2.54E-03                 | 5.28E-02                     | 8.97E-01                  | +--+                 | <i>NT5C2</i>           |
|           |          | Lead migraine SNP | rs7905968  | 105,125,309 | 9.00E-03            | 3.65E-06                 | 1.68E-02                     | 8.62E-03                  | +---                 | <i>TAF5</i>            |
| 8         | 2q33     | Lead CAD SNP      | rs3845800  | 203,442,610 | <b>4.47E-11</b>     | 2.90E-02                 | 3.32E-02                     | 9.53E-01                  | +---                 | <i>ICAIL</i>           |

|    |       |                   |            |             |                 |          |          |          |      |                         |
|----|-------|-------------------|------------|-------------|-----------------|----------|----------|----------|------|-------------------------|
|    |       | Lead migraine SNP | rs934287   | 203,416,552 | <b>3.93E-08</b> | 9.49E-03 | 8.91E-03 | 7.92E-01 | +--- | <i>ICA1L</i>            |
| 9  | 10q24 | Lead CAD SNP      | rs11191425 | 104,615,960 | 1.16E-05        | 2.83E-02 | 4.88E-02 | 7.55E-01 | +--- | <i>C10orf32-AS3MT</i>   |
|    |       | Lead migraine SNP | rs1890185  | 104,738,708 | 1.92E-03        | 5.58E-06 | 2.21E-02 | 9.18E-03 | +--- | <i>CNNM2</i>            |
| 10 | 6q13  | Lead CAD SNP      | rs9351814  | 72,250,428  | <b>9.90E-09</b> | 7.51E-03 | 3.47E-03 | 7.52E-02 | ++++ | <i>LINC00472, RIMS1</i> |
|    |       | Lead migraine SNP | rs1889277  | 72,386,917  | 3.26E-04        | 4.15E-04 | 2.47E-02 | 6.64E-02 | ++++ | <i>LINC00472, RIMS1</i> |
| 11 | 8q21  | Lead CAD SNP      | rs1580508  | 89,639,576  | 9.40E-04        | 3.95E-03 | 1.25E-07 | 3.60E-01 | ++++ | <i>MMP16, RIPK2</i>     |
|    |       | Lead migraine SNP | rs716881   | 89,585,557  | 3.29E-03        | 1.44E-03 | 2.36E-07 | 3.81E-01 | ++++ | <i>MMP16, RIPK2</i>     |
| 12 | 19q13 | Lead CAD SNP      | rs2231940  | 46,636,077  | 4.13E-03        | 2.07E-04 | 5.51E-04 | 6.14E-01 | +--- | <i>ATP5SL</i>           |
|    |       | Lead migraine SNP | rs4803455  | 46,543,349  | 8.56E-01        | 1.80E-07 | 5.47E-05 | 6.42E-03 | +--- | <i>TGFB1</i>            |
| 13 | 12q24 | Lead CAD SNP      | rs871921   | 109,599,496 | 6.66E-05        | 1.27E-02 | 8.82E-04 | 3.43E-01 | ++++ | <i>HVCN1</i>            |
|    |       | Lead migraine SNP | rs3864937  | 109,567,467 | 6.98E-01        | 8.12E-04 | 8.48E-02 | 3.71E-03 | +--- | <i>TCTN1</i>            |
| 14 | 8q21  | Lead CAD SNP      | rs7004601  | 89,440,710  | 2.32E-04        | 1.66E-03 | 1.78E-06 | 3.83E-01 | ++++ | <i>MMP16, RIPK2</i>     |
|    |       | Lead migraine SNP | rs6469372  | 89,443,032  | 1.84E-03        | 2.35E-04 | 3.66E-07 | 3.70E-01 | ++++ | <i>MMP16, RIPK2</i>     |
| 15 | 16q24 | Lead CAD SNP      | rs12924776 | 88,114,093  | 1.80E-06        | 5.73E-02 | 8.79E-01 | 4.13E-02 | ++-+ | <i>SPG7</i>             |
|    |       | Lead migraine SNP | rs7359417  | 88,144,059  | 6.60E-2         | 6.65E-04 | 2.53E-02 | 3.60E-02 | ++++ | <i>SPG7</i>             |
| 16 | 9p21  | Lead CAD SNP      | rs190661   | 23,444,661  | 2.57E-03        | 3.05E-03 | 1.27E-02 | 4.59E-01 | +--- | <i>FLJ35282, ELAVL2</i> |
|    |       | Lead migraine SNP | rs274934   | 23,476,403  | 1.00E-02        | 2.37E-06 | 9.01E-05 | 2.40E-01 | +--- | <i>FLJ35282, ELAVL2</i> |

CAD = coronary artery disease. \*Positions refer to build NCBI36/hg18. †P values <5.0 x10<sup>-8</sup> are highlighted in bold. ‡Direction of effect for CAD, migraine, migraine without aura and migraine with aura respectively. Direction of effect for association to CAD is set as positive (+). §RefSeq genes. For intergenic SNPs the nearest gene on either side is listed.

**Table e6. Functional variants (non-synonymous or splice site variants) in LD ( $r^2 > 0.8$ ) with lead SNPs at overlapping loci.**

| Locus no. | Chr band |                   | Lead SNP   | Nearest gene to lead SNP‡ | Proxy SNP  | Distance from lead SNP | Gene*          | $r^2$ | D'   | Coding change                       | Type           |
|-----------|----------|-------------------|------------|---------------------------|------------|------------------------|----------------|-------|------|-------------------------------------|----------------|
| 2         | 17q21    | Lead CAD SNP      | rs46522    | UBE2Z                     | rs2291725  | 50535                  | <i>GIP</i>     | 0.94  | 1.0  | p.Ser103Gly                         | non-synonymous |
|           |          |                   |            |                           | rs2291726  | 50657                  | <i>GIP</i>     | 0.91  | 1.0  | c.258-73A>G                         | splice-site    |
|           |          | Lead migraine SNP | rs11079844 | SNF8, <i>GIP</i>          | rs2291725  | 10798                  | <i>GIP</i>     | 0.93  | 0.97 | p.Ser103Gly                         | non-synonymous |
|           |          |                   |            |                           | rs2291726  | 10920                  | <i>GIP</i>     | 0.97  | 1.0  | c.258-73A>G                         | splice-site    |
| 8         | 2q33     | Lead CAD SNP      | rs3845800  | ICA1L                     | rs35212307 | 31391                  | <i>WDR12</i>   | 1.0   | 1.0  | p.Ile75Val                          | non-synonymous |
|           |          |                   |            |                           | rs72932557 | 112452                 | <i>ALS2CR8</i> | 1.0   | 1.0  | p.Tyr571Phe                         | non-synonymous |
| 9         | 10q24    | Lead CAD SNP      | rs11191425 | C10orf32-AS3MT            | rs17115100 | -34577                 | <i>CYP17A1</i> | 1.0   | 1.0  | c.1140-25C>A                        | splice-site    |
| 12        | 19q13    | Lead CAD SNP      | rs2231940  | ATP5SL                    | rs10853751 | -41017                 | <i>EXOSC5</i>  | 1.0   | 1.0  | p.Thr5Met                           | non-synonymous |
|           |          |                   |            |                           | rs284662   | -11962                 | <i>B3GNT8</i>  | 0.91  | 1.0  | p.Ser137Gly                         | non-synonymous |
|           |          |                   |            |                           | rs1043413  | -4940                  | <i>ATP5SL</i>  | 1.0   | 1.0  | p.[Cys165Ser, Cys132Ser, Cys159Ser] | non-synonymous |
|           |          |                   |            |                           | rs2231940  | 0                      | <i>ATP5SL</i>  | 1.0   | 1.0  | p.[Asn40Ser, Asn34Ser]              | non-synonymous |
| 15        | 16q24    | Lead migraine SNP | rs7359417  | SPG7                      | rs2292954  | -3435                  | <i>SPG7</i>    | 1.0   | 1.0  | p.Thr503Ala                         | non-synonymous |
|           |          |                   |            |                           | rs12960    | 3770                   | <i>SPG7</i>    | 0.94  | 1.0  | p.Arg688Gln                         | non-synonymous |

CAD = coronary artery disease.

\*RefSeq genes. For intergenic SNPs the nearest gene on either side is listed.

LD calculations are based on 1000 genomes phase 1 CEU

**Table e7. Expression quantitative trait loci (eQTLs) at overlapping loci determined from gene expression in peripheral blood.**

| <b>Locus no.</b> | <b>Chr band</b> | <b>Locus SNP</b> | <b>eQTL SNP</b> | <b>eQTL <i>P</i> value*</b> | <b>eQTL probe</b> | <b>eQTL gene</b> | <b><i>P</i> value for correlation with eQTL locus†</b> |
|------------------|-----------------|------------------|-----------------|-----------------------------|-------------------|------------------|--|
| 2                | 17q21           | rs11079844       | rs1985785       | 1.94E-26                    | 11745885_a_at     | UBE2Z            | 3.18E-03   |
| 2                | 17q21           | rs11079844       | rs4597361       | 5.39E-08                    | 11715988_x_at     | ATP5G1           | 0.90   |
| 4                | 12q24           | rs7136874        | rs668774        | 4.74E-11                    | 11731248_a_at     | TMEM116          | 1.0  |
| 4                | 12q24           | rs7136874        | rs7956495       | 1.95E-06                    | 11743486_a_at     | NAA25            | 1.0  |
| 5                | 17p11           | rs12951376       | rs6502629       | 5.26E-06                    | 11758738_a_at     | SREBF1           | 0.18   |
| 15               | 16q24           | rs7359417        | rs2377056       | 2.10E-46                    | 11725404_x_at     | RPL13            | 1.0  |

The table shows eQTLs at which the credible set of causative SNPs at the eQTL locus intersect with the credible set of causative SNPs at the overlap locus, represented by the migraine dataset.

\**P* value for association between eQTL SNP and expression of the eQTL probe.

†*P* value for a test of significant correlation between association z-scores in the migraine credible set compared to the overlapping eQTL credible set. Correlation was measured using Pearson's correlation coefficient and significance assessed by a two-tailed t-test with n-2 degrees of freedom, where n is the number of SNPs overlapping in the credible sets. The final p-values given here are Bonferroni corrected for 6 tests.