**Supplementary Materials**

**Contents**

|  |  |
| --- | --- |
| Table S1. Rucker’s Q Tests of heterogeneity in the SNP effects | Page 2 |
| Table S2. MR Egger intercept test of directional pleiotropy | Page 3 |
| Table S3. Summary level MR results after Steiger filtering | Page 4 |
| Table S4. Association of lifetime smoking score and polygenic risk score on the baseline confounders | Page 5 |
| Table S5. Baseline characteristics of 335,918 participants in the UK Biobank according to smoking status and number of rs1051730 effect alleles | Page 6 |
| Table S6: Mendelian randomisation analyses using summary level data of smoking initiation and risk-taking. | Page 7 |
| Table S7. Mendelian randomisation analyses using summary level data of smoking initiation on suicide attempts with smoking initiation SNPs restricted to independence at 10000kb and r2<0.001. | Page 8 |
|  |  |
|  |  |

**Table S1. Rucker’s Q Tests of heterogeneity in the SNP effects**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Exposure** | **Outcome** | **Method** | **Q** | **df** | **P-value** |
| Smoking initiation (378 SNPs) | Suicide attempts | IVW | 325.35 | 320 | 0.41 |
|  |  | MR Egger | 324.87 | 319 | 0.40 |
|  |  | Q’ | 0.48 | 1 | 0.50 |
| Smoking initiation (206 SNPs) | Suicide attempts | IVW | 182.76 | 179 | 0.41 |
|  |  | MR Egger | 182.26 | 178 | 0.40 |
|  |  | Q’ | 0.49 | 1 | 0.48 |
| Smoking initiation  | Risk-taking | IVW | 1093.70 | 346 | <0.001 |
|  |  | MR Egger | 1043.79 | 345 | <0.001 |
|  |  | Q’ | 49.91 | 1 | <0.001 |
| Risk-taking | Smoking initiation | IVW | 192.75 | 100 | <0.001 |
|  |  | MR Egger | 191.28 | 99 | <0.001 |
|  |  | Q’ | 1.48 | 1 | 0.22 |

**Table S2. MR Egger intercept test of directional pleiotropy**

|  |  |  |  |
| --- | --- | --- | --- |
| **Exposure** | **Outcome** | **Intercept (95% CI)** | **P-value** |
| Smoking initiation (378 SNPs) | Suicide attempts | 0.003 (-0.006, 0.013) | 0.494 |
| Smoking initiation (206 SNPs) | Suicide attempts | 0.005 (-0.009, 0.019) | 0.489 |
| Smoking initiation | Risk-taking | 0.002 (0.001, 0.004) | <0.001 |
| Risk-taking | Smoking initiation | -0.002 (-0.005, -0.002) | 0.384 |

**Table S3. Summary level MR results after Steiger filtering**

|  |  |  |
| --- | --- | --- |
| **Exposure** | **Outcome** | **N SNP** |
| **Smoking initiation (378 SNPs)**  | **Suicide attempt** | 153/367 (42%) |
| **Smoking initiation (206 SNPs)**  | **Suicide attempt** | 78/180 (43%) |
| **Smoking initiation** | **Risk-taking** | 304/347 (88%) |
| **Risk-taking** | **Smoking initiation** | 118/123 (96%) |

**Table S4. Association of lifetime smoking score and polygenic risk score on the baseline confounder**

|  |  |  |
| --- | --- | --- |
|  | **Observed association with lifetime smoking** | **Genetic association with lifetime smoking polygenic score** |
|  | **Test statistic** | **p-value** | **Test statistic** | **p-value** |
| **Sex** | t = -29.52 (1, 154080) | P<0.001 | t = 0.96 (1, 164010) | P=0.338 |
| **Age** | $β$ = 0.002 (SE = 0.0002) | P<0.001 | $β$ = -0.0006 (SE = 0.0003) | P=0.035 |
| **Socio-economic position** | $β$ = 0.046 (SE = 0.0006) | P<0.001 | $β$ = 0.005 (SE = 0.0008) | P<0.001 |
| **Educational attainment** | $β$ = -0.164 (SE = 0.002) | P<0.001 | $β$ = -0.028 (SE = 0.004) | P<0.001 |
| **Alcohol consumption** | $β$ = -0.004 (SE = 0.001) | P=0.011 | $β$ = -0.005 (SE = 0.002) | P=0.017 |

# **Table S5: Baseline characteristics of 335,918 participants in the UK Biobank according to smoking status and number of rs1051730 effect alleles**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | Never smokers |  |  |  | Ever smokers |  |  |
|  |  | **0** | **1** | **2** | **p-value** |  | **0** | **1** | **2** | **p-value** |
| Study sample (n) |  | 82,130 | 81,580 | 20,334 |  |  | 68,562 | 66,953 | 16,307 |  |
| Cigarettes per day (mean) |  |  |  |  |  | 14.88 | 15.89 | 16.72 | <0.001 |
|  Missing (n) |  |  |  |  |  |  | 3807 | 3371 | 739 |  |
| Smoking status (%)a |  |  |  |  |  |  |  |  |  |  |
|  Current |  |  |  |  |  |  | 22 | 22 | 22 |  |
|  Former |  |  |  |  |  |  | 78 | 78 | 78 | 0.057 |
| Men (%) |  | 42 | 41 | 41 | 0.121 |  | 52 | 52 | 52 | 0.539 |
| Age (mean) |  | 56.1 | 56.2 | 56.2 | 0.092 |  | 57.8 | 57.7 | 57.6 | 0.002 |
| Education (%) |  |  |  |  |  |  |  |  |  |
|  Primary |  | 14 | 14 | 14 |  |  | 21 | 21 | 20 |  |
|  Secondary |  | 51 | 50 | 50 |  |  | 51 | 52 | 52 |  |
|  Tertiary |  | 36 | 36 | 36 | 0.776 |  | 27 | 27 | 28 | 0.020 |
|  Missing (n) |  | 683 | 704 | 202 |  |  | 634 | 685 | 133 |  |
| Alcohol intake (%) |  |  |  |  |  |  |  |  |  |  |
|  Never |  | 7 | 7 | 7 |  |  | 5 | 6 | 6 |  |
|  Special occasions |  | 11 | 12 | 11 |  |  | 9 | 9 | 9 |  |
|  Monthly |  | 12 | 13 | 12 |  |  | 9 | 10 | 10 |  |
|  Weekly |  | 53 | 52 | 53 |  |  | 49 | 48 | 47 |  |
|  Daily/almost daily |  | 16 | 16 | 16 | 0.161 |  | 28 | 28 | 28 | 0.074 |
|  Missing (n) |  | 33 | 47 | 16 |  |  | 47 | 55 | 13 |  |
| Suicidal Ideation (%) |  | 3.6 | 3.6 | 3.1 | 0.068 |  | 4.9 | 4.7 | 5.3 | 0.242 |
|  Missing (N) |  | 53,810 | 53,424 | 13,250 |  |  | 47,941 | 46,651 | 11,352 |  |
| Attempted suicide (%) |  | 1.6 | 1.6 | 1.4 | 0.596 |  | 3.2 | 3.0 | 2.6 | 0.086 |
|  Missing (N) |  | 53,719 | 53,327 | 13,237 |  |  | 47,843 | 46,574 | 11,341 |  |

**Table S6. Mendelian randomisation analyses using summary level data of smoking initiation and risk-taking.**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Exposure** | **Method** | **N SNP** | **Beta (95% CI)** | **P-value** |
| **Smoking initiation** | Inverse-Variance Weighted | 347 | 0.284 (0.228, 0.341) | <0.001 |
|  | Weighted Median | 347 | 0.205 (0.149, 0.261) | <0.001 |
|  | Weighted Mode | 347 | 0.210 (0.061, 0.360) | 0.006 |
|  | MR RAPS | 347 | 0.303 (0.240, 0.365) | <0.001 |
| **Risk-taking** | Inverse-Variance Weighted | 101 | 0.152 (0.081, 0.225) | <0.001 |
|  | Weighted Median | 101 | 0.172 (0.092, 0.252) | <0.001 |
|  | Weighted Mode | 101 | 0.192 (0.017, 0.366) | 0.03 |
|  | MR RAPS | 101 | 0.176 (0.103, 0.248) | <0.001 |

**Table S7. Mendelian randomisation analyses using summary level data of smoking initiation on suicide attempts with smoking initiation SNPs restricted to independence at 10000kb and r2<0.001.**

|  |  |  |  |
| --- | --- | --- | --- |
| **Method** | **N SNP** | **OR (95% CI)** | **P-value** |
| Inverse-Variance Weighted | 180 | 2.84 (1.62, 5.00) | <0.001 |
| Weighted Median | 180 | 2.68 (1.14, 6.30) | 0.02 |
| Weighted Mode | 180 | 3.24 (0.48, 22.00) | 0.23 |
| MR RAPS | 180 | 3.30 (1.69, 6.43) | <0.001 |