

**Figure 5:** Association of genetic risk scores for lifetime smoking and smoking initiation with visceral adipose tissue (VAT), gluteofemoral fat (GSAT), and abdominal subcutaneous adipose tissue (ASAT) volumes, with and without adjustment for BMI (adjBMI). The associations of the genetic risk scores with VAT/GSAT, VAT/ASAT and ASAT/GSAT ratios are also shown. We constructed genetic risk scores using variants from the inverse variance-weighted model for the causal association between smoking initiation and WHR (121 variants), smoking initiation and WHRadjBMI (130 variants), lifetime smoking and WHR (76 variants), and lifetime smoking and WHRadjBMI (83 variants). The smoking variants causally associated with WHR were used to study associations with BMI-unadjusted fat depots, while the smoking variants causally associated with WHRadjBMI were used to study associations with BMI-adjusted fat depots. We computed weighted genetic scores using the beta of the variants for a smoking trait as weights with gtx.package’s (v0.0.8) grs.summary function [36]. This function approximates the results of a genetic risk score using GWAS summary statistics by calculating the joint effect of genetic variants on an outcome trait.



**Supplementary Figure 5.** Association of genetic risk scores for lifetime smoking and smoking initiation with hormonal levels, including cortisol, testosterone, oestradiol and sex hormone-binding globulin (SHBG). We constructed genetic risk scores using variants from the inverse variance-weighted model for the causal association between smoking initiation and WHRadjBMI (110 variants) and lifetime smoking and WHRadjBMI (69 variants). We computed weighted genetic scores using the beta of the variants for the smoking trait as weights with gtx.package’s (v0.0.8) grs.summary function. This function approximates the results of a genetic risk score using GWAS summary statistics by calculating the joint effect of genetic variants on an outcome trait.

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|  | **Supplementary Table 11: Association of genetic risk scores for smoking traits with fat depot volumes and their ratios.** | | | | | | | | | | | | | |
|  | **Lifetime smoking - WHR** | | | | | |  | | **Lifetime smoking - WHRadjBMI** | | | | | |
| **Fat depot** | **N** | **effect size** | **SE** | **lower 95% CI** | **upper 95% CI** | **P** | **Fat depot** | **N** | | **effect size** | **SE** | **lower 95%**  **CI** | **upper**  **95% CI** | **P** |
| VAT | 76 | 0.31 | 0.09 | 0.13 | 0.48 | 5.08E-04 | VATadjBMI | 83 | | 0.1 | 0.08 | -0.06 | 0.27 | 2.08E-01 |
| GSAT | 76 | 0.26 | 0.09 | 0.09 | 0.43 | 2.97E-03 | GSATadjBMI | 83 | | -0.003 | 0.08 | -0.16 | 0.16 | 9.75E-01 |
| ASAT | 76 | 0.21 | 0.09 | 0.04 | 0.39 | 1.56E-02 | ASATadjBMI | 83 | | -0.13 | 0.08 | -0.30 | 0.03 | 1.15E-01 |
| VAT/GSAT | 76 | 0.22 | 0.09 | 0.05 | 0.39 | 1.00E-02 | VAT/GSAT | NA | | NA | NA | NA | NA | NA |
| VAT/ASAT | 76 | 0.25 | 0.09 | 0.08 | 0.42 | 3.17E-03 | VAT/ASAT | NA | | NA | NA | NA | NA | NA |
| ASAT/GSAT | 76 | 0.06 | 0.09 | -0.11 | 0.23 | 4.78E-01 | ASAT/GSAT | NA | | NA | NA | NA | NA | NA |
|  | **Smoking initiation - WHR** | | | | | |  | | **Smoking initiation - WHRadjBMI** | | | | | |
| VAT | 121 | 0.13 | 0.04 | 0.06 | 0.20 | 5.66E-04 | VATadjBMI | 130 | | -0.04 | 0.04 | -0.11 | 0.03 | 2.89E-01 |
| GSAT | 121 | 0.10 | 0.04 | 0.02 | 0.17 | 8.98E-03 | GSATadjBMI | 130 | | -0.03 | 0.04 | -0.10 | 0.04 | 3.50E-01 |
| ASAT | 121 | 0.09 | 0.04 | 0.02 | 0.16 | 1.65E-02 | ASATadjBMI | 130 | | -0.11 | 0.04 | -0.18 | -0.04 | 3.54E-03 |
| VAT/GSAT | 121 | 0.10 | 0.04 | 0.03 | 0.17 | 5.93E-03 | VAT/GSAT | NA | | NA | NA | NA | NA | NA |
| VAT/ASAT | 121 | 0.10 | 0.04 | 0.02 | 0.17 | 8.42E-03 | VAT/ASAT | NA | | NA | NA | NA | NA | NA |
| ASAT/GSAT | 121 | 0.05 | 0.04 | -0.03 | 0.12 | 2.12E-01 | ASAT/GSAT | NA | | NA | NA | NA | NA | NA |
| We constructed genetic risk scores using variants from the inverse variance-weighted model for the causal association between smoking initiation and WHR (121 variants), smoking initiation and WHRadjBMI (130 variants), lifetime smoking and WHR (76 variants), and lifetime smoking and WHRadjBMI (83 variants). The smoking variants causally associated with WHR were used to study associations with BMI-unadjusted fat depots, while the smoking variants causally associated with WHRadjBMI were used to study associations with BMI-adjusted fat depots. We computed weighted genetic scores using the beta of the variants for a smoking trait as weights with gtx.package’s (v0.0.8) grs.summary function. This function approximates the results of a genetic risk score using GWAS summary statistics by calculating the joint effect of genetic variants on an outcome trait. N, number of variants used; SE, standard error; P, p-value; CI, confidence interval; VAT, visceral adipose tissue; ASAT, abdominal subcutaneous adipose tissue; GSAT, gluteofemoral subcutaneous adipose tissue. | | | | | | | | | | | | | | |

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| **Supplementary Table 12: Association of genetic risk scores for smoking traits with hormones.** | | | | | | |
|  | **Lifetime smoking - WHRadjBMI** | | | | | |
| **Hormones** | **N** | **effect size** | **SE** | **lower  95% CI** | **upper**  **95% CI** | **P** |
| Cortisol | 69 | -0.01 | 0.11 | -0.23 | 0.22 | 9.60E-01 |
| Oestradiol | 69 | 0.12 | 0.11 | -0.10 | 0.33 | 2.90E-01 |
| Testosterone | 69 | -0.01 | 0.02 | -0.04 | 0.03 | 7.12E-01 |
| SHBG | 69 | -0.002 | 0.01 | -0.02 | 0.02 | 8.79E-01 |
|  | **Smoking initiation - WHRadjBMI** | | | | | |
| Cortisol | 110 | -0.07 | 0.05 | -0.17 | 0.03 | 1.77E-01 |
| Oestradiol | 110 | 0.01 | 0.05 | -0.08 | 0.11 | 7.74E-01 |
| Testosterone | 110 | -0.01 | 0.01 | -0.02 | 0.01 | 3.02E-01 |
| SHBG | 110 | -0.02 | 0.01 | -0.03 | -0.01 | 4.56E-05 |
| We constructed genetic risk scores using variants from the inverse variance-weighted model for the causal association between smoking initiation and WHRadjBMI (110 variants), and lifetime smoking and WHRadjBMI (69 variants). We computed weighted genetic scores using the beta of the variants for a smoking trait as weights with gtx.package’s (v0.0.8) grs.summary function. This function approximates the results of a genetic risk score using GWAS summary statistics by calculating the joint effect of genetic variants on an outcome trait. N, number of variants used; SE, standard error; P, p-value; CI, confidence interval. | | | | | | |