

SUPPLEMENTAL MATERIAL

Supplemental material for:

Modifiable Risk Factors for Intracranial Aneurysm and Aneurysmal Subarachnoid Hemorrhage: A Mendelian Randomization Study

Table S1

Table S2

Figure S1

Table S1. Minimum detectable odds ratios*

| Exposure | Intracranial aneurysm | Subarachnoid hemorrhage |
|---|--------------------------|----------------------------|
| Alcohol consumption | > 1.98, < 0.50 | > 2.44, < 0.41 |
| Body mass index | > 1.14, < 0.88 | > 1.18, < 0.85 |
| Blood urea nitrogen | > 1.30, < 0.77 | > 1.39, < 0.72 |
| Caffeine consumption | > 1.99, < 0.50 | > 2.29, < 0.44 |
| Chronic kidney disease | NA | NA |
| Coffee consumption | > 1.86, < 0.54 | > 2.15, < 0.47 |
| Diastolic blood pressure | > 1.16, < 0.86 | > 1.21, < 0.83 |
| eGFR | > 1.25, < 0.80 | > 1.32, < 0.76 |
| Fasting glucose | > 1.25, < 0.80 | > 1.31, < 0.76 |
| Fasting insulin | > 2.05, < 0.49 | > 2.45, < 0.41 |
| HbA1c | > 1.31, < 0.77 | > 1.39, < 0.72 |
| High-density lipoprotein cholesterol | > 1.14, < 0.88 | > 1.18, < 0.85 |
| Interleukin-6 receptor | > 1.73, < 0.58 | > 1.93, < 0.52 |
| Insomnia | NA | NA |
| Low-density lipoprotein cholesterol | > 1.13, < 0.88 | > 1.14, < 0.87 |
| Physical activity | > 3.75, < 0.27 | > 5.55, < 0.18 |
| Systolic blood pressure | > 1.22, < 0.82 | > 1.30, < 0.77 |
| Sleep duration | > 1.70, < 0.59 | > 1.97, < 0.51 |
| Long sleep duration | NA | NA |
| Short sleep duration | NA | NA |
| Smoking index | > 1.48, < 0.68 | > 1.69, < 0.59 |
| Smoking initiation | NA | NA |
| Type 2 diabetes mellitus | NA | NA |
| Triglycerides | > 1.17, < 0.85 | > 1.21, < 0.82 |

*Minimum detectable odds ratio for the continuous exposures with 80% power ($\alpha = 0.05$) and based on the exposure genome-wide association study sample size and the sum of the variance explained by the individual genetic instruments.

Table S2. Associations of genetically predicted exposures and intracranial aneurysm and aneurysmal subarachnoid hemorrhage in main and sensitivity analyses

| Group | Exposure | Outcome | Method | SNPs | OR | 95%_CI_low | 95%_CI_high | p-value | p-value pleiotropy |
|-----------|----------------------|---------|-----------------|------|--------|------------|-------------|----------|-----------------------|
| Lifestyle | Smoking index | IA | IVW-RE | 85 | 3,1985 | 1,9347 | 5,2878 | 5,82E-06 | |
| Lifestyle | Smoking index | IA | MR-Egger | 85 | 8,0469 | 0,9194 | 70,4329 | 0,0596 | 0,3915 |
| Lifestyle | Smoking index | IA | Weighted Median | 85 | 3,3335 | 1,7879 | 6,2155 | 0,0002 | |
| Lifestyle | Smoking index | IA | Weighted Mode | 85 | 2,0699 | 0,3743 | 11,4477 | 0,4045 | |
| Lifestyle | Smoking initiation | IA | IVW-RE | 235 | 1,8484 | 1,4952 | 2,2850 | 0,0000 | |
| Lifestyle | Smoking initiation | IA | MR-Egger | 235 | 2,7557 | 1,1367 | 6,6805 | 0,0249 | 0,3626 |
| Lifestyle | Smoking initiation | IA | Weighted Median | 235 | 2,0337 | 1,5197 | 2,7216 | 1,37E-08 | |
| Lifestyle | Smoking initiation | IA | Weighted Mode | 235 | 1,6888 | 0,7564 | 3,7705 | 0,2010 | |
| Lifestyle | Insomnia | IA | IVW-RE | 143 | 1,2382 | 1,0978 | 1,3965 | 0,0005 | |
| Lifestyle | Insomnia | IA | MR-Egger | 143 | 1,1186 | 0,6081 | 2,0574 | 0,7186 | 0,7389 |
| Lifestyle | Insomnia | IA | Weighted Median | 143 | 1,2743 | 1,0767 | 1,5081 | 0,0048 | |
| Lifestyle | Insomnia | IA | Weighted Mode | 143 | 1,2266 | 0,7388 | 2,0366 | 0,4298 | |
| Lifestyle | Caffeine consumption | IA | IVW-RE | 2 | 1,2257 | 0,9297 | 1,6160 | 0,1490 | |
| Lifestyle | Short sleep duration | IA | IVW-RE | 19 | 1,1220 | 0,7032 | 1,7903 | 0,6292 | |
| Lifestyle | Short sleep duration | IA | MR-Egger | 19 | 1,0288 | 0,1147 | 9,2258 | 0,9798 | 0,9367 |
| Lifestyle | Short sleep duration | IA | Weighted Median | 19 | 1,0992 | 0,6332 | 1,9083 | 0,7367 | |
| Lifestyle | Short sleep duration | IA | Weighted Mode | 19 | 1,1241 | 0,4724 | 2,6748 | 0,7915 | |
| Lifestyle | Alcohol consumption | IA | IVW-RE | 56 | 0,8622 | 0,3885 | 1,9137 | 0,7155 | |
| Lifestyle | Alcohol consumption | IA | MR-Egger | 56 | 0,5845 | 0,0700 | 4,8821 | 0,6200 | 0,6982 |
| Lifestyle | Alcohol consumption | IA | Weighted Median | 56 | 0,7160 | 0,2599 | 1,9731 | 0,5184 | |
| Lifestyle | Alcohol consumption | IA | Weighted Mode | 56 | 0,4892 | 0,1184 | 2,0214 | 0,3233 | |
| Lifestyle | Coffee consumption | IA | IVW-RE | 10 | 0,8269 | 0,4875 | 1,4028 | 0,4810 | |
| Lifestyle | Coffee consumption | IA | MR-Egger | 10 | 1,1072 | 0,3563 | 3,4409 | 0,8602 | 0,5641 |
| Lifestyle | Coffee consumption | IA | Weighted Median | 10 | 1,0034 | 0,5472 | 1,8398 | 0,9913 | |
| Lifestyle | Coffee consumption | IA | Weighted Mode | 10 | 1,1311 | 0,6027 | 2,1228 | 0,7013 | |
| Lifestyle | Long sleep duration | IA | IVW-RE | 4 | 0,7968 | 0,4875 | 1,3023 | 0,3648 | |

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|-----------------|--------------------------|----|-----------------|-----|--------|--------|----------|----------|--------|
| Lifestyle | Long sleep duration | IA | MR-Egger | 4 | 1,1545 | 0,1654 | 8,0601 | 0,8848 | 0,6991 |
| Lifestyle | Long sleep duration | IA | Weighted Median | 4 | 0,7161 | 0,3968 | 1,2924 | 0,2677 | |
| Lifestyle | Long sleep duration | IA | Weighted Mode | 4 | 0,6545 | 0,3130 | 1,3687 | 0,2601 | |
| Lifestyle | Sleep duration | IA | IVW-RE | 54 | 0,7134 | 0,4228 | 1,2040 | 0,2060 | |
| Lifestyle | Sleep duration | IA | MR-Egger | 54 | 1,0103 | 0,1473 | 6,9304 | 0,9917 | 0,7127 |
| Lifestyle | Sleep duration | IA | Weighted Median | 54 | 0,6403 | 0,3084 | 1,3291 | 0,2315 | |
| Lifestyle | Sleep duration | IA | Weighted Mode | 54 | 0,5593 | 0,1722 | 1,8167 | 0,3337 | |
| Lifestyle | Physical activity | IA | IVW-RE | 6 | 0,2196 | 0,0322 | 1,4982 | 0,1218 | |
| Lifestyle | Physical activity | IA | MR-Egger | 6 | 0,0011 | 0,0000 | 78,5456 | 0,2314 | 0,3442 |
| Lifestyle | Physical activity | IA | Weighted Median | 6 | 0,0999 | 0,0130 | 0,7686 | 0,0269 | |
| Lifestyle | Physical activity | IA | Weighted Mode | 6 | 0,0553 | 0,0031 | 0,9971 | 0,0498 | |
| Cardiometabolic | Diastolic blood pressure | IA | IVW-RE | 721 | 2,9227 | 2,4925 | 3,4271 | 8,38E-40 | |
| Cardiometabolic | Diastolic blood pressure | IA | MR-Egger | 721 | 5,4346 | 3,5999 | 8,2041 | 8,88E-16 | 0,0014 |
| Cardiometabolic | Diastolic blood pressure | IA | Weighted Median | 721 | 2,8770 | 2,2997 | 3,5993 | 2,29E-20 | |
| Cardiometabolic | Diastolic blood pressure | IA | Weighted Mode | 721 | 2,6370 | 1,1465 | 6,0651 | 0,0225 | |
| Cardiometabolic | Blood urea nitrogen | IA | IVW-RE | 67 | 1,9416 | 0,7231 | 5,2134 | 0,1880 | |
| Cardiometabolic | Blood urea nitrogen | IA | MR-Egger | 67 | 2,7888 | 0,1878 | 41,4029 | 0,4562 | 0,7772 |
| Cardiometabolic | Blood urea nitrogen | IA | Weighted Median | 67 | 1,1348 | 0,2854 | 4,5131 | 0,8575 | |
| Cardiometabolic | Blood urea nitrogen | IA | Weighted Mode | 67 | 0,4220 | 0,0613 | 2,9073 | 0,3809 | |
| Cardiometabolic | Systolic blood pressure | IA | IVW-RE | 214 | 1,8696 | 1,6117 | 2,1687 | 1,42E-16 | |
| Cardiometabolic | Systolic blood pressure | IA | MR-Egger | 214 | 3,6572 | 2,2723 | 5,8861 | 9,29E-08 | 0,0037 |
| Cardiometabolic | Systolic blood pressure | IA | Weighted Median | 214 | 1,7832 | 1,4970 | 2,1242 | 9,18E-11 | |
| Cardiometabolic | Systolic blood pressure | IA | Weighted Mode | 214 | 1,4929 | 0,9253 | 2,4089 | 0,1007 | |
| Cardiometabolic | eGFR | IA | IVW-RE | 235 | 1,6261 | 0,4839 | 5,4645 | 0,4317 | |
| Cardiometabolic | eGFR | IA | MR-Egger | 235 | 0,0588 | 0,0030 | 1,1632 | 0,0628 | 0,0173 |
| Cardiometabolic | eGFR | IA | Weighted Median | 235 | 1,5335 | 0,2371 | 9,9198 | 0,6536 | |
| Cardiometabolic | eGFR | IA | Weighted Mode | 235 | 3,2552 | 0,0544 | 194,9203 | 0,5719 | |
| Cardiometabolic | Triglycerides | IA | IVW-RE | 60 | 1,1870 | 1,0196 | 1,3819 | 0,0271 | |
| Cardiometabolic | Triglycerides | IA | MR-Egger | 60 | 1,0621 | 0,8386 | 1,3452 | 0,6170 | 0,2295 |
| Cardiometabolic | Triglycerides | IA | Weighted Median | 60 | 1,1392 | 0,9120 | 1,4231 | 0,2508 | |

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|-----------------|--------------------------|----|-----------------|-----|--------|--------|---------|--------|--------|
| Cardiometabolic | Triglycerides | IA | Weighted Mode | 60 | 1,1751 | 0,9535 | 1,4482 | 0,1302 | |
| Cardiometabolic | Body mass index | IA | IVW-RE | 967 | 1,1537 | 1,0095 | 1,3186 | 0,0359 | |
| Cardiometabolic | Body mass index | IA | MR-Egger | 967 | 0,9867 | 0,6767 | 1,4386 | 0,9445 | 0,3848 |
| Cardiometabolic | Body mass index | IA | Weighted Median | 967 | 1,1991 | 0,9742 | 1,4760 | 0,0866 | |
| Cardiometabolic | Body mass index | IA | Weighted Mode | 967 | 1,4877 | 0,9178 | 2,4114 | 0,1070 | |
| Cardiometabolic | Chronic kidney disease | IA | IVW-RE | 21 | 1,1440 | 0,9001 | 1,4539 | 0,2714 | |
| Cardiometabolic | Chronic kidney disease | IA | MR-Egger | 21 | 1,9347 | 1,0206 | 3,6677 | 0,0431 | 0,0847 |
| Cardiometabolic | Chronic kidney disease | IA | Weighted Median | 21 | 1,3581 | 1,0875 | 1,6959 | 0,0069 | |
| Cardiometabolic | Chronic kidney disease | IA | Weighted Mode | 21 | 1,3350 | 1,0083 | 1,7675 | 0,0436 | |
| Cardiometabolic | Type 2 diabetes mellitus | IA | IVW-RE | 422 | 1,0136 | 0,9458 | 1,0863 | 0,7024 | |
| Cardiometabolic | Type 2 diabetes mellitus | IA | MR-Egger | 422 | 0,8829 | 0,7568 | 1,0300 | 0,1132 | 0,0496 |
| Cardiometabolic | Type 2 diabetes mellitus | IA | Weighted Median | 422 | 0,9718 | 0,8753 | 1,0790 | 0,5925 | |
| Cardiometabolic | Type 2 diabetes mellitus | IA | Weighted Mode | 422 | 0,8695 | 0,7288 | 1,0373 | 0,1204 | |
| Cardiometabolic | HbA1c | IA | IVW-RE | 34 | 0,9683 | 0,5378 | 1,7434 | 0,9144 | |
| Cardiometabolic | HbA1c | IA | MR-Egger | 34 | 0,9770 | 0,1810 | 5,2742 | 0,9784 | 0,9911 |
| Cardiometabolic | HbA1c | IA | Weighted Median | 34 | 0,9230 | 0,3941 | 2,1614 | 0,8535 | |
| Cardiometabolic | HbA1c | IA | Weighted Mode | 34 | 0,9447 | 0,2964 | 3,0109 | 0,9234 | |
| Cardiometabolic | Fasting insulin | IA | IVW-RE | 9 | 0,9585 | 0,1691 | 5,4332 | 0,9618 | |
| Cardiometabolic | Fasting insulin | IA | MR-Egger | 9 | 0,2732 | 0,0000 | 4248511 | 0,8779 | 0,8812 |
| Cardiometabolic | Fasting insulin | IA | Weighted Median | 9 | 0,4446 | 0,0762 | 2,5954 | 0,3679 | |
| Cardiometabolic | Fasting insulin | IA | Weighted Mode | 9 | 0,1236 | 0,0026 | 5,9757 | 0,2907 | |
| Cardiometabolic | HDL cholesterol | IA | IVW-RE | 113 | 0,9317 | 0,8244 | 1,0531 | 0,2576 | |
| Cardiometabolic | HDL cholesterol | IA | MR-Egger | 113 | 1,0550 | 0,8452 | 1,3168 | 0,6359 | 0,1882 |
| Cardiometabolic | HDL cholesterol | IA | Weighted Median | 113 | 0,9145 | 0,7597 | 1,1010 | 0,3453 | |
| Cardiometabolic | HDL cholesterol | IA | Weighted Mode | 113 | 0,9361 | 0,7769 | 1,1279 | 0,4874 | |
| Cardiometabolic | LDL cholesterol | IA | IVW-RE | 88 | 0,8959 | 0,7842 | 1,0234 | 0,1054 | |
| Cardiometabolic | LDL cholesterol | IA | MR-Egger | 88 | 0,9669 | 0,7810 | 1,1970 | 0,7570 | 0,3705 |
| Cardiometabolic | LDL cholesterol | IA | Weighted Median | 88 | 0,9705 | 0,8179 | 1,1515 | 0,7314 | |
| Cardiometabolic | LDL cholesterol | IA | Weighted Mode | 88 | 0,9845 | 0,8373 | 1,1576 | 0,8504 | |
| Cardiometabolic | Interleukin-6 receptor | IA | IVW-RE | 2 | 0,8049 | 0,4865 | 1,3318 | 0,3983 | |

| | | | | | | | | | |
|-----------------|----------------------|------|-----------------|-----|---------|--------|----------|----------|--------|
| Cardiometabolic | Fasting glucose | IA | IVW-RE | 32 | 0,6391 | 0,4278 | 0,9548 | 0,0288 | |
| Cardiometabolic | Fasting glucose | IA | MR-Egger | 32 | 1,0586 | 0,5040 | 2,2238 | 0,8804 | 0,1165 |
| Cardiometabolic | Fasting glucose | IA | Weighted Median | 32 | 0,8572 | 0,5222 | 1,4072 | 0,5424 | |
| Cardiometabolic | Fasting glucose | IA | Weighted Mode | 32 | 0,8269 | 0,5193 | 1,3167 | 0,4233 | |
| Lifestyle | Smoking index | aSAH | IVW-RE | 66 | 2,9861 | 1,5538 | 5,7388 | 0,0010 | |
| Lifestyle | Smoking index | aSAH | MR-Egger | 66 | 25,6901 | 1,6637 | 396,6874 | 0,0201 | 0,1128 |
| Lifestyle | Smoking index | aSAH | Weighted Median | 66 | 2,0573 | 0,9239 | 4,5814 | 0,0774 | |
| Lifestyle | Smoking index | aSAH | Weighted Mode | 66 | 1,6760 | 0,2102 | 13,3657 | 0,6259 | |
| Lifestyle | Smoking initiation | aSAH | IVW-RE | 190 | 1,6217 | 1,2372 | 2,1257 | 0,0005 | |
| Lifestyle | Smoking initiation | aSAH | MR-Egger | 190 | 5,1285 | 1,7086 | 15,3938 | 0,0036 | 0,0343 |
| Lifestyle | Smoking initiation | aSAH | Weighted Median | 190 | 2,1689 | 1,5006 | 3,1348 | 3,79E-05 | |
| Lifestyle | Smoking initiation | aSAH | Weighted Mode | 190 | 3,0090 | 1,2050 | 7,5142 | 0,0183 | |
| Lifestyle | Insomnia | aSAH | IVW-RE | 109 | 1,1986 | 1,0252 | 1,4014 | 0,0231 | |
| Lifestyle | Insomnia | aSAH | MR-Egger | 109 | 1,1289 | 0,5396 | 2,3618 | 0,7475 | 0,8706 |
| Lifestyle | Insomnia | aSAH | Weighted Median | 109 | 1,1832 | 0,9527 | 1,4694 | 0,1280 | |
| Lifestyle | Insomnia | aSAH | Weighted Mode | 109 | 1,1230 | 0,6164 | 2,0460 | 0,7047 | |
| Lifestyle | Caffeine consumption | aSAH | IVW-RE | 2 | 1,2035 | 0,8719 | 1,6611 | 0,2601 | |
| Lifestyle | Short sleep duration | aSAH | IVW-RE | 14 | 1,4819 | 0,8809 | 2,4929 | 0,1383 | |
| Lifestyle | Short sleep duration | aSAH | MR-Egger | 14 | 2,9471 | 0,1939 | 44,7913 | 0,4363 | 0,6139 |
| Lifestyle | Short sleep duration | aSAH | Weighted Median | 14 | 1,4557 | 0,7107 | 2,9815 | 0,3047 | |
| Lifestyle | Short sleep duration | aSAH | Weighted Mode | 14 | 1,3632 | 0,4629 | 4,0150 | 0,5740 | |
| Lifestyle | Alcohol consumption | aSAH | IVW-RE | 46 | 0,7232 | 0,3164 | 1,6530 | 0,4423 | |
| Lifestyle | Alcohol consumption | aSAH | MR-Egger | 46 | 0,9197 | 0,1040 | 8,1298 | 0,9400 | 0,8150 |
| Lifestyle | Alcohol consumption | aSAH | Weighted Median | 46 | 0,5593 | 0,1594 | 1,9622 | 0,3642 | |
| Lifestyle | Alcohol consumption | aSAH | Weighted Mode | 46 | 0,5455 | 0,0941 | 3,1627 | 0,4991 | |
| Lifestyle | Coffee consumption | aSAH | IVW-RE | 9 | 1,0027 | 0,5251 | 1,9147 | 0,9935 | |
| Lifestyle | Coffee consumption | aSAH | MR-Egger | 9 | 0,9359 | 0,2310 | 3,7912 | 0,9260 | 0,9115 |
| Lifestyle | Coffee consumption | aSAH | Weighted Median | 9 | 1,1272 | 0,5448 | 2,3320 | 0,7469 | |
| Lifestyle | Coffee consumption | aSAH | Weighted Mode | 9 | 1,1713 | 0,5101 | 2,6893 | 0,7093 | |
| Lifestyle | Long sleep duration | aSAH | IVW-RE | 4 | 0,7291 | 0,4032 | 1,3186 | 0,2960 | |

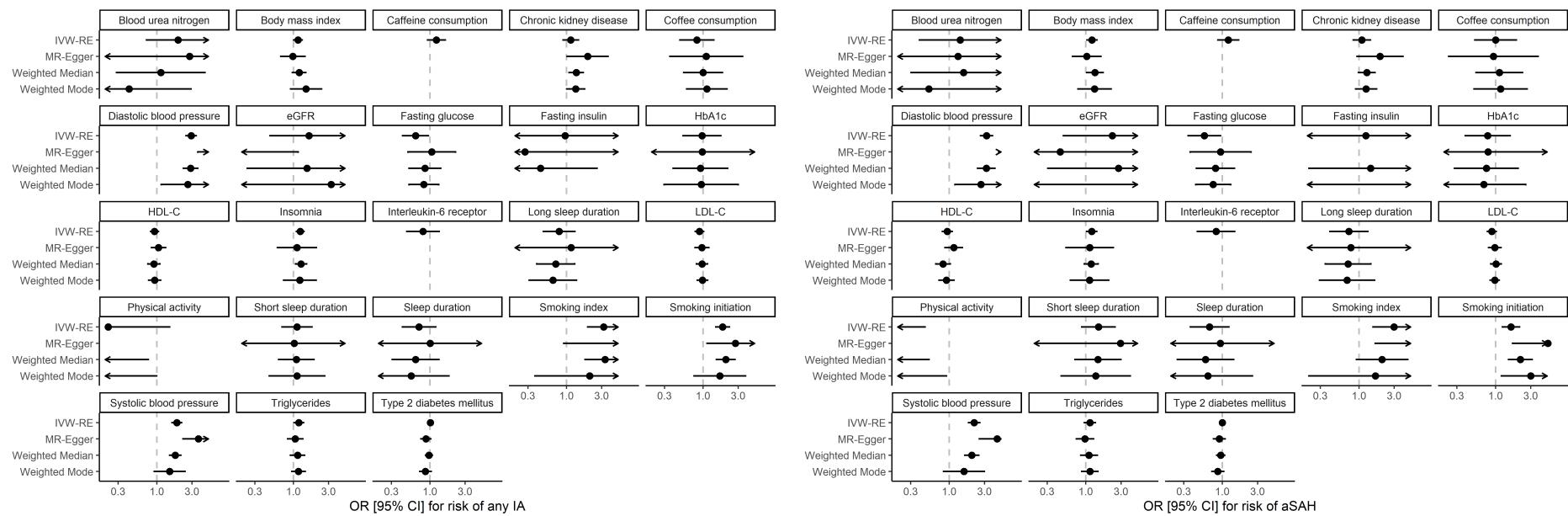
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|-----------------|--------------------------|------|-----------------|-----|--------|--------|-----------|----------|--------|
| Lifestyle | Long sleep duration | aSAH | MR-Egger | 4 | 0,7792 | 0,0761 | 7,9758 | 0,8335 | 0,9538 |
| Lifestyle | Long sleep duration | aSAH | Weighted Median | 4 | 0,7131 | 0,3504 | 1,4515 | 0,3511 | |
| Lifestyle | Long sleep duration | aSAH | Weighted Mode | 4 | 0,6907 | 0,2918 | 1,6347 | 0,3998 | |
| Lifestyle | Sleep duration | aSAH | IVW-RE | 47 | 0,6708 | 0,3669 | 1,2266 | 0,1947 | |
| Lifestyle | Sleep duration | aSAH | MR-Egger | 47 | 0,9375 | 0,1059 | 8,2972 | 0,9538 | 0,7540 |
| Lifestyle | Sleep duration | aSAH | Weighted Median | 47 | 0,5888 | 0,2445 | 1,4181 | 0,2376 | |
| Lifestyle | Sleep duration | aSAH | Weighted Mode | 47 | 0,6383 | 0,1593 | 2,5576 | 0,5261 | |
| Lifestyle | Physical activity | aSAH | IVW-RE | 5 | 0,0543 | 0,0063 | 0,4678 | 0,0080 | |
| Lifestyle | Physical activity | aSAH | MR-Egger | 5 | 0,0003 | 0,0000 | 133,9815 | 0,2250 | 0,4345 |
| Lifestyle | Physical activity | aSAH | Weighted Median | 5 | 0,0425 | 0,0034 | 0,5328 | 0,0144 | |
| Lifestyle | Physical activity | aSAH | Weighted Mode | 5 | 0,0181 | 0,0004 | 0,9122 | 0,0449 | |
| Cardiometabolic | Diastolic blood pressure | aSAH | IVW-RE | 651 | 3,2096 | 2,6627 | 3,8690 | 2,05E-34 | |
| Cardiometabolic | Diastolic blood pressure | aSAH | MR-Egger | 651 | 7,6051 | 4,6743 | 12,3735 | 2,22E-16 | 0,0002 |
| Cardiometabolic | Diastolic blood pressure | aSAH | Weighted Median | 651 | 3,1726 | 2,4245 | 4,1515 | 3,93E-17 | |
| Cardiometabolic | Diastolic blood pressure | aSAH | Weighted Mode | 651 | 2,6823 | 1,1950 | 6,0204 | 0,0168 | |
| Cardiometabolic | Blood urea nitrogen | aSAH | IVW-RE | 64 | 1,4062 | 0,3942 | 5,0162 | 0,5993 | |
| Cardiometabolic | Blood urea nitrogen | aSAH | MR-Egger | 64 | 1,3093 | 0,0387 | 44,2434 | 0,8807 | 0,9660 |
| Cardiometabolic | Blood urea nitrogen | aSAH | Weighted Median | 64 | 1,5625 | 0,3023 | 8,0763 | 0,5943 | |
| Cardiometabolic | Blood urea nitrogen | aSAH | Weighted Mode | 64 | 0,5288 | 0,0409 | 6,8434 | 0,6258 | |
| Cardiometabolic | Systolic blood pressure | aSAH | IVW-RE | 188 | 2,1696 | 1,8236 | 2,5814 | 2,40E-18 | |
| Cardiometabolic | Systolic blood pressure | aSAH | MR-Egger | 188 | 4,4641 | 2,5548 | 7,8001 | 1,49E-07 | 0,0078 |
| Cardiometabolic | Systolic blood pressure | aSAH | Weighted Median | 188 | 2,0175 | 1,6240 | 2,5063 | 2,30E-10 | |
| Cardiometabolic | Systolic blood pressure | aSAH | Weighted Mode | 188 | 1,5856 | 0,8395 | 2,9948 | 0,1554 | |
| Cardiometabolic | eGFR | aSAH | IVW-RE | 216 | 2,2873 | 0,4951 | 10,5671 | 0,2893 | |
| Cardiometabolic | eGFR | aSAH | MR-Egger | 216 | 0,4500 | 0,0095 | 21,2913 | 0,6849 | 0,3680 |
| Cardiometabolic | eGFR | aSAH | Weighted Median | 216 | 2,7807 | 0,3043 | 25,4133 | 0,3650 | |
| Cardiometabolic | eGFR | aSAH | Weighted Mode | 216 | 7,5182 | 0,0283 | 1999,2246 | 0,4788 | |
| Cardiometabolic | Triglycerides | aSAH | IVW-RE | 54 | 1,1356 | 0,9571 | 1,3474 | 0,1450 | |
| Cardiometabolic | Triglycerides | aSAH | MR-Egger | 54 | 0,9701 | 0,7424 | 1,2678 | 0,8242 | 0,1352 |
| Cardiometabolic | Triglycerides | aSAH | Weighted Median | 54 | 1,1027 | 0,8510 | 1,4290 | 0,4595 | |

| | | | | | | | | | |
|-----------------|--------------------------|------|-----------------|-----|--------|--------|----------|--------|--------|
| Cardiometabolic | Triglycerides | aSAH | Weighted Mode | 54 | 1,1340 | 0,8821 | 1,4577 | 0,3266 | |
| Cardiometabolic | Body mass index | aSAH | IVW-RE | 911 | 1,2077 | 1,0324 | 1,4129 | 0,0184 | |
| Cardiometabolic | Body mass index | aSAH | MR-Egger | 911 | 1,0281 | 0,6605 | 1,6002 | 0,9024 | 0,4455 |
| Cardiometabolic | Body mass index | aSAH | Weighted Median | 911 | 1,3317 | 1,0308 | 1,7204 | 0,0284 | |
| Cardiometabolic | Body mass index | aSAH | Weighted Mode | 911 | 1,3125 | 0,7831 | 2,1999 | 0,3021 | |
| Cardiometabolic | Chronic kidney disease | aSAH | IVW-RE | 21 | 1,0935 | 0,8356 | 1,4309 | 0,5149 | |
| Cardiometabolic | Chronic kidney disease | aSAH | MR-Egger | 21 | 1,9333 | 0,9454 | 3,9536 | 0,0709 | 0,0942 |
| Cardiometabolic | Chronic kidney disease | aSAH | Weighted Median | 21 | 1,2754 | 0,9836 | 1,6539 | 0,0664 | |
| Cardiometabolic | Chronic kidney disease | aSAH | Weighted Mode | 21 | 1,2497 | 0,8998 | 1,7355 | 0,1835 | |
| Cardiometabolic | Type 2 diabetes mellitus | aSAH | IVW-RE | 383 | 0,9985 | 0,9208 | 1,0827 | 0,9708 | |
| Cardiometabolic | Type 2 diabetes mellitus | aSAH | MR-Egger | 383 | 0,9080 | 0,7568 | 1,0894 | 0,2990 | 0,2538 |
| Cardiometabolic | Type 2 diabetes mellitus | aSAH | Weighted Median | 383 | 0,9493 | 0,8387 | 1,0745 | 0,4102 | |
| Cardiometabolic | Type 2 diabetes mellitus | aSAH | Weighted Mode | 383 | 0,8650 | 0,7194 | 1,0401 | 0,1232 | |
| Cardiometabolic | HbA1c | aSAH | IVW-RE | 31 | 0,7825 | 0,3876 | 1,5797 | 0,4939 | |
| Cardiometabolic | HbA1c | aSAH | MR-Egger | 31 | 0,7914 | 0,1049 | 5,9727 | 0,8205 | 0,9907 |
| Cardiometabolic | HbA1c | aSAH | Weighted Median | 31 | 0,7521 | 0,2782 | 2,0337 | 0,5746 | |
| Cardiometabolic | HbA1c | aSAH | Weighted Mode | 31 | 0,6961 | 0,1882 | 2,5754 | 0,5874 | |
| Cardiometabolic | Fasting insulin | aSAH | IVW-RE | 8 | 1,2434 | 0,1952 | 7,9211 | 0,8176 | |
| Cardiometabolic | Fasting insulin | aSAH | MR-Egger | 8 | 0,0561 | 0,0000 | 6533732 | 0,7612 | 0,7423 |
| Cardiometabolic | Fasting insulin | aSAH | Weighted Median | 8 | 1,4436 | 0,2098 | 9,9319 | 0,7091 | |
| Cardiometabolic | Fasting insulin | aSAH | Weighted Mode | 8 | 6,4921 | 0,1167 | 361,0099 | 0,3616 | |
| Cardiometabolic | HDL cholesterol | aSAH | IVW-RE | 102 | 0,9378 | 0,8047 | 1,0930 | 0,4112 | |
| Cardiometabolic | HDL cholesterol | aSAH | MR-Egger | 102 | 1,1488 | 0,8753 | 1,5078 | 0,3174 | 0,0782 |
| Cardiometabolic | HDL cholesterol | aSAH | Weighted Median | 102 | 0,8227 | 0,6587 | 1,0274 | 0,0852 | |
| Cardiometabolic | HDL cholesterol | aSAH | Weighted Mode | 102 | 0,9166 | 0,7257 | 1,1577 | 0,4648 | |
| Cardiometabolic | LDL cholesterol | aSAH | IVW-RE | 84 | 0,8890 | 0,7744 | 1,0205 | 0,0946 | |
| Cardiometabolic | LDL cholesterol | aSAH | MR-Egger | 84 | 0,9771 | 0,8064 | 1,1838 | 0,8126 | 0,1677 |
| Cardiometabolic | LDL cholesterol | aSAH | Weighted Median | 84 | 1,0165 | 0,8650 | 1,1946 | 0,8421 | |
| Cardiometabolic | LDL cholesterol | aSAH | Weighted Mode | 84 | 0,9756 | 0,8481 | 1,1223 | 0,7294 | |
| Cardiometabolic | Interleukin-6 receptor | aSAH | IVW-RE | 2 | 0,8197 | 0,4573 | 1,4695 | 0,5045 | |

| | | | | | | | | | |
|-----------------|-----------------|------|-----------------|----|--------|--------|--------|--------|--------|
| Cardiometabolic | Fasting glucose | aSAH | IVW-RE | 27 | 0,5694 | 0,3435 | 0,9439 | 0,0290 | |
| Cardiometabolic | Fasting glucose | aSAH | MR-Egger | 27 | 0,9449 | 0,3643 | 2,4506 | 0,9072 | 0,2208 |
| Cardiometabolic | Fasting glucose | aSAH | Weighted Median | 27 | 0,8041 | 0,4430 | 1,4598 | 0,4737 | |
| Cardiometabolic | Fasting glucose | aSAH | Weighted Mode | 27 | 0,7492 | 0,4346 | 1,2916 | 0,2987 | |

Abbreviations: aSAH, aneurysmal subarachnoid hemorrhage; CI, confidence interval; eGFR, estimated glomerular filtration rate; HDL, high-density lipoprotein cholesterol; IA, intracranial aneurysm; IVW-RE, inverse-variance weighted random effects; LDL, low-density lipoprotein; MR, Mendelian randomization; OR, odds ratio; SE, standard error; SNPs, single-nucleotide polymorphisms.

Figure S1. Associations of genetically predicted exposures and intracranial aneurysm and aneurysmal subarachnoid hemorrhage in main and sensitivity analyses



Abbreviations: aSAH, aneurysmal subarachnoid hemorrhage; CI, confidence interval; eGFR, estimated glomerular filtration rate; HDL, high-density lipoprotein cholesterol; IA, intracranial aneurysm; IVW-RE, inverse-variance weighted random effects; LDL, low-density lipoprotein; MR, Mendelian randomization; OR, odds ratio.