Supplementary Table 1. Publicly available GWAS summary statistics that used in the current study.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Trait name** | **Source** | **Sample size** | **SNP number** | **Ethnicity** | **URL** |
| Major depression | Meta-analysis | 191,005 | 13,554,551 | European | https://www.med.unc.edu/pgc/results-and-downloads/mdd/ |
| Current tobacco smoking | UKBB, Ben Neale | 337,030 | 10,894,597 | European | http://ldsc.broadinstitute.org/ |
| Past tobacco smoking | UKBB, Ben Neale | 310,749 | 10,894,597 | European | http://ldsc.broadinstitute.org/ |

Supplementary Table 2. Genomic regions where the presence of variants that influence both MDD and Current smoking.

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Chr | Start(bp) | Stop(bp) | Top MDD SNP | MDD SNP P | Top SMK SNP | SMK SNP P | PP | Gene Context |
| Hypothesis 2 | ***5*** | ***166847740*** | ***168524897*** | ***rs10039321*** | 6.93E-06 | rs1549214 | 5.62E-11 | 0.990 | TENM2 |
|  | 1 | 212842330 | 214577612 | rs12125521 | 2.24E-05 | rs12126101 | 8.05E-07 | 0.984 | SMYD2 |
|  | 2 | 21051529 | 23341246 | rs61533748 | 1.13E-05 | rs61533748 | 2.96E-06 | 0.975 | AC068490.2 |
|  | 15 | 46619479 | 48135629 | rs1025145 | 1.03E-05 | rs8033799 | 3.90E-08 | 0.957 | CTD-2050N2.1 |
|  | ***7*** | ***116780383*** | ***118351333*** | ***rs1548461*** | 3.09E-06 | rs7807019 | 1.03E-08 | 0.948 | CTTNBP2 |
|  | 18 | 35075250 | 36365021 | rs12959642 | 1.71E-04 | rs1557341 | 7.75E-07 | 0.939 | CELF4 |
|  | 1 | 96151539 | 97885200 | rs161678 | 6.90E-05 | rs1931263 | 1.50E-05 | 0.932 | RP5-898J17.1/ RP11-286B14.1 |
|  | 1 | 71687454 | 74326484 | rs12129573 | 5.45E-09 | rs11209756 | 2.80E-05 | 0.931 | RP4-598G3.1/ ZRANB2-AS2 |
| Hypothesis 3 | ***10*** | ***104380686*** | ***106694980*** | ***rs11192230*** | 5.05E-06 | rs3736922 | 1.05E-07 | 0.920 | SORCS3/ NT5C2 |
|  | 6 | 25684587 | 26762667 | rs9379871 | 1.24E-08 | rs6935954 | 3.55E-07 | 0.940 | BTN3A2/ HIST1H2BH |
|  | 14 | 103012102 | 105001680 | rs11350625 | 1.17E-07 | rs56206644 | 1.42E-07 | 0.961 | TRMT61A/ C14orf2 |
|  | 5 | 90423162 | 91840153 | rs72777075 | 1.55E-06 | rs17640214 | 5.09E-06 | 0.960 | RP11-348J24.2/ARRDC3 |

Abbreviations: MDD, major depression disorder; SMK, smoking; PP, posterior probability. For each region, the chromosome, start and stop position in basepairs (bp) and the most strongly associated SNP for MDD and smoking are given. Chromosome coordinates are in hg19. Hypothesis 2 = one causal variant; Hypothesis 3 = two distinct causal variants.

Supplementary Table 3. Genomic regions where the presence of variants that influence both MDD and former smoking.

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Chr | Start(bp) | Stop(bp) | Top MDD SNP | MDD SNP P | Top SMK SNP | SMK SNP P | PP | Gene Context |
| Hypothesis 2 | 6 | 28917832 | 29737871 | rs71550120 | 7.77E-10 | rs1555244 | 1.34E-06 | 0.997 | OR5V1 |
|  | ***5*** | ***166847740*** | ***168524897*** | ***rs10039321*** | 6.93E-06 | rs986391 | 1.37E-09 | 0.989 | TENM2 |
|  | 6 | 30798252 | 31569782 | rs147854926 | 1.24E-09 | rs2244546 | 1.18E-06 | 0.962 | DPCR1/HCP5 |
|  | ***7*** | ***116780383*** | ***118351333*** | ***rs1548461*** | 3.09E-06 | rs10233018 | 1.28E-07 | 0.959 | CTTNBP2 |
|  | 20 | 44839203 | 47199240 | chr20\_45824587\_I | 3.60E-06 | rs8121471 | 1.10E-04 | 0.935 | ZMYND8 |
|  | 6 | 26798640 | 28017250 | rs6934329 | 1.42E-09 | rs200956 | 1.40E-06 | 0.926 | MIR3143/HIST1H3I |
|  | 15 | 46619479 | 48135629 | rs1025145 | 1.03E-05 | rs8034783 | 5.96E-09 | 0.925 | CTD-2050N2.1/ SEMA6D |
|  | ***10*** | ***85458703*** | ***87937400*** | ***rs77198573*** | 1.71E-05 | rs7907900 | 2.70E-06 | 0.916 | GRID1 |
|  | 13 | 53339622 | 54682393 | rs12552 | 3.90E-07 | rs7326087 | 1.46E-05 | 0.912 | OLFM4/Metazoa\_SRP |
|  | 6 | 25684587 | 26762667 | rs9379871 | 1.24E-08 | rs9379873 | 3.22E-06 | 0.908 | BTN3A2/ BTN3A1 |
| Hypothesis 3 | 6 | 28018353 | 28917057 | rs6905391 | 3.47E-11 | rs9468350 | 3.33E-08 | 0.933 | PGBD1/ ZKSCAN3 |
|  | 14 | 103012102 | 105001680 | rs11350625 | 1.17E-07 | rs34161718 | 1.42E-05 | 0.920 | TRMT61A/ KIF26A |
|  | 5 | 90423162 | 91840153 | rs72777075 | 1.55E-06 | rs1863946 | 2.90E-05 | 0.930 | RP11-348J24.2 |
|  | 5 | 103321005 | 104848525 | rs76025409 | 2.32E-11 | rs12186738 | 4.20E-08 | 0.972 | RP11-6N13.1 |
|  | ***10*** | ***104380686*** | ***106694980*** | ***rs11192230*** | 5.05E-06 | rs12244388 | 3.19E-13 | 0.920 | SORCS3/ AS3MT |
|  | ***20*** | ***47200367*** | ***49239082*** | ***rs4811079*** | 6.56E-08 | rs62212763 | 5.98E-06 | 0.963 | PTPN1/ DDX27 |
|  | 5 | 43983499 | 50163085 | rs78955704 | 1.42E-07 | rs13180635 | 1.35E-06 | 0.953 | HCN1 |

Abbreviations: MDD, major depression disorder; SMK, smoking; PP, posterior probability. For each region, the chromosome, start and stop position in basepairs (bp) and the most strongly associated SNP for MDD and smoking are given. Chromosome coordinates are in hg19. Hypothesis 2 = one causal variant; Hypothesis 3 = two distinct causal variants.

Supplementary Table 4. A list of 43 prioritized common genes.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| AKT1 | GABRB3 | MAPK8 | CXCL12 | LDLRAP1 | CD2AP | MAP3K7 | FGF8 |
| GDF2 | GRM3 | GABRA5 | TTR | DSG2 | KCNIP2 | ABCB1 | SRI |
| HADHA | CYP17A1 | HADHB | TUBB2A | RAB10 | GDF10 | RUNX2 | STMN1 |
| ABCB4 | PLA2G7 | KCNQ5 | JAG2 | TUBB2B | GABRG3 | NR2F2 | ERCC5 |
| SOX11 | NCDN | OTOF | RIMS1 | DLGAP3 | SIVA1 | PACS2 | FBXW4 |
| FAM21B | MGEA5 | SEPN1 |  |  |  |  |  |

|  |  |  |  |
| --- | --- | --- | --- |
| Supplementary Table 5. Tests of Heterogeneity in the SNP-exposure association | | | |
|  | Q | df | P-value |
| Current tob smk > Depression | 86.73 | 23 | < 0.0001 |
| Past tob smk > Depression | 173.8 | 84 | < 0.0001 |
| Depression > Current tob smk | 1858.02 | 360 | < 0.0001 |
| Depression > Past tob smk | 5912.7 | 360 | < 0.0001 |

Supplementary Table 6. MR Egger regression test for directional pleiotropy

|  |  |  |
| --- | --- | --- |
| Outcome | Intercept | P-value |
| Current tob smk > Depression | -0.014 | 0.349 |
| Past tob smk > Depression | 0.007 | 0.238 |
| Depression > Current tob smk | -0.001 | 0.422 |
| Depression > Past tob smk | 0.011 | 0.134 |