Supplemental Material

Sex hormones and risk of aneurysmal subarachnoid hemorrhage: a Mendelian randomization study

Rob Molenberg BSc, Chris H.L. Thio PhD, Marlien W. Aalbers MD PhD, Maarten Uyttenboogaart MD PhD, ISGC Intracranial Aneurysm Working Group, Susanna C. Larsson PhD, Mark K. Bakker MSc, Ynte M. Ruigrok MD PhD, Harold Snieder PhD, J. Marc C. van Dijk MD PhD

Contents
- Data sources
- Table S1. SNPs and proxies used for age at menarche
- Table S2. SNPs and proxies used for age at menopause
- Table S3. SNPs and proxies used for SHBG in men
- Table S4. SNPs and proxies used for SHBG in women
- Table S5. SNPs and proxies used for bioavailable testosterone in men
- Table S6. SNPs and proxies used for bioavailable testosterone in women
- Table S7. Study characteristics and SNP effects for estradiol
- Table S8. Mendelian randomization results after cluster filtering
- Table S9. Multivariable Mendelian randomization results
- Table S10. Mendelian randomization results for the different exposures on aSAH risk among women
- Table S11. Sensitivity analyses for the different exposures on aSAH risk among men
- Table S12. Mendelian randomization results after MR-Steiger filtering
- ISGC Intracranial Aneurysm Working Group contributors
- STROBE-MR checklist
Data sources

Detailed information (e.g. summary-level GWAS statistics and lists of underlying cohorts) can be obtained via the links provided below.

Exposure data
Summary statistics for the GWASs on age at menopause and age at menarche can be accessed from the ReproGen website (www.reprogen.org). Summary-level data for the exposures SHBG and Bioavailable testosterone are available via the supplemental tables belonging to the original article (https://doi.org/10.1038/s41591-020-0751-5).

Outcome data
GWAS summary-level data regarding aneurysmal subarachnoid hemorrhage can be accessed from the Cerebrovascular Disease Knowledge Portal (www.cerebrovascularportal.org).
| NO. | SNP        | CHR | POSITION (B37) | EA/OA | EAF   | BETA  | SE   | P-VALUE | PROXY SNP | PROXY EA/OA | R²   | PROXY EAF |
|-----|------------|-----|----------------|-------|-------|-------|------|---------|-----------|-------------|------|-----------|
| 1   | rs6678140  | 1   | 8436802        | T/C   | 0.6731| -0.0269| 0.0041| 7.54E-11|           |             |      |           |
| 2   | rs141847393| 1   | 27212209       | T/C   | 0.9182| 0.0396 | 0.0071| 2.96E-08|           |             |      |           |
| 3   | rs11209331 | 1   | 4145689        | T/C   | 0.5713| 0.0238 | 0.0039| 9.83E-10|           |             |      |           |
| 4   | rs11210871 | 1   | 44029353       | C/G   | 0.2981| 0.04   | 0.0042| 3.07E-21| rs3001723 | A/G         | 0.9077| 0.3260    |
| 5   | rs643428   | 1   | 54728858       | T/C   | 0.5926| -0.0219| 0.004 | 3.21E-08| rs679200  | G/A         | 0.8243| 0.5209    |
| 6   | rs7516763  | 1   | 65972250       | A/C   | 0.4691| 0.0232 | 0.0038| 1.49E-09|           |             |      |           |
| 7   | rs1040070  | 1   | 74977870       | C/G   | 0.5654| 0.05   | 0.0039| 7.01E-38| rs953567  | A/G         | 0.86  | 0.5885    |
| 8   | rs11165924 | 1   | 98375448       | A/G   | 0.6767| 0.0312 | 0.0041| 4.83E-14|           |             |      |           |
| 9   | rs4561063  | 1   | 102520898      | T/G   | 0.4614| 0.0312 | 0.0039| 7.89E-16|           |             |      |           |
| 10  | rs6661100  | 1   | 150758727      | T/C   | 0.0921| 0.0471 | 0.0067| 2.18E-12|           |             |      |           |
| 11  | rs2661339  | 1   | 163018934      | T/G   | 0.054 | 0.0534 | 0.0088| 1.34E-09| rs17440397| G/A         | 0.9833| 0.0626    |
| 12  | rs157877   | 1   | 165398744      | A/G   | 0.1265| -0.0843| 0.0058| 2.25E-48|           |             |      |           |
| 13  | rs506589   | 1   | 177894287      | T/C   | 0.8029| 0.0695 | 0.0048| 1.54E-47|           |             |      |           |
| 14  | rs4951261  | 1   | 20571823       | A/C   | 0.6144| 0.0269 | 0.0039| 5.36E-12|           |             |      |           |
| 15  | rs7576624  | 2   | 625029         | T/C   | 0.8261| -0.0741| 0.005 | 4.98E-50|           |             |      |           |
| 16  | rs10175423 | 2   | 42970161       | T/C   | 0.2967| -0.0247| 0.0042| 4.25E-09|           |             |      |           |
| 17  | rs111567162| 2   | 56588406       | A/T   | 0.1742| 0.0675 | 0.0051| 2.49E-40| rs6545574 | T/C         | 0.9217| 0.1720    |
| 18  | rs12467441 | 2   | 61685826       | T/C   | 0.8739| -0.0408| 0.006 | 8.99E-12| rs34823499| A/G         | 0.8069| 0.8529    |
| 19  | rs2723065  | 2   | 65279414       | A/G   | 0.613 | -0.0247| 0.0039| 2.59E-10|           |             |      |           |
| 20  | rs35935052 | 2   | 142032503      | T/G   | 0.148 | 0.0437 | 0.0054| 5.01E-16|           |             |      |           |
| 21  | rs142058842| 2   | 156621725      | C/G   | 0.8297| -0.0681| 0.0051| 2.42E-40| rs72899095| C/T         | 1     | 0.8469    |
| 22  | rs2271758  | 2   | 172701157      | T/G   | 0.4106| -0.0214| 0.0039| 3.96E-08|           |             |      |           |
| 23  | rs842567   | 2   | 184291116      | A/C   | 0.7939| -0.034 | 0.005 | 9.38E-12| rs1992645 | A/G         | 0.8725| 0.7982    |
| 24  | rs10931831 | 2   | 199621641      | T/C   | 0.3556| -0.0531| 0.004 | 1.87E-39|           |             |      |           |
|   |   | rs16841867 | rs6735626 | rs73820560 | rs9867904 | rs73035994 | rs1984870 | rs6445624 | rs7431217 | rs9758500 | rs10934420 | rs2461794 | rs6439713 | rs11711674 | rs2300922 | rs2108753 | rs4340786 | rs3113862 | rs3733632 | rs17035311 | rs13120031 | rs10521021 | rs7712046 | rs813301 | rs256350 | rs13173441 | rs17085593 | rs654354 | rs247520 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 25 | 2 | 203168235 | C/G | 0.8845 | 0.0456 | 0.006 | 2.56E-14 | rs12464254 | T/C | 1 | 0.8598  |
| 26 | 2 | 213403972 | A/G | 0.4374 | 0.0215 | 0.0039 | 2.96E-08  |
| 27 | 3 | 1906245  | A/C | 0.8562 | -0.0319 | 0.0057 | 1.68E-08 |
| 28 | 3 | 18442437 | C/G | 0.3869 | -0.0278 | 0.004 | 3.42E-12 | rs9812165 | C/T | 1 | 0.3539  |
| 29 | 3 | 24206463 | T/C | 0.9716 | -0.0907 | 0.0116 | 5.22E-15 |
| 30 | 3 | 24715135 | T/G | 0.4728 | 0.0422  | 0.0039 | 5.61E-27 |
| 31 | 3 | 51358019 | A/G | 0.1473 | 0.0422  | 0.0056 | 6.41E-14 | rs4687569 | T/C | 0.9164 | 0.1183 |
| 32 | 3 | 68595634 | A/C | 0.412  | 0.0229  | 0.0039 | 6.19E-09 |
| 33 | 3 | 86910329 | A/G | 0.375  | -0.0457 | 0.004 | 1.36E-30 |
| 34 | 3 | 117552111 | T/C | 0.5054 | -0.0546 | 0.0038 | 1.54E-47 |
| 35 | 3 | 127870060 | A/G | 0.2763 | 0.0342  | 0.0043 | 2.10E-15 |
| 36 | 3 | 137128815 | A/C | 0.315  | 0.0259  | 0.0041 | 2.13E-10 |
| 37 | 3 | 156532953 | T/C | 0.5708 | 0.0216  | 0.0038 | 1.77E-08 |
| 38 | 3 | 185651469 | T/C | 0.4144 | 0.0432  | 0.0039 | 1.11E-28 |
| 39 | 4 | 3266860  | T/C | 0.565  | 0.0284  | 0.0038 | 1.20E-13 |
| 40 | 4 | 28746246 | A/T | 0.7412 | 0.037  | 0.0043 | 9.25E-18 | rs10013470 | G/T | 1 | 0.7316 |
| 41 | 4 | 95143122 | A/G | 0.5994 | -0.0373 | 0.0039 | 9.69E-22 |
| 42 | 4 | 104640935 | A/G | 0.8437 | -0.0536 | 0.0052 | 1.04E-24 |
| 43 | 4 | 106066293 | A/C | 0.854  | 0.036  | 0.0054 | 2.26E-11 |
| 44 | 4 | 177465182 | T/C | 0.3243 | 0.0274  | 0.0041 | 1.57E-11 |
| 45 | 5 | 35030311 | T/G | 0.6577 | -0.024  | 0.0041 | 4.77E-09 |
| 46 | 5 | 43134968 | T/C | 0.6962 | -0.0333 | 0.0042 | 9.42E-16 |
| 47 | 5 | 52909927 | T/C | 0.6259 | 0.0274  | 0.0039 | 2.84E-12 |
| 48 | 5 | 59140876 | T/C | 0.7259 | -0.0238 | 0.0043 | 2.84E-08 |
| 49 | 5 | 77048448 | T/C | 0.8787 | 0.0331  | 0.0059 | 1.86E-08 | rs34541757 | C/T | 0.9912 | 0.8718 |
| 50 | 5 | 95630705 | C/G | 0.6841 | 0.0246  | 0.0042 | 3.53E-09 | rs2350002 | A/G | 0.9954 | 0.6879 |
| 51 | 5 | 110503301 | A/T | 0.3828 | -0.0233 | 0.0039 | 2.36E-09 | rs32701  | A/C | 1 | 0.3708 |
| 52 | 5 | 110876057 | T/C | 0.7652 | 0.0361  | 0.0045 | 1.99E-15 |
|   | SNP         | Chr | Start | Strand | Ref Allele  | Var Allele  | Minor allele freq | r^2 | P val  |
|---|-------------|-----|-------|--------|-------------|-------------|-------------------|-----|--------|
| 53 | rs3815212   | 5   | 137761555 | T/C | 0.7829 | 0.0337 | 0.0046 | 3.21E-13 |
| 54 | rs1428120   | 5   | 153541904 | T/G | 0.5718 | 0.025  | 0.0038 | 7.72E-11 |
| 55 | rs437836    | 5   | 156715068 | T/C | 0.1671 | 0.035  | 0.0052 | 1.15E-11 |
| 56 | rs9647570   | 5   | 167370263 | T/G | 0.8544 | -0.0363 | 0.0056 | 6.26E-11 |
| 57 | rs6864818   | 5   | 168734867 | T/C | 0.2107 | 0.0364 | 0.0046 | 4.67E-15 | rs12716241 | T/C   | 1  | 0.2256 |
| 58 | rs446745    | 6   | 14918298 | T/C | 0.2407 | -0.0258 | 0.0046 | 2.81E-08 | rs6930513 | T/C   | 0.96 | 0.2167 |
| 59 | rs6927679   | 6   | 18559687 | T/C | 0.718  | 0.027  | 0.0043 | 2.52E-10 |
| 60 | rs1539310   | 6   | 22562485 | A/G | 0.7568 | 0.0244 | 0.0045 | 4.59E-08 |
| 61 | rs9349203   | 6   | 41893323 | A/G | 0.5463 | -0.0395 | 0.0038 | 5.93E-25 |
| 62 | rs9474996   | 6   | 54640512 | A/T | 0.5553 | -0.0343 | 0.0038 | 3.82E-19 | rs9474997 | T/C   | 1  | 0.5845 |
| 63 | rs9382676   | 6   | 56859084 | T/C | 0.7767 | 0.0373 | 0.0046 | 8.77E-16 | rs9396246 | C/T   | 0.9946 | 0.7555 |
| 64 | rs7753896   | 6   | 76347020 | A/G | 0.3681 | 0.031  | 0.0039 | 2.46E-15 |
| 65 | rs7757654   | 6   | 77173780 | T/C | 0.2956 | -0.0306 | 0.0042 | 2.51E-13 |
| 66 | rs9403051   | 6   | 100194846 | A/G | 0.5701 | 0.0365 | 0.0038 | 1.76E-21 |
| 67 | rs395962    | 6   | 105397418 | T/G | 0.3163 | 0.1266 | 0.0041 | 2.26E-213 |
| 68 | rs4897178   | 6   | 126727908 | T/G | 0.5545 | 0.0426 | 0.0039 | 1.02E-27 | rs4897179 | G/A   | 0.996 | 0.5457 |
| 69 | rs6911527   | 6   | 148285329 | T/C | 0.2275 | 0.0269 | 0.0045 | 3.18E-09 |
| 70 | rs6933660   | 6   | 151803754 | A/C | 0.3173 | -0.0343 | 0.0041 | 8.99E-17 |
| 71 | rs10268051  | 7   | 27763590 | A/C | 0.7769 | 0.0249 | 0.0045 | 3.88E-08 |
| 72 | rs17171852  | 7   | 41392815 | A/C | 0.8078 | -0.038  | 0.0048 | 3.42E-15 |
| 73 | rs1470750   | 7   | 50576648 | C/G | 0.5923 | -0.0223 | 0.0039 | 1.44E-08 | rs12718572 | C/T   | 0.9287 | 0.6431 |
| 74 | rs2267812   | 7   | 74138121 | A/C | 0.7951 | 0.0417 | 0.0049 | 1.69E-17 | rs4717907 | G/A   | 0.8269 | 0.73613 |
| 75 | rs1030015   | 7   | 78139581 | T/G | 0.5217 | -0.0206 | 0.0038 | 4.45E-08 |
| 76 | rs149226155 | 7   | 93215658 | A/G | 0.3474 | -0.0238 | 0.0041 | 5.67E-09 | rs13247665 | C/T   | 0.9912 | 0.35608 |
| 77 | rs999885    | 7   | 99701176 | A/G | 0.5164 | 0.0241 | 0.0038 | 2.79E-10 |
| 78 | rs11767400  | 7   | 122160742 | A/C | 0.2959 | 0.0289 | 0.0042 | 5.41E-12 |
| 79 | rs12707076  | 7   | 132729814 | C/G | 0.3844 | 0.0273 | 0.004 | 4.88E-12 | rs6953845 | C/T   | 1  | 0.3936 |
| 80 | rs7004265   | 8   | 1523903  | T/C | 0.4769 | 0.023  | 0.0039 | 5.12E-09 | rs12546094 | T/C   | 0.9297 | 0.4851 |
|     | Gene ID     | Ref SNP | Alt SNP | Minor Allele Frequency | Odds Ratio |Log Odds Ratio | P-Value | SNP ID     | Gene       |
|----|-------------|---------|---------|------------------------|------------|---------------|---------|------------|------------|
| 81 | rs2724961   | T/C     | 0.4682  | -0.0459               | 0.0038     | 3.76E-33      |         | rs4871939  | G/A        |
| 82 | rs6185      | C/G     | 0.7296  | -0.0301               | 0.0044     | 9.48E-12      |         | rs7837649  | G/A        |
| 83 | rs1691837   | T/C     | 0.8769  | 0.0478                | 0.0059     | 9.08E-16      |         | rs72663709 | T/C        |
| 84 | rs1178686   | C/G     | 0.837   | 0.0321                | 0.0051     | 4.27E-10      |         | rs2514656  | G/A        |
| 85 | rs10094506  | T/C     | 0.2807  | -0.0454               | 0.0043     | 2.46E-26      |         | rs4464946  | A/G        |
| 86 | rs7465046   | T/C     | 0.322   | -0.0409               | 0.0046     | 1.52E-18      |         | rs2514656  | G/A        |
| 87 | rs2441873   | T/G     | 0.4106  | 0.0235                | 0.0039     | 1.74E-09      |         | rs2514656  | G/A        |
| 88 | rs2542420   | C/G     | 0.5384  | 0.0327                | 0.004     | 1.52E-16      |         | rs2615377  | T/C        |
| 89 | rs552491    | A/G     | 0.6375  | -0.0294               | 0.004     | 1.11E-13      |         | rs4571809  | T/G        |
| 90 | rs1601615   | T/C     | 0.3964  | -0.028                | 0.0039     | 7.57E-13      |         | rs9286380  | T/C        |
| 91 | rs7849973   | C/G     | 0.6547  | 0.024                 | 0.004     | 2.82E-09      |         | rs9286380  | T/C        |
| 92 | rs1329767   | A/C     | 0.3487  | -0.0292               | 0.004     | 2.43E-13      |         | rs13286861 | C/T        |
| 93 | rs1571536   | T/C     | 0.4852  | 0.0331                | 0.0038     | 2.19E-18      |         | rs7040225  | C/T        |
| 94 | rs9330454   | A/G     | 0.4299  | -0.0307               | 0.0042     | 1.44E-13      |         | rs11599257 | G/A        |
| 95 | rs10156597  | A/T     | 0.6774  | 0.1024                | 0.0041     | 5.04E-13      |         | rs11599257 | G/A        |
| 96 | rs7852169   | C/G     | 0.9117  | -0.0973               | 0.0068     | 1.82E-46      |         | rs7040225  | C/T        |
| 97 | rs2780243   | T/C     | 0.5646  | -0.0234               | 0.0039     | 2.31E-09      |         | rs10751883 | C/T        |
| 98 | rs7912468   | T/C     | 0.5775  | -0.0239               | 0.0039     | 1.20E-09      |         | rs11599257 | G/A        |
| 99 | rs10906395  | T/C     | 0.6109  | -0.0233               | 0.0039     | 2.28E-09      |         | rs11599257 | G/A        |
|100 | rs61846901  | T/C     | 0.3113  | -0.0257               | 0.0042     | 1.21E-09      |         | rs11599257 | G/A        |
|101 | rs6415872   | A/G     | 0.4931  | 0.0236                | 0.0039     | 1.52E-09      |         | rs11599257 | G/A        |
|102 | rs4746113   | A/G     | 0.3094  | -0.0244               | 0.0042     | 8.79E-09      |         | rs11599257 | G/A        |
|103 | rs77532868  | T/C     | 0.0446  | 0.0573                | 0.0097     | 3.31E-09      |         | rs11599257 | G/A        |
|104 | rs2066323   | A/G     | 0.6021  | -0.0237               | 0.0039     | 1.31E-09      |         | rs11599257 | G/A        |
|105 | rs10400136  | A/G     | 0.5627  | -0.0259               | 0.0039     | 2.73E-11      |         | rs1198754  | G/A        |
|106 | rs12571664  | T/C     | 0.7998  | 0.0367                | 0.0048     | 1.85E-14      |         | rs1199129  | A/G        |
|107 | rs7077302   | A/G     | 0.9852  | 0.0497                | 0.007     | 1.08E-12      |         | rs72839625 | A/C        |
|108 | rs4576738   | C/G     | 0.4455  | 0.0266                | 0.0043     | 7.20E-10      |         | rs7904728  | A/G        |

6
| #  | rsID         | Chromosome | Position | Reference Allele | Minor Allele | Minor Allele Frequency | Minor Allele Frequency |
|----|--------------|------------|----------|------------------|--------------|------------------------|------------------------|
| 109| rs3782120    | 11         | 206089   | A                | G            | 0.2583                 | 0.0334                 |
| 110| rs10832021   | 11         | 13324530 | A                | G            | 0.7095                 | 0.047                  |
| 111| rs4359170    | 11         | 16596152 | A/T              |              | 0.673                  | 0.0282                 |
| 112| rs11606190   | 11         | 28033473 | A                | G            | 0.1457                 | 0.041                  |
| 113| rs11031040   | 11         | 30317733 | T/G              |              | 0.8378                 | 0.0404                 |
| 114| rs1023955    | 11         | 43608835 | T/G              |              | 0.3976                 | 0.0279                 |
| 115| rs10897450   | 11         | 63593219 | C                | G            | 0.5304                 | 0.0229                 |
| 116| rs7115444    | 11         | 77555824 | T/C              |              | 0.2085                 | 0.0333                 |
| 117| rs4402316    | 11         | 84780098 | C/G              |              | 0.2407                 | 0.0313                 |
| 118| rs6950889    | 11         | 101438191| T/C              |              | 0.3404                 | 0.0437                 |
| 119| rs7114175    | 11         | 122813983| A/T              |              | 0.4963                 | 0.0599                 |
| 120| rs7132908    | 12         | 50263148 | A                | G            | 0.3883                 | 0.0424                 |
| 121| rs1148006    | 12         | 75978358 | A/G              |              | 0.2442                 | 0.0259                 |
| 122| rs7979001    | 12         | 97506357 | A/G              |              | 0.5078                 | 0.0219                 |
| 123| rs660549     | 12         | 121300988| T/C              |              | 0.5671                 | 0.0212                 |
| 124| rs9548873    | 13         | 40238492 | T/C              |              | 0.663                  | 0.0311                 |
| 125| rs9568123    | 13         | 49475780 | A/G              |              | 0.8478                 | 0.0291                 |
| 126| rs1925047    | 13         | 74600274 | A/C              |              | 0.3213                 | 0.0341                 |
| 127| rs11619721   | 13         | 112082513| T/G              |              | 0.0836                 | 0.0413                 |
| 128| rs9522262    | 13         | 112186283| C/G              |              | 0.4915                 | 0.0411                 |
| 129| rs10136330   | 14         | 30514335 | T/C              |              | 0.0426                 | 0.0579                 |
| 130| rs10138913   | 14         | 60943106 | T/C              |              | 0.3062                 | 0.056                  |
| 131| rs941520     | 14         | 99709702 | A/C              |              | 0.4936                 | 0.0223                 |
| 132| rs12894936   | 14         | 100846991| T/C              |              | 0.2936                 | 0.0522                 |
| 133| rs4924538    | 15         | 41494364 | A/T              |              | 0.5129                 | 0.0255                 |
| 134| rs1435753    | 15         | 47925066 | T/C              |              | 0.6467                 | 0.0278                 |
| 135| rs3743266    | 15         | 60781513 | T/C              |              | 0.668                  | 0.0416                 |
| 136| rs72756954   | 15         | 64537300 | C/G              |              | 0.938                  | 0.0577                 |
| SNP       | Chr | Position   | Allele | Effect Allele Frequency | Standard Error | p Value   |
|-----------|-----|------------|--------|-------------------------|----------------|-----------|
| rs5742915 | 15  | 74336633   | T/C    | 0.5463                  | -0.0234        | 1.02E-09  |
| rs1971554 | 15  | 83406228   | T/C    | 0.2654                  | 0.032          | 2.35E-13  |
| rs12915845| 15  | 89042467   | T/C    | 0.4244                  | -0.0403        | 3.70E-25  |
| rs153793  | 16  | 15542199   | A/G    | 0.5198                  | -0.0234        | 9.27E-10  |
| rs112991346| 16  | 19967668   | T/C    | 0.8575                  | -0.0446        | 6.47E-16  |
| rs143461173| 16  | 52283158   | A/G    | 0.8063                  | 0.0288         | 6.10E-09  |
| rs9972653 | 16  | 53814363   | T/G    | 0.4002                  | -0.0509        | 6.47E-40  |
| rs7359336 | 16  | 69733460   | A/G    | 0.5789                  | -0.0534        | 5.33E-44  |
| rs142643995| 17  | 2017993    | T/C    | 0.0302                  | 0.0646         | 3.25E-08  |
| rs12603280 | 17  | 6034754    | A/G    | 0.244                   | -0.037         | 2.66E-16  |
| rs5560968 | 17  | 7774047    | A/G    | 0.9282                  | -0.0455        | 1.17E-09  |
| rs9635759 | 17  | 49613785   | A/G    | 0.3067                  | 0.059          | 2.78E-46  |
| rs2787487 | 17  | 53209382   | C/G    | 0.6037                  | 0.0311         | 1.62E-15  |
| rs66508321| 17  | 78739672   | A/G    | 0.3235                  | -0.0303        | 2.84E-13  |
| rs8087304 | 18  | 31765736   | A/T    | 0.4823                  | 0.0222         | 6.54E-09  |
| rs1512238 | 18  | 44748467   | A/G    | 0.4207                  | -0.0537        | 2.48E-44  |
| rs484353  | 19  | 7891767    | A/G    | 0.5389                  | 0.0316         | 8.28E-16  |
| rs4804117 | 19  | 9984509    | T/G    | 0.5568                  | 0.0455         | 3.58E-31  |
| rs4804025 | 19  | 47609223   | A/G    | 0.7038                  | -0.0409        | 3.11E-22  |
| rs2548458 | 19  | 49209325   | T/C    | 0.5061                  | 0.0212         | 3.53E-08  |
| rs852061  | 20  | 17109159   | A/C    | 0.3645                  | -0.0365        | 1.58E-20  |
| rs1535252 | 20  | 19682834   | T/C    | 0.4547                  | -0.0252        | 4.82E-11  |
| rs2295094 | 20  | 33447915   | A/G    | 0.1585                  | 0.0364         | 5.86E-12  |
| rs36093651| 20  | 37287102   | T/C    | 0.2378                  | 0.0371         | 6.51E-16  |
| rs3746619 | 20  | 54823805   | A/C    | 0.0862                  | 0.0475         | 5.52E-12  |
| rs151680  | 22  | 22273242   | T/C    | 0.524                   | 0.028          | 2.52E-13  |
| rs9614460 | 22  | 45745229   | T/G    | 0.6779                  | -0.0249        | 1.38E-09  |

SNP, single nucleotide polymorphism; Chr, chromosome; EA, effect allele; OA, other allele; EAF, effect allele frequency; SE, standard error.
| NO. | SNP       | CHR | POSITION (B37) | EA/OA | EAF  | BETA | SE  | P-VALUE   | PROXY SNP | PROXY EA/OA | R²   | PROXY EAF |
|-----|-----------|-----|----------------|-------|------|------|-----|-----------|-----------|-------------|------|-----------|
| 1   | rs9438982 | 1   | 39358143       | C/A   | 0.3219 | 0.214 | 0.013 | 6.40E-62 | rs9438979 | G/T         | 0.9955 | 0.328     |
| 2   | rs12046563| 1   | 43137280       | A/G   | 0.7609 | 0.1   | 0.014 | 1.70E-12 |           |             |      |           |
| 3   | rs12133213| 1   | 110191395      | G/A   | 0.4657 | 0.08  | 0.013 | 5.30E-10 | rs542338  | A/G         | 0.9521 | 0.4105    |
| 4   | rs72708144| 1   | 149815740      | C/T   | 0.0404 | 0.282 | 0.032 | 1.10E-18 | rs41265172| T/C         | 0.8968 | 0.0378    |
| 5   | rs2736609 | 1   | 156202640      | T/C   | 0.3592 | 0.079 | 0.013 | 3.00E-10 |           |             |      |           |
| 6   | rs11582336| 1   | 178230945      | A/G   | 0.7951 | 0.106 | 0.015 | 2.00E-12 |           |             |      |           |
| 7   | rs1044595 | 1   | 180943529      | T/C   | 0.5979 | 0.132 | 0.012 | 1.30E-26 | rs12754041| G/T         | 0.9639 | 0.5686    |
| 8   | rs7515939 | 1   | 225623627      | A/T   | 0.3336 | 0.103 | 0.013 | 8.40E-16 | rs6702538  | A/C         | 1     | 0.3588    |
| 9   | rs7414807 | 1   | 231476874      | A/G   | 0.6326 | 0.088 | 0.013 | 4.00E-12 |           |             |      |           |
| 10  | rs7539755 | 1   | 244598815      | C/T   | 0.5766 | 0.101 | 0.012 | 1.40E-16 | rs6684936  | T/C         | 0.9919 | 0.5646    |
| 11  | rs7779   | 1   | 246930564      | C/G   | 0.0733 | 0.148 | 0.024 | 3.90E-10 | rs72764632| T/C         | 0.984  | 0.0656    |
| 12  | rs780088 | 2   | 27716004      | T/C   | 0.606  | 0.2   | 0.012 | 1.20E-58 |           |             |      |           |
| 13  | rs12053063| 2   | 28350611       | G/A   | 0.7212 | 0.103 | 0.014 | 2.40E-14 | rs1948922  | A/G         | 0.964  | 0.7147    |
| 14  | rs17425341| 2   | 44324287       | T/G   | 0.6567 | 0.085 | 0.013 | 2.30E-11 |           |             |      |           |
| 15  | rs76982781| 2   | 48005821       | G/A   | 0.1896 | 0.198 | 0.016 | 2.10E-37 |           |             |      |           |
| 16  | rs62156756| 2   | 67671015       | A/G   | 0.8963 | 0.263 | 0.02  | 2.20E-40 |           |             |      |           |
| 17  | rs4852777 | 2   | 71534161       | G/C   | 0.404  | 0.074 | 0.012 | 2.10E-09 | rs4852778 | G/A         | 0.926  | 0.4443    |
| 18  | rs6772766 | 2   | 112007716      | G/A   | 0.5057 | 0.079 | 0.012 | 9.90E-11 |           |             |      |           |
| 19  | rs16830019| 2   | 152267359      | T/G   | 0.2626 | 0.118 | 0.014 | 2.10E-17 |           |             |      |           |
| 20  | rs4668354 | 2   | 171814750      | G/C   | 0.6262 | 0.187 | 0.012 | 5.50E-51 | rs6731774  | T/C         | 0.9957 | 0.6402    |
| 21  | rs72934556| 2   | 203990789      | G/T   | 0.1258 | 0.101 | 0.018 | 3.70E-08 |           |             |      |           |
| 22  | rs6736096 | 2   | 216958369      | C/T   | 0.5235 | 0.098 | 0.012 | 3.10E-16 |           |             |      |           |
| 23  | rs7558434 | 2   | 223705337      | T/G   | 0.4388 | 0.07  | 0.012 | 9.10E-09 |           |             |      |           |
| 24  | rs12636454| 3   | 12360214       | C/T   | 0.2451 | 0.092 | 0.014 | 6.90E-11 |           |             |      |           |
|   | rs62244773 | 3 | 30518433 | A/T | 0.6987 | 0.083 | 0.014 | 1.80E-09 | rs62244772 | T/C | 0.8484 | 0.6581 |
|---|------------|---|----------|-----|--------|-------|-------|---------|-----------|------|--------|-------|
| 26 | rs12487736 | 3 | 47459679 | C/T | 0.4205 | 0.078 | 0.012 | 3.50E-10 | rs6972461 | T/C | 0.936  | 0.3936 |
| 27 | rs9968117  | 3 | 52838654 | T/C | 0.1188 | 0.106 | 0.019 | 1.80E-08 |          |      |        |       |
| 28 | rs2885255  | 3 | 57722613 | C/G | 0.5976 | 0.071 | 0.012 | 8.60E-09 | rs7624585 | T/C | 1     | 0.6024 |
| 29 | rs7610102  | 3 | 101246803| G/A  | 0.6052 | 0.077 | 0.013 | 1.30E-09 | rs7634759 | C/A | 1     | 0.5915 |
| 30 | rs6793835  | 3 | 135819934| G/A  | 0.7383 | 0.141 | 0.014 | 1.80E-24 |          |      |        |       |
| 31 | rs10154963 | 3 | 150169559| C/T  | 0.2798 | 0.077 | 0.014 | 1.80E-08 |          |      |        |       |
| 32 | rs10804920 | 3 | 189438689| T/C  | 0.4389 | 0.084 | 0.012 | 6.00E-12 |          |      |        |       |
| 33 | rs13070791 | 3 | 193385275| T/C  | 0.433  | 0.074 | 0.012 | 1.40E-09 |          |      |        |       |
| 34 | rs2052160  | 4 | 13576578 | C/G  | 0.8928 | 0.168 | 0.02  | 1.90E-17 | rs7661090 | C/T | 0.9905 | 0.8817 |
| 35 | rs6824237  | 4 | 38071911 | T/C  | 0.7506 | 0.077 | 0.014 | 3.50E-08 |          |      |        |       |
| 36 | rs76540949 | 4 | 48527209 | T/C  | 0.5221 | 0.141 | 0.012 | 9.60E-31 | rs12512637| A/G | 0.8693 | 0.4811 |
| 37 | rs12651246 | 4 | 84367605 | A/G  | 0.4875 | 0.261 | 0.012 | 2.20E-103|          |     |        |       |
| 38 | rs6810489  | 4 | 99877445 | T/G  | 0.5958 | 0.09  | 0.012 | 4.40E-13 |          |      |        |       |
| 39 | rs9990489  | 4 | 188916240| C/T  | 0.5899 | 0.098 | 0.013 | 8.50E-15 |          |      |        |       |
| 40 | rs274701   | 5 | 6728707  | C/A  | 0.5921 | 0.144 | 0.012 | 3.20E-31 |          |      |        |       |
| 41 | rs62356073 | 5 | 36241922 | G/A  | 0.4264 | 0.07  | 0.012 | 1.60E-08 |          |      |        |       |
| 42 | rs17206591 | 5 | 51997134 | A/C  | 0.5634 | 0.074 | 0.012 | 1.40E-09 |          |      |        |       |
| 43 | rs7728833  | 5 | 82000737 | A/G  | 0.4997 | 0.079 | 0.012 | 5.10E-11 |          |      |        |       |
| 44 | rs10070308 | 5 | 107281621| C/T  | 0.844  | 0.099 | 0.017 | 2.80E-09 |          |      |        |       |
| 45 | rs10477172 | 5 | 141682090| T/C  | 0.4883 | 0.092 | 0.012 | 2.80E-14 |          |      |        |       |
| 46 | rs888694   | 5 | 154307485| A/C  | 0.0862 | 0.16  | 0.022 | 1.30E-13 | rs2688187 | G/A | 0.99   | 0.1123 |
| 47 | rs353478   | 5 | 176370988| C/T  | 0.4855 | 0.318 | 0.012 | 4.20E-154|          |      |        |       |
| 48 | rs9348724  | 6 | 10887276 | C/G  | 0.1724 | 0.306 | 0.016 | 6.90E-80 | rs9379896 | C/T | 0.9037 | 0.1849 |
| 49 | rs113967617| 6 | 111663858| A/G  | 0.1544 | 0.122 | 0.017 | 5.70E-13 |          |      |        |       |
| 50 | rs6569648  | 6 | 130349119| C/T  | 0.2358 | 0.123 | 0.014 | 6.90E-18 |          |      |        |       |
| 51 | rs11767307 | 7 | 23584496 | C/G  | 0.7697 | 0.084 | 0.014 | 4.90E-09 | rs7799435 | C/T | 1     | 0.7773 |
| 52 | rs10255049 | 7 | 56121304 | G/A  | 0.3121 | 0.14  | 0.013 | 1.00E-26 |          |      |        |       |
|   |    |   |   |   |   |   |   |   |   |
|---|----|----|----|----|----|----|----|----|----|
| 53 | rs2056726 | 7 | 99780283 | G/A | 0.7803 | 0.107 | 0.015 | 3.40E-13 |
| 54 | rs2392836 | 7 | 105973193 | G/A | 0.3726 | 0.115 | 0.013 | 4.00E-20 |
| 55 | rs4731541 | 7 | 12867236 | C/G | 0.3733 | 0.099 | 0.013 | 2.40E-15 |
| 56 | rs2013 | 7 | 158523888 | C/T | 0.1659 | 0.091 | 0.017 | 4.90E-08 |
| 57 | rs3735828 | 8 | 61592425 | G/A | 0.3594 | 0.115 | 0.013 | 4.80E-19 |
| 58 | rs1467044 | 8 | 120887041 | G/A | 0.4597 | 0.07 | 0.012 | 9.70E-09 |
| 59 | rs6470583 | 7 | 129018915 | A/T | 0.7837 | 0.094 | 0.015 | 1.30E-10 |
| 60 | rs1476164 | 8 | 129620616 | A/T | 0.7837 | 0.094 | 0.015 | 1.30E-10 |
| 61 | rs4879656 | 9 | 13208912 | G/A | 0.9436 | 0.216 | 0.027 | 1.20E-15 |
| 62 | rs10818873 | 9 | 126599993 | A/G | 0.9576 | 0.289 | 0.031 | 3.20E-21 |
| 63 | rs7087644 | 10 | 97826334 | A/G | 0.9576 | 0.289 | 0.031 | 3.20E-21 |
| 64 | rs7091889 | 10 | 104793723 | G/A | 0.214 | 0.121 | 0.015 | 2.80E-16 |
| 65 | rs7298823 | 10 | 9475372 | A/G | 0.4285 | 0.069 | 0.012 | 2.20E-08 |
| 66 | rs11031006 | 11 | 30226528 | A/G | 0.146 | 0.201 | 0.017 | 1.50E-31 |
| 67 | rs10899493 | 11 | 78117534 | C/T | 0.1664 | 0.12 | 0.016 | 1.90E-13 |
| 68 | rs7308068 | 12 | 6669706 | C/T | 0.4705 | 0.119 | 0.012 | 2.90E-22 |
| 69 | rs12825762 | 12 | 122983973 | G/A | 0.4495 | 0.09 | 0.012 | 1.90E-13 |
| 70 | rs35067339 | 12 | 123760109 | G/T | 0.7961 | 0.178 | 0.015 | 7.40E-32 |
| 71 | rs7318091 | 13 | 31203339 | C/T | 0.5954 | 0.068 | 0.012 | 4.10E-08 |
| 72 | rs3736830 | 13 | 50306221 | C/G | 0.8453 | 0.116 | 0.017 | 4.00E-12 |
| 73 | rs3722160 | 13 | 61061456 | C/T | 0.3325 | 0.186 | 0.013 | 7.20E-48 |
| 74 | rs12879626 | 14 | 34721134 | T/G | 0.3876 | 0.093 | 0.013 | 1.00E-13 |
|   | rs61488898 | 14 | 35086437 | C/T | 0.9738 | 0.356 | 0.04 | 2.70E-19 |
|---|-----------|----|-----------|-----|--------|-------|-------|---------|
| 82 | rs1969713 | 14 | 45623460 | C/T | 0.1044 | 0.168 | 0.02 | 5.30E-17 |
| 83 | rs762643  | 14 | 54422767 | G/T | 0.5561 | 0.076 | 0.012 | 6.20E-10 |
| 84 | rs1986616 | 14 | 73540936 | G/A | 0.4773 | 0.08  | 0.012 | 4.30E-11 |
| 85 | rs9796    | 15 | 41271447 | A/T | 0.5351 | 0.181 | 0.017 | 1.90E-19 |
| 86 | rs11071756| 16 | 63831636 | C/G | 0.8603 | 0.12  | 0.017 | 4.90E-12 |
| 87 | rs716886  | 15 | 83715853 | A/G | 0.3294 | 0.084 | 0.013 | 7.10E-11 |
| 88 | rs12898357| 15 | 89801391 | A/G | 0.6145 | 0.183 | 0.013 | 1.50E-48 |
| 89 | rs9673473 | 16 | 12011212 | C/G | 0.4029 | 0.212 | 0.012 | 3.40E-66 |
| 90 | rs11075466| 16 | 52375540 | G/A | 0.1764 | 0.095 | 0.016 | 4.10E-09 |
| 91 | rs8045027 | 16 | 79388209 | G/A | 0.4644 | 0.073 | 0.012 | 2.50E-09 |
| 92 | rs200293726| 16 | 79754440 | T/A | 0.3098 | 0.106 | 0.016 | 1.60E-11 |
| 93 | rs2108839 | 16 | 89860182 | T/G | 0.6903 | 0.136 | 0.013 | 6.90E-25 |
| 94 | rs34856659| 17 | 5327572 | C/T | 0.2431 | 0.168 | 0.014 | 7.80E-33 |
| 95 | rs111637825| 17 | 40134782 | G/A | 0.9357 | 0.139 | 0.025 | 1.90E-08 |
| 96 | rs1815198 | 17 | 55360585 | A/G | 0.3564 | 0.09  | 0.013 | 1.30E-12 |
| 97 | rs34609096 | 17 | 7123680 | A/G | 0.4696 | 0.068 | 0.012 | 2.30E-08 |
| 98 | rs12605881 | 18 | 60941441 | T/A | 0.4055 | 0.07  | 0.012 | 2.00E-08 |
| 99 | rs11670032 | 19 | 23166913 | T/C | 0.8557 | 0.182 | 0.017 | 1.60E-25 |
| 100| rs424223  | 19 | 23485893 | T/G | 0.2633 | 0.1   | 0.014 | 4.60E-13 |
| 101| rs7249357 | 19 | 33465388 | G/A | 0.811  | 0.136 | 0.016 | 1.40E-18 |
| 102| rs11668344 | 19 | 55833664 | A/G | 0.6403 | 0.447 | 0.013 | 1.00E-20 |
| 103| rs236117  | 20 | 5937175 | G/T | 0.8899 | 0.225 | 0.019 | 1.00E-31 |
| 104| rs58065489 | 20 | 32052912 | C/G | 0.8292 | 0.098 | 0.016 | 1.90E-09 |
| 105| rs11699793 | 20 | 34271574 | C/T | 0.8972 | 0.123 | 0.02  | 7.00E-10 |
| 106| rs483508  | 20 | 48499609 | T/C | 0.3847 | 0.117 | 0.013 | 6.80E-21 |
| 107| rs7266248 | 20 | 55183547 | G/A | 0.1986 | 0.115 | 0.015 | 3.60E-14 |
| 108| rs10854167 | 20 | 61533039 | G/C | 0.7893 | 0.175 | 0.015 | 1.40E-32 |

12
| SNP ID | Chromosome | Position | Allele | Effect Allele Frequency | Other Allele Frequency | P-Value |
|--------|------------|----------|--------|-------------------------|------------------------|---------|
| rs9975728 | 21         | 40662749 | T/G    | 0.8711                  | 0.104                  | 0.018   | 7.50E-09 |
| rs5754100 | 22         | 21916166 | C/T    | 0.1906                  | 0.097                  | 0.016   | 1.90E-09 |
| rs5762852 | 22         | 29242473 | C/T    | 0.1545                  | 0.131                  | 0.017   | 5.80E-15 |
| rs2272805 | 22         | 45809698 | G/A    | 0.8545                  | 0.108                  | 0.017   | 4.30E-10 |

SNP, single nucleotide polymorphism; Chr, chromosome; EA, effect allele; OA, other allele; EAF, effect allele frequency; SE, standard error.
Table S3. SNPs and proxies used for SHBG in men

| NO. | SNP        | CHR | POSITION (B37) | EA/OA | EAF | BETA  | SE   | P-VALUE | PROXY SNP | PROXY EA/OA | R^2 | PROXY EAF |
|-----|------------|-----|----------------|-------|-----|-------|------|---------|-----------|-------------|-----|----------|
| 1   | rs36086195 | 1   | 16510894       | T/C   | 0.579 | 0.017 | 0.001 | 2.3E-52 | rs6656611 | C/T         | 0.8302 | 0.5835   |
| 2   | rs59708846 | 1   | 61687651       | A/G   | 0.076 | 0.019 | 0.002 | 1.3E-20 | rs17311684 | G/A         | 0.8409 | 0.0686   |
| 3   | rs1730865  | 1   | 10760561       | G/T   | 0.345 | 0.028 | 0.001 | 8.0E-127| rs3108680 | C/T         | 0.9513 | 0.331    |
| 4   | rs12059956 | 1   | 17106326       | G/A   | 0.583 | 0.007 | 0.001 | 3.4E-10 |           |             |       |          |
| 5   | rs17583875 | 1   | 19792477       | A/G   | 0.021 | 0.023 | 0.004 | 1.1E-09 | rs115328872| A/G         | 1    | 0.0219   |
| 6   | rs10864086 | 1   | 21431874       | C/A   | 0.256 | 0.015 | 0.001 | 2.9E-32 |           |             |       |          |
| 7   | rs2820441  | 1   | 21973496       | C/A   | 0.318 | 0.009 | 0.001 | 2.7E-13 |           |             |       |          |
| 8   | rs2247213  | 1   | 22105546       | G/A   | 0.670 | 0.015 | 0.001 | 1.3E-36 |           |             |       |          |
| 9   | rs1870927  | 1   | 22642633       | A/T   | 0.620 | 0.007 | 0.001 | 2.3E-08 | rs6605032 | T/C         | 0.8303 | 0.6799   |
| 10  | rs144647926| 1   | 23546760       | A/G   | 0.087 | 0.013 | 0.002 | 1.3E-10 |           |             |       |          |
| 11  | rs1260326  | 2   | 27730940       | C/T   | 0.606 | 0.041 | 0.001 | 1.3E-298|           |             |       |          |
| 12  | rs17050272 | 2   | 12130644       | A/G   | 0.410 | 0.007 | 0.001 | 1.4E-10 | rs6706968 | A/C         | 0.9796 | 0.4592   |
| 13  | rs13389219 | 2   | 16552887       | T/C   | 0.394 | 0.012 | 0.001 | 2.3E-26 |           |             |       |          |
| 14  | rs72948115 | 2   | 17816708       | C/T   | 0.905 | 0.012 | 0.002 | 2.2E-10 |           |             |       |          |
| 15  | rs8176526  | 2   | 18834532       | C/T   | 0.730 | 0.008 | 0.001 | 1.6E-10 |           |             |       |          |
| 16  | rs4675682  | 2   | 20840275       | T/C   | 0.540 | 0.009 | 0.001 | 9.2E-16 |           |             |       |          |
| 17  | rs62182125 | 2   | 21927414       | G/A   | 0.449 | 0.008 | 0.001 | 1.2E-12 | rs2303561 | T/C         | 0.855  | 0.4066   |
| 18  | rs12694450 | 2   | 22001963       | T/C   | 0.325 | 0.007 | 0.001 | 3.0E-10 | rs6725951 | T/C         | 0.9957 | 0.3579   |
| 19  | rs222018   | 2   | 22709522       | C/A   | 0.352 | 0.014 | 0.001 | 5.1E-31 |           |             |       |          |
| 20  | rs10153880 | 2   | 24217934       | A/G   | 0.230 | 0.007 | 0.001 | 2.9E-08 |           |             |       |          |
| 21  | rs17036326 | 3   | 12389313       | G/A   | 0.122 | 0.019 | 0.002 | 1.2E-26 |           |             |       |          |
| 22  | rs2564923  | 3   | 53103262       | A/G   | 0.443 | 0.006 | 0.001 | 8.1E-11 |           |             |       |          |
| 23  | rs13315174 | 3   | 10540646       | G/A   | 0.784 | 0.008 | 0.001 | 1.5E-10 | rs4627779 | G/A         | 0.893  | 0.7624   |
| 24  | rs687339   | 3   | 13593235       | C/T   | 0.228 | 0.025 | 0.001 | 5.3E-08 | rs6779146 | C/T         | 0.9454 | 0.2356   |
| 25  | rs234051   | 3   | 17231171       | A/G   | 0.284 | 0.009 | 0.001 | 1.8E-15 |           |             |       |          |
|   | rs    |   |                  |   |               |   |   |   |    |               |   |   |   |    |   |   |    |
|---|-------|---|-----------------|---|-------------|---|---|---|---|---------------|---|---|---|---|---|---|---|
| 26| rs7631981 | 3 | 185273510        | G/A | 0.697 | 0.008 | 0.001 | 6.5E-13 |
| 27| rs11734408 | 4 | 23882519         | G/A | 0.293 | 0.008 | 0.001 | 2.1E-13 |
| 28| rs28507491 | 4 | 77197651         | A/G | 0.376 | 0.014 | 0.001 | 2.0E-31 |
| 29| rs7694379  | 4 | 88186509         | G/A | 0.567 | 0.020 | 0.001 | 5.5E-71 |
| 30| rs6831352  | 4 | 100063525        | T/C | 0.302 | 0.020 | 0.001 | 2.9E-58 |
| 31| rs7665064  | 4 | 120106348        | T/C | 0.875 | 0.008 | 0.002 | 4.0E-08 |
| 32| rs10027275 | 4 | 148981496        | G/C | 0.259 | 0.013 | 0.001 | 3.9E-26 |
| 33| rs72729610 | 4 | 154190965        | A/G | 0.834 | 0.009 | 0.002 | 9.1E-11 |
| 34| rs11732763 | 4 | 171010101        | A/G | 0.106 | 0.011 | 0.002 | 1.9E-10 |
| 35| rs7735249  | 5 | 53310139         | C/G | 0.887 | 0.020 | 0.002 | 4.9E-31 |
| 36| rs40270    | 5 | 55804552         | A/C | 0.228 | 0.014 | 0.001 | 4.0E-26 |
| 37| rs11739158 | 5 | 72927292         | T/C | 0.428 | 0.008 | 0.001 | 1.7E-13 |
| 38| rs6595447  | 5 | 122750847        | T/C | 0.807 | 0.010 | 0.001 | 1.2E-12 |
| 39| rs329122   | 5 | 133864599        | G/A | 0.581 | 0.008 | 0.001 | 1.5E-14 |
| 40| rs11743810 | 5 | 137802404        | T/C | 0.560 | 0.008 | 0.001 | 3.6E-11 |
| 41| rs2431752  | 5 | 162882702        | A/G | 0.106 | 0.011 | 0.002 | 7.5E-10 |
| 42| rs55646464 | 5 | 173324971        | G/T | 0.700 | 0.009 | 0.001 | 1.3E-11 |
| 43| rs17185536 | 6 | 100620931        | T/C | 0.244 | 0.007 | 0.001 | 3.2E-09 |
| 44| rs1890426  | 6 | 116338065        | C/T | 0.401 | 0.007 | 0.001 | 1.8E-09 |
| 45| rs6900473  | 6 | 130375810        | A/G | 0.312 | 0.010 | 0.001 | 4.8E-16 |
| 46| rs501470   | 6 | 160770918        | G/T | 0.475 | 0.017 | 0.001 | 3.4E-55 |
| 47| rs2106727  | 7 | 17287998        | G/A | 0.637 | 0.006 | 0.001 | 2.8E-08 |
| 48| rs860262   | 7 | 28194397        | A/C | 0.502 | 0.011 | 0.001 | 3.1E-23 |
| 49| rs6965401  | 7 | 46269012        | G/A | 0.936 | 0.015 | 0.002 | 9.0E-10 |
| 50| rs12536766 | 7 | 70158864        | T/G | 0.570 | 0.007 | 0.001 | 5.9E-09 |
| 51| rs17145750 | 7 | 73026378        | T/C | 0.161 | 0.013 | 0.002 | 1.4E-16 |
| 52| rs1229492  | 7 | 81564122        | T/C | 0.268 | 0.011 | 0.001 | 1.2E-18 |
| 53| rs445      | 7 | 92408370        | C/T | 0.905 | 0.013 | 0.002 | 7.9E-12 |
|   | rs   | Chromosome | Position (bp) | Minor Allele | Minor Allele Frequency | Major Allele Frequency | Minor Allele Frequency of Reference Allele | Major Allele Frequency of Reference Allele | P-value | Minor Allele Frequency of Reference Allele | Major Allele Frequency of Reference Allele |
|---|------|------------|---------------|--------------|-----------------------|-----------------------|------------------------------------------|------------------------------------------|---------|------------------------------------------|------------------------------------------|
| 54 | rs6950023 | 7 | 97915635 | G/T | 0.814 | 0.030 | 0.001 | 2.1E-101 | rs112758337 | G/A | 0.9417 | 0.8181 |
| 55 | rs187437 | 7 | 116445091 | G/A | 0.547 | 0.009 | 0.001 | 3.2E-17 |
| 56 | rs157935 | 7 | 130585553 | G/T | 0.304 | 0.012 | 0.001 | 5.0E-27 |
| 57 | rs3812275 | 7 | 135064882 | C/A | 0.403 | 0.007 | 0.001 | 9.6E-09 |
| 58 | rs114949263 | 7 | 150498245 | C/T | 0.111 | 0.017 | 0.002 | 9.1E-23 |
| 59 | rs12543287 | 8 | 42334511 | C/G | 0.371 | 0.010 | 0.001 | 2.9E-21 | rs10808961 | A/G | 0.8247 | 0.337 |
| 60 | rs10107182 | 8 | 59392737 | T/C | 0.663 | 0.013 | 0.001 | 1.1E-27 |
| 61 | rs75349541 | 8 | 71152803 | C/T | 0.867 | 0.009 | 0.002 | 2.0E-08 |
| 62 | rs11994858 | 8 | 81273210 | G/A | 0.654 | 0.011 | 0.001 | 4.4E-23 |
| 63 | rs10116426 | 9 | 4145648 | C/A | 0.432 | 0.008 | 0.001 | 9.2E-13 |
| 64 | rs820503 | 9 | 6667928 | C/A | 0.863 | 0.011 | 0.002 | 2.9E-11 |
| 65 | rs35234337 | 9 | 35661243 | C/T | 0.743 | 0.007 | 0.001 | 4.5E-08 |
| 66 | rs10868080 | 9 | 86626769 | T/A | 0.256 | 0.021 | 0.001 | 9.5E-63 | rs296893 | T/C | 1 | 0.2783 |
| 67 | rs56237852 | 9 | 100343212 | C/A | 0.826 | 0.008 | 0.002 | 1.0E-08 |
| 68 | rs62580766 | 9 | 113034490 | T/C | 0.182 | 0.010 | 0.002 | 1.6E-11 |
| 69 | rs79717793 | 10 | 5262267 | G/A | 0.845 | 0.023 | 0.002 | 4.8E-58 |
| 70 | rs3781085 | 10 | 13370958 | T/G | 0.585 | 0.006 | 0.001 | 3.6E-09 |
| 71 | rs3006593 | 10 | 31171626 | C/G | 0.380 | 0.007 | 0.001 | 2.7E-09 | rs3006594 | C/T | 0.9874 | 0.3777 |
| 72 | rs34390319 | 10 | 63960611 | C/T | 0.100 | 0.015 | 0.002 | 2.2E-13 |
| 73 | rs10822153 | 10 | 65056813 | A/C | 0.472 | 0.063 | 0.001 | 3.9E-714 |
| 74 | rs2259305 | 10 | 93615903 | G/A | 0.523 | 0.012 | 0.001 | 8.3E-28 |
| 75 | rs856534 | 10 | 94810665 | A/G | 0.387 | 0.011 | 0.001 | 1.3E-22 |
| 76 | rs7096937 | 10 | 113950418 | T/C | 0.269 | 0.009 | 0.001 | 1.4E-12 | rs2255141 | A/G | 0.9585 | 0.3091 |
| 77 | rs1037169 | 11 | 13361005 | T/C | 0.313 | 0.010 | 0.001 | 4.0E-16 |
| 78 | rs12797706 | 11 | 65561369 | A/G | 0.235 | 0.013 | 0.001 | 1.4E-22 |
| 79 | rs631695 | 11 | 69283303 | T/G | 0.418 | 0.018 | 0.001 | 2.0E-61 |
| 80 | rs10895277 | 11 | 102084940 | A/G | 0.659 | 0.010 | 0.001 | 1.3E-17 |
| 81 | rs2156805 | 11 | 122610568 | G/A | 0.508 | 0.006 | 0.001 | 4.4E-08 |
|   | rs1871395 | 12 | 21352315 | A/G | 0.848 | 0.032 | 0.002 | 2.7E-100 |
|---|-----------|----|----------|-----|-------|-------|-------|----------|
| 83| rs75130744 | 12 | 25410741 | G/C | 0.928 | 0.029 | 0.002 | 3.0E-44  |
|   | rs12818938 | 12 | 53783182 | T/G | 0.832 | 0.008 | 0.002 | 1.1E-08  |
| 85| rs540730 | 12 | 57807114 | T/C | 0.246 | 0.018 | 0.001 | 1.9E-48  |
|   | rs11111274 | 12 | 102838128 | G/A | 0.263 | 0.008 | 0.001 | 1.3E-10  |
| 87| rs9738226 | 12 | 121423659 | G/A | 0.623 | 0.019 | 0.001 | 7.8E-61  |
| 88| rs11621792 | 14 | 24871926 | C/T | 0.546 | 0.013 | 0.001 | 2.0E-28  |
|   | rs2239222 | 14 | 73011885 | G/A | 0.350 | 0.012 | 0.001 | 8.8E-20  |
| 90| rs13379043 | 14 | 74250126 | C/T | 0.280 | 0.008 | 0.001 | 2.9E-11  |
|   | rs28929474 | 14 | 94844947 | T/C | 0.020 | 0.133 | 0.004 | 1.2E-252 |
| 92| rs3742366 | 14 | 104198351 | C/T | 0.346 | 0.009 | 0.001 | 3.6E-17  |
| 93| rs7175361 | 15 | 41048058 | A/G | 0.158 | 0.009 | 0.002 | 3.4E-09  |
|   | rs139974673 | 15 | 44027885 | T/C | 0.975 | 0.078 | 0.004 | 4.6E-110 |
| 95| rs56187480 | 15 | 63789479 | G/A | 0.655 | 0.014 | 0.001 | 1.2E-33  |
|   | rs8038465 | 15 | 73978337 | T/C | 0.425 | 0.007 | 0.001 | 4.6E-10  |
| 97| rs72753908 | 15 | 8334856 | C/T | 0.925 | 0.013 | 0.002 | 1.9E-09  |
| 98| rs11856926 | 15 | 96223649 | G/A | 0.551 | 0.011 | 0.001 | 1.1E-24  |
| 99| rs56332871 | 15 | 96714816 | A/C | 0.272 | 0.031 | 0.001 | 6.0E-140 |
|   | rs12928099 | 16 | 15150505 | A/C | 0.295 | 0.009 | 0.001 | 7.2E-13  |
| 101| rs2288004 | 16 | 31054040 | G/C | 0.619 | 0.009 | 0.001 | 3.4E-16  |
|   | rs246192 | 16 | 58544295 | G/C | 0.480 | 0.008 | 0.001 | 9.8E-14  |
| 103| rs28650012 | 16 | 80497341 | G/C | 0.271 | 0.008 | 0.001 | 4.5E-11  |
|   | rs8066941 | 17 | 9588450 | T/G | 0.761 | 0.016 | 0.001 | 7.7E-33  |
| 105| rs2905801 | 17 | 29524974 | T/C | 0.705 | 0.013 | 0.001 | 1.2E-28  |
| 106| rs11655704 | 17 | 47448172 | C/T | 0.315 | 0.030 | 0.001 | 1.5E-147 |
| 107| rs7210574 | 17 | 73824121 | C/T | 0.329 | 0.010 | 0.001 | 2.3E-20  |
| 108| rs36013981 | 17 | 79493307 | A/G | 0.604 | 0.006 | 0.001 | 8.2E-11  |
| 109| rs10871794 | 18 | 59342210 | A/G | 0.697 | 0.007 | 0.001 | 6.0E-09  |
|   | SNP          | Chr | Position   | EA  | OA  | EAF  | SE  | p_value   |   | SNP          | Chr | Position   | EA  | OA  | EAF  | SE  | p_value   |
|---|--------------|-----|------------|-----|-----|------|-----|-----------|---|--------------|-----|------------|-----|-----|------|-----|-----------|
| 110| rs1788641    | 18  | 71949629   | A/G |     | 0.688| 0.008| 0.001    | 8.0E-12|   | rs941410    | A/G | 0.8807    |    | 0.3171  |
| 111| rs1640267    | 19  | 2789337    | C/T |     | 0.286| 0.017| 0.001    | 1.9E-45|   | rs11981233  | G/T | 0.079     | 0.025| 0.002    | 7.7E-36|
| 112| rs45512696   | 19  | 35550878   | T/C |     | 0.174| 0.021| 0.002    | 9.8E-47|
| 113| rs34255979   | 19  | 46384830   | T/C |     | 0.119| 0.028| 0.002    | 2.7E-63|
| 114| rs111981233  | 19  | 50016479   | G/T |     | 0.079| 0.025| 0.002    | 7.7E-36|
| 115| rs13042148   | 20  | 32298286   | C/T |     | 0.844| 0.013| 0.002    | 5.6E-20|
| 116| rs3795128    | 20  | 39774163   | C/T |     | 0.484| 0.010| 0.001    | 1.7E-23|
| 117| rs3746575    | 20  | 43058096   | G/C |     | 0.597| 0.017| 0.001    | 4.7E-49|   | rs3212198   | T/C | 0.8066    |    | 0.5606  |
| 118| rs6005840    | 22  | 29101357   | A/G |     | 0.327| 0.016| 0.001    | 1.5E-40|
| 119| rs738409     | 22  | 44324727   | G/C |     | 0.216| 0.029| 0.001    | 3.4E-98|   | rs2294915   | T/C | 0.8526    |    | 0.2525  |

SNP, single nucleotide polymorphism; Chr, chromosome; EA, effect allele; OA, other allele; EAF, effect allele frequency; SE, standard error.
Table S4. SNPs and proxies used for SHBG in women

| NO. | SNP     | CH R | POSITION (B37) | EA/OA | EAF  | BETA  | SE    | P-VALUE | PROXY SNP | PROXY EA/OA | R²  | PROXY EAF |
|-----|---------|------|----------------|-------|------|-------|-------|---------|-----------|-------------|-----|-----------|
| 1   | rs198358| 1    | 11904076       | C/T   | 0.248| 0.008| 0.001| 9.0E-11 | rs17311684 | G/A         | 1   | 0.002     |
| 2   | rs74090351 | 1 | 61705898       | A/G   | 0.069| 0.019| 0.002| 5.9E-18 | rs3108680 | C/T         | 0.9337| 0.331     |
| 3   | rs469721 | 1    | 91530001       | C/T   | 0.803| 0.011| 0.002| 5.4E-12 | rs198358  | C/T         | 0.9337| 0.331     |
| 4   | rs1730862 | 1 | 107614003      | G/A   | 0.342| 0.023| 0.001| 1.7E-73 | rs267733  | G/A         | 0.9337| 0.331     |
| 5   | rs267733 | 1    | 150958836      | A/G   | 0.839| 0.014| 0.002| 3.7E-21 | rs469721  | C/T         | 0.9337| 0.331     |
| 6   | rs9426829 | 1  | 154592201      | C/T   | 0.481| 0.014| 0.001| 1.5E-30 | rs267733  | G/A         | 0.9337| 0.331     |
| 7   | rs2064074 | 1  | 214323347      | G/C   | 0.164| 0.014| 0.002| 8.4E-19 | rs3001032 | G/A         | 0.9337| 0.331     |
| 8   | rs12138803 | 1 | 172348823      | C/T   | 0.731| 0.009| 0.001| 9.8E-10 | rs12138803| C/T         | 0.9337| 0.331     |
| 9   | rs34331968 | 1 | 196659753      | T/C   | 0.534| 0.011| 0.001| 7.8E-20 | rs12138803| C/T         | 0.9337| 0.331     |
| 10  | rs1418652 | 1  | 205646458      | C/T   | 0.386| 0.007| 0.001| 3.3E-08 | rs12138803| C/T         | 0.9337| 0.331     |
| 11  | rs1223796 | 1    | 214323347      | G/C   | 0.164| 0.014| 0.002| 8.4E-19 | rs12138803| C/T         | 0.9337| 0.331     |
| 12  | rs3001032 | 1    | 219727779      | C/T   | 0.320| 0.015| 0.001| 3.6E-29 | rs12138803| C/T         | 0.9337| 0.331     |
| 13  | rs61830291 | 1  | 221001142      | C/A   | 0.097| 0.012| 0.002| 1.7E-08 | rs12138803| C/T         | 0.9337| 0.331     |
| 14  | rs1870927 | 1    | 226426337      | A/T   | 0.622| 0.008| 0.001| 2.0E-11 | rs12138803| C/T         | 0.9337| 0.331     |
| 15  | rs1260326 | 2    | 27730940       | C/T   | 0.607| 0.035| 0.001| 1.7E-18 | rs12138803| C/T         | 0.9337| 0.331     |
| 16  | rs11690748 | 2  | 48584575       | C/G   | 0.623| 0.008| 0.001| 9.7E-11 | rs12138803| C/T         | 0.9337| 0.331     |
| 17  | rs921153  | 2    | 61563408       | A/G   | 0.159| 0.009| 0.002| 2.8E-10 | rs12138803| C/T         | 0.9337| 0.331     |
| 18  | rs13394092 | 2  | 85815954       | C/T   | 0.170| 0.008| 0.002| 1.4E-08 | rs12138803| C/T         | 0.9337| 0.331     |
| 19  | rs13018007 | 2  | 114971913      | G/A   | 0.082| 0.013| 0.002| 1.2E-08 | rs12138803| C/T         | 0.9337| 0.331     |
| 20  | rs1128249 | 2    | 165528624      | T/G   | 0.392| 0.022| 0.001| 1.3E-73 | rs12138803| C/T         | 0.9337| 0.331     |
| 21  | rs2364717 | 2    | 178101234      | T/C   | 0.538| 0.008| 0.001| 2.3E-12 | rs12138803| C/T         | 0.9337| 0.331     |
| 22  | rs1047891 | 2    | 211540507      | A/C   | 0.315| 0.018!| 0.001| 1.5E-44 | rs12138803| C/T         | 0.9337| 0.331     |
| 23  | rs10189479 | 2  | 219287276      | A/C   | 0.434| 0.009| 0.001| 4.8E-14 | rs12138803| C/T         | 0.9337| 0.331     |
| 24  | rs2176040 | 2    | 227092802      | A/G   | 0.354| 0.015| 0.001| 2.7E-36 | rs12138803| C/T         | 0.9337| 0.331     |
| 25  | rs1801282 | 3    | 12393125       | G/C   | 0.120| 0.024| 0.002| 8.9E-43 | rs12138803| C/T         | 0.9337| 0.331     |
| SNP          | MAF | rsID      | Effect | z-score | p-value | Effect  | p-value |
|--------------|-----|-----------|--------|---------|---------|---------|---------|
| rs10461018   | 3   | 46995242  | T/C    | 0.420   | 0.011   | 0.001   | 2.5E-19 |
| rs11130982   | 3   | 64728312  | T/G    | 0.293   | 0.009   | 0.001   | 3.8E-11 |
| rs4530527    | 3   | 86800085  | C/A    | 0.361   | 0.008   | 0.001   | 1.8E-09 |
| rs17202341   | 3   | 105452593 | G/A    | 0.348   | 0.007   | 0.001   | 1.3E-09 |
| rs11720108   | 3   | 123069058 | T/C    | 0.249   | 0.008   | 0.001   | 5.4E-11 |
| rs687339     | 3   | 135932359 | C/T    | 0.227   | 0.031   | 0.001   | 5.3E-104|
| rs9872754    | 3   | 138117985 | C/T    | 0.840   | 0.010   | 0.002   | 9.0E-11 |
| rs9834503    | 3   | 149994882 | A/C    | 0.540   | 0.008   | 0.001   | 1.9E-09 |
| rs1126161    | 3   | 172228827 | G/A    | 0.673   | 0.008   | 0.001   | 5.6E-09 |
| rs57158761   | 3   | 185371172 | A/G    | 0.564   | 0.010   | 0.001   | 9.3E-18 |
| rs34311866   | 4   | 951947    | T/C    | 0.824   | 0.011   | 0.002   | 6.1E-14 |
| rs925098     | 4   | 17919811  | G/A    | 0.265   | 0.009   | 0.001   | 2.8E-09 |
| rs2970871    | 4   | 23890582  | T/C    | 0.441   | 0.007   | 0.001   | 3.2E-08 |
| rs6531735    | 4   | 39686332  | G/A    | 0.492   | 0.006   | 0.001   | 1.3E-08 |
| rs28636815   | 4   | 77197397  | G/A    | 0.377   | 0.012   | 0.001   | 1.5E-21 |
| rs13150068   | 4   | 88203828  | A/G    | 0.564   | 0.017   | 0.001   | 6.2E-47 |
| rs6831257    | 4   | 100018260 | G/A    | 0.340   | 0.008   | 0.001   | 3.3E-11 |
| rs14333210   | 4   | 124766956 | C/A    | 0.245   | 0.010   | 0.001   | 2.9E-12 |
| rs10857228   | 4   | 148979700 | C/A    | 0.257   | 0.010   | 0.001   | 2.6E-13 |
| rs28712547   | 4   | 157646955 | G/A    | 0.321   | 0.010   | 0.001   | 2.9E-14 |
| rs11738093   | 5   | 53301425  | A/G    | 0.748   | 0.014   | 0.001   | 6.0E-24 |
| rs40270      | 5   | 55804552  | A/C    | 0.227   | 0.018   | 0.001   | 8.7E-35 |
| rs34651      | 5   | 72144005  | T/C    | 0.918   | 0.011   | 0.002   | 3.0E-08 |
| rs6860245    | 5   | 127367998 | C/G    | 0.247   | 0.011   | 0.001   | 9.6E-14 |
| rs2057655    | 5   | 131807624 | A/G    | 0.187   | 0.011   | 0.002   | 2.4E-11 |
| rs1650527    | 5   | 158022724 | C/T    | 0.768   | 0.014   | 0.001   | 4.1E-22 |
| rs6879874    | 5   | 176730775 | T/A    | 0.724   | 0.008   | 0.001   | 1.8E-09 |
| rs9366291    | 6   | 19381870  | C/G    | 0.577   | 0.006   | 0.001   | 4.2E-08 |
|   | SNP ID     | Chr | POS   | Ref | Alt | MAF  | Effect Size | P-value |
|---|-----------|-----|-------|-----|-----|------|-------------|---------|
| 54| rs28360642| 6   | 41667506 | A/C | 0.839 | 0.020 | 0.002 | 5.8E-36 |
| 55| rs150115323| 6   | 117506408 | G/C | 0.372 | 0.006 | 0.001 | 4.1E-09 |
| 56| rs58321169| 6   | 126868567 | C/T | 0.732 | 0.010 | 0.001 | 5.6E-14 |
| 57| rs199607859| 6   | 139835418 | T/G | 0.594 | 0.010 | 0.001 | 3.7E-17 |
| 58| rs1738386| 6   | 151990235 | C/T | 0.380 | 0.008 | 0.001 | 1.9E-11 |
| 59| rs555754| 6   | 160769423 | A/G | 0.468 | 0.018 | 0.001 | 1.7E-59 |
| 60| rs2246223| 7   | 6701189 | T/C | 0.555 | 0.009 | 0.002 | 1.3E-10 |
| 61| rs28459049| 7   | 21567331 | C/T | 0.787 | 0.009 | 0.002 | 1.3E-10 |
| 62| rs4563785| 7   | 26349213 | G/T | 0.913 | 0.014 | 0.002 | 6.6E-12 |
| 63| rs13237750| 7   | 46456878 | C/T | 0.952 | 0.016 | 0.003 | 1.6E-09 |
| 64| rs17492269| 7   | 70047405 | G/A | 0.292 | 0.010 | 0.001 | 1.1E-16 |
| 65| rs848476| 7   | 77541673 | G/A | 0.067 | 0.014 | 0.002 | 6.5E-09 |
| 66| rs10238028| 7   | 99208899 | G/A | 0.067 | 0.014 | 0.002 | 6.5E-09 |
| 67| rs6706| 7   | 100471044 | T/C | 0.184 | 0.017 | 0.002 | 2.5E-29 |
| 68| rs114949263| 7   | 150498245 | C/T | 0.111 | 0.014 | 0.002 | 2.7E-14 |
| 69| rs9644032| 8   | 23414822 | T/G | 0.368 | 0.008 | 0.001 | 1.2E-11 |
| 70| rs12543287| 8   | 42334511 | C/G | 0.372 | 0.011 | 0.001 | 1.8E-18 |
| 71| rs10095930| 8   | 116974302 | C/T | 0.417 | 0.010 | 0.001 | 1.1E-15 |
| 72| rs4871015| 8   | 128314516 | A/G | 0.581 | 0.008 | 0.001 | 5.1E-10 |
| 73| rs820504| 9   | 6668278 | G/A | 0.864 | 0.014 | 0.002 | 2.2E-16 |
| 74| rs10961205| 9   | 13722479 | A/G | 0.583 | 0.007 | 0.001 | 4.6E-08 |
| 75| rs696825| 9   | 86583076 | T/C | 0.252 | 0.024 | 0.001 | 4.5E-63 |
| 76| rs62580766| 9   | 113034490 | T/C | 0.181 | 0.011 | 0.002 | 7.5E-16 |
| 77| rs4837794| 9   | 123507855 | T/C | 0.332 | 0.010 | 0.001 | 1.4E-16 |
| 78| rs8176741| 9   | 136131461 | G/A | 0.938 | 0.016 | 0.003 | 1.7E-10 |
| 79| rs7475279| 10   | 5252866 | A/C | 0.846 | 0.018 | 0.002 | 1.3E-30 |
| 80| rs899865| 10   | 36473044 | T/C | 0.600 | 0.007 | 0.001 | 1.0E-08 |
| 81| rs1530439| 10   | 63645959 | T/G | 0.309 | 0.011 | 0.001 | 9.7E-19 |
| SNP     | Chromosome | Position | Reference Allele | Reference Allele Frequency | Study Allele Frequency | P-Value  |
|---------|------------|----------|------------------|----------------------------|------------------------|----------|
| rs206888 | 10         | 94839642 | A                  | 0.451                      | 0.013                  | 2.0E-26  |
| rs10883451| 10         | 101924418| C                  | 0.499                      | 0.009                  | 8.2E-11  |
| rs140312320| 10        | 103992418| G                   | 0.933                      | 0.017                  | 1.1E-11  |
| rs35198068 | 10         | 114754784| T                   | 0.710                      | 0.011                  | 2.0E-19  |
| rs1037169 | 11         | 13361005 | C                  | 0.499                      | 0.009                  | 8.2E-11  |
| rs174537  | 11         | 61552680 | G                   | 0.654                      | 0.012                  | 5.5E-21  |
| rs12804411| 11         | 69284200 | T                   | 0.231                      | 0.014                  | 2.6E-24  |
| rs11021232| 11         | 95320808 | T                   | 0.820                      | 0.013                  | 4.0E-17  |
| rs10893876| 11         | 123853007| C                  | 0.766                      | 0.008                  | 3.5E-08  |
| rs17887160| 12         | 6877721  | C                  | 0.720                      | 0.009                  | 7.4E-12  |
| rs4149056 | 12         | 21331549 | T                   | 0.849                      | 0.030                  | 1.5E-74  |
| rs11047237| 12         | 24206326 | A                  | 0.965                      | 0.028                  | 8.2E-17  |
| rs4307773 | 12         | 51144432 | T                   | 0.419                      | 0.014                  | 5.9E-31  |
| rs8756    | 12         | 66359752 | C                  | 0.485                      | 0.008                  | 1.7E-13  |
| rs3751129 | 12         | 102455712| A                 | 0.216                      | 0.011                  | 1.7E-13  |
| rs7139079 | 12         | 121415293| A                | 0.593                      | 0.013                  | 5.4E-28  |
| rs12311848| 12         | 124486851| G                 | 0.333                      | 0.014                  | 1.6E-29  |
| rs9556403 | 13         | 95236825 | G                   | 0.350                      | 0.007                  | 6.8E-10  |
| rs7321688 | 13         | 115000365| C                  | 0.767                      | 0.009                  | 1.7E-09  |
| rs11621792| 14         | 24871926 | C                  | 0.548                      | 0.026                  | 4.0E-102 |
| rs2239222 | 14         | 73011885 | G                  | 0.349                      | 0.010                  | 2.1E-16  |
| rs13379043| 14         | 74250126 | C                  | 0.278                      | 0.011                  | 2.2E-16  |
| rs28929474| 14         | 94844947 | T                  | 0.020                      | 0.061                  | 3.1E-43  |
| rs2498786 | 14         | 105262368| C                  | 0.385                      | 0.011                  | 5.5E-19  |
| rs275177  | 15         | 39449003 | C                  | 0.150                      | 0.010                  | 5.5E-09  |
| rs139974673| 15         | 44027885 | T                  | 0.974                      | 0.054                  | 1.4E-49  |
| rs12438742| 15         | 61947280 | G                 | 0.570                      | 0.007                  | 2.9E-08  |
| rs12906447| 15         | 96224270 | C                  | 0.552                      | 0.009                  | 4.3E-14  |
| SNP ID     | Chromosome | Position | Genotype     | Minor Allele Frequency | Major Allele Frequency | p-value | Minor Allele Frequency | Major Allele Frequency |
|------------|------------|----------|--------------|------------------------|------------------------|---------|------------------------|------------------------|
| rs56332871 | 15         | 96714816 | A/C          | 0.272                  | 0.039                  | 9.2E-188 | rs8023580               | C/T                    |
| rs4122352  | 16         | 15174571 | A/G          | 0.296                  | 0.011                  | 1.8E-16  | rs11644601              | C/T                    |
| rs858519   | 17         | 7531965  | C/T          | 0.557                  | 0.099                  | 1.7E-1533| rs72844546              | C/T                    |
| rs2525570  | 17         | 29681245 | G/A          | 0.601                  | 0.007                  | 1.0E-09  | rs71493850              | T/G                    |
| rs140302625| 17         | 47379867 | T/G          | 0.087                  | 0.062                  | 4.2E-193 | rs72844546              | T/G                    |
| rs7250869  | 19         | 33887405 | C/T          | 0.690                  | 0.011                  | 2.7E-20  | rs889140                | A/G                    |
| rs2018519  | 19         | 35559787 | C/T          | 0.181                  | 0.020                  | 3.4E-40  | rs1790813               | T/G                    |
| rs73036519 | 19         | 45748362 | G/C          | 0.700                  | 0.009                  | 7.3E-10  | rs151165225             | C/T                    |
| rs34255979 | 19         | 46384830 | T/C          | 0.121                  | 0.028                  | 7.9E-52  | rs9774409               | T/C                    |
| rs59774409 | 19         | 50016748 | T/C          | 0.082                  | 0.018                  | 5.2E-16  | rs1741344               | T/C                    |
| rs1741344  | 20         | 4101800  | T/C          | 0.634                  | 0.007                  | 3.4E-09  | rs13042148              | T/C                    |
| rs13042148 | 20         | 32298286 | C/T          | 0.845                  | 0.016                  | 1.9E-21  | rs6073431               | T/C                    |
| rs6073431  | 20         | 43040569 | T/C          | 0.532                  | 0.017                  | 6.2E-43  | rs4810580               | T/G                    |
| rs4810580  | 20         | 45594295 | T/G          | 0.782                  | 0.010                  | 6.2E-10  | rs16995626              | C/T                    |
| rs16995626 | 20         | 49540925 | C/T          | 0.072                  | 0.018                  | 3.7E-15  | rs5753111               | T/C                    |
| rs5753111  | 22         | 30779211 | T/C          | 0.291                  | 0.013                  | 4.4E-23  | rs3747207               | T/C                    |

SNP, single nucleotide polymorphism; Chr, chromosome; EA, effect allele; OA, other allele; EAF, effect allele frequency; SE, standard error.
| NO. | SNP            | CHR | POSITION (B37) | EA/OA | EAF  | BETA | SE  | P-VALUE | PROXY SNP | PROXY EA/OA | R²   | PROXY EAF |
|-----|----------------|-----|---------------|-------|------|------|-----|---------|-----------|-------------|------|-----------|
| 1   | rs71519251     | 1   | 163251833     | A/G   | 0.167| 0.024| 0.004| 1.5E-09 | rs12724399 | C/T         | 0.9277| 0.1829    |
| 2   | rs6729954      | 2   | 18286651      | T/A   | 0.435| 0.019| 0.003| 3.3E-10 | rs6742679  | A/G         | 0.9837| 0.4155    |
| 3   | rs829593       | 2   | 30641234      | G/A   | 0.687| 0.018| 0.003| 1.5E-08 |           |             |      |           |
| 4   | rs6718154      | 2   | 180497923     | T/C   | 0.275| 0.032| 0.003| 1.2E-22 |           |             |      |           |
| 5   | rs2011425      | 2   | 234627608     | T/G   | 0.920| 0.050| 0.006| 6.4E-20 |           |             |      |           |
| 6   | rs1112195      | 3   | 24085166      | G/A   | 0.495| 0.018| 0.003| 4.7E-10 |           |             |      |           |
| 7   | rs9824196      | 3   | 28807441      | T/G   | 0.721| 0.026| 0.003| 4.1E-16 |           |             |      |           |
| 8   | rs3821866      | 3   | 53805577      | G/C   | 0.622| 0.022| 0.003| 4.1E-14 | rs11918583 | A/G         | 0.9956| 0.662     |
| 9   | rs13065463     | 3   | 61662996      | G/A   | 0.869| 0.032| 0.005| 8.8E-13 |           |             |      |           |
| 10  | rs10510939     | 3   | 65507808      | C/T   | 0.375| 0.017| 0.003| 1.6E-08 |           |             |      |           |
| 11  | rs34040779     | 3   | 107235109     | T/C   | 0.924| 0.035| 0.006| 2.2E-09 | rs16853512 | A/G         | 1     | 0.9215    |
| 12  | rs4678408      | 3   | 138053187     | G/A   | 0.630| 0.026| 0.003| 7.6E-17 | rs1002766  | A/G         | 0.9077| 0.666     |
| 13  | rs7679843      | 4   | 22028079      | G/C   | 0.095| 0.050| 0.005| 3.8E-22 | rs11728819 | A/C         | 0.8863| 0.1064    |
| 14  | rs4274916      | 4   | 69988378      | C/T   | 0.542| 0.017| 0.003| 3.2E-09 |           |             |      |           |
| 15  | rs950716       | 5   | 135680540     | A/G   | 0.863| 0.034| 0.004| 3.1E-14 |           |             |      |           |
| 16  | rs2961853      | 5   | 165932048     | C/T   | 0.469| 0.019| 0.003| 3.2E-10 |           |             |      |           |
| 17  | rs34192788     | 6   | 17416258      | T/A   | 0.690| 0.020| 0.003| 4.2E-09 | rs17379883 | G/A         | 1     | 0.672     |
| 18  | rs7454964      | 6   | 52728059      | T/C   | 0.428| 0.017| 0.003| 1.8E-08 | rs11969435 | T/C         | 0.9959| 0.4254    |
| 19  | rs9322822      | 6   | 105369598     | C/T   | 0.679| 0.049| 0.003| 2.1E-52 |           |             |      |           |
| 20  | rs2184968      | 6   | 126760994     | C/T   | 0.451| 0.020| 0.003| 9.1E-11 |           |             |      |           |
| 21  | rs10279715     | 7   | 40870935      | A/G   | 0.538| 0.022| 0.003| 3.1E-13 |           |             |      |           |
| 22  | rs55795858     | 7   | 146123500     | C/T   | 0.329| 0.018| 0.003| 1.5E-08 | rs2888335  | C/T         | 0.8808| 0.2753    |
| 23  | rs2631864      | 8   | 21112084      | G/A   | 0.104| 0.033| 0.005| 8.3E-12 |           |             |      |           |
| 24  | rs4872310      | 8   | 25247181      | G/A   | 0.753| 0.023| 0.004| 3.7E-12 |           |             |      |           |
| 25  | rs4562360      | 8   | 61704817      | G/A   | 0.757| 0.032| 0.004| 3.6E-20 |           |             |      |           |
| SNP     | Chr | Start Position | Allele 1 | Allele 2 | Effect Allele | Effect Allele Frequency | p-Value | Alternative Allele Frequency | p-Value |
|---------|-----|----------------|----------|----------|---------------|-------------------------|---------|-------------------------------|---------|
| rs71529289 | 8   | 77879487       | C/T      | 0.748    | 0.036         | 0.003                   | 2.0E-25 | rs7857865                     | A/G     | 0.9562  | 0.4374 |
| rs4483209  | 9   | 1960629        | T/G      | 0.472    | 0.017         | 0.003                   | 4.3E-09 | rs6478869                     | C/T     | 1       | 0.7147 |
| rs745486   | 9   | 11242155       | C/T      | 0.719    | 0.021         | 0.003                   | 1.2E-10 | rs7097461                     | A/G     | 0.9798  | 0.4284 |
| rs10738700 | 9   | 24973797       | A/G      | 0.569    | 0.020         | 0.003                   | 5.6E-11 | rs7872329                     | A/T     | 0.689   | 0.017  |
| rs912202   | 9   | 77225603       | C/G      | 0.343    | 0.040         | 0.003                   | 2.5E-38 | rs6478869                     | T/G     | 0.798   | 0.021  |
| rs2090409  | 9   | 108967088      | C/A      | 0.684    | 0.031         | 0.003                   | 1.7E-21 | rs4919686                     | C/A     | 0.569   | 0.020  |
| rs7872329  | 9   | 131956152      | A/T      | 0.689    | 0.017         | 0.003                   | 3.8E-08 | rs6478869                     | C/T     | 0.719   | 0.021  |
| rs7912521  | 10  | 67262089       | C/T      | 0.416    | 0.061         | 0.003                   | 6.2E-94 | rs7097461                     | A/G     | 0.9798  | 0.4284 |
| rs4919686  | 10  | 104592249      | A/G      | 0.710    | 0.023         | 0.003                   | 3.9E-13 | rs6478869                     | T/G     | 0.798   | 0.021  |
| rs7915430  | 10  | 121660465      | T/G      | 0.798    | 0.021         | 0.004                   | 9.7E-09 | rs4919686                     | A/C     | 0.569   | 0.020  |
| rs2035837  | 11  | 29200527       | T/C      | 0.852    | 0.073         | 0.004                   | 6.7E-67 | rs55765314                    | C/A     | 0.838   | 0.025  |
| rs55765314 | 11  | 72360935       | C/A      | 0.838    | 0.025         | 0.004                   | 4.6E-10 | rs303542                       | T/C     | 0.852   | 0.073  |
| rs10892924 | 11  | 122773715      | T/A      | 0.568    | 0.039         | 0.003                   | 2.8E-37 | rs4936759                     | C/T     | 0.9897  | 0.5696 |
| rs61932784 | 12  | 114132310      | C/A      | 0.783    | 0.022         | 0.004                   | 4.0E-09 | rs10892924                    | C/A     | 0.838   | 0.025  |
| rs10137488 | 14  | 35797122       | C/T      | 0.027    | 0.053         | 0.010                   | 2.1E-08 | rs10483727                    | T/C     | 0.9713  | 0.4036 |
| rs1272131  | 14  | 60886150       | C/T      | 0.387    | 0.027         | 0.003                   | 1.4E-17 | rs10483727                    | T/C     | 0.9713  | 0.4036 |
| rs1454836  | 15  | 47551054       | T/A      | 0.601    | 0.017         | 0.003                   | 3.4E-08 | rs766132                       | C/T     | 0.9107  | 0.6083 |
| rs17703883 | 15  | 51530097       | C/T      | 0.255    | 0.044         | 0.004                   | 7.5E-40 | rs7915430                     | A/G     | 0.424   | 0.019  |
| rs13835    | 15  | 89056040       | A/C      | 0.424    | 0.019         | 0.003                   | 4.9E-10 | rs61932784                    | C/A     | 0.783   | 0.022  |
| rs62041532 | 16  | 73922719       | G/T      | 0.213    | 0.023         | 0.004                   | 1.6E-10 | rs17703883                    | A/G     | 0.739   | 0.034  |
| rs1799941  | 17  | 7533423        | G/A      | 0.739    | 0.034         | 0.003                   | 7.7E-23 | rs149932962                   | G/A     | 0.8877  | 0.7604 |
| rs2668776  | 18  | 44750365       | C/T      | 0.469    | 0.029         | 0.003                   | 1.7E-22 | rs62041532                    | G/T     | 0.9906  | 0.6998 |
| rs2327121  | 20  | 8878250        | C/G      | 0.657    | 0.018         | 0.003                   | 1.3E-08 | rs6056230                     | G/T     | 0.9906  | 0.6998 |
| rs7265992  | 20  | 33525407       | G/A      | 0.821    | 0.032         | 0.004                   | 4.0E-16 | rs7915430                     | C/T     | 0.9798  | 0.4284 |

SNP, single nucleotide polymorphism; Chr, chromosome; EA, effect allele; OA, other allele; EAF, effect allele frequency; SE, standard error.
| NO. | SNP          | CHR | POSITION (B37) | EA/OA | EAF  | BETA   | SE   | P-VALUE | PROXY SNP | PROXY EA/OA | R²     | PROXY EAF |
|-----|--------------|-----|----------------|-------|------|--------|------|---------|-----------|-------------|--------|-----------|
| 1   | rs1989147    | 1   | 7909373        | C/T   | 0.807| 0.024  | 0.003| 7.0E-14 |           |             |        |           |
| 2   | rs6684361    | 1   | 101737743      | C/T   | 0.307| 0.040  | 0.003| 5.4E-48 |           |             |        |           |
| 3   | rs12564492   | 1   | 168234645      | A/G   | 0.691| 0.015  | 0.003| 5.0E-09 | rs4656150 | C/T         | 0.9678 | 0.6909    |
| 4   | rs2266782    | 1   | 171079696      | A/G   | 0.417| 0.016  | 0.003| 2.6E-11 |           |             |        |           |
| 5   | rs2152318    | 1   | 179293511      | T/C   | 0.245| 0.032  | 0.003| 1.8E-27 |           |             |        |           |
| 6   | rs34269793   | 1   | 125516445      | A/G   | 0.691| 0.015  | 0.003| 5.0E-09 |           |             |        |           |
| 7   | rs6684361    | 1   | 101737743      | C/T   | 0.307| 0.040  | 0.003| 5.4E-48 |           |             |        |           |
| 8   | rs2266782    | 1   | 171079696      | A/G   | 0.417| 0.016  | 0.003| 2.6E-11 |           |             |        |           |
| 9   | rs34269793   | 1   | 125516445      | A/G   | 0.691| 0.015  | 0.003| 5.0E-09 |           |             |        |           |
| 10  | rs2152318    | 1   | 179293511      | T/C   | 0.245| 0.032  | 0.003| 1.8E-27 |           |             |        |           |
| 11  | rs34269793   | 1   | 125516445      | A/G   | 0.691| 0.015  | 0.003| 5.0E-09 |           |             |        |           |
| 12  | rs2266782    | 1   | 171079696      | A/G   | 0.417| 0.016  | 0.003| 2.6E-11 |           |             |        |           |
| 13  | rs34269793   | 1   | 125516445      | A/G   | 0.691| 0.015  | 0.003| 5.0E-09 |           |             |        |           |
| 14  | rs2266782    | 1   | 171079696      | A/G   | 0.417| 0.016  | 0.003| 2.6E-11 |           |             |        |           |
| 15  | rs2152318    | 1   | 179293511      | T/C   | 0.245| 0.032  | 0.003| 1.8E-27 |           |             |        |           |
| 16  | rs34269793   | 1   | 125516445      | A/G   | 0.691| 0.015  | 0.003| 5.0E-09 |           |             |        |           |
| 17  | rs2266782    | 1   | 171079696      | A/G   | 0.417| 0.016  | 0.003| 2.6E-11 |           |             |        |           |
| 18  | rs34269793   | 1   | 125516445      | A/G   | 0.691| 0.015  | 0.003| 5.0E-09 |           |             |        |           |
| 19  | rs2266782    | 1   | 171079696      | A/G   | 0.417| 0.016  | 0.003| 2.6E-11 |           |             |        |           |
|   | SNP ID       | Chr | Position   | Genotype | HWE (p) | MAF   | MAF (s) | OR       | 95% CI   |
|---|-------------|-----|------------|----------|---------|-------|---------|----------|----------|
| 26| rs62396733  | 6   | 41679691   | T/C      | 0.137   | 0.021 | 0.004   | 5.7E-09  |          |
| 27| rs1214759   | 6   | 43352980   | G/A      | 0.679   | 0.018 | 0.003   | 2.8E-12  |          |
| 28| rs2397112   | 6   | 52684333   | A/G      | 0.576   | 0.016 | 0.003   | 4.0E-10  | rs6932500| G/A      | 0.9959   | 0.5755   |
| 29| rs9399469   | 6   | 144318529  | A/T      | 0.610   | 0.020 | 0.003   | 2.6E-14  | rs9376802| T/C      | 0.9547   | 0.6103   |
| 30| rs4869893   | 6   | 157117322  | C/A      | 0.282   | 0.016 | 0.003   | 1.1E-08  |          |
| 31| rs4544698   | 7   | 99332948   | T/G      | 0.951   | 0.161 | 0.006   | 5.1E-12  | rs14898277| T/C      | 0.81     | 0.9513   |
| 32| rs12054255  | 8   | 59398435   | G/A      | 0.377   | 0.017 | 0.003   | 6.1E-10  |          |
| 33| rs11334795  | 8   | 97136852   | G/A      | 0.976   | 0.045 | 0.008   | 1.2E-08  |          |
| 34| rs35783704  | 8   | 10596625   | A/G      | 0.101   | 0.033 | 0.004   | 4.7E-16  |          |
| 35| rs12543598  | 8   | 143955318  | T/G      | 0.407   | 0.020 | 0.003   | 6.6E-15  | rs4581033| A/C      | 0.9918   | 0.4066   |
| 36| rs10757893  | 9   | 29599001   | A/G      | 0.532   | 0.014 | 0.003   | 9.3E-09  | rs10757895| A/G      | 0.8275   | 0.5318   |
| 37| rs1171617   | 10  | 61467182   | T/G      | 0.767   | 0.030 | 0.003   | 3.6E-23  |          |
| 38| rs7089122   | 10  | 93647412   | T/C      | 0.199   | 0.024 | 0.003   | 1.7E-14  | rs2259287| G/A      | 0.9204   | 0.1988   |
| 39| rs9527      | 10  | 104623578  | C/T      | 0.758   | 0.023 | 0.003   | 5.9E-15  |          |
| 40| rs7078330   | 10  | 122834163  | T/C      | 0.088   | 0.031 | 0.004   | 5.7E-13  |          |
| 41| rs6486122   | 11  | 13361524   | T/C      | 0.690   | 0.017 | 0.003   | 1.7E-09  |          |
| 42| rs11031005  | 11  | 30226356   | C/T      | 0.144   | 0.023 | 0.004   | 1.5E-10  |          |
| 43| rs113172275| 11  | 62905115   | C/T      | 0.066   | 0.049 | 0.005   | 1.4E-22  |          |
| 44| rs3814707   | 11  | 65560785   | G/A      | 0.758   | 0.020 | 0.003   | 5.5E-11  |          |
| 45| rs850294    | 11  | 123437669  | T/C      | 0.114   | 0.034 | 0.004   | 5.2E-18  |          |
| 46| rs4149056   | 12  | 21331549   | C/T      | 0.151   | 0.043 | 0.004   | 3.0E-35  |          |
| 47| rs11047261  | 12  | 24257228   | G/A      | 0.041   | 0.037 | 0.006   | 6.4E-09  |          |
| 48| rs56205943  | 12  | 57679414   | G/A      | 0.759   | 0.021 | 0.003   | 3.9E-13  |          |
| 49| rs7301634   | 12  | 98901200   | A/G      | 0.810   | 0.019 | 0.003   | 2.8E-09  |          |
| 50| rs10778215  | 12  | 103537266  | A/T      | 0.506   | 0.024 | 0.003   | 2.6E-22  | rs4764939| T/C      | 0.9764   | 0.506    |
| 51| rs7139079   | 12  | 121415293  | G/A      | 0.407   | 0.022 | 0.003   | 1.1E-16  |          |
| 52| rs2954111   | 12  | 122134415  | C/T      | 0.361   | 0.017 | 0.003   | 3.1E-10  |          |
| 53| rs629042    | 13  | 22318506   | C/G      | 0.603   | 0.028 | 0.003   | 7.4E-29  | rs631660 | G/T      | 0.9959   | 0.6034   |
| SNP        | Chr | Position | Allele | Effect Allele Fr | Other Allele Fr | P-value | Other SNP        | Chr | Position | Allele | Effect Allele Fr | Other Allele Fr | P-value |
|------------|-----|----------|--------|-----------------|----------------|---------|-----------------|-----|----------|--------|-----------------|----------------|---------|
| rs17245822 | 13  | 73131694 | C/A    | 0.360           | 0.014          | 0.003   | rs1337985       | C/T | 0.9957   | 0.3598 |
| rs11621792 | 14  | 24871926 | T/C    | 0.481           | 0.025          | 0.003   | rs11626929      | T/C | 0.8147   | 0.4811 |
| rs112635299| 14  | 94838142 | G/T    | 0.979           | 0.102          | 0.009   | rs924416        | T/G | 0.9462   | 0.3241 |
| rs7183977  | 15  | 40377092 | C/T    | 0.324           | 0.029          | 0.003   | rs11626929      | T/C | 0.8147   | 0.4811 |
| rs10851395 | 15  | 40718534 | C/T    | 0.524           | 0.019          | 0.003   | rs11626929      | T/C | 0.8147   | 0.4811 |
| rs62025141 | 15  | 79850183 | A/G    | 0.855           | 0.026          | 0.004   | rs11626929      | T/C | 0.8147   | 0.4811 |
| rs56332871 | 15  | 96714816 | C/A    | 0.698           | 0.030          | 0.003   | rs8023580       | T/C | 0.9626   | 0.6978 |
| rs388430   | 16  | 4135562  | C/T    | 0.688           | 0.017          | 0.003   | rs8023580       | T/C | 0.9626   | 0.6978 |
| rs8046391  | 16  | 30836648 | C/G    | 0.305           | 0.017          | 0.003   | rs28421305      | A/G | 1        | 0.3052 |
| rs58072681 | 16  | 81590541 | C/T    | 0.070           | 0.061          | 0.005   | rs11626929      | T/C | 0.8147   | 0.4811 |
| rs727428   | 17  | 7537792  | T/C    | 0.444           | 0.095          | 0.003   | rs11626929      | T/C | 0.8147   | 0.4811 |
| rs11653686 | 17  | 47362991 | C/T    | 0.913           | 0.066          | 0.004   | rs11626929      | T/C | 0.8147   | 0.4811 |
| rs7239564  | 18  | 71967031 | C/T    | 0.856           | 0.031          | 0.004   | rs11626929      | T/C | 0.8147   | 0.4811 |
| rs1640272  | 19  | 2800192  | A/T    | 0.683           | 0.021          | 0.003   | rs941410        | G/A | 0.9021   | 0.6829 |
| rs7248104  | 19  | 7224431  | G/A    | 0.584           | 0.016          | 0.003   | rs941410        | G/A | 0.9021   | 0.6829 |
| rs34255979 | 19  | 46384830 | C/T    | 0.879           | 0.023          | 0.004   | rs941410        | G/A | 0.9021   | 0.6829 |
| rs6020423  | 20  | 48909667 | C/T    | 0.760           | 0.025          | 0.003   | rs941410        | G/A | 0.9021   | 0.6829 |
| rs6008259  | 22  | 46633782 | G/A    | 0.821           | 0.021          | 0.003   | rs941410        | G/A | 0.9021   | 0.6829 |

SNP, single nucleotide polymorphism; Chr, chromosome; EA, effect allele; OA, other allele; EAF, effect allele frequency; SE, standard error.
TABLE S7. Study characteristics and SNP effects for estradiol

| STUDY            | SEX     | N    | SNP    | GENE      | EA/OA | EAF  | BETA* | SE  | P-VALUE | ADJUSTMENTS                                      | ANCESTRY     |
|------------------|---------|------|--------|-----------|-------|------|-------|-----|---------|-------------------------------------------------|--------------|
| Thompson et al,  | Females | 2,767| rs727479 | CYP19A1 | A/C   | 0.656| 0.096 | 0.018| 7.40E-8 | Laboratory batch, study, age at blood draw, BMI, HRT use and menopausal status (2–5 years, or >5 years since menopause) | European     |
| (2016)           |         |      |        |           |       |      |       |     |         |                                                 |              |
| Eriksson et al,  | Males   | 11,097| rs727479 | CYP19A1 | A/C   | 0.63 | 1.39  | 0.12 | 8.2E-30 | Age, BMI                                        | European     |
| (2018)           |         |      |        |           |       |      |       |     |         |                                                 |              |

*Beta for the study by Thompson is in log-transformed estradiol concentration, for Eriksson et al it is the effect in picogram per milliliter. SNP, single nucleotide polymorphism; EA, Effect allele; OA, Other allele; EAF, Effect allele frequency; SE, Standard error; BMI, Body mass index.
Table S8. Mendelian randomization results after cluster filtering

| EXPOSURE                     | SEX | UNIT       | METHOD               | SNPS | ODDS RADIO | 95% CI    | P-VALUE | Q     | P-HET |
|------------------------------|-----|------------|----------------------|------|------------|-----------|---------|-------|-------|
| Bioavailable testosterone    | F   | 1 s.d. increase | IVW (random effects) | 17   | 1.24       | 0.81-1.91 | 0.313   | 12.33 | 0.721 |
|                              |     |            | Weighted median      | 17   | 1.38       | 0.72-2.66 | 0.337   |       |       |
|                              |     |            | MR-Egger intercept   | 17   | β= -0.00113| s.e.= 0.01715 | 0.948   |       |       |
| SHBG                         | F   | 1 s.d. increase | IVW (random effects) | 126  | 1.21       | 1.05-1.40 | 0.008   | 112.20| 0.787 |
|                              |     |            | Weighted median      | 126  | 1.31       | 1.02-1.70 | 0.032   |       |       |
|                              |     |            | MR-Egger intercept   | 126  | β=-0.0074636 | s.e.=0.0075638 | 0.325   |       |       |

SNPs used for bioavailable testosterone have effects independent of SHBG. SNPs used for SHBG have a primary effect on SHBG, and secondary (opposite) effects on bioavailable testosterone. ‘P-het’ represents the p-value belonging to the Q-statistic. F, Females; M, Males; s.e., standard error; s.d., standard deviation; N/A, Not Applicable;
Table S9. Multivariable Mendelian randomization results

| EXPOSURE                  | SEX | UNIT         | METHOD                              | SNPS | ODDS | 95% CI     | P-VALUE | Q       | P-HET | P-EGGER |
|---------------------------|-----|--------------|-------------------------------------|------|------|------------|---------|---------|--------|---------|
| Bioavailable testosterone | F   | 1 s.d. increase | MV-IVW (random effects)             | 162  | 1.02 | 0.61-1.69  | 0.952   | 138.24  | 0.89   | 0.15    |
| SHBG                      | F   | 1 s.d. increase | MV-IVW (random effects)             | 162  | 1.17 | 0.94-1.46  | 0.169   |         |        |         |

Estimates represent the estimated direct causal effect of the exposure, while accounting for the other exposure. ‘P-het’ represents the p-value belonging to the Q-statistic. ‘P-Egger’ represents the p-value belonging to the Egger-intercept. F, Females; M, Males; s.e., standard error; s.d., standard deviation; N/A, Not Applicable.
Table S10. Mendelian randomization results for the different exposures on aSAH risk among women

| EXPOSURE                        | SEX | UNIT            | METHOD                  | SNPS | ODDS RADIO | 95% CI       | P-VALUE | Q     | P-HET |
|---------------------------------|-----|-----------------|-------------------------|------|------------|--------------|---------|-------|-------|
| Age at menarche                 | F   | 1-year increase | IVW (random effects)    | 163  | 0.96       | 0.82-1.12    | 0.576   | 159.78| 0.534 |
|                                 |     |                 | Weighted median         | 163  | 1.04       | 0.82-1.33    | 0.737   |        |       |
|                                 |     |                 | MR-Egger intercept      | 163  | β=-0.0074636 | s.e.=0.0075638 | 0.325   |        |       |
|                                 |     |                 | MR-Egger                | 163  | 1.15       | 0.78-1.69    | 0.493   |        |       |
|                                 |     |                 | MR-PRESSO               | N/A  | N/A        | N/A          | N/A     | N/A   |       |
| Age at menopause                | F   | 1-year increase | IVW (random effects)    | 112  | 1.01       | 0.96-1.06    | 0.807   | 97.26 | 0.821 |
|                                 |     |                 | Weighted median         | 112  | 1.00       | 0.92-1.09    | 0.975   |        |       |
|                                 |     |                 | MR-Egger intercept      | 112  | β=0.008318  | s.e.=0.007939 | 0.297   |        |       |
|                                 |     |                 | MR-Egger                | 112  | 0.95       | 0.85-1.07    | 0.415   |        |       |
|                                 |     |                 | MR-PRESSO               | N/A  | N/A        | N/A          | N/A     | N/A   |       |
| Bioavailable testosterone       | F   | 1 s.d. increase | IVW (random effects)    | 71   | 0.73       | 0.55-0.95    | 0.020   | 67.92 | 0.548 |
|                                 |     |                 | Weighted median         | 71   | 0.64       | 0.42-0.98    | 0.038   |        |       |
|                                 |     |                 | MR-Egger intercept      | 71   | β=-0.00023  | s.e.=0.008943 | 0.979   |        |       |
|                                 |     |                 | MR-Egger                | 71   | 0.73       | 0.44-1.21    | 0.229   |        |       |
|                                 |     |                 | MR-PRESSO               | N/A  | N/A        | N/A          | N/A     | N/A   |       |
| SHBG                            | F   | 1 s.d. increase | IVW (random effects)    | 129  | 1.18       | 1.05-1.34    | 0.007   | 112.44| 0.835 |
|                         | Weighted median | 129 | 1.27 | 1.02-1.59 | 0.035 |
|-------------------------|-----------------|-----|------|-----------|-------|
| MR-Egger intercept      | β=-0.00257      | 129 | 1.23 | 1.00-1.52 | 0.053 |
| MR-Egger                | s.e.=0.005459   |     |      |           |       |
| MR-PRESSO               | N/A             | N/A | N/A  | N/A       | N/A   |
| **SHBG (unadjusted for BMI)** |               |     |      |           |       |
| F                      | 1 s.d. increase | IVW (random effects) | 129 | 1.24 | 1.05-1.47 | 0.009 | 112.91 | 0.827 |
| Weighted median         | 129             | 1.36 | 1.02-1.83 | 0.039 |
| MR-Egger intercept      | β=-0.00151      | 129 | 1.28 | 0.98-1.68 | 0.077 |
| MR-Egger                | s.e.=0.0053     |     |      |           |       |
| MR-PRESSO               | N/A             | N/A | N/A  | N/A       | N/A   |
| **Estradiol**           | F               | 1 s.d. increase | Wald estimate | 1 | 0.85 | 0.43-1.67 | 0.642 |

‘P-het’ represents the p-value belonging to the Q-statistic. F, Females; M, Males; s.e., standard error; s.d., standard deviation; N/A, Not Applicable; BMI, body mass index.
Table S11. Sensitivity analyses for the different exposures on aSAH risk among men

| EXPOSURE                | SEX | UNIT            | METHOD                  | SNPS | ODDS RADIO | 95% CI       | P-VALUE | Q    | P- HET |
|-------------------------|-----|-----------------|-------------------------|------|------------|--------------|---------|------|--------|
| Age at menarche         | M   | 1-year increase | IVW (random effects)    | 163  | 1.12       | 0.92-1.36    | 0.279   | 156.36 | 0.610  |
|                         |     |                 | Weighted median         | 163  | 1.23       | 0.87-1.73    | 0.244   |       |        |
|                         |     |                 | MR-Egger intercept      | 163  | β=-0.00035 | s.e.=0.009781| 0.971   |       |        |
|                         |     |                 | MR-Egger                | 163  | 1.13       | 0.68-1.86    | 0.644   |       |        |
|                         |     | MR-PRESSO       | N/A                     | N/A  | N/A        | N/A          | N/A     | N/A   | N/A    |
| Age at menopause        | M   | 1-year increase | IVW (random effects)    | 112  | 1.04       | 0.97-1.12    | 0.235   | 119.53 | 0.273  |
|                         |     |                 | Weighted median         | 112  | 1.05       | 0.93-1.18    | 0.451   |       |        |
|                         |     |                 | MR-Egger intercept      | 112  | β=0.002552 | s.e.=0.01072 | 0.812   |       |        |
|                         |     |                 | MR-Egger                | 112  | 1.03       | 0.88-1.19    | 0.732   |       |        |
|                         |     | MR-PRESSO       | N/A                     | N/A  | N/A        | N/A          | N/A     | N/A   | N/A    |
| Bioavailable testosterone| M   | 1 s.d. increase | IVW (random effects)    | 51   | 0.86       | 0.56-1.34    | 0.516   | 58.65 | 0.188  |
|                         |     |                 | Weighted median         | 51   | 0.80       | 0.42-1.51    | 0.489   |       |        |
|                         |     |                 | MR-Egger intercept      | 51   | β=0.011498 | s.e.=0.018964| 0.547   |       |        |
|                         |     |                 | MR-Egger                | 51   | 0.63       | 0.21-1.90    | 0.419   |       |        |
|                         |     | MR-PRESSO       | N/A                     | N/A  | N/A        | N/A          | N/A     | N/A   | N/A    |
| SHBG                    | M   | 1 s.d. increase | IVW (random effects)    | 119  | 0.97       | 0.80-1.16    | 0.703   | 135.04 | 0.135  |
| Method               | N  | Wald estimate | Lower 95% | Upper 95% | P (het) |
|----------------------|----|---------------|-----------|-----------|---------|
| Weighted median      | 119| 1.09          | 0.81-1.48 | 0.561     |
| MR-Egger intercept   | 119| β=-0.00984    | s.e. =0.008511 | 0.250 |
| MR-Egger             | 119| 1.12          | 0.82-1.54 | 0.563     |
| MR-PRESSO            | N/A| N/A           | N/A       | N/A       |

| Estradiol            | M  | 1 s.d. increase | Wald estimate | Lower 95% | Upper 95% | P (het) |
|----------------------|----|-----------------|---------------|-----------|-----------|---------|
|                      | 1  | 1.02            | 0.96-1.08     | 0.589     |

‘P-het’ represents the p-value belonging to the Q-statistic. F, Females; M, Males; s.e., standard error; N/A, Not Applicable;
### Table S12. Mendelian randomization results after MR-Steiger filtering

| EXPOSURE               | SEX | UNIT          | METHOD                      | SNPS | ODDS RADIO | 95% CI     | P-VALUE | Q      | P-HE   |
|------------------------|-----|---------------|-----------------------------|------|-------------|-------------|---------|--------|--------|
| **Age at menarche**    | F   | 1-year increase | IVW (random effects)       | 117  | 0.95        | 0.78-1.16   | 0.633   | 125.16 | 0.264  |
|                        |     |               | Weighted median            | 117  | 0.87        | 0.64-1.17   | 0.353   |         |        |
|                        |     |               | MR-Egger intercept         | 117  | β=-0.00156  | s.e. = 0.01011 | 0.878   |         |        |
|                        |     |               | MR-Egger                   | 117  | 0.99        | 0.57-1.71   | 0.975   |         |        |
|                        |     |               | MR-PRESSO                  | N/A  | N/A         | N/A         | N/A     | N/A    | N/A    |
| **Age at menopause**   | F   | 1-year increase | IVW (random effects)       | 96   | 1.00        | 0.95-1.05   | 0.948   | 79.09  | 0.880  |
|                        |     |               | Weighted median            | 96   | 1.01        | 0.92-1.10   | 0.875   |         |        |
|                        |     |               | MR-Egger intercept         | 96   | β=0.00470   | s.e. = 0.00836 | 0.575   |         |        |
|                        |     |               | MR-Egger                   | 96   | 0.97        | 0.87-1.09   | 0.603   |         |        |
|                        |     |               | MR-PRESSO                  | N/A  | N/A         | N/A         | N/A     | N/A    | N/A    |
| **Bioavailable**       | F   | 1 s.d. increase | IVW (random effects)       | 56   | 0.69        | 0.52-0.93   | 0.016   | 53.89  | 0.517  |
| testosterone           |     |               | Weighted median            | 56   | 0.65        | 0.41-1.03   | 0.068   |         |        |
|                        |     |               | MR-Egger intercept         | 56   | β=-0.00625  | s.e. = 0.00955 | 0.516   |         |        |
|                        |     |               | MR-Egger                   | 56   | 0.80        | 0.48-1.35   | 0.411   |         |        |
|                        |     |               | MR-PRESSO                  | N/A  | N/A         | N/A         | N/A     | N/A    | N/A    |
| **Bioavailable**       | M   | 1 s.d. increase | IVW (random effects)       | 35   | 1.04        | 0.62-1.74   | 0.881   | 39.41  | 0.241  |
| testosterone           |     |               |                             |      |             |             |         |        |        |
|                | Weighted median | MR-Egger intercept | MR-Egger | MR-PRESSO |
|----------------|----------------|--------------------|----------|-----------|
|                |                | 35                 | 35       | N/A       |
|                | β=0.00940      | s.e.=0.02497       | 0.81     | 1.08      |
|                | β=0.00197      | s.e.=0.0058        | 1.06     | 1.06      |
|                | s.e.=0.00998   |                    | 0.74     | 0.77      |
|                | β=0.01112      | s.e.=0.00998       | 0.268    | 0.664     |
|                | β=-0.01112     | s.e.=0.00998       | 0.268    | 0.664     |
|                | β=-0.01112     | s.e.=0.00998       | 0.268    | 0.664     |
|                | β=-0.01112     | s.e.=0.00998       | 0.268    | 0.664     |
|                | β=-0.01112     | s.e.=0.00998       | 0.268    | 0.664     |
|                | β=-0.01112     | s.e.=0.00998       | 0.268    | 0.664     |
|                | β=-0.01112     | s.e.=0.00998       | 0.268    | 0.664     |
|                | β=-0.01112     | s.e.=0.00998       | 0.268    | 0.664     |
|                | β=-0.01112     | s.e.=0.00998       | 0.268    | 0.664     |
|                | β=-0.01112     | s.e.=0.00998       | 0.268    | 0.664     |
|                | β=-0.01112     | s.e.=0.00998       | 0.268    | 0.664     |
|                | β=-0.01112     | s.e.=0.00998       | 0.268    | 0.664     |
|                | β=-0.01112     | s.e.=0.00998       | 0.268    | 0.664     |
|                | β=-0.01112     | s.e.=0.00998       | 0.268    | 0.664     |
|                | β=-0.01112     | s.e.=0.00998       | 0.268    | 0.664     |
|                | β=-0.01112     | s.e.=0.00998       | 0.268    | 0.664     |
|                | β=-0.01112     | s.e.=0.00998       | 0.268    | 0.664     |
|                | β=-0.01112     | s.e.=0.00998       | 0.268    | 0.664     |
|                | β=-0.01112     | s.e.=0.00998       | 0.268    | 0.664     |
|                | β=-0.01112     | s.e.=0.00998       | 0.268    | 0.664     |
|                | β=-0.01112     | s.e.=0.00998       | 0.268    | 0.664     |
|                | β=-0.01112     | s.e.=0.00998       | 0.268    | 0.664     |
|                | β=-0.01112     | s.e.=0.00998       | 0.268    | 0.664     |
|                | β=-0.01112     | s.e.=0.00998       | 0.268    | 0.664     |
International Stroke Genetics Consortium (ISGC) Intracranial Aneurysm Working Group:

Mark K. Bakker¹, Romain Bourcier², Robin G. Walters³, Rainer Malik⁶, Martin Dichgans⁶,⁷,⁸, Muralidharan Sargurupremraj⁹,¹⁰, Turgut Tatlisumak¹¹, Stéphanie Debette⁹,¹⁰, Gabriel J.E. Rinkel¹, Bradford B. Worrall¹², Joanna Pera¹³, Agnieszka Slowik¹³, Joseph P. Broderick¹⁴, David J. Werring¹⁵, Daniel Woo¹⁴, Philippe Bijlenga¹⁶, Yoichiro Kamatani¹⁷, Ynte M. Ruigrok¹

¹Department of Neurology and Neurosurgery, University Medical Center Utrecht Brain Center, Utrecht University, Utrecht, The Netherlands. ²Université de Nantes, CHU Nantes, INSERM, CNRS, l’institut du thorax, Nantes, France. ³CHU Nantes, Department of Neuroradiology, Nantes, France. ⁴Clinical Trial Service Unit and Epidemiological Studies Unit, Nuffield Department of Population Health, University of Oxford, Oxford, U.K. ⁵Medical Research Council Population Health Research Unit, University of Oxford, Oxford, U.K. ⁶Institute for Stroke and Dementia Research, University Hospital, Ludwig-Maximilians-University, Munich. ⁷Munich Cluster for Systems Neurology (SyNergy), Munich, Germany. ⁸Deutsches Zentrum für Neurodegenerative Erkrankungen (DZNE), Munich, Germany. ⁹INSERM U1219 Bordeaux Population Health Research Center, University of Bordeaux, Bordeaux, France. ¹⁰Department of Neurology, Institute for Neurodegenerative Disease, Bordeaux University Hospital, Bordeaux, France. ¹¹Department of Clinical Neuroscience at Institute of Neuroscience and Physiology, University of Gothenburg, Sweden. ¹²Departments of Neurology and Public Health Sciences, University of Virginia School of Medicine, Charlottesville, VA, USA. ¹³Department of Neurology, Faculty of Medicine, Jagiellonian University Medical College, ul. Botaniczna 3, 31-503, Krakow, Poland. ¹⁴University of Cincinnati College of Medicine, Cincinnati, OH, USA. ¹⁵Stroke Research Centre, University College London Queen Square Institute of Neurology, London, UK. ¹⁶Neurosurgery Division, Department of Clinical Neurosciences, Faculty of Medicine, Geneva University Hospitals, Geneva, Switzerland. ¹⁷Graduate School of Frontier Sciences, The University of Tokyo, Tokyo, Japan.
### STROBE-MR checklist

| Item No. | Section                          | Checklist item                                                                 | Section (paragraph number) |
|----------|----------------------------------|-------------------------------------------------------------------------------|-----------------------------|
| 1        | TITLE and ABSTRACT              | Indicate Mendelian randomization as the study’s design in the title and/or the abstract if that is a main purpose of the study | Title page                 |
| 2        | Background                       | Explain the scientific background and rationale for the reported study. What is the exposure? Is a potential causal relationship between exposure and outcome plausible? Justify why MR is a helpful method to address the study question | Introduction (paragraphs 1-3) |
| 3        | Objectives                       | State specific objectives clearly, including pre-specified causal hypotheses (if any). State that MR is a method that, under specific assumptions, intends to estimate causal effects | Introduction (paragraph 3)  |
| 4        | Study design and data sources    | Present key elements of the study design early in the article. Consider including a table listing sources of data for all phases of the study. For each data source contributing to the analysis, describe the following: |                             |
|          |                                  | **a)** Setting: Describe the study design and the underlying population, if possible. Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection, when available. | Methods (paragraph 2,3)     |
|          |                                  | **b)** Participants: Give the eligibility criteria, and the sources and methods of selection of participants. Report the sample size, and whether any power or sample size calculations were carried out prior to the main analysis | Methods (paragraph 2,3), Table 1 |
|          |                                  | **c)** Describe measurement, quality control and selection of genetic variants | Methods (paragraph 2,3)     |
|          |                                  | **d)** For each exposure, outcome, and other relevant variables, describe methods of assessment and diagnostic criteria for diseases | Table 1                     |
|          |                                  | **e)** Provide details of ethics committee approval and participant informed consent, if relevant | N/A                         |

39
|   | Assumptions | Explicitly state the three core IV assumptions for the main analysis (relevance, independence and exclusion restriction) as well assumptions for any additional or sensitivity analysis | Methods (paragraph 4) |
|---|-------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------|
| 6 | Statistical methods: main analysis | Describe statistical methods and statistics used | |
|   | a) | Describe how quantitative variables were handled in the analyses (i.e., scale, units, model) | Table 1 |
|   | b) | Describe how genetic variants were handled in the analyses and, if applicable, how their weights were selected | Methods (paragraphs 4, 5) |
|   | c) | Describe the MR estimator (e.g. two-stage least squares, Wald ratio) and related statistics. Detail the included covariates and, in case of two-sample MR, whether the same covariate set was used for adjustment in the two samples | Methods (paragraphs 4, 5) |
|   | d) | Explain how missing data were addressed | N/A |
|   | e) | If applicable, indicate how multiple testing was addressed | Methods (paragraph 6) |
| 7 | Assessment of assumptions | Describe any methods or prior knowledge used to assess the assumptions or justify their validity | Methods (paragraphs 4) |
| 8 | Sensitivity analyses and additional analyses | Describe any sensitivity analyses or additional analyses performed (e.g. comparison of effect estimates from different approaches, independent replication, bias analytic techniques, validation of instruments, simulations) | Methods (paragraphs 4, 5) |
| 9 | Software and pre-registration | | |
|   | a) | Name statistical software and package(s), including version and settings used | Methods (paragraph 6) |
|   | b) | State whether the study protocol and details were pre-registered (as well as when and where) | N/A |
| 10 | Descriptive data | | |
|   | a) | Report the numbers of individuals at each stage of included studies and reasons for exclusion. Consider use of a flow-diagram | N/A |
### Main results

|   |   |
|---|---|
| a) | Report the associations between genetic variant and exposure, and between genetic variant and outcome, preferably on an interpretable scale |
| b) | Report MR estimates of the relationship between exposure and outcome, and the measures of uncertainty from the MR analysis, on an interpretable scale, such as odds ratio or relative risk per SD difference |
| c) | If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period |
| d) | Consider plots to visualize results (e.g. forest plot, scatterplot of associations between genetic variants and outcome versus between genetic variants and exposure) |

### Assessment of assumptions

|   |   |
|---|---|
| a) | Report the assessment of the validity of the assumptions |
| b) | Report any additional statistics (e.g., assessments of heterogeneity across genetic variants, such as $I^2$, Q statistic or E-value) |

### Sensitivity analyses and additional analyses

|   |   |
|---|---|
| a) | Report any sensitivity analyses to assess the robustness of the main results to violations of the assumptions |
|   |   |   |
|---|---|---|
| b) | Report results from other sensitivity analyses or additional analyses | Results (paragraphs 1, 2), Tables S8-12 |
| c) | Report any assessment of direction of causal relationship (e.g., bidirectional MR) | Results (paragraph 2), Table S12 |
| d) | When relevant, report and compare with estimates from non-MR analyses | N/A |
| e) | Consider additional plots to visualize results (e.g., leave-one-out analyses) | N/A |

### DISCUSSION

|   |   |   |
|---|---|---|
| 14 | **Key results** | Summarize key results with reference to study objectives | Discussion (paragraph 1) |
| 15 | **Limitations** | Discuss limitations of the study, taking into account the validity of the IV assumptions, other sources of potential bias, and imprecision. Discuss both direction and magnitude of any potential bias and any efforts to address them | Discussion (paragraph 5) |

### Interpretation

|   |   |   |
|---|---|---|
| a) | Meaning: Give a cautious overall interpretation of results in the context of their limitations and in comparison with other studies | Discussion (paragraphs 2, 3) |
| b) | Mechanism: Discuss underlying biological mechanisms that could drive a potential causal relationship between the investigated exposure and the outcome, and whether the gene-environment equivalence assumption is reasonable. Use causal language carefully, clarifying that IV estimates may provide causal effects only under certain assumptions | Discussion (paragraphs 3) |
| c) | Clinical relevance: Discuss whether the results have clinical or public policy relevance, and to what extent they inform effect sizes of possible interventions | Discussion (paragraph 4), Conclusion |

### Generalizability

|   |   |   |
|---|---|---|
| 17 | **Generalizability** | Discuss the generalizability of the study results (a) to other populations, (b) across other exposure periods/timings, and (c) across other levels of exposure | Discussion (paragraph 4) |

### OTHER INFORMATION

|   |   |   |
|---|---|---|
| 18 | **Funding** | Describe sources of funding and the role of funders in the present study and, if applicable, sources of funding for the databases and original study or studies on which the present study is based | N/A |
| 19 | **Data and data sharing** | Provide the data used to perform all analyses or report where and how the data can be accessed, and reference these sources in the article. Provide the statistical code needed to | Data availability section in Methods |
reproduce the results in the article, or report whether the code is publicly accessible and if so, where

| 20 | **Conflicts of Interest** | All authors should declare all potential conflicts of interest | Disclosure section |