

Supplementary Table 1 Look up of genome-wide significant SNPs for risk-taking in UK Biobank for 'Ever smoking'

| SNP | Chr | Base pair | Effect allele | Other allele | Effect allele frequency | Info | Beta | SE | P-val |
|------------|-----|-----------|---------------|--------------|-------------------------|----------|------------|----------|----------|
| rs6762267 | 3 | 85513115 | C | A | 0.381262 | 0.998347 | 0.0094076 | 0.001051 | 3.40E-19 |
| rs727644 | 7 | 114109349 | G | A | 0.595406 | 0.992547 | 0.0013696 | 0.001045 | 1.90E-01 |
| rs62519827 | 8 | 65481947 | T | C | 0.887242 | 1 | 0.0011878 | 0.001616 | 4.60E-01 |
| rs9841382 | 3 | 181408124 | C | T | 0.144996 | 0.992706 | 0.0059097 | 0.001453 | 4.70E-05 |
| rs58560561 | 1 | 243537729 | G | T | 0.651824 | 0.985229 | -8.50E-05 | 0.001078 | 9.40E-01 |
| rs992493 | 4 | 106180264 | T | C | 0.188643 | 0.99873 | 0.0049033 | 0.001307 | 1.80E-04 |
| rs6923811 | 6 | 27289776 | T | C | 0.678951 | 1 | 0.004272 | 0.001097 | 9.90E-05 |
| rs7817124 | 8 | 81404008 | C | G | 0.239069 | 0.997976 | 0.0022905 | 0.001199 | 5.60E-02 |
| rs4801000 | 18 | 53456943 | G | A | 0.33539 | 0.997479 | 0.0023003 | 0.001083 | 3.40E-02 |
| rs4653015 | 1 | 33776431 | T | C | 0.26086 | 0.994959 | 0.0026161 | 0.001164 | 2.50E-02 |
| rs12476923 | 2 | 145830053 | A | C | 0.336033 | 0.999171 | -0.0007015 | 0.001078 | 5.20E-01 |
| rs283914 | 3 | 17330649 | T | C | 0.531356 | 0.997244 | 0.0019071 | 0.001024 | 6.20E-02 |
| rs4233093 | 1 | 73446245 | A | G | 0.516179 | 0.997724 | 0.0050554 | 0.001022 | 7.60E-07 |
| rs7829912 | 8 | 33479228 | T | C | 0.555727 | 0.991336 | 0.001943 | 0.001031 | 6.00E-02 |
| rs3117340 | 6 | 29210596 | G | T | 0.622344 | 0.999729 | 0.0051953 | 0.001055 | 8.50E-07 |
| rs1381287 | 14 | 98597552 | T | C | 0.456905 | 0.986444 | 0.0050533 | 0.001032 | 9.80E-07 |
| rs28520003 | 22 | 46411969 | G | A | 0.68587 | 1 | 0.0057744 | 0.001102 | 1.60E-07 |
| rs12115650 | 9 | 126367705 | G | A | 0.725133 | 0.986183 | -0.00184 | 0.001151 | 1.10E-01 |
| rs11226319 | 11 | 104221573 | A | G | 0.160313 | 0.994423 | -0.0015943 | 0.001394 | 2.50E-01 |
| rs1358391 | 7 | 115111838 | G | T | 0.505524 | 0.986954 | 0.0050478 | 0.001027 | 8.80E-07 |
| rs12617392 | 2 | 27336827 | C | A | 0.558239 | 0.992674 | -0.0003932 | 0.00103 | 7.00E-01 |
| rs542883 | 2 | 45143382 | C | G | 0.559253 | 0.995628 | 0.0079359 | 0.001029 | 1.20E-14 |
| rs10823791 | 10 | 73338334 | T | A | 0.398774 | 0.997238 | 0.00158 | 0.001045 | 1.30E-01 |
| rs34905321 | 6 | 109131107 | T | C | 0.567814 | 0.995805 | 0.0013402 | 0.001033 | 1.90E-01 |
| rs891124 | 16 | 71440756 | T | C | 0.710131 | 0.988667 | 0.0036719 | 0.001132 | 1.20E-03 |
| rs35914833 | 14 | 94182383 | C | T | 0.684169 | 0.978438 | 0.000966 | 0.001111 | 3.80E-01 |

The highlighting indicates nominal statistical significance in the ever smoking dataset (P<0.05)

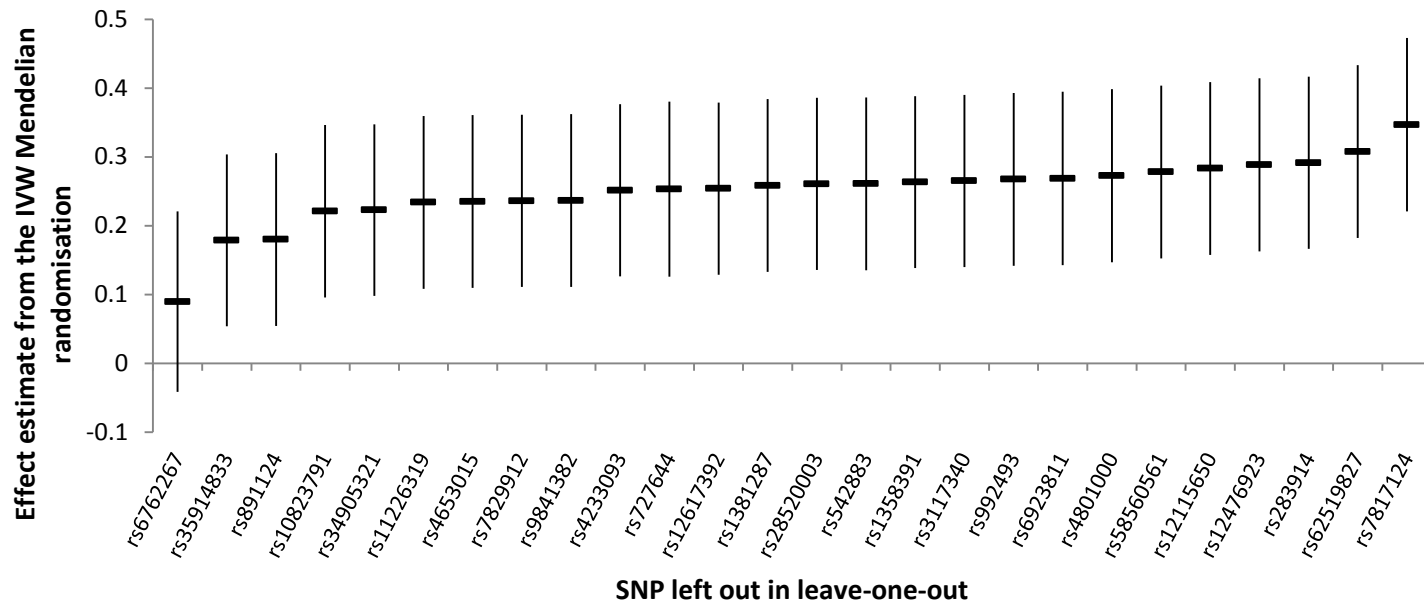
Supplementary Table 2 Associations between four risk-taking loci that are genome-wide significant for BMI and the eating behaviours in the Fenland cohort

| Variant | Implicated gene | BMI | | Emotional eating | | Uncontrolled eating | | Cognitive restraint | |
|------------|-----------------|---------------|-----------------------|------------------|----------------|---------------------|----------------|---------------------|----------------|
| | | Beta (SE) | <i>P</i> -val. | Beta (SE) | <i>P</i> -val. | Beta (SE) | <i>P</i> -val. | Beta (SE) | <i>P</i> -val. |
| rs891124 | CALB2 | 0.01 (0.002) | 3.5x10 ⁻¹⁰ | 1.12 (0.71) | 0.11 | 0.48 (0.47) | 0.30 | 0.03 (0.51) | 0.96 |
| rs35914833 | PRIMA1 | 0.02 (0.002) | 5.3x10 ⁻¹⁴ | 0.06 (0.71) | 0.93 | -0.01 (0.47) | 0.98 | -0.11 (0.51) | 0.83 |
| rs6762267 | CADM2 | 0.02 (0.002) | 1.7x10 ⁻¹⁵ | 0.95 (0.65) | 0.15 | 0.69 (0.43) | 0.11 | 0.33 (0.47) | 0.48 |
| rs7817124 | ZBTB10 | -0.01 (0.002) | 1.8x10 ⁻⁹ | 0.31 (0.73) | 0.67 | 0.17 (0.48) | 0.72 | 0.37 (0.52) | 0.48 |

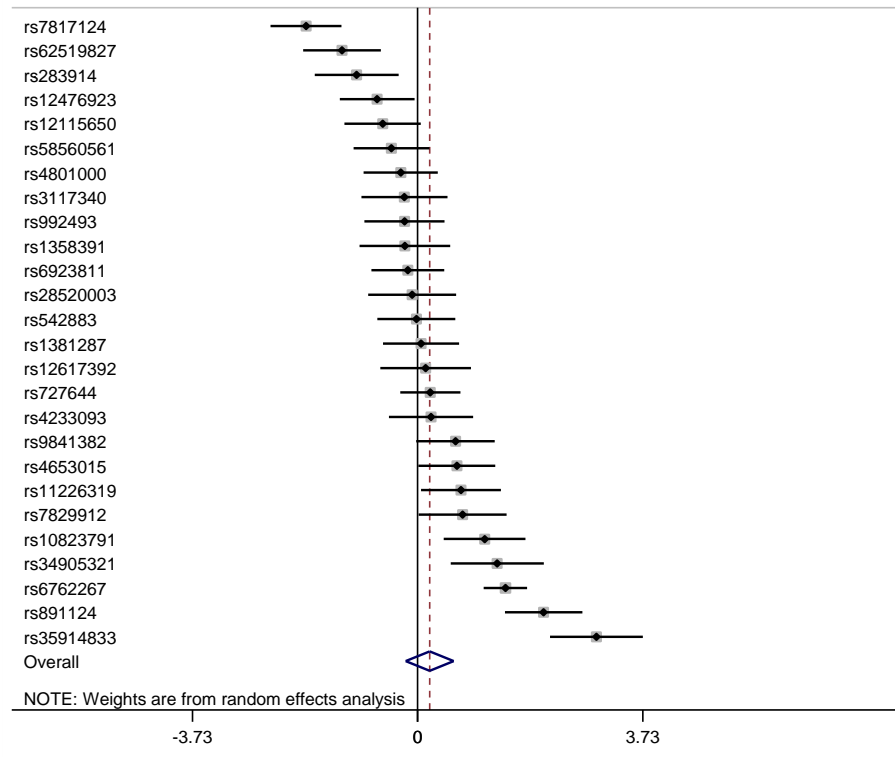
SNPs were aligned to the risk taking propensity-increasing allele. Effect estimates (beta and standard error, SE) were derived from linear regressions of the variant to the named trait, adjusted for age and sex. BMI was a continuous outcome standardised within the BMI meta-analysis.

Supplementary Table 3 Associations between the principal components and risk-taking

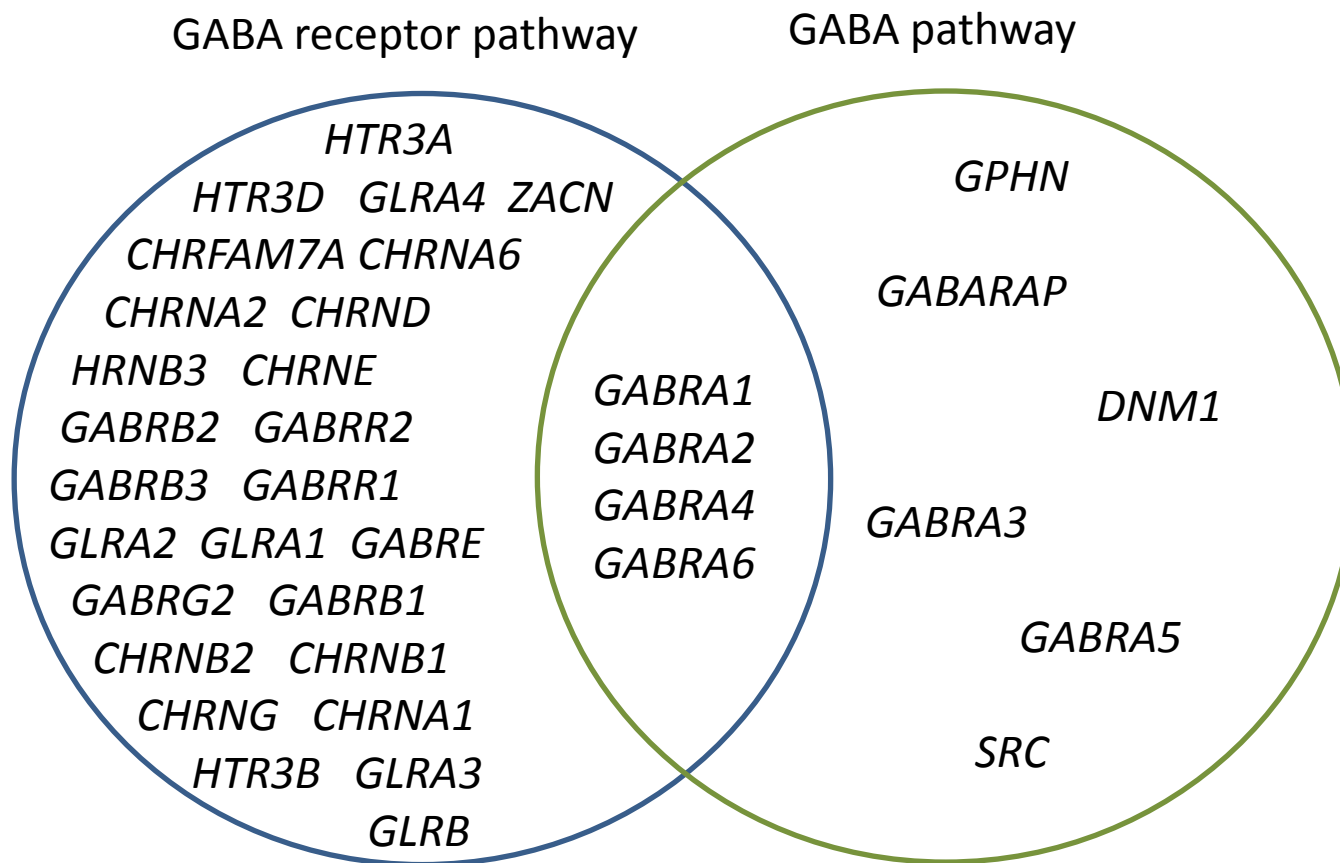
| | Odds ratio | 95% CI | P-value |
|-------------|-------------------|----------------|----------------|
| PC1 | 1.008 | (1.005, 1.011) | <0.001 |
| PC2 | 0.995 | (0.992, 0.998) | 0.002 |
| PC3 | 1.004 | (1.000, 1.008) | 0.036 |
| PC4 | 0.990 | (0.988, 0.992) | <0.001 |
| PC5 | 1.012 | (1.010, 1.013) | <0.001 |
| PC6 | 1.004 | (1.001, 1.008) | 0.013 |
| PC7 | 0.995 | (0.992, 0.998) | <0.001 |
| PC8 | 1.009 | (1.006, 1.012) | <0.001 |
| PC9 | 0.998 | (0.996, 0.999) | 0.004 |
| PC10 | 1.003 | (1.000, 1.006) | 0.037 |



Supplementary Figure 1. Leave-one-out analysis. The figure shows the effect estimates and 95% confidence intervals from a series of inverse weighted variance (IVW) Mendelian randomisation analyses, each with one of the genome wide significant risk-taking propensity SNPs removed. The removed SNP is indicated on the x-axis. Comparison of the effect estimates for the four SNPs that reached genome-wide significance for BMI (rs6762267, rs35914833, rs891124 and rs7817124) with the mean of the effect estimates from the sample with that SNP removed, showed a significant difference ($P < 0.0001$).



Supplementary Figure 2. Results of a random effects IVW Mendelian randomisation analysis of risk-taking to BMI. This analysis combined the effect estimates ascertained when treating each of the genome-wide significant SNPs for risk-taking (displayed on the y-axis) as an individual instrument. Points indicate effect estimates, bars indicate 95% confidence intervals.



Supplementary Figure 3 Overlap between the GABA pathway and the GABA receptor pathway