**Supplement to ‘Investigating the causal nature of the relationship between subcortical brain volume and substance use.‘**

***Emma Logtenberg1\*, Martin F Overbeek1\*, Joëlle A Pasman2, Abdel Abdellaoui1, Maartje Luijten2, Ruth J van Holst1, Jacqueline M Vink2, Damiaan Denys1, Sarah E Medland3, Karin JH Verweij1, Jorien L Treur1***

***\*Shared first author***

*1. Department of Psychiatry, Amsterdam UMC, University of Amsterdam, the Netherlands*

*2. Behavioural Science Institute, Radboud University Nijmegen, the Netherlands*

*3. QIMR Berghofer Medical Research Instititute, Brisbane, QLD, Australia*

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**Guidelines followed for this study**

Please note that this is not a traditional observational / epidemiological study and therefore the traditional STROBE guidelines could not be used. No standard, validated guidelines are currently available for Mendelian randomization studies, but we did adhere to the stead, we adhere as much as possible to the STROBE-MR guidelines (Davey Smith et al., 2019). These are available online as a pre-print, and currently still under development (<https://peerj.com/preprints/27857/>).

**GWAS and meta-analysis procedures**

*GWAS subcortical brain volumes*

To perform the GWAS on subcortical brain volumes in UK Biobank participants, we first extracted UKB participants of European ancestry. Individuals of non-European ancestry, as determined by Principal Component Analysis in GCTA1, were excluded. We performed Single Nucleotide Polymorphism (SNP) quality control on unrelated Europeans (N=312,927) – using the Hapmap 3 reference panel – filtering out SNPs with MAF < 0.01, missingess > 0.05 and HWE p < 10-10, leaving 1,246,531 SNPs. After also adding related participants, we created a dataset of 1,246,531 common, QC-ed SNPs for 456,064 UK Biobank participants of European ancestry. For a more detailed description of our QC and data processing pipeline, see Abdellaoui et al., 20192.

Of the total, QC-ed UK Biobank dataset, 37,119 participants had MRI-imaging data on subcortical brain volumes available. We performed GWAS for seven subcortical brain regions; nucleus accumbens (UKB data fields 25023 (left) and 25024 (right)), amygdala (25021 (left) and 25022 (right)), caudate (25013 (left) and 25014 (right)), hippocampus (25019 (left) and 25020 (right)), pallidum (25017 (left) and 25018 (right)), putamen (25015 (left) and 25016 (right)), and thalamus (25011 (left) and 25012 (right)). For each brain region, we first summed the left and right volume measures (in mm3). For the GWAS, we ran a linear mixed model (LMM) GWAS using fastGWA3. As covariates, we added a sparse genetic relatedness matrix (GRM) which controls for cryptic relatedness as well as population stratification4 and the first 25 principle components (PCs), and we applied LDSC-intercept based genomic control (GC)2. Other covariates that were added were sex, age and total brain volume (UKB data field 25010).

After performing GWAS for subcortical brain structures in all participants, we also ran GWAS for subcortical brain structures stratified for smoking status (to allow Mendelian randomization analyses with cigarettes per day as the exposure variable, see main paper). All 37,119 UK Biobank participants described above had provided information on their lifetime smoking behaviour (UKB data field 20160), falling into the category of either ever smoker (n=14,564) or never smoker (n=22,555). We performed GWAS using the exact same approach described above, in these two groups separately.

*Meta-analysis GWAS samples subcortical brain volumes*

We performed a meta-analysis of the summary statistics from our GWAS analyses on UK Biobank participants (the complete sample described above) and the summary statistics from a previous ENIGMA GWAS5 for all brain regions. We performed this meta-analysis in METAL6, and it was based on sample size (instead of standard error) because there was measurement variance in the original samples. SNPs with a sample size below 1,000 were not included in the meta-analysis. Subsequently, the LD score regression intercept was calculated using LDSC7. Z-scores resulting from the meta-analysis were converted to betas using the formula $β=\frac{z-score}{\sqrt{N}\*\frac{1}{\sqrt{EAF(1-EAF)}}}$ (following procedures from Taylor et al., 20168). The corresponding standard error was computed using$ se=\frac{β}{z-score}$. We corrected the standard error for genomic inflation with the LD score regression intercept with $se\_{corrected}=\sqrt{se^{2}\*intercept}$ and computed corresponding p-values in R. To create genetic instruments for exposures, we clumped significant (5e-08 / 1e-05) hits using PLINK, using R2 <0.01 and 10,000 kb as our independence threshold.

*Meta-analysis GWAS samples substance use*

We performed a meta-analysis of the summary statistics from the single largest available GWAS on smoking and alcohol use9 (excl. UK-Biobank) and the summary statistics from 23andMe (requested from 23andMe, Inc) for smoking initiation, cigarettes per day, smoking cessation, and alcohol per week in METAL6, based on sample size. Subsequently, the LD score regression intercept was calculated using LDSC7. Z-scores resulting from the meta-analysis were converted to betas with similar procedures as described above. To create genetic instruments for exposures, we selected the SNPs (rs-numbers) that were reported to be significantly related with the traits in the original GSCAN paper9 and extracted their estimates (betas, standard errors and p-values) from our own meta-analysis.

**References**

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**Supplementary Figure 1.** Visual overview of all the datasets and (exposure and outcome) measures that were used in our Mendelian randomization analyses

**Scatterplots main findings**

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**Supplementary Figure 2a.** Scatterplot with IVW, weighted median, weighted mode, and MR-Egger results for cigarettes per day as the exposure and hippocampal volume as the outcome – *in smokers*

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**Supplementary Figure 2b.** Scatterplot with IVW, weighted median, weighted mode, and MR-Egger results for cigarettes per day as the exposure and hippocampal volume as the outcome – *in never smokers*

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**Supplementary Figure 3.** Scatterplot with IVW, weighted median, weighted mode, and MR-Egger results for alcohol dependence as the exposure and hippocampal volume as the outcome

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**Supplementary Figure 4.** Scatterplot with IVW, weighted median, weighted mode, and MR-Egger results for alcohol dependence as the exposure and amygdala volume as the outcome

**SNPs included in the genetic instruments**

Below is an overview of the SNPs that were included in the various genetic instruments used for Mendelian randomization analyses. Note that we selected SNPs which had initially, that is, in the original, full GWAS study, been reported as genome-wide associated (*p*<5E-08), to include in the instruments. In the case of smoking initiation, smoking cessation, cigarettes smoked per day and alcohol drinks per week, we excluded UK Biobank from the original GWAS study to prevent sample overlap (which causes bias in MR), and then took the effect estimates from meta-analyses of the remaining samples. This means that for some of the included SNPs for those exposures the significance level may not be *p*<5E-08.

***SNPs included for subcortical brain volumes as exposures:***

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Nucleus accumbens** | **Amygdala 5E-08** | **Amygdala 1E-05** | **Caudate** | **Hippocampus** | **Pallidum** | **Putamen** | **Thalamus** |
| 1 | rs1178320 | rs2347701 | rs10130307 | rs10439608 | rs10494303 | rs11196876 | rs10439608 | rs11827239 |
| 2 | rs11916858 | rs79340609 | rs10504722 | rs10800064 | rs11068205 | rs11639504 | rs10765500 | rs12146713 |
| 3 | rs2153960 |  | rs10850141 | rs10887759 | rs11245365 | rs11976703 | rs11196979 | rs16956241 |
| 4 | rs2608301 |  | rs10868746 | rs112510871 | rs11737577 | rs12445022 | rs11197861 | rs1789167 |
| 5 | rs321414 |  | rs111592563 | rs115053453 | rs12189145 | rs12703184 | rs11204421 | rs321348 |
| 6 | rs34255419 |  | rs11230889 | rs11669745 | rs12523793 | rs1291602 | rs11576262 | rs385301 |
| 7 | rs34312154 |  | rs116991338 | rs11676147 | rs13089287 | rs1328360 | rs11765218 | rs429358 |
| 8 | rs3789364 |  | rs11790097 | rs117407140 | rs2279681 | rs196798 | rs1187155 | rs45499402 |
| 9 | rs4148557 |  | rs118133428 | rs1187155 | rs2287509 | rs2231142 | rs12197456 | rs62288104 |
| 10 | rs62288106 |  | rs118182651 | rs12256016 | rs3111623 | rs28439696 | rs12457893 | rs7026018 |
| 11 | rs6658111 |  | rs12251016 | rs12749024 | rs429358 | rs2844510 | rs12806934 | rs75179968 |
| 12 | rs66717543 |  | rs12363897 | rs12952581 | rs58499557 | rs2974367 | rs13403450 | rs76928645 |
| 13 | rs7940646 |  | rs12586189 | rs13172721 | rs61921502 | rs34658078 | rs1346914 | rs806794 |
| 14 |  |  | rs12605433 | rs1347008 | rs62063437 | rs34736685 | rs1430332 |  |
| 15 |  |  | rs13100173 | rs1422191 | rs62374671 | rs4887023 | rs1544528 |  |
| 16 |  |  | rs13124981 | rs1743179 | rs6664992 | rs6037025 | rs2139559 |  |
| 17 |  |  | rs132867 | rs17764251 | rs6876370 | rs6058317 | rs2244479 |  |
| 18 |  |  | rs17150071 | rs17773700 | rs7040792 | rs62079082 | rs2710880 |  |
| 19 |  |  | rs202923 | rs208829 | rs77956314 | rs6723226 | rs3131633 |  |
| 20 |  |  | rs2336943 | rs2196448 |  | rs73186053 | rs314688 |  |
| 21 |  |  | rs2347701 | rs2817145 |  | rs76891681 | rs3815071 |  |
| 22 |  |  | rs28399637 | rs28366595 |  | rs7950543 | rs398652 |  |
| 23 |  |  | rs4586727 | rs28535536 |  | rs8014725 | rs4714854 |  |
| 24 |  |  | rs4797344 | rs2910056 |  | rs9426738 | rs4748999 |  |
| 25 |  |  | rs4818252 | rs2926043 |  | rs9922520 | rs4916907 |  |
| 26 |  |  | rs61353762 | rs34259020 |  |  | rs556151 |  |
| 27 |  |  | rs61921502 | rs34811474 |  |  | rs6138937 |  |
| 28 |  |  | rs62282701 | rs3820870 |  |  | rs62136802 |  |
| 29 |  |  | rs62359209 | rs4888010 |  |  | rs634368 |  |
| 30 |  |  | rs6658111 | rs4984975 |  |  | rs6428671 |  |
| 31 |  |  | rs6979446 | rs4985152 |  |  | rs7101609 |  |
| 32 |  |  | rs7014578 | rs55830072 |  |  | rs7734654 |  |
| 33 |  |  | rs707097 | rs56000151 |  |  | rs79787807 |  |
| 34 |  |  | rs7539819 | rs6135525 |  |  | rs8017172 |  |
| 35 |  |  | rs7604451 | rs62037364 |  |  | rs806794 |  |
| 36 |  |  | rs76436457 | rs62082217 |  |  | rs9838026 |  |
| 37 |  |  | rs79340609 | rs62365541 |  |  |  |  |
| 38 |  |  | rs80223973 | rs6483195 |  |  |  |  |
| 39 |  |  | rs895330 | rs6703416 |  |  |  |  |
| 40 |  |  | rs9853475 | rs7040561 |  |  |  |  |
| 41 |  |  |  | rs7084454 |  |  |  |  |
| 42 |  |  |  | rs7198936 |  |  |  |  |
| 43 |  |  |  | rs7245004 |  |  |  |  |
| 44 |  |  |  | rs72631228 |  |  |  |  |
| 45 |  |  |  | rs73144681 |  |  |  |  |
| 46 |  |  |  | rs75268943 |  |  |  |  |
| 47 |  |  |  | rs7747401 |  |  |  |  |
| 48 |  |  |  | rs7949956 |  |  |  |  |
| 49 |  |  |  | rs8017172 |  |  |  |  |
| 50 |  |  |  | rs888234 |  |  |  |  |
| 51 |  |  |  | rs9369275 |  |  |  |  |
| 52 |  |  |  | rs9903088 |  |  |  |  |
| 53 |  |  |  | rs994539 |  |  |  |  |

Note that if the number of SNPs differed slightly for different exposure-outcome combinations, we report the instrument with the largest amount of SNPs here.

***SNPs included for substance use behaviours as exposures:***

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Smoking initiation** | **Cigarettes per day** | **Alcohol dependence** | **Alcohol drinks per week** |
| 1 | rs10042827 | rs1024323 | rs113659074 | rs10004020 |
| 2 | rs1004787 | rs10454798 | rs1154445 | rs10028756 |
| 3 | rs10060196 | rs10519203 | rs1229863 | rs1004787 |
| 4 | rs1008078 | rs10742683 | rs1229984 | rs10085696 |
| 5 | rs1022376 | rs1115019 | rs34929220 | rs10236149 |
| 6 | rs1022528 | rs11264100 | rs3811802 | rs10438820 |
| 7 | rs10233018 | rs113001570 | rs4388946 | rs10506274 |
| 8 | rs10272990 | rs117824460 | rs6827898 | rs10750025 |
| 9 | rs10279261 | rs11846838 | rs79171978 | rs10753661 |
| 10 | rs1030015 | rs11940255 | rs894368 | rs10876188 |
| 11 | rs10446419 | rs12438181 |  | rs10978550 |
| 12 | rs10490159 | rs12924872 |  | rs11030084 |
| 13 | rs1050847 | rs13253502 |  | rs1123285 |
| 14 | rs1059490 | rs143200968 |  | rs113443718 |
| 15 | rs10698713 | rs146009840 |  | rs1154414 |
| 16 | rs10789369 | rs1592485 |  | rs11625650 |
| 17 | rs10805858 | rs182317 |  | rs11692435 |
| 18 | rs10853981 | rs2084533 |  | rs11739827 |
| 19 | rs10858334 | rs215600 |  | rs11940694 |
| 20 | rs10873871 | rs2236951 |  | rs12088813 |
| 21 | rs10885480 | rs2273500 |  | rs1217091 |
| 22 | rs10905461 | rs258321 |  | rs1229984 |
| 23 | rs10914684 | rs2741351 |  | rs12499107 |
| 24 | rs10935779 | rs28681284 |  | rs1260326 |
| 25 | rs10945141 | rs28813180 |  | rs12655091 |
| 26 | rs10953957 | rs3025383 |  | rs12795042 |
| 27 | rs10966092 | rs34973462 |  | rs12907323 |
| 28 | rs11057005 | rs4144686 |  | rs13024996 |
| 29 | rs1106363 | rs4236926 |  | rs13032049 |
| 30 | rs11076962 | rs4485470 |  | rs13066454 |
| 31 | rs11078713 | rs56113850 |  | rs13094887 |
| 32 | rs1108130 | rs59208569 |  | rs13107325 |
| 33 | rs1109480 | rs6078373 |  | rs13250583 |
| 34 | rs11162019 | rs62447179 |  | rs13383034 |
| 35 | rs1116690 | rs632811 |  | rs17029090 |
| 36 | rs11191269 | rs699165 |  | rs1713676 |
| 37 | rs11192347 | rs7125588 |  | rs17177078 |
| 38 | rs11258417 | rs72740955 |  | rs17665139 |
| 39 | rs1126757 | rs7281463 |  | rs2011092 |
| 40 | rs112725451 | rs73229090 |  | rs2165670 |
| 41 | rs113230003 | rs7431710 |  | rs2178197 |
| 42 | rs1139897 | rs75596189 |  | rs2180870 |
| 43 | rs114976176 | rs7599488 |  | rs2472297 |
| 44 | rs1150668 | rs7766641 |  | rs2764771 |
| 45 | rs11587399 | rs78408772 |  | rs281379 |
| 46 | rs11594623 | rs790564 |  | rs2854334 |
| 47 | rs11611651 | rs7951365 |  | rs28601761 |
| 48 | rs11642231 | rs8040868 |  | rs28680958 |
| 49 | rs11651955 | rs8192726 |  | rs28929474 |
| 50 | rs11678980 |  |  | rs35034355 |
| 51 | rs11692435 |  |  | rs35538052 |
| 52 | rs11713899 |  |  | rs36052336 |
| 53 | rs1173461 |  |  | rs3748034 |
| 54 | rs117657830 |  |  | rs378421 |
| 55 | rs11766326 |  |  | rs3803800 |
| 56 | rs11768481 |  |  | rs3809162 |
| 57 | rs117734003 |  |  | rs4092465 |
| 58 | rs11780471 |  |  | rs4501255 |
| 59 | rs11783093 |  |  | rs4548913 |
| 60 | rs11791671 |  |  | rs4690727 |
| 61 | rs118202 |  |  | rs4699791 |
| 62 | rs11872397 |  |  | rs4815364 |
| 63 | rs1187820 |  |  | rs4842786 |
| 64 | rs11889814 |  |  | rs4916723 |
| 65 | rs11956866 |  |  | rs4938230 |
| 66 | rs12022778 |  |  | rs500321 |
| 67 | rs12027999 |  |  | rs5024204 |
| 68 | rs12053870 |  |  | rs55872084 |
| 69 | rs12130857 |  |  | rs55932213 |
| 70 | rs12195240 |  |  | rs56030824 |
| 71 | rs12244388 |  |  | rs56337305 |
| 72 | rs12474587 |  |  | rs58107686 |
| 73 | rs12517438 |  |  | rs60654199 |
| 74 | rs12530388 |  |  | rs62044525 |
| 75 | rs12563365 |  |  | rs62250685 |
| 76 | rs12633090 |  |  | rs6460047 |
| 77 | rs12642744 |  |  | rs6787172 |
| 78 | rs12714017 |  |  | rs682011 |
| 79 | rs12739243 |  |  | rs6951574 |
| 80 | rs12740789 |  |  | rs705687 |
| 81 | rs12755632 |  |  | rs7074871 |
| 82 | rs12855717 |  |  | rs7185555 |
| 83 | rs12878369 |  |  | rs72859280 |
| 84 | rs12918191 |  |  | rs77165542 |
| 85 | rs1291821 |  |  | rs79139602 |
| 86 | rs13007361 |  |  | rs7950166 |
| 87 | rs13066050 |  |  | rs79616692 |
| 88 | rs13109980 |  |  | rs823114 |
| 89 | rs13110073 |  |  | rs828867 |
| 90 | rs13261666 |  |  | rs9607814 |
| 91 | rs13319205 |  |  | rs9838144 |
| 92 | rs13392222 |  |  | rs9950000 |
| 93 | rs13437771 |  |  |  |
| 94 | rs1373178 |  |  |  |
| 95 | rs1381287 |  |  |  |
| 96 | rs1381775 |  |  |  |
| 97 | rs1385108 |  |  |  |
| 98 | rs1389171 |  |  |  |
| 99 | rs13906 |  |  |  |
| 100 | rs139896 |  |  |  |
| 101 | rs1413119 |  |  |  |
| 102 | rs1435479 |  |  |  |
| 103 | rs1435672 |  |  |  |
| 104 | rs1435741 |  |  |  |
| 105 | rs1445649 |  |  |  |
| 106 | rs1449012 |  |  |  |
| 107 | rs147052174 |  |  |  |
| 108 | rs1514176 |  |  |  |
| 109 | rs1518393 |  |  |  |
| 110 | rs1549979 |  |  |  |
| 111 | rs1555445 |  |  |  |
| 112 | rs1561112 |  |  |  |
| 113 | rs1565735 |  |  |  |
| 114 | rs160631 |  |  |  |
| 115 | rs1632941 |  |  |  |
| 116 | rs16826827 |  |  |  |
| 117 | rs16828799 |  |  |  |
| 118 | rs1713676 |  |  |  |
| 119 | rs1714521 |  |  |  |
| 120 | rs17165769 |  |  |  |
| 121 | rs17197663 |  |  |  |
| 122 | rs1722666 |  |  |  |
| 123 | rs17229285 |  |  |  |
| 124 | rs1733760 |  |  |  |
| 125 | rs1737329 |  |  |  |
| 126 | rs1759433 |  |  |  |
| 127 | rs17616642 |  |  |  |
| 128 | rs17692129 |  |  |  |
| 129 | rs1772572 |  |  |  |
| 130 | rs1799068 |  |  |  |
| 131 | rs1811739 |  |  |  |
| 132 | rs181508347 |  |  |  |
| 133 | rs1834306 |  |  |  |
| 134 | rs1863161 |  |  |  |
| 135 | rs1889571 |  |  |  |
| 136 | rs1901477 |  |  |  |
| 137 | rs1910236 |  |  |  |
| 138 | rs1927901 |  |  |  |
| 139 | rs1930371 |  |  |  |
| 140 | rs1935571 |  |  |  |
| 141 | rs1944689 |  |  |  |
| 142 | rs2010921 |  |  |  |
| 143 | rs2028269 |  |  |  |
| 144 | rs2063976 |  |  |  |
| 145 | rs2155646 |  |  |  |
| 146 | rs2173019 |  |  |  |
| 147 | rs2196356 |  |  |  |
| 148 | rs221988 |  |  |  |
| 149 | rs2276825 |  |  |  |
| 150 | rs2279829 |  |  |  |
| 151 | rs2289791 |  |  |  |
| 152 | rs2306866 |  |  |  |
| 153 | rs2319545 |  |  |  |
| 154 | rs2344976 |  |  |  |
| 155 | rs2378662 |  |  |  |
| 156 | rs238896 |  |  |  |
| 157 | rs2526390 |  |  |  |
| 158 | rs2539706 |  |  |  |
| 159 | rs2587507 |  |  |  |
| 160 | rs2637869 |  |  |  |
| 161 | rs2710634 |  |  |  |
| 162 | rs2734390 |  |  |  |
| 163 | rs2796793 |  |  |  |
| 164 | rs281296 |  |  |  |
| 165 | rs28408682 |  |  |  |
| 166 | rs28441558 |  |  |  |
| 167 | rs28717373 |  |  |  |
| 168 | rs2901785 |  |  |  |
| 169 | rs290601 |  |  |  |
| 170 | rs2925128 |  |  |  |
| 171 | rs2938134 |  |  |  |
| 172 | rs2939756 |  |  |  |
| 173 | rs2952251 |  |  |  |
| 174 | rs2959084 |  |  |  |
| 175 | rs301807 |  |  |  |
| 176 | rs3098272 |  |  |  |
| 177 | rs3115418 |  |  |  |
| 178 | rs3172494 |  |  |  |
| 179 | rs3218116 |  |  |  |
| 180 | rs329124 |  |  |  |
| 181 | rs34342129 |  |  |  |
| 182 | rs34399632 |  |  |  |
| 183 | rs34553878 |  |  |  |
| 184 | rs34940743 |  |  |  |
| 185 | rs34970111 |  |  |  |
| 186 | rs35375873 |  |  |  |
| 187 | rs35656245 |  |  |  |
| 188 | rs357304 |  |  |  |
| 189 | rs359247 |  |  |  |
| 190 | rs359431 |  |  |  |
| 191 | rs3740977 |  |  |  |
| 192 | rs3764351 |  |  |  |
| 193 | rs3800227 |  |  |  |
| 194 | rs3810496 |  |  |  |
| 195 | rs3811038 |  |  |  |
| 196 | rs3820277 |  |  |  |
| 197 | rs3843905 |  |  |  |
| 198 | rs3847244 |  |  |  |
| 199 | rs3909281 |  |  |  |
| 200 | rs3934797 |  |  |  |
| 201 | rs4044321 |  |  |  |
| 202 | rs42417 |  |  |  |
| 203 | rs4264267 |  |  |  |
| 204 | rs4275621 |  |  |  |
| 205 | rs4310804 |  |  |  |
| 206 | rs4476253 |  |  |  |
| 207 | rs4543050 |  |  |  |
| 208 | rs45444697 |  |  |  |
| 209 | rs4674916 |  |  |  |
| 210 | rs4674993 |  |  |  |
| 211 | rs4727189 |  |  |  |
| 212 | rs4752018 |  |  |  |
| 213 | rs4759229 |  |  |  |
| 214 | rs4785187 |  |  |  |
| 215 | rs4788676 |  |  |  |
| 216 | rs4790874 |  |  |  |
| 217 | rs4818005 |  |  |  |
| 218 | rs4822102 |  |  |  |
| 219 | rs4837631 |  |  |  |
| 220 | rs4877285 |  |  |  |
| 221 | rs4886207 |  |  |  |
| 222 | rs4912332 |  |  |  |
| 223 | rs540860 |  |  |  |
| 224 | rs55786907 |  |  |  |
| 225 | rs55913542 |  |  |  |
| 226 | rs55944129 |  |  |  |
| 227 | rs56208390 |  |  |  |
| 228 | rs56367474 |  |  |  |
| 229 | rs56902655 |  |  |  |
| 230 | rs57153235 |  |  |  |
| 231 | rs58400863 |  |  |  |
| 232 | rs586699 |  |  |  |
| 233 | rs59537158 |  |  |  |
| 234 | rs6011779 |  |  |  |
| 235 | rs6050446 |  |  |  |
| 236 | rs6058782 |  |  |  |
| 237 | rs6073075 |  |  |  |
| 238 | rs60833441 |  |  |  |
| 239 | rs61533748 |  |  |  |
| 240 | rs61884449 |  |  |  |
| 241 | rs61886926 |  |  |  |
| 242 | rs619087 |  |  |  |
| 243 | rs61959481 |  |  |  |
| 244 | rs62007780 |  |  |  |
| 245 | rs62052916 |  |  |  |
| 246 | rs62098013 |  |  |  |
| 247 | rs62106258 |  |  |  |
| 248 | rs62137126 |  |  |  |
| 249 | rs62180324 |  |  |  |
| 250 | rs62193862 |  |  |  |
| 251 | rs62246017 |  |  |  |
| 252 | rs62340589 |  |  |  |
| 253 | rs62618693 |  |  |  |
| 254 | rs6265 |  |  |  |
| 255 | rs6437769 |  |  |  |
| 256 | rs6438436 |  |  |  |
| 257 | rs644740 |  |  |  |
| 258 | rs6452785 |  |  |  |
| 259 | rs6497840 |  |  |  |
| 260 | rs6568832 |  |  |  |
| 261 | rs67050670 |  |  |  |
| 262 | rs6730325 |  |  |  |
| 263 | rs6731872 |  |  |  |
| 264 | rs6750107 |  |  |  |
| 265 | rs6750529 |  |  |  |
| 266 | rs6756212 |  |  |  |
| 267 | rs67777803 |  |  |  |
| 268 | rs6782116 |  |  |  |
| 269 | rs6874731 |  |  |  |
| 270 | rs6890961 |  |  |  |
| 271 | rs6936160 |  |  |  |
| 272 | rs6948707 |  |  |  |
| 273 | rs6968380 |  |  |  |
| 274 | rs6986430 |  |  |  |
| 275 | rs6993429 |  |  |  |
| 276 | rs7024924 |  |  |  |
| 277 | rs7026534 |  |  |  |
| 278 | rs7072776 |  |  |  |
| 279 | rs7134009 |  |  |  |
| 280 | rs71367544 |  |  |  |
| 281 | rs71592686 |  |  |  |
| 282 | rs71602617 |  |  |  |
| 283 | rs7188873 |  |  |  |
| 284 | rs7192140 |  |  |  |
| 285 | rs72780746 |  |  |  |
| 286 | rs72789626 |  |  |  |
| 287 | rs72790288 |  |  |  |
| 288 | rs72898831 |  |  |  |
| 289 | rs72938304 |  |  |  |
| 290 | rs73008357 |  |  |  |
| 291 | rs7333559 |  |  |  |
| 292 | rs73831818 |  |  |  |
| 293 | rs74697736 |  |  |  |
| 294 | rs748832 |  |  |  |
| 295 | rs7505855 |  |  |  |
| 296 | rs75210106 |  |  |  |
| 297 | rs75674569 |  |  |  |
| 298 | rs75919030 |  |  |  |
| 299 | rs7600835 |  |  |  |
| 300 | rs7631379 |  |  |  |
| 301 | rs7640107 |  |  |  |
| 302 | rs76460663 |  |  |  |
| 303 | rs7657022 |  |  |  |
| 304 | rs76608582 |  |  |  |
| 305 | rs76841737 |  |  |  |
| 306 | rs7696257 |  |  |  |
| 307 | rs77215829 |  |  |  |
| 308 | rs77283305 |  |  |  |
| 309 | rs7743165 |  |  |  |
| 310 | rs7802996 |  |  |  |
| 311 | rs7809303 |  |  |  |
| 312 | rs7836565 |  |  |  |
| 313 | rs7867822 |  |  |  |
| 314 | rs7901883 |  |  |  |
| 315 | rs7929518 |  |  |  |
| 316 | rs7943721 |  |  |  |
| 317 | rs79476395 |  |  |  |
| 318 | rs7969559 |  |  |  |
| 319 | rs8005334 |  |  |  |
| 320 | rs80054503 |  |  |  |
| 321 | rs8027457 |  |  |  |
| 322 | rs8050598 |  |  |  |
| 323 | rs8083764 |  |  |  |
| 324 | rs8096225 |  |  |  |
| 325 | rs8103660 |  |  |  |
| 326 | rs876793 |  |  |  |
| 327 | rs910912 |  |  |  |
| 328 | rs925524 |  |  |  |
| 329 | rs9288999 |  |  |  |
| 330 | rs9302604 |  |  |  |
| 331 | rs9323328 |  |  |  |
| 332 | rs9331343 |  |  |  |
| 333 | rs951740 |  |  |  |
| 334 | rs9538162 |  |  |  |
| 335 | rs9540731 |  |  |  |
| 336 | rs9545155 |  |  |  |
| 337 | rs9627272 |  |  |  |
| 338 | rs963354 |  |  |  |
| 339 | rs9787523 |  |  |  |
| 340 | rs9826984 |  |  |  |
| 341 | rs9841807 |  |  |  |
| 342 | rs9850597 |  |  |  |
| 343 | rs9922607 |  |  |  |
| 344 | rs9936784 |  |  |  |
| 345 | rs9941217 |  |  |  |
| 346 | rs9987376 |  |  |  |

Note that if the number of SNPs differed slightly for different exposure-outcome combinations, we report the instrument with the largest amount of SNPs here.