**Supplementary information for:**

**Physical activity and risk of coronary artery disease, myocardial infarction and stroke: a two-sample Mendelian randomization study**

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Suppl. Table 1 – Association of genetic instruments (SNPs) related to self-reported moderate-to-vigorous physical activity from the GWAS by Klimentidis et al.1 with coronary artery disease, myocardial infarction and ischemic stroke.

| SNP | CHR | POS (hg38) | EA | OA | EAF | BETA | SE | P-value |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| *Coronary artery disease* (SNPs from GWAS by Nikpay3) | | | | | | | | |
| rs2942127 | 1 | 204450939 | G | A | 0.254 | 0.025 | 0.011 | 0.025 |
| rs1974771 | 2 | 54051406 | G | A | 0.886 | 0.012 | 0.015 | 0.418 |
| rs2114286 | 3 | 41152792 | A | G | 0.428 | 0.006 | 0.010 | 0.509 |
| rs877483 | 3 | 53812714 | T | C | 0.418 | -0.007 | 0.010 | 0.501 |
| rs2035562 | 3 | 85007370 | A | G | 0.351 | -0.002 | 0.010 | 0.851 |
| rs1972763 | 4 | 158939411 | C | T | 0.340 | -0.015 | 0.010 | 0.138 |
| rs77742115 | 5 | 18330315 | T | C | 0.858 | -0.004 | 0.013 | 0.787 |
| rs2854277 | 6 | 32660307 | C | T | 0.890 | -0.003 | 0.019 | 0.894 |
| rs1186721 | 7 | 34934990 | G | A | 0.716 | 0.015 | 0.010 | 0.147 |
| rs921915 | 7 | 50188985 | T | C | 0.436 | 0.004 | 0.009 | 0.634 |
| rs1043595 | 7 | 128769958 | G | A | 0.780 | 0.010 | 0.012 | 0.391 |
| rs7804463 | 7 | 133762898 | T | C | 0.519 | 0.000 | 0.009 | 0.985 |
| rs2988004 | 9 | 37044391 | T | G | 0.558 | -0.013 | 0.010 | 0.167 |
| rs7326482 | 13 | 53463668 | G | T | 0.391 | 0.004 | 0.009 | 0.659 |
| rs10145335 | 14 | 98081411 | G | A | 0.770 | -0.017 | 0.011 | 0.117 |
| rs12912808 | 15 | 94748994 | C | T | 0.843 | 0.014 | 0.013 | 0.305 |
| rs1921981 | 21 | 41050620 | G | A | 0.706 | -0.010 | 0.010 | 0.357 |
| *Myocardial infarction* (SNPs from GWAS by Nikpay3) | | | | | | | | |
| rs2942127 | 1 | 204450939 | G | A | 0.283 | 0.031 | 0.012 | 0.011 |
| rs1974771 | 2 | 54051406 | G | A | 0.896 | 0.032 | 0.016 | 0.055 |
| rs2114286 | 3 | 41152792 | A | G | 0.440 | -0.003 | 0.011 | 0.801 |
| rs877483 | 3 | 53812714 | T | C | 0.434 | -0.008 | 0.011 | 0.441 |
| rs2035562 | 3 | 85007370 | A | G | 0.372 | 0.005 | 0.011 | 0.627 |
| rs1972763 | 4 | 158939411 | C | T | 0.361 | -0.018 | 0.011 | 0.101 |
| rs77742115 | 5 | 18330315 | T | C | 0.866 | 0.001 | 0.014 | 0.971 |
| rs2854277 | 6 | 32660307 | C | T | 0.906 | 0.019 | 0.021 | 0.357 |
| rs1186721 | 7 | 34934990 | G | A | 0.724 | 0.012 | 0.011 | 0.301 |
| rs921915 | 7 | 50188985 | T | C | 0.456 | 0.004 | 0.010 | 0.686 |
| rs1043595 | 7 | 128769958 | G | A | 0.784 | 0.008 | 0.013 | 0.544 |
| rs7804463 | 7 | 133762898 | T | C | 0.539 | 0.005 | 0.010 | 0.639 |
| rs2988004 | 9 | 37044391 | T | G | 0.569 | -0.019 | 0.011 | 0.069 |
| rs7326482 | 13 | 53463668 | G | T | 0.409 | -0.007 | 0.010 | 0.502 |
| rs10145335 | 14 | 98081411 | G | A | 0.774 | -0.015 | 0.012 | 0.226 |
| rs12912808 | 15 | 94748994 | C | T | 0.846 | 0.005 | 0.015 | 0.731 |
| rs1921981 | 21 | 41050620 | G | A | 0.721 | 0.002 | 0.012 | 0.873 |
| *Ischemic stroke* (SNPs from GWAS by Malik4) | | | | | | | | |
| rs2942127 | 1 | 204450939 | G | A | 0.188 | 0.022 | 0.013 | 0.076 |
| rs1974771 | 2 | 54051406 | G | A | 0.889 | -0.007 | 0.016 | 0.678 |
| rs2114286 | 3 | 41152792 | A | G | 0.447 | -0.006 | 0.010 | 0.582 |
| rs877483 | 3 | 53812714 | T | C | 0.424 | -0.011 | 0.010 | 0.290 |
| rs2035562 | 3 | 85007370 | A | G | 0.323 | -0.011 | 0.011 | 0.301 |
| rs1972763 | 4 | 158939411 | C | T | 0.339 | 0.008 | 0.010 | 0.444 |
| rs77742115 | 5 | 18330315 | T | C | 0.848 | -0.005 | 0.014 | 0.740 |
| rs2854277 | 6 | 32660307 | C | T | 0.894 | 0.002 | 0.021 | 0.928 |
| rs1186721 | 7 | 34934990 | G | A | 0.692 | 0.004 | 0.011 | 0.700 |
| rs921915 | 7 | 50188985 | T | C | 0.415 | 0.011 | 0.011 | 0.317 |
| rs1043595 | 7 | 128769958 | G | A | 0.729 | 0.010 | 0.011 | 0.390 |
| rs7804463 | 7 | 133762898 | T | C | 0.541 | -0.001 | 0.010 | 0.938 |
| rs2988004 | 9 | 37044391 | T | G | 0.567 | -0.011 | 0.010 | 0.272 |
| rs7326482 | 13 | 53463668 | G | T | 0.393 | 0.009 | 0.010 | 0.378 |
| rs10145335 | 14 | 98081411 | G | A | 0.752 | -0.002 | 0.012 | 0.843 |
| rs12912808 | 15 | 94748994 | C | T | 0.847 | -0.006 | 0.014 | 0.645 |
| rs1921981 | 21 | 41050620 | G | A | 0.679 | -0.001 | 0.011 | 0.896 |

EA, effect allele. OA, other allele. EAF, effect allele frequency. SE, standard error; bold font indicate nominal significant SNP outcome association

Suppl. Table 2 – Association of genetic instruments (SNPs) related to average accelerations from the GWAS by Klimentidis et al.1 with coronary artery disease, myocardial infarction and ischemic stroke.

| SNP | CHR | POS (hg38) | EA | OA | EAF | BETA | SE | P-value |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| *Coronary artery disease* (SNPs from GWAS by Nikpay3) | | | | | | | | |
| rs34517439 | 1 | 77984833 | C | A | 0.906 | -0.038 | 0.019 | 0.042 |
| rs6775319 | 3 | 18717009 | A | T | 0.316 | -0.005 | 0.010 | 0.594 |
| rs9293503 | 5 | 88653144 | T | C | 0.878 | 0.033 | 0.014 | 0.023 |
| rs12522261 | 5 | 152675265 | G | A | 0.659 | -0.003 | 0.010 | 0.740 |
| rs11012732 | 10 | 21541175 | A | G | 0.702 | -0.002 | 0.011 | 0.827 |
| rs148193266 | 11 | 104657953 | A | C | 0.957 | -0.033 | 0.026 | 0.203 |
| rs59499656 | 18 | 43188344 | A | T | 0.645 | 0.000 | 0.010 | 0.995 |
| *Myocardial infarction* (SNPs from GWAS by Nikpay3) | | | | | | | | |
| rs34517439 | 1 | 77984833 | C | A | 0.911 | -0.045 | 0.021 | 0.031 |
| rs6775319 | 3 | 18717009 | A | T | 0.338 | -0.004 | 0.011 | 0.710 |
| rs9293503 | 5 | 88653144 | T | C | 0.882 | 0.025 | 0.016 | 0.108 |
| rs12522261 | 5 | 152675265 | G | A | 0.677 | -0.001 | 0.011 | 0.898 |
| rs11012732 | 10 | 21541175 | A | G | 0.704 | -0.002 | 0.012 | 0.891 |
| rs148193266 | 11 | 104657953 | A | C | 0.961 | -0.017 | 0.029 | 0.560 |
| rs59499656 | 18 | 43188344 | A | T | 0.650 | 0.009 | 0.011 | 0.379 |
| *Ischemic stroke* (SNPs from GWAS by Malik4) | | | | | | | | |
| rs34517439 | 1 | 77984833 | C | A | 0.884 | -0.029 | 0.016 | 0.078 |
| rs6775319 | 3 | 18717009 | A | T | 0.282 | -0.023 | 0.012 | 0.049 |
| rs9293503 | 5 | 88653144 | T | C | 0.886 | 0.035 | 0.016 | 0.031 |
| rs12522261 | 5 | 152675265 | G | A | 0.667 | -0.026 | 0.010 | 0.015 |
| rs11012732 | 10 | 21541175 | A | G | 0.668 | 0.016 | 0.011 | 0.141 |
| rs148193266 | 11 | 104657953 | A | C | 0.954 | -0.003 | 0.026 | 0.898 |
| rs59499656 | 18 | 43188344 | A | T | 0.652 | 0.009 | 0.010 | 0.368 |

EA, effect allele. OA, other allele. EAF, effect allele frequency. SE, standard error;

Suppl. Table 3 – Association of genetic instruments (SNPs) related to fraction accelerations > 425 milli-gravities from the GWAS by Klimentidis et al.1 and coronary artery disease, myocardial infarction and ischemic stroke

| SNP | CHR | POS (hg38) | EA | OA | EAF | BETA | SE | P-value |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| *Coronary artery disease* (SNPs from GWAS by Nikpay3) | | | | | | | | |
| rs1856329 | 1 | 219766281 | A | C | 0.767 | 0.019 | 0.011 | 0.068 |
| rs6433478 | 2 | 174376754 | T | C | 0.512 | 0.003 | 0.010 | 0.734 |
| rs62443625 | 7 | 39013531 | T | C | 0.792 | 0.004 | 0.012 | 0.743 |
| rs72633364 | 8 | 34329370 | G | A | 0.740 | 0.021 | 0.011 | 0.062 |
| rs4754194 | 11 | 107219461 | C | T | 0.758 | 0.022 | 0.011 | 0.038 |
| rs743580 | 15 | 74035775 | A | G | 0.492 | -0.020 | 0.009 | 0.035 |
| rs1668835 | 18 | 24898988 | T | A | 0.720 | -0.007 | 0.011 | 0.500 |
| *Myocardial infarction* (SNPs from GWAS by Nikpay3) | | | | | | | | |
| rs1856329 | 1 | 219766281 | A | C | 0.774 | 0.015 | 0.012 | 0.209 |
| rs6433478 | 2 | 174376754 | T | C | 0.518 | 0.012 | 0.011 | 0.265 |
| rs62443625 | 7 | 39013531 | T | C | 0.798 | 0.002 | 0.013 | 0.906 |
| rs72633364 | 8 | 34329370 | G | A | 0.742 | 0.021 | 0.012 | 0.080 |
| rs4754194 | 11 | 107219461 | C | T | 0.764 | 0.017 | 0.012 | 0.153 |
| rs743580 | 15 | 74035775 | A | G | 0.502 | -0.020 | 0.010 | 0.053 |
| rs1668835 | 18 | 24898988 | T | A | 0.722 | -0.009 | 0.012 | 0.442 |
| *Ischemic stroke* (SNPs from GWAS by Malik4) | | | | | | | | |
| rs1856329 | 1 | 219766281 | A | C | 0.786 | -0.003 | 0.012 | 0.794 |
| rs6433478 | 2 | 174376754 | T | C | 0.480 | 0.005 | 0.010 | 0.615 |
| rs62443625 | 7 | 39013531 | T | C | 0.771 | 0.010 | 0.012 | 0.385 |
| rs72633364 | 8 | 34329370 | G | A | 0.715 | 0.021 | 0.011 | 0.061 |
| rs4754194 | 11 | 107219461 | C | T | 0.771 | 0.027 | 0.012 | 0.023 |
| rs743580 | 15 | 74035775 | A | G | 0.506 | 0.008 | 0.010 | 0.460 |
| rs1668835 | 18 | 24898988 | T | A | 0.687 | -0.008 | 0.011 | 0.474 |

EA, effect allele. OA, other allele. EAF, effect allele frequency. SE, standard error

Suppl. Table 4 – Association of genetic instruments (SNPs) related to sedentary behavior from a GWAS by Doherty et al.2 and coronary artery disease, myocardial infarction and ischemic stroke

| SNP | CHR | POS (hg38) | EA | OA | EAF | BETA | SE | P-value |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| *Coronary artery disease* (SNPs from GWAS by Nikpay3) | | | | | | | | |
| rs61776614 | 1 | 2234967 | C | T | 0.944 | 0.062 | 0.026 | 0.018 |
| rs1858242 | 3 | 68477984 | A | G | 0.300 | 0.006 | 0.010 | 0.539 |
| rs26579 | 5 | 88689478 | G | C | 0.454 | -0.007 | 0.010 | 0.483 |
| rs25981 | 5 | 107487207 | G | C | 0.519 | 0.004 | 0.010 | 0.695 |
| rs6870096 | 5 | 152566250 | C | G | 0.341 | 0.007 | 0.010 | 0.493 |
| rs34858520 | 7 | 72258898 | A | G | 0.614 | -0.028 | 0.010 | 0.005 |
| *Myocardial infarction* (SNPs from GWAS by Nikpay3) | | | | | | | | |
| rs61776614 | 1 | 2234967 | C | T | 0.945 | 0.052 | 0.029 | 0.073 |
| rs1858242 | 3 | 68477984 | A | G | 0.319 | 0.010 | 0.011 | 0.353 |
| rs26579 | 5 | 88689478 | G | C | 0.472 | -0.004 | 0.011 | 0.726 |
| rs25981 | 5 | 107487207 | G | C | 0.505 | 0.001 | 0.011 | 0.912 |
| rs6870096 | 5 | 152566250 | C | G | 0.364 | -0.001 | 0.011 | 0.924 |
| rs34858520 | 7 | 72258898 | A | G | 0.626 | -0.030 | 0.011 | 0.006 |
| *Ischemic stroke* (SNPs from GWAS by Malik4) | | | | | | | | |
| rs61776614 | 1 | 2234967 | C | T | 0.921 | 0.014 | 0.022 | 0.524 |
| rs1858242 | 3 | 68477984 | A | G | 0.260 | 0.006 | 0.012 | 0.620 |
| rs26579 | 5 | 88689478 | G | C | 0.420 | -0.005 | 0.010 | 0.638 |
| rs25981 | 5 | 107487207 | G | C | 0.532 | 0.002 | 0.010 | 0.861 |
| rs6870096 | 5 | 152566250 | C | G | 0.317 | -0.018 | 0.011 | 0.101 |
| rs34858520 | 7 | 72258898 | A | G | 0.607 | -0.018 | 0.011 | 0.111 |

EA, effect allele. OA, other allele. EAF, effect allele frequency. SE, standard error;

Suppl. Table 5 – Association (P<5x10-8) of the candidate genetic instruments (SNPs) with confounders or the outcomes

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| SNP | Chr. | Position (hg38) | Trait |  |
| *Self-reported moderate to vigorous physical activity (SNPs* by Klimentidis et al.1*)* | | | | |
| rs2942127 | 1 | 204450939 | forced vital capacity5 |  |
| rs1974771 | 2 | 54051406 |  |  |
| rs2114286 | 3 | 41152792 | whole body fat free mass, weight (UK Biobank - Neale) |  |
| rs877483 | 3 | 53812714 | high blood pressure6 |  |
| rs2035562 | 3 | 85007370 | whole body fat free mass, weight, waist circumference (UK Biobank - Neale) |  |
| rs1972763 | 4 | 158939411 |  |  |
| rs77742115 | 5 | 18330315 |  |  |
| rs2854277 | 6 | 32660307 | waist-to-hip ratio7 |  |
| rs1186721 | 7 | 34934990 | impedance of whole body (UK Biobank - Neale) |  |
| rs921915 | 7 | 50188985 |  |  |
| rs1043595 | 7 | 128769958 | education8 |  |
| rs7804463 | 7 | 133762898 | education8 |  |
| rs2988004 | 9 | 37044391 | body mass index7 |  |
| rs7326482 | 13 | 53463668 | hip circumference (UK Biobank - Neale) |  |
| rs10145335 | 14 | 98081411 | systolic blood pressure9 |  |
| rs4886868 | 15 | 74061220 | forced vital capacity (UK Biobank - Neale) |  |
| rs12912808 | 15 | 94748994 |  |  |
| rs429358 | 19 | 44908684 | coronary artery disease 10, body mass index7 |  |
| rs1921981 | 21 | 41050620 |  |  |
| *Average accelerations (SNPs by Klimentidis et al.*1*)* | | | | |
| rs34517439 | 1 | 77984833 | whole body fat free mass, weight, hip circumference (UK Biobank - Neale) |  |
| rs6775319 | 3 | 18717009 | body fat, body mass index (UK Biobank - Neale) |  |
| rs9293503 | 5 | 88653144 | self-reported hypertension, trunk fat free mass (UK Biobank - Neale) |  |
| rs12522261 | 5 | 152675265 |  |  |
| rs11012732 | 10 | 21541175 | waist circumference, body mass index, body fat percentage (UK Biobank - Neale) |  |
| rs148193266 | 11 | 104657953 |  |  |
| rs56194509 | 17 | 45767193 | forced vital capacity, red blood cell count (UK Biobank - Neale) |  |
| rs59499656 | 18 | 43188344 | body fat percentage, body mass index |  |
| *Fration accelerations > 425 milli-gravities (SNPs by Klimentidis et al.*1*)* | | | | |
| rs1856329 | 1 | 219766281 | FEV1/FVC ratio5 |  |
| rs6433478 | 2 | 174376754 | hand grip strength left, trunk fat percentage (UK Biobank - Neale) |  |
| rs62443625 | 7 | 39013531 | body fat percentage, whole body fat mass (UK Biobank - Neale) |  |
| rs72633364 | 8 | 34329370 |  |  |
| rs4754194 | 11 | 107219461 | systolic blood pressure (UK Biobank - Neale) |  |
| rs743580 | 15 | 74035775 | BMI, body fat percentage (UK Biobank - Neale) |  |
| rs80028338 | 17 | 46084104 | forced vital capacity (UK Biobank - Neale) |  |
| rs1668835 | 18 | 24898988 |  |  |
| *Sedentary behavior (SNPs by Doherty et al.2)* | | | | |
| rs61776614 | 1 | 2166405 |  |  |
| rs1858242 | 3 | 68477984 |  |  |
| rs26579 | 5 | 88689478 | body fat percentage (UK Biobank - Neale) |  |
| rs25981 | 5 | 107487207 | body mass index, hip circumference (UK Biobank - Neale) |  |
| rs6870096 | 5 | 152566250 |  |  |
| rs34858520 | 7 | 72258898 |  |  |

Suppl. Table 6 – Sample size and a priori power estimates

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Exposure | OR=0.9 | OR=0.85 | OR=0.8 | OR=0.75 | OR=0.7 | Sample size for outcome | Proportion of cases |
| *Coronary artery disease (*GWAS by Nikpay3) |  |  |  |  |  |  |  |
| Self-reported moderate-to-vigorous | 0.095 | 0.168 | 0.278 | 0.424 | 0.592 | 141,217 | 0.30 |
| Average accelerations (mg) | 0.128 | 0.245 | 0.414 | 0.613 | 0.795 | 141,217 | 0.30 |
| Fraction accelerations > 425 mg | 0.121 | 0.229 | 0.387 | 0.578 | 0.762 | 141,217 | 0.30 |
| Sedentary behavior | 0.120 | 0.226 | 0.381 | 0.57 | 0.755 | 141,217 | 0.30 |
| *Myocardial infarction (*GWAS by Nikpay3) |  |  |  |  |  |  |  |
| Self-reported moderate-to-vigorous | 0.081 | 0.136 | 0.219 | 0.332 | 0.473 | 126,630 | 0.22 |
| Average accelerations (mg) | 0.106 | 0.193 | 0.323 | 0.491 | 0.670 | 126,630 | 0.22 |
| Fraction accelerations > 425 mg | 0.100 | 0.181 | 0.302 | 0.406 | 0.635 | 126,630 | 0.22 |
| Sedentary behavior | 0.099 | 0.179 | 0.298 | 0.453 | 0.627 | 126,630 | 0.22 |
| *Ischemic stroke (*GWAS by Malik4) |  |  |  |  |  |  |  |
| Self-reported moderate-to-vigorous | 0.105 | 0.191 | 0.319 | 0.485 | 0.664 | 440,328 | 0.08 |
| Average accelerations (mg) | 0.143 | 0.280 | 0.473 | 0.684 | 0.856 | 440,328 | 0.08 |
| Fraction accelerations > 425 mg | 0.135 | 0.262 | 0.443 | 0.649 | 0.827 | 440,328 | 0.08 |
| Sedentary behavior | 0.133 | 0.258 | 0.436 | 0.641 | 0.82 | 440,328 | 0.08 |

R² – explained variation by SNPs, OR – odds ratio, PA – physical activity, mg - milli-gravities

Suppl. Table 7 – Between SNP-heterogeneity for SNPs associated with self-reported moderate-to-vigorous physical activity, average accelerations, fraction accelerations > 425 milli-gravities and sedentary behavior.

|  |  |  |  |
| --- | --- | --- | --- |
| Exposure | Cochran’s Q | D. f. | P-value |
| *Coronary artery disease (*GWAS by Nikpay3) | | |  |
| Self-reported moderate-to-vigorous PA | 18.39 | 16 | 0.301 |
| Average accelerations (mg) | 11.21 | 6 | 0.082 |
| Fraction accelerations > 425 mg | 13.73 | 6 | 0.033 |
| Sedentary behavior | 14.54 | 5 | 0.013 |
| *Myocardial infarction (*GWAS by Nikpay3) | |  |  |
| Self-reported moderate-to-vigorous PA | 21.22 | 16 | 0.17 |
| Average accelerations (mg) | 8.36 | 6 | 0.213 |
| Fraction accelerations > 425 mg | 9.52 | 6 | 0.147 |
| Sedentary behavior | 11.58 | 5 | 0.041 |
| *Ischemic stroke (*GWAS by Malik4) | |  |  |
| Self-reported moderate-to-vigorous PA | 10.08 | 16 | 0.863 |
| Average accelerations (mg) | 19.17 | 6 | 0.004 |
| Fraction accelerations > 425 mg | 8.38 | 6 | 0.212 |
| Sedentary behavior | 6.02 | 5 | 0.304 |

PA – physical activity, D.f. – degrees of freedom, mg – milli-gravities; bold font indicate nominal significant heterogeneity statistic Cochran’s Q

Suppl. Table 8 – Results for the leave one out analysis for the association between self-reported moderate-to-vigorous physical activity and coronary artery disease, myocardial infarction and ischemic stroke

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| SNP | OR | 95% LL | 95% UL | P-value |
| *Coronary artery disease (*GWAS by Nikpay3) | | | |  |
| rs10145335 | 0.97 | 0.67 | 1.39 | 0.856 |
| rs1043595 | 1.00 | 0.68 | 1.46 | 0.988 |
| rs1186721 | 1.09 | 0.76 | 1.58 | 0.630 |
| rs12912808 | 0.99 | 0.68 | 1.45 | 0.948 |
| rs1921981 | 1.07 | 0.73 | 1.57 | 0.724 |
| rs1972763 | 1.10 | 0.76 | 1.58 | 0.617 |
| rs1974771 | 1.07 | 0.73 | 1.58 | 0.723 |
| rs2035562 | 1.02 | 0.69 | 1.52 | 0.910 |
| rs2114286 | 1.06 | 0.72 | 1.56 | 0.769 |
| rs2854277 | 1.04 | 0.70 | 1.55 | 0.844 |
| rs2942127 | 0.93 | 0.65 | 1.32 | 0.673 |
| rs2988004 | 0.97 | 0.67 | 1.41 | 0.872 |
| rs7326482 | 1.05 | 0.71 | 1.56 | 0.796 |
| rs77742115 | 1.02 | 0.69 | 1.51 | 0.924 |
| rs7804463 | 1.03 | 0.70 | 1.54 | 0.870 |
| rs877483 | 1.06 | 0.72 | 1.56 | 0.766 |
| rs921915 | 1.06 | 0.71 | 1.56 | 0.783 |
| All | 1.03 | 0.71 | 1.49 | 0.875 |
| *Myocardial infarction (*GWAS by Nikpay3) | | | |  |
| rs10145335 | 1.10 | 0.70 | 1.73 | 0.676 |
| rs1043595 | 1.13 | 0.71 | 1.80 | 0.595 |
| rs1186721 | 1.22 | 0.78 | 1.91 | 0.385 |
| rs12912808 | 1.15 | 0.72 | 1.83 | 0.566 |
| rs1921981 | 1.16 | 0.73 | 1.84 | 0.542 |
| rs1972763 | 1.26 | 0.82 | 1.93 | 0.293 |
| rs1974771 | 1.29 | 0.85 | 1.96 | 0.226 |
| rs2035562 | 1.20 | 0.75 | 1.91 | 0.448 |
| rs2114286 | 1.15 | 0.72 | 1.84 | 0.553 |
| rs2854277 | 1.11 | 0.69 | 1.77 | 0.678 |
| rs2942127 | 1.02 | 0.68 | 1.52 | 0.927 |
| rs2988004 | 1.07 | 0.69 | 1.65 | 0.774 |
| rs7326482 | 1.13 | 0.71 | 1.80 | 0.613 |
| rs77742115 | 1.17 | 0.73 | 1.87 | 0.513 |
| rs7804463 | 1.14 | 0.71 | 1.83 | 0.591 |
| rs877483 | 1.21 | 0.76 | 1.90 | 0.422 |
| rs921915 | 1.19 | 0.75 | 1.90 | 0.456 |
| All | 1.16 | 0.74 | 1.80 | 0.519 |
| *Ischemic stroke (*GWAS by Malik4) | | |  |  |
| rs10145335 | 1.16 | 0.79 | 1.69 | 0.451 |
| rs1043595 | 1.12 | 0.77 | 1.64 | 0.554 |
| rs1186721 | 1.19 | 0.81 | 1.73 | 0.374 |
| rs12912808 | 1.19 | 0.82 | 1.74 | 0.361 |
| rs1921981 | 1.17 | 0.80 | 1.71 | 0.408 |
| rs1972763 | 1.13 | 0.77 | 1.65 | 0.540 |
| rs1974771 | 1.15 | 0.78 | 1.68 | 0.486 |
| rs2035562 | 1.11 | 0.76 | 1.62 | 0.589 |
| rs2114286 | 1.14 | 0.78 | 1.66 | 0.501 |
| rs2854277 | 1.17 | 0.79 | 1.71 | 0.431 |
| rs2942127 | 1.07 | 0.74 | 1.57 | 0.712 |
| rs2988004 | 1.11 | 0.76 | 1.62 | 0.597 |
| rs7326482 | 1.22 | 0.83 | 1.78 | 0.308 |
| rs77742115 | 1.15 | 0.79 | 1.68 | 0.472 |
| rs7804463 | 1.18 | 0.80 | 1.73 | 0.402 |
| rs877483 | 1.22 | 0.84 | 1.79 | 0.296 |
| rs921915 | 1.23 | 0.84 | 1.79 | 0.293 |
| All | 1.16 | 0.80 | 1.67 | 0.436 |

OR – odds ratio, 95%LL – 95% lower limit, 95% UL – 95% upper limit

Suppl. Table 9 – Results for the leave one out analysis for the association between average accelerations and coronary artery disease, myocardial infarction and ischemic stroke

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| SNP | OR | 95% LL | 95% UL | P-value |
| *Coronary artery disease (*GWAS by Nikpay3) | | |  |  |
| rs11012732 | 1.01 | 0.95 | 1.07 | 0.756 |
| rs12522261 | 1.01 | 0.96 | 1.07 | 0.729 |
| rs148193266 | 1.00 | 0.95 | 1.05 | 0.941 |
| rs34517439 | 1.02 | 0.98 | 1.06 | 0.385 |
| rs59499656 | 1.01 | 0.95 | 1.07 | 0.798 |
| rs6775319 | 1.01 | 0.96 | 1.07 | 0.675 |
| rs9293503 | 0.99 | 0.95 | 1.03 | 0.559 |
| All | 1.01 | 0.96 | 1.06 | 0.801 |
| *Myocardial infarction (*GWAS by Nikpay3) | | |  |  |
| rs11012732 | 0.99 | 0.94 | 1.05 | 0.785 |
| rs12522261 | 0.99 | 0.94 | 1.05 | 0.783 |
| rs148193266 | 0.99 | 0.94 | 1.04 | 0.621 |
| rs34517439 | 1.01 | 0.97 | 1.05 | 0.796 |
| rs59499656 | 1.00 | 0.95 | 1.05 | 0.991 |
| rs6775319 | 1.00 | 0.94 | 1.05 | 0.845 |
| rs9293503 | 0.98 | 0.94 | 1.02 | 0.252 |
| All | 0.99 | 0.95 | 1.04 | 0.748 |
| *Ischemic stroke (*GWAS by Malik4) | |  |  |  |
| rs11012732 | 0.96 | 0.90 | 1.03 | 0.268 |
| rs12522261 | 0.99 | 0.93 | 1.06 | 0.871 |
| rs148193266 | 0.97 | 0.90 | 1.05 | 0.501 |
| rs34517439 | 0.99 | 0.92 | 1.06 | 0.754 |
| rs59499656 | 0.98 | 0.91 | 1.06 | 0.653 |
| rs6775319 | 0.99 | 0.92 | 1.06 | 0.791 |
| rs9293503 | 0.96 | 0.90 | 1.01 | 0.154 |
| All | 0.98 | 0.92 | 1.05 | 0.515 |

OR – odds ratio, 95%LL – 95% lower limit, 95% UL – 95% upper limit

Suppl. Table 10 – Results for the leave one out analysis for the association between fraction accelerations > 425 milli-gravities and coronary artery disease, myocardial infarction and ischemic stroke

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| SNP | OR | 95% LL | 95% UL | P-value |
| *Coronary artery disease (*GWAS by Nikpay3) | | |  |  |
| rs1668835 | 0.72 | 0.43 | 1.21 | 0.214 |
| rs1856329 | 0.63 | 0.43 | 0.93 | 0.021 |
| rs4754194 | 0.86 | 0.52 | 1.43 | 0.562 |
| rs62443625 | 0.76 | 0.44 | 1.33 | 0.340 |
| rs6433478 | 0.76 | 0.43 | 1.34 | 0.339 |
| rs72633364 | 0.84 | 0.50 | 1.41 | 0.508 |
| rs743580 | 0.87 | 0.52 | 1.48 | 0.614 |
| All | 0.77 | 0.48 | 1.25 | 0.293 |
| *Myocardial infarction (*GWAS by Nikpay3) | | |  |  |
| rs1668835 | 0.68 | 0.43 | 1.07 | 0.096 |
| rs1856329 | 0.63 | 0.43 | 0.92 | 0.017 |
| rs4754194 | 0.79 | 0.48 | 1.31 | 0.361 |
| rs62443625 | 0.72 | 0.43 | 1.20 | 0.205 |
| rs6433478 | 0.77 | 0.46 | 1.30 | 0.329 |
| rs72633364 | 0.81 | 0.51 | 1.29 | 0.370 |
| rs743580 | 0.84 | 0.52 | 1.35 | 0.458 |
| All | 0.75 | 0.48 | 1.16 | 0.188 |
| *Ischemic stroke (*GWAS by Malik4) | |  |  |  |
| rs1668835 | 0.70 | 0.47 | 1.06 | 0.092 |
| rs1856329 | 0.75 | 0.47 | 1.19 | 0.223 |
| rs4754194 | 0.87 | 0.61 | 1.24 | 0.441 |
| rs62443625 | 0.79 | 0.50 | 1.25 | 0.306 |
| rs6433478 | 0.76 | 0.48 | 1.22 | 0.258 |
| rs72633364 | 0.84 | 0.56 | 1.26 | 0.404 |
| rs743580 | 0.69 | 0.46 | 1.03 | 0.067 |
| All | 0.77 | 0.52 | 1.14 | 0.192 |

OR – odds ratio, 95%LL – 95% lower limit, 95% UL – 95% upper limit; bold font indicate influential SNP towards attenuation of association results.

Suppl. Table 11 – Results for the leave one out analysis for the association between sedentary behavior and coronary artery disease, myocardial infarction and ischemic stroke

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| SNP | OR | 95% LL | 95% UL | P-value |
| *Coronary artery disease (*GWAS by Nikpay3) | | | |  |
| rs1858242 | 0.84 | 0.46 | 1.53 | 0.576 |
| rs25981 | 0.86 | 0.47 | 1.58 | 0.634 |
| rs26579 | 0.94 | 0.51 | 1.73 | 0.847 |
| rs34858520 | 1.10 | 0.73 | 1.66 | 0.655 |
| rs61776614 | 0.81 | 0.54 | 1.23 | 0.321 |
| rs6870096 | 0.94 | 0.52 | 1.71 | 0.836 |
| All | 0.91 | 0.56 | 1.49 | 0.709 |
| *Myocardial infarction (*GWAS by Nikpay3) | | | |  |
| rs1858242 | 0.87 | 0.49 | 1.54 | 0.623 |
| rs25981 | 0.94 | 0.51 | 1.71 | 0.831 |
| rs26579 | 0.98 | 0.53 | 1.79 | 0.935 |
| rs34858520 | 1.18 | 0.83 | 1.68 | 0.348 |
| rs61776614 | 0.87 | 0.55 | 1.39 | 0.560 |
| rs6870096 | 0.94 | 0.52 | 1.70 | 0.838 |
| All | 0.96 | 0.59 | 1.56 | 0.855 |
| *Ischemic stroke (*GWAS by Malik4) | | |  |  |
| rs1858242 | 1.03 | 0.68 | 1.55 | 0.896 |
| rs25981 | 1.06 | 0.69 | 1.60 | 0.803 |
| rs26579 | 1.11 | 0.75 | 1.67 | 0.598 |
| rs34858520 | 1.20 | 0.86 | 1.68 | 0.286 |
| rs61776614 | 1.02 | 0.69 | 1.52 | 0.912 |
| rs6870096 | 0.94 | 0.67 | 1.32 | 0.725 |
| All | 1.06 | 0.75 | 1.48 | 0.748 |

OR – odds ratio, 95%LL – 95% lower limit, 95% UL – 95% upper limit

Suppl. Table 12 – MR-Egger test on intercept table for the association between self-reported moderate to vigorous physical activity, average accelerations, fraction accelerations > 425 milli-gravities and sedentary behavior with coronary artery disease, myocardial infarction and ischemic stroke

|  |  |  |  |
| --- | --- | --- | --- |
| Outcome | Intercept | SE | P-value |
| Self-reported moderate-to-vigorous PA (by *Klimentidis et al.*1*)* | | | |
| CAD | -0.009 | 0.013 | 0.524 |
| Myocardial infarction | -0.005 | 0.016 | 0.772 |
| Ischemic stroke | -0.004 | 0.013 | 0.765 |
| Average accelerations (in mg *by Klimentidis et al.*1) | | | |
| CAD | -0.032 | 0.025 | 0.205 |
| Myocardial infarction | -0.021 | 0.026 | 0.420 |
| Ischemic stroke | -0.032 | 0.036 | 0.367 |
| Fraction accelerations > 425mg (*by Klimentidis et al.*1) | | | |
| CAD | -0.085 | 0.107 | 0.430 |
| Myocardial infarction | -0.084 | 0.097 | 0.386 |
| Ischemic stroke | 0.020 | 0.093 | 0.826 |
| Sedentary behavior (*by Doherty et al.2)* | | | |
| CAD | -0.104 | 0.039 | 0.008 |
| Myocardial infarction | -0.093 | 0.045 | 0.040 |
| Ischemic Stroke | -0.020 | 0.035 | 0.568 |

SE – standard error, CAD – coronary artery disease, PA – physical activity, mg – milli-gravities; bold font indicate nominal significance of the MR-Egger directional pleiotropy test

Suppl. Table 13 – Body mass index and education adjusted Mendelian randomization estimates between self-reported moderate-to-vigorous physical activity identified by Klimentidis et al.1 and coronary artery disease, myocardial infarction, and ischemic stroke using multivariable MR analysis

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Method | N SNPs | OR a | 95% CI | P value |
| *Coronary artery disease* | | | | |
| Inverse variance weighted | 17 | 1.11 | (0.82 – 1.51) | 0.500 |
| Weighted median | 17 | 1.10 | (0.77 – 1.56) | 0.609 |
| MR Egger | 17 | 1.10 | (0.81 – 1.50) | 0.551 |
| *Myocardial infarction* | | | | |
| Inverse variance weighted | 17 | 1.00 | (0.72 – 1.38) | 0.976 |
| Weighted median | 17 | 0.96 | (0.65 – 1.41) | 0.823 |
| MR Egger | 17 | 1.00 | (0.72 – 1.38) | 0.992 |
| *Ischemic stroke* | | | | |
| Inverse variance weighted | 17 | 1.02 | (0.74 – 1.41) | 0.891 |
| Weighted median | 17 | 1.24 | (0.85 – 1.81) | 0.274 |
| MR Egger | 17 | 1.01 | (0.73 – 1.40) | 0.943 |

OR (odds ratio) per increase in MET/h per week for self-reported physical activity. CI, confidence interval. MET, metabolic equivalent tasks

Suppl. Table 14 – Body mass index and education adjusted Mendelian randomization estimates between accelerometer-derived average accelerations identified by Klimentidis et al. *1* in relation to coronary artery disease, myocardial infarction, and ischemic stroke using multivariable MR analysis

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Method | N SNPs | OR a | 95% CI | P value |
| *Coronary artery disease* | | | | |
| Inverse variance weighted | 7 | 1.01 | (0.99 – 1.03) | 0.313 |
| Weighted median | 7 | 1.01 | (0.99 – 1.03) | 0.519 |
| MR Egger | 7 | 1.02 | (0.99 – 1.06) | 0.145 |
| *Myocardial infarction* | | | | |
| Inverse variance weighted | 7 | 1.01 | (0.99 – 1.03) | 0.409 |
| Weighted median | 7 | 1.01 | (0.98 – 1.03) | 0.647 |
| MR Egger | 7 | 1.02 | (0.98 – 1.05) | 0.340 |
| *Ischemic stroke* | | | | |
| Inverse variance weighted | 7 | 0.98 | (0.96 – 1.00) | 0.022 |
| Weighted median | 7 | 0.96 | (0.94 – 0.99) | 0.001 |
| MR Egger | 7 | 0.95 | (0.92 – 0.98) | 0.001 |

OR (odds ratio) per increase in milligravities for accelerometer derived physical activity. CI, confidence interval

Suppl. Table 15 – Body mass index and education adjusted Mendelian randomization estimates between fraction acceleration > 425 milli-gravities identified by Klimentidis et al. *1* in relation to coronary artery disease, myocardial infarction, and ischemic stroke using multivariable MR analysis

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Method | N SNPs | OR a | 95% CI | P value |
| *Coronary artery disease* | | | | |
| Inverse variance weighted | 7 | 1.01 | (0.83 – 1.22) | 0.926 |
| Weighted median | 7 | 0.97 | (0.79 – 1.20) | 0.803 |
| MR Egger | 7 | 1.00 | (0.82 – 1.21) | 0.970 |
| *Myocardial infarction* | | | | |
| Inverse variance weighted | 7 | 1.04 | (0.85 – 1.28) | 0.685 |
| Weighted median | 7 | 1.04 | (0.82 – 1.32) | 0.734 |
| MR Egger | 7 | 1.04 | (0.85 – 1.28) | 0.688 |
| *Ischemic stroke* | | | | |
| Inverse variance weighted | 7 | 0.86 | (0.71 – 1.05) | 0.149 |
| Weighted median | 7 | 0.79 | (0.63 – 0.99) | 0.039 |
| MR Egger | 7 | 0.86 | (0.70 – 1.05) | 0.132 |

OR (odds ratio) for engaging in vigorous physical activity (≥ 425 milli-gravities). CI, confidence interval.

Suppl. Table 16 – Body mass index and education adjusted Mendelian randomization estimates between sedentary behavior identified by Doherty et al.2 in relation to coronary artery disease, myocardial infarction, and ischemic stroke using multivariable MR analysis

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Method | N SNPs | OR a | 95% CI | P value |
| *Coronary artery disease* | | | | |
| Inverse variance weighted | 6 | 1.01 | (0.99 – 1.03) | 0.313 |
| Weighted median | 6 | 1.01 | (0.99 – 1.03) | 0.516 |
| MR Egger | 6 | 1.01 | (0.99 – 1.03) | 0.364 |
| *Myocardial infarction* | | | | |
| Inverse variance weighted | 6 | 1.01 | (0.99 – 1.03) | 0.409 |
| Weighted median | 6 | 1.01 | (0.98 – 1.03) | 0.651 |
| MR Egger | 6 | 1.01 | (0.99 – 1.03) | 0.417 |
| *Ischemic stroke* | | | | |
| Inverse variance weighted | 6 | 0.98 | (0.96 – 1.00) | 0.022 |
| Weighted median | 6 | 0.96 | (0.94 – 0.99) | 0.002 |
| MR Egger | 6 | 0.98 | (0.96 – 1.00) | 0.020 |

OR (odds ratio) for displaying sedentary behavior (energy expenditure ≤ 1.5MET/h)

Suppl. Table 17 – False discovery rate adjusted11 p-values for the main (inverse variance weighted) analysis of the univariate and multivariate 2-sample MR analysis between self-reported moderate-to-vigorous physical activity, accelerometer-derived average accelerations, vigorous physical activity and sedentary behavior with coronary artery disease, myocardial infarction and ischemic stroke

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Exposure | OR a | 95% CI | P value | q-value |
| *Univariate MR analysis*  *Coronary artery disease* | | | | | |  |
| Self-reported moderate-to-vigorous PA | 1.03 | (0.71 – 1.49) | 0.875 | 0.956 |
| Accelerometer derived PA | 1.01 | (0.96 – 1.06) | 0.802 | 0.956 |
| Fraction accelerations > 425mg | 0.77 | (0.48 – 1.25) | 0.293 | 0.795 |
| Sedentary behavior | 0.91 | (0.56 – 1-49) | 0.709 | 0.956 |
| *Myocardial infarction* | | | | | |  |
| Self-reported moderate-to-vigorous PA | 1.01 | (0.96 – 1.06) | 0.802 | 0.956 |
| Accelerometer derived PA | 0.99 | (0.95 – 1.04) | 0.748 | 0.956 |
| Fraction accelerations > 425mg | 0.75 | (0.48 – 1.14) | 0.188 | 0.683 |
| Sedentary behavior | 0.96 | (0.59 – 1.56) | 0.855 | 0.956 |
| *Ischemic stroke* | | | | | |  |
| Self-reported moderate-to-vigorous PA | 1.16 | (0.80 – 1.67) | 0.436 | 0.821 |
| Accelerometer derived PA | 0.98 | (0.92 – 1.05) | 0.515 | 0.830 |
| Fraction accelerations > 425mg | 0.77 | (0.52 – 1.14) | 0.192 | 0.683 |
| Sedentary behavior | 1.06 | (0.75 – 1.48) | 0.748 | 0.956 |
| *Multivariable MR analysis*  *Coronary artery disease* | | | | | |
| Self-reported moderate-to-vigorous PA | 1.11 | (0.82 – 1.51) | 0.501 | 0.830 |
| Accelerometer derived PA | 1.01 | (0.99 – 1.03) | 0.313 | 0.795 |
| Fraction accelerations > 425mg | 1.01 | (0.83 – 1.22) | 0.926 | 0.956 |
| Sedentary behavior | 1.01 | (0.99 – 1.03) | 0.313 | 0.795 |
| *Myocardial infarction* | | | | | |
| Self-reported moderate-to-vigorous PA | 1.00 | (0.72 – 1.38) | 0.976 | 0.976 |
| Accelerometer derived PA | 1.01 | (0.99 – 1.03) | 0.409 | 0.818 |
| Fraction accelerations > 425mg | 1.04 | (0.85 – 1.28) | 0.685 | 0.956 |
| Sedentary behavior | 1.01 | (0.99 – 1.03) | 0.409 | 0.818 |
| *Ischemic stroke* | | | | | |
| Self-reported moderate-to-vigorous PA | 1.02 | (0.74 – 1.41) | 0.891 | 0.956 |
| Accelerometer derived PA | 0.98 | (0.96 – 1.00) | 0.022 | 0.176 |
| Fraction accelerations > 425mg | 0.86 | (0.71 – 1.05) | 0.149 | 0.681 |
| Sedentary behavior | 0.98 | (0.96 – 1.00) | 0.022 | 0.176 |

OR – odds ratio, CI – confidence interval

Suppl. Table 18 – Studies included from Nikpay et al3

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Study | Coronary artery disease cases (N) | Myocardial infarction cases (N) | Controls (N) | Ethnicity |
| PROCARDIS12,13 | 5,719 | 4,575 | 6,545\* | EUR |
| HSDS14,15 | 206 | 94 | 259 | EUR |
| ADVANCE16 | 278 | 278 | 312 | EUR |
| CARDIOGENICS17 | 392 | 49 | 410 | EUR |
| CCGB\_218 | 1,628 | 982 | 368 | EUR |
| COROGENE19 | 2,083 | 1,875 | 2,048 | EUR |
| DUKE\_218 | 1,216 | 585 | 653 | EUR |
| EGCUT20 | 658 | 1,29 | 5,841 | EUR |
| GERMIFS I17 | 634 | 634 | 1,608 | EUR |
| GERMIFS II21 | 1,207 | 1,207 | 1,288 | EUR |
| GERMIFS III (KORA)22 | 1,061 | 1,061 | 1,467 | EUR |
| GERMIFS\_IV | 1,089 | 1,089 | 1,147 | EUR |
| GODARTS23 | 877 |  | 2,187 | EUR |
| HPS12,24 | 2,700 | 1,755 | 2,758 | EUR |
| IPM\_EA25 | 487 | 148 | 1,381 | EUR |
| LURIC26 | 2,095 | 1,318 | 503 | EUR |
| MEDSTAR27 | 933 | 933 | 468 | EUR |
| MIGen28 | 2,905 | 2,905 | 2,998 | EUR |
| OHGS\_A218 | 947 | 609 | 1,008 | EUR |
| OHGS\_B218 | 1,294 | 719 | 1,529 | EUR |
| OHGS\_C218 | 843 | 373 | 318 | EUR |
| PENNCATH27 | 933 | 933 | 468 | EUR |
| PIVUS29 | 119 |  | 830 | EUR |
| PREDICTCVD30 | 631 | 252 | 334 | EUR |
| THISEAS31 | 426 | 256 | 594 | EUR |
| TWINGENE32 | 814 |  | 5,999 | EUR |
| ULSAM33 | 322 |  | 857 | EUR |
| WTCCC17,34 | 1,926 | 1,377 | 2,938 | EUR |
| LIFE-HEART35 | 1,535 | 675 | 772 | EUR |
| WGHS36 | 1,007 | 383 | 22,286 | EUR |
| ITH\_237 | 402 | 402 | 448 | EUR |
| MAYO-VDB38 | 745 |  | 1,389 | EUR |
| AGES39 | 397 | 317 | 2,474 | EUR |
| RS40 | 506 | 419 | 5,335 | EUR |
| FHS41 | 259 | 15 | 4,202 | EUR |
| FamHS42 | 334 | 29 | 3,446 | EUR |
| PROSPER43 | 2,034 | 763 | 3,210 | EUR |
| ARIC44 | 454 | 370 | 8,443 | EUR |
| **Total** | **42,096** | **27,509** | **101,879** |  |

Suppl. Table 19 – Studies included from Malik et al.4

|  |  |  |  |
| --- | --- | --- | --- |
| Study | Ischemic stroke (N) | Controls (N) | Ethnicity |
| CHARGE consortium45 | 3,028 | 80,613 | EUR |
| METASTROKE consortium46 47 | 10,307 | 19,326 | EUR |
| NINDS-SiGN consortium48 | 7,743 | 17,970 | EUR |
| deCODE study49 | 4,483 | 255,213 | EUR |
| EPIC-CVD50 | 2,226 | 7,897 | EUR |
| young lacunar stroke DNA resource51 | 1,268 | 970 | EUR |
| SIFAP-GER/KORA51 | 981 | 1,824 | EUR |
| INTERSTROKE (EUR) 52 | 826 | 863 | EUR |
| Heart and Vascular Health Study 153 | 577 | 1,331 | EUR |
| Heart and Vascular Health Study 253 | 103 | 570 | EUR |
| Glasgow Stroke Sampe54 | 599 | 1,775 | EUR |
| CADISP55 | 555 | 9,259 | EUR |
| VHIR-FMT-Barcelona | 520 | 315 | EUR |
| Helsinki 2000 Ischemic Stroke Genetics Study56 | 501 | 1,813 | EUR |
| SAHLSIS57 | 298 | 596 | EUR |
| MDC58 | 202 | 4,295 | EUR |
| **Total** | **34,217** | **404,630** |  |

**MEGASTROKE CONSORTIUM**

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