

SUPPLEMENTARY MATERIALS

Supplementary Table 1 Results of linkage disequilibrium regression analysis for seven anthropometric traits against TGCT.

Supplementary Table 2 Results of Egger regression for each of the traits for which Mendelian randomisation was performed.

Supplementary Table 3 Results of inverse weighted variance for each of the traits for which Mendelian randomisation was performed.

Supplementary Figures 1-11 Effect sizes of TGCT and each of the traits for which Mendelian randomisation was performed.

Supplementary Figures 12-15 Power estimates of our MR analysis to demonstrate an association between TGCT and anthropometric traits over a range of effect sizes.

| Phenotype | Heritability of Phenotype | | | | Genetic Covariance (with TGCT) | | | Genetic Correlation (with TGCT) | | |
|-------------------------------------|---|--------------|---------------|------------------------|--|---------------|------------------------|-------------------------------------|---------|----------------|
| | Total Liability Scale h^2 (Std.Err) | Lambda GC | Mean x^2 | Intercept (Std.Err) | Total Liability Scale gencov (Std.Err) | Mean z1*z2 | Intercept (Std.Err) | Genetic Correlation (Std.Err) | Z-score | <i>P</i> value |
| Birth Weight | 0.11 (0.021) | 1.05 | 1.06 | 1.01 (0.0084) | 0.036 (0.019) | 0.017 | -0.0041 (0.0064) | 0.17 (0.093) | 1.83 | 0.068 |
| Childhood Obesity | 0.41 (0.046) | 1.02 | 1.03 | 0.92 (0.0098) | -0.058 (0.027) | 0.0023 | 0.025 (0.0069) | -0.14 (0.064) | -2.15 | 0.032 |
| Adult BMI | 0.14 (0.0095) | 1.12 | 1.33 | 0.63 (0.016) | -0.0008 (0.0073) | 0.0018 | 0.0056 (0.0073) | -0.0035 (0.034) | -0.1 | 0.92 |
| WHRadjBMI | 0.093 (0.008) | 1.05 | 1.13 | 0.85 (0.013) | 0.0069 (0.0081) | 0.025 | 0.014 (0.0077) | 0.035 (0.04) | 0.87 | 0.39 |
| WHRadjBMI (Male only) | 0.12 (0.011) | 1.05 | 1.06 | 0.91 (0.0089) | -0.0012 (0.013) | 0.009 | 0.0086 (0.0077) | -0.0054 (0.055) | -0.099 | 0.92 |
| WCadjBMI | 0.11 (0.0078) | 1.05 | 1.18 | 0.82 (0.012) | 0.0052 (0.009) | 0.0053 | -0.005 (0.0075) | 0.024 (0.042) | 0.57 | 0.57 |
| WCadjBMI (Male only) | 0.18 (0.014) | 1.05 | 1.11 | 0.88 (0.01) | -0.0029 (0.014) | -0.0068 | -0.0067 (0.0077) | -0.011 (0.052) | -0.2 | 0.84 |
| HIPadjBMI | 0.15 (0.011) | 1.1 | 1.26 | 0.79 (0.015) | -0.0031 (0.0099) | -0.024 | -0.022 (0.0076) | -0.012 (0.039) | -0.31 | 0.76 |
| HIPadjBMI (Male only) | 0.22 (0.017) | 1.05 | 1.13 | 0.85 (0.012) | -0.0094 (0.014) | -0.013 | -0.0074 (0.0074) | -0.031 (0.046) | -0.68 | 0.5 |
| Adult Height | 0.33 (0.021) | 2.09 | 3.16 | 1.28 (0.049) | -0.015 (0.013) | -0.045 | -0.024 (0.01) | -0.039 (0.034) | -1.15 | 0.25 |
| Adult Height (Male only) | 0.26 (0.022) | 1.05 | 1.18 | 0.83 (0.015) | -0.025 (0.017) | -0.018 | -0.0003 (0.0074) | -0.073 (0.049) | -1.5 | 0.13 |

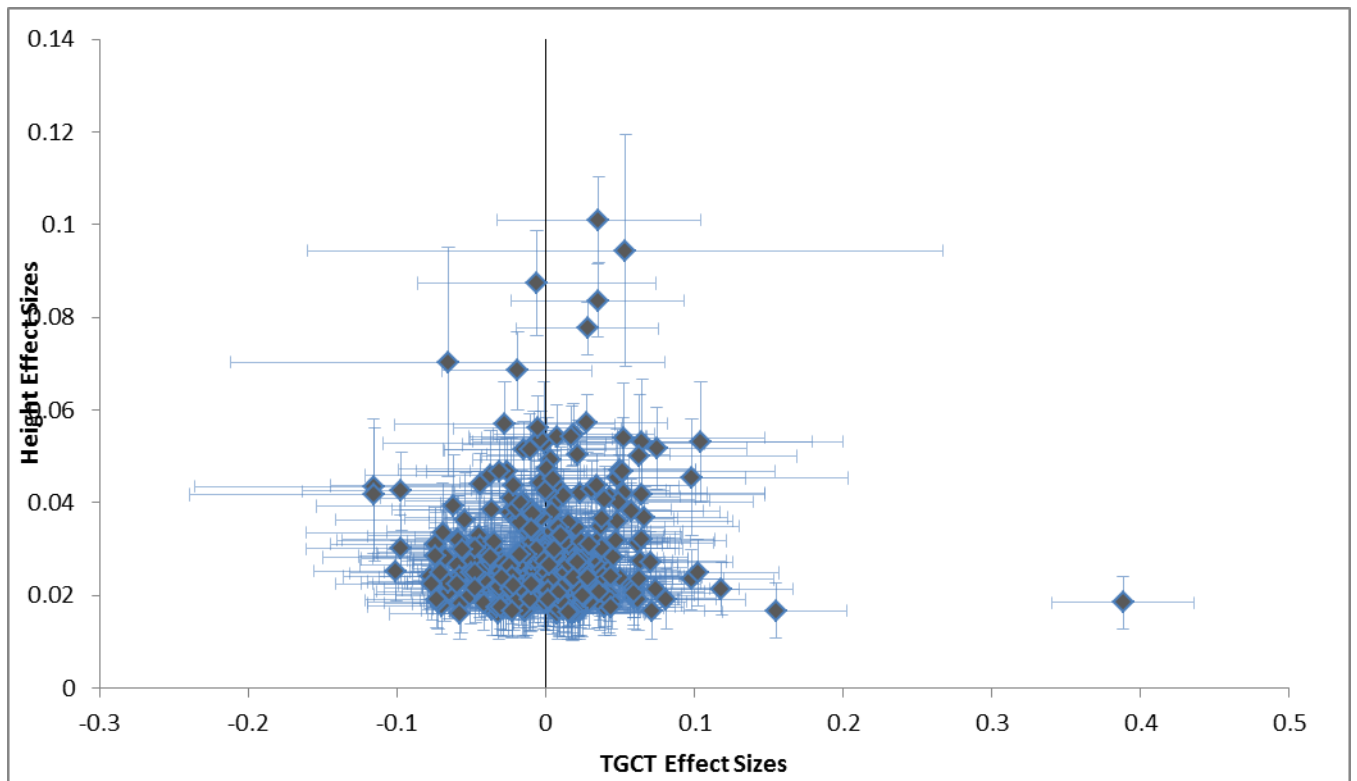
Supplementary Table 1 Results of linkage disequilibrium regression analysis for seven anthropometric traits against TGCT, as well as male-specific components for four of these traits.

| Trait | x – intercept | | | slope | | |
|----------------------------------|-----------------|----------------|-----------------|----------|--------------|-----------------|
| | Estimate | 95% CI | <i>P</i> -value | Estimate | 95% CI | <i>P</i> -value |
| BMI | 0.00031 | [-0.026,0.027] | 0.98 | -0.18 | [-1.19,0.84] | 0.73 |
| Height | 0.00023 | [-0.011,0.012] | 0.97 | 0.054 | [-0.35,0.45] | 0.79 |
| Height (Male only) | 0.046 | [-0.040,0.13] | 0.27 | -1.51 | [-4.21,1.19] | 0.25 |
| HIPadjBMI | -0.039 | [-0.11,0.030] | 0.23 | 1.87 | [-0.67,4.41] | 0.13 |
| HIPadjBMI (Male only) | 0.13 | [-0.17,0.43] | 0.2 | -3.19 | [-10.8,4.38] | 0.21 |
| WCadjBMI | -0.0072 | [-0.059,0.044] | 0.77 | 0.41 | [-1.50,2.32] | 0.66 |
| WCadjBMI (Male only) | -0.041 | [-0.30,0.22] | 0.72 | 1.49 | [-6.74,9.73] | 0.68 |
| WHRadjBMI | 0.038 | [-0.015,0.091] | 0.16 | -1.39 | [-3.30,0.52] | 0.15 |
| WHRadjBMI (Male only) | -0.17 | [-0.49,0.14] | 0.22 | 5.77 | [-4.24,15.8] | 0.2 |
| Birth Weight | 0.007 | [-0.102,0.12] | 0.88 | 0.006 | [-2.14,2.15] | 0.99 |
| Childhood Obesity | -0.015 | [-0.28,0.25] | 0.89 | 0.04 | [-3.25,3.33] | 0.98 |

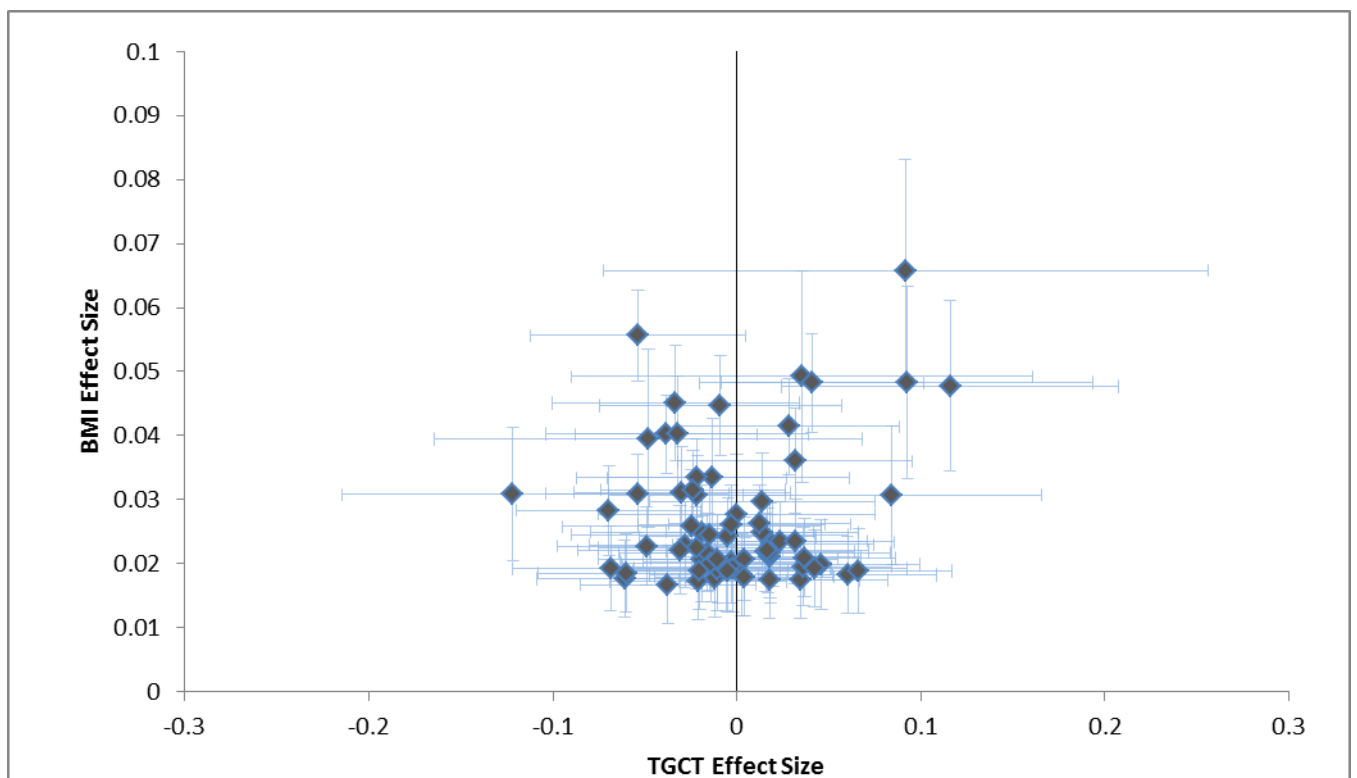
Supplementary Table 2 Egger regression results for each of the traits for which Mendelian randomisation was performed.

| Trait | IVW Estimate | 95% CI | P-value |
|------------------------------|---------------------|---------------|----------------|
| BMI | -0.16 | [-0.49,0.16] | 0.32 |
| Height | 0.061 | [-0.09,0.21] | 0.42 |
| Height (Male only) | -0.082 | [-0.55,0.39] | 0.72 |
| HIPadjBMI | 0.50 | [-0.27,1.28] | 0.17 |
| HIPadjBMI (Male only) | -0.007 | [-2.05,2.04] | 0.99 |
| WCadjBMI | 0.15 | [-0.33,0.63] | 0.53 |
| WCadjBMI (Male only) | 0.21 | [-0.65,1.08] | 0.58 |
| WHRadjBMI | -0.043 | [-0.39,0.31] | 0.80 |
| WHRadjBMI (Male only) | 0.32 | [-0.54,1.19] | 0.40 |
| Birth Weight | 0.14 | [-0.34,0.62] | 0.50 |
| Childhood Obesity | -0.15 | [-0.57,0.28] | 0.43 |

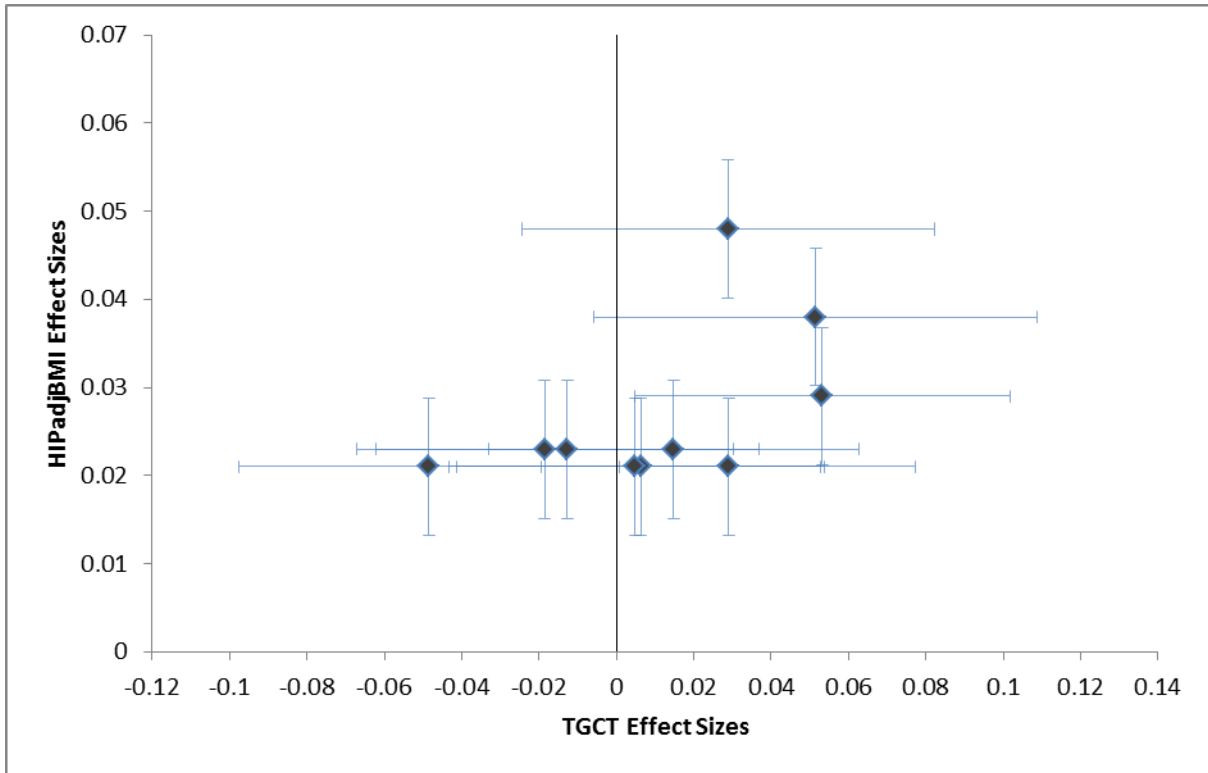
Supplementary Table 3 Inverse weighted variance results for each of the traits for which Mendelian randomisation was performed.



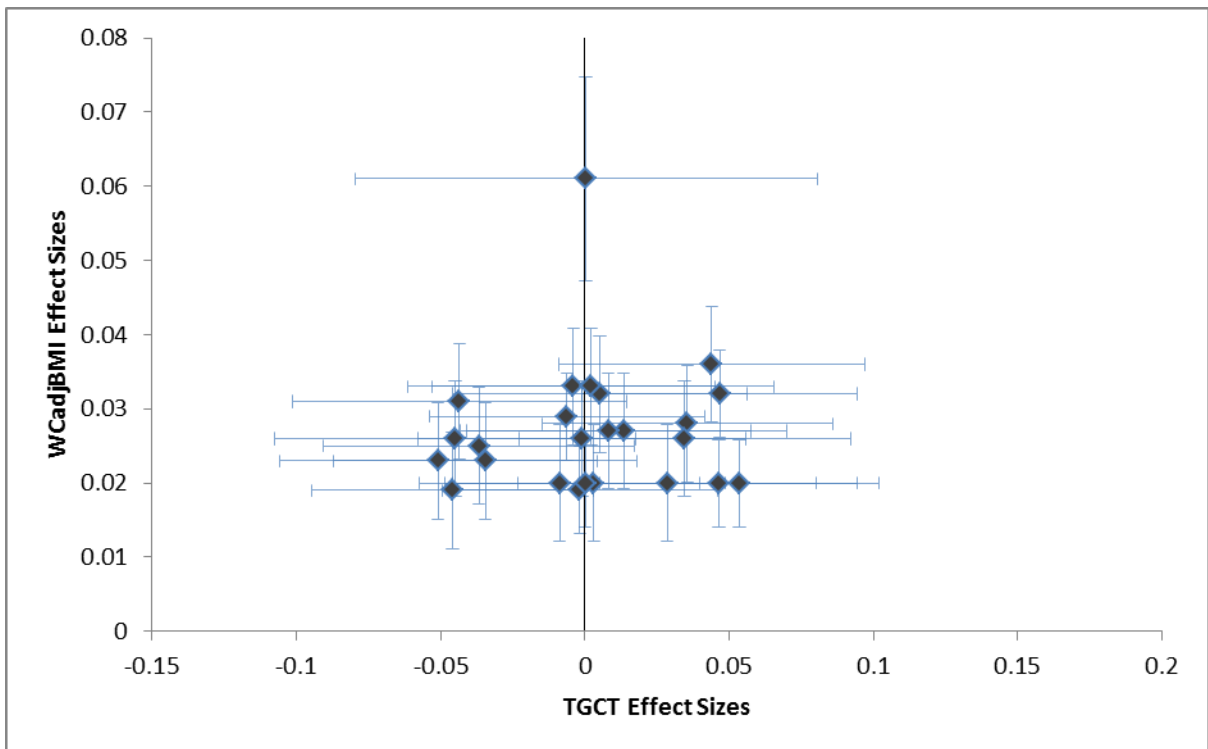
Supplementary Fig. 1 TGCT and adult height effect sizes (and 95% CI) for 379 adult height risk SNPs.



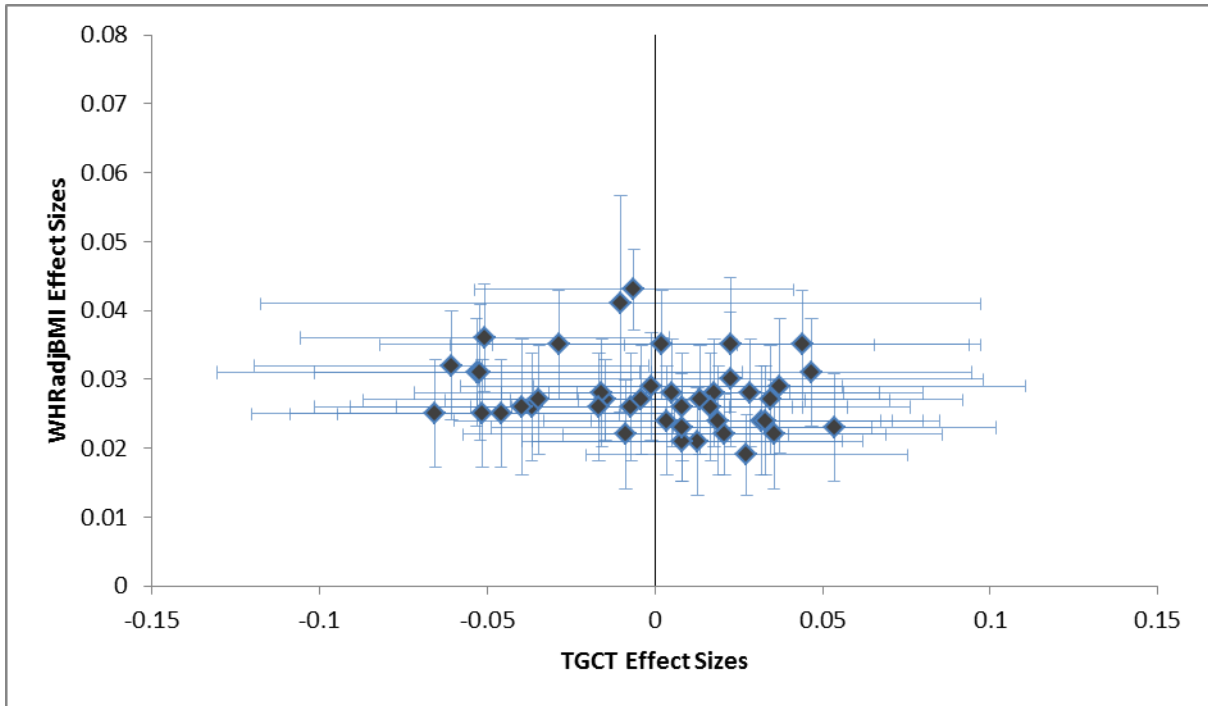
Supplementary Fig. 2 TGCT and BMI effect sizes (and 95% CI) for 69 BMI risk SNPs.



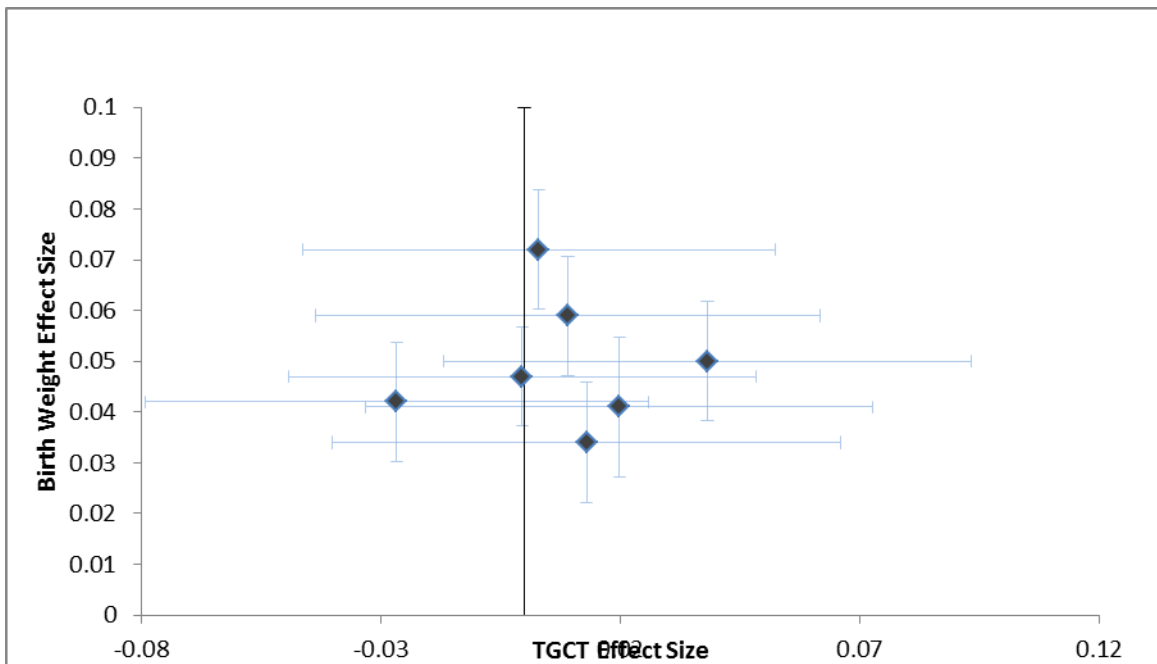
Supplementary Fig. 3 TGCT and HIPadjBMI effect sizes (and 95% CI) for ten HIPadjBMI risk SNPs.



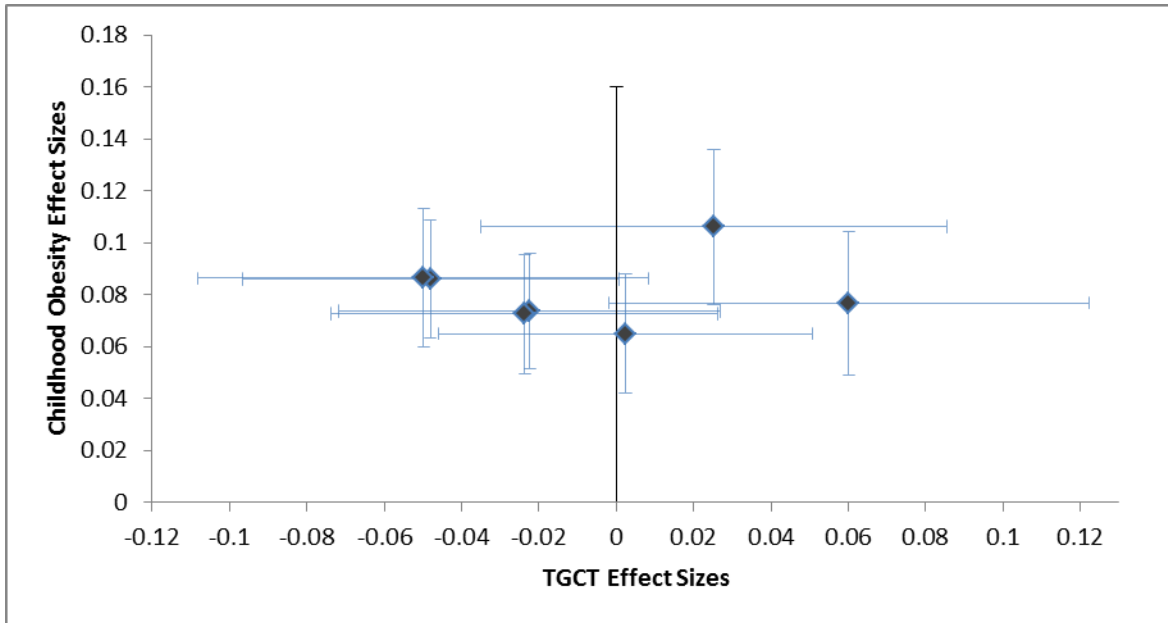
Supplementary Fig. 4 TGCT and WCadjBMI effect sizes (and 95% CI) for 25 WCadjBMI risk SNPs.



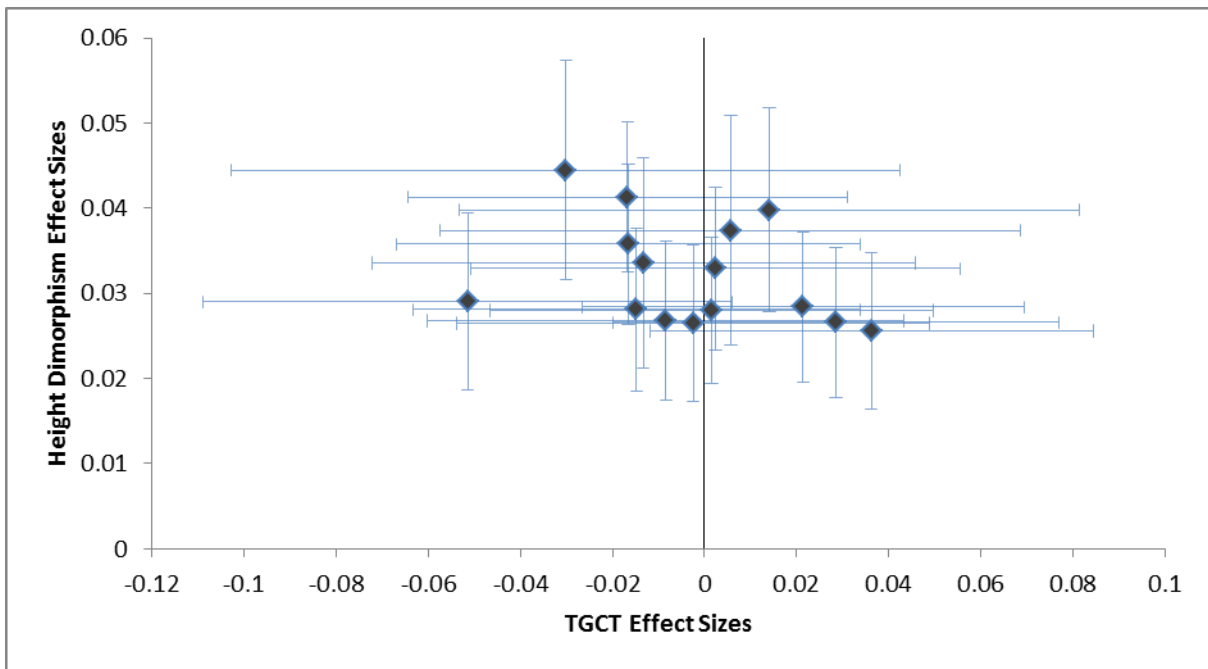
Supplementary Fig. 5 TGCT and WHRadjBMI effect sizes (and 95% CI) for 44 WHRadjBMI risk SNPs.



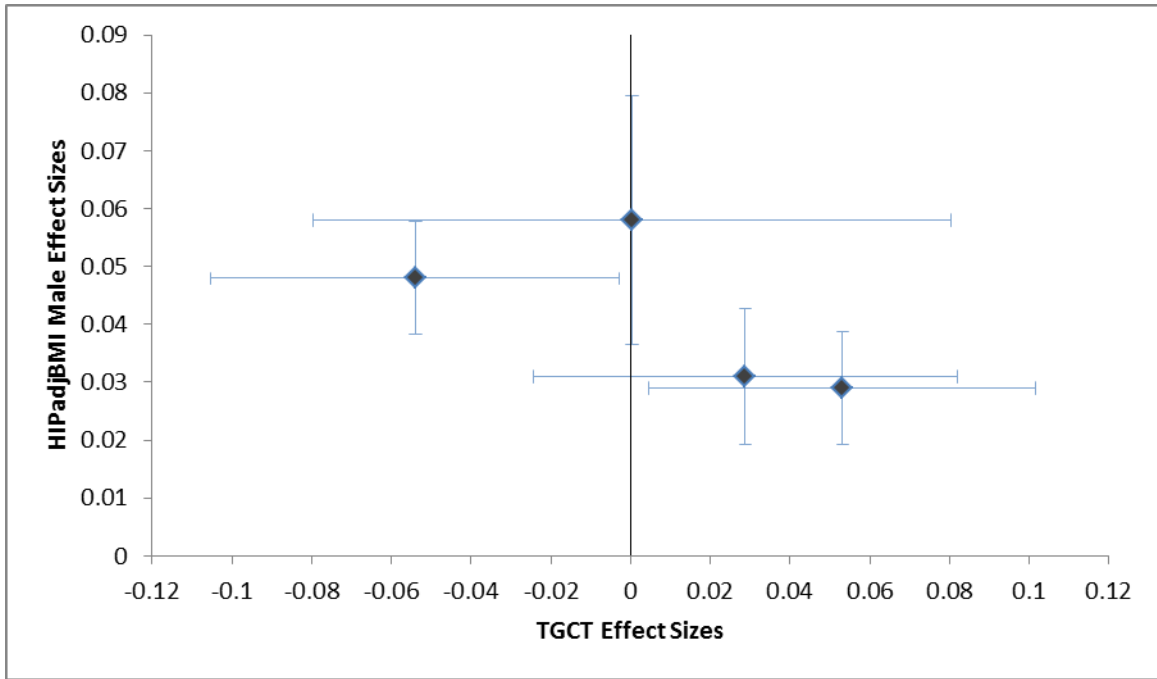
Supplementary Fig. 6 TGCT and birth weight effect sizes (and 95% CI) for seven birth weight risk SNPs.



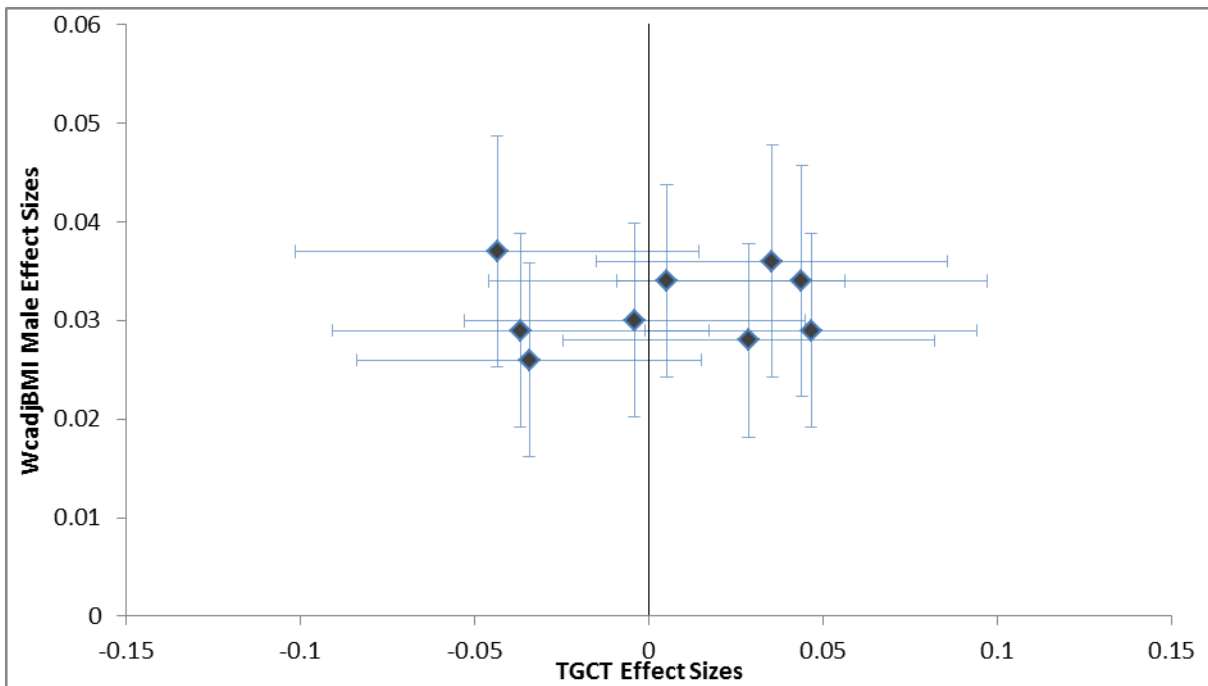
Supplementary Fig. 7 TGCT and childhood obesity effect sizes (and 95% CI) for seven childhood obesity risk SNPs.



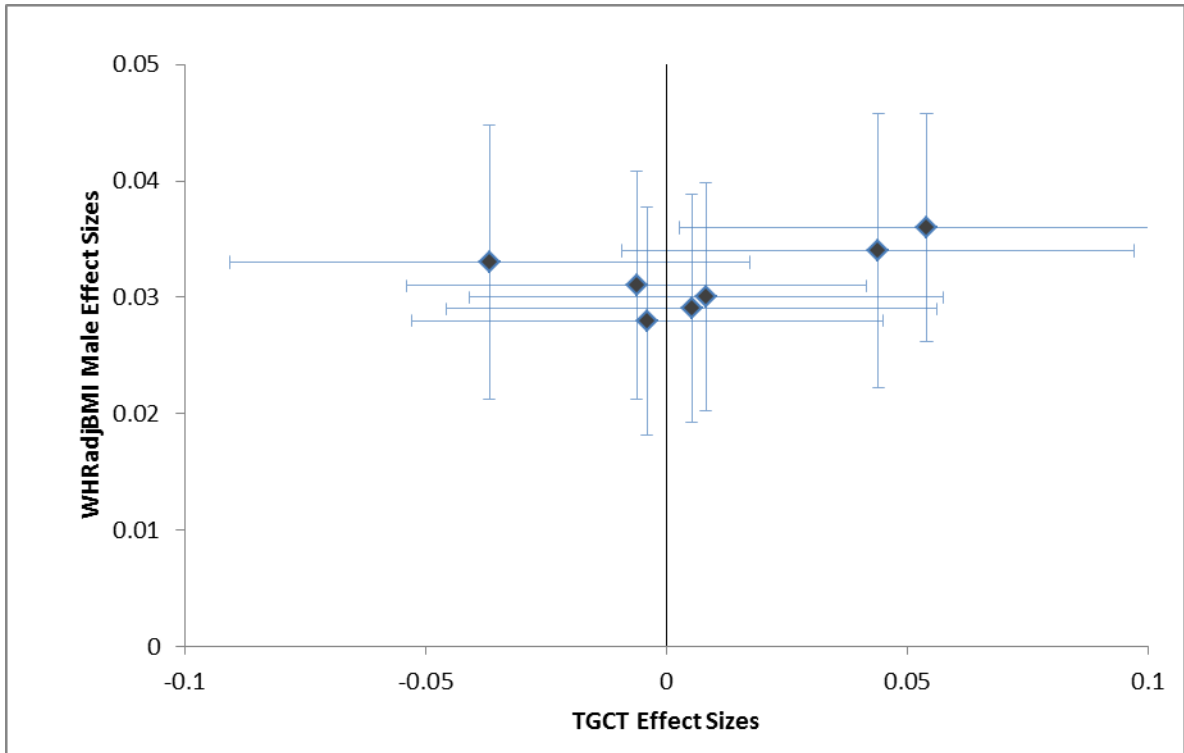
Supplementary Fig. 8 TGCT and height (male dimorphism) effect sizes (and 95% CI) for 15 height (male dimorphism) risk SNPs.



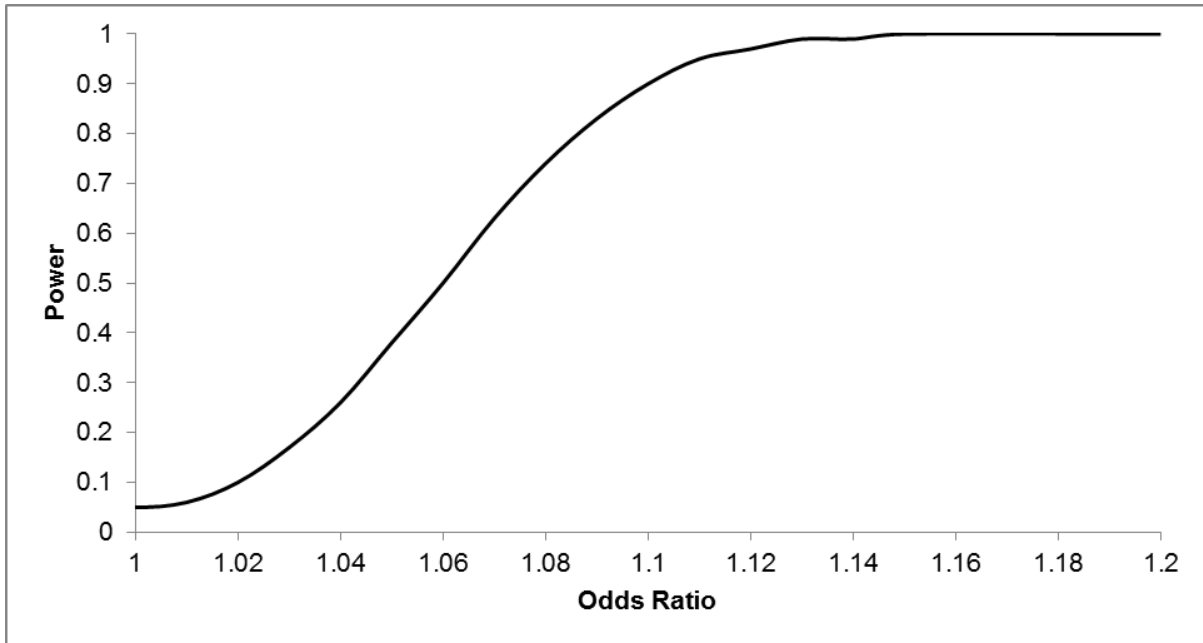
Supplementary Fig. 9 TGCT and HIPadjBMI (male specific) effect sizes (and 95% CI) for four HIPadjBMI (male-specific) risk SNPs.



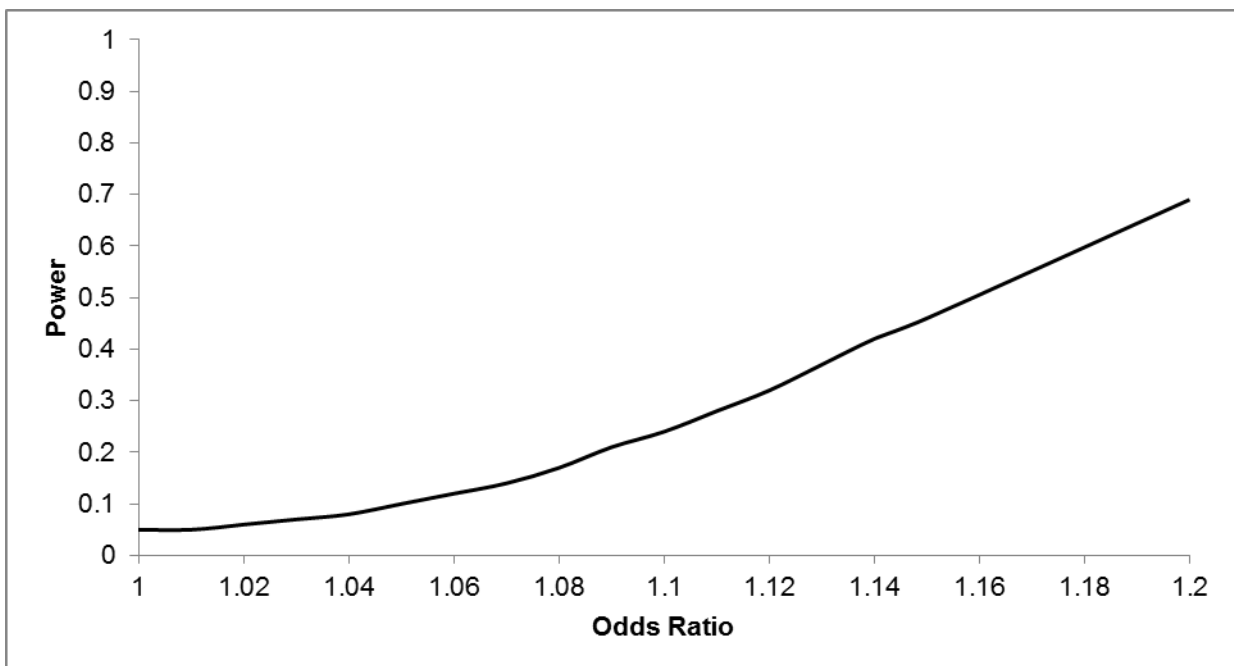
Supplementary Fig. 10 TGCT and WCadjBMI (male specific) effect sizes (and 95% CI) for nine WCadjBMI (male specific) risk SNPs.



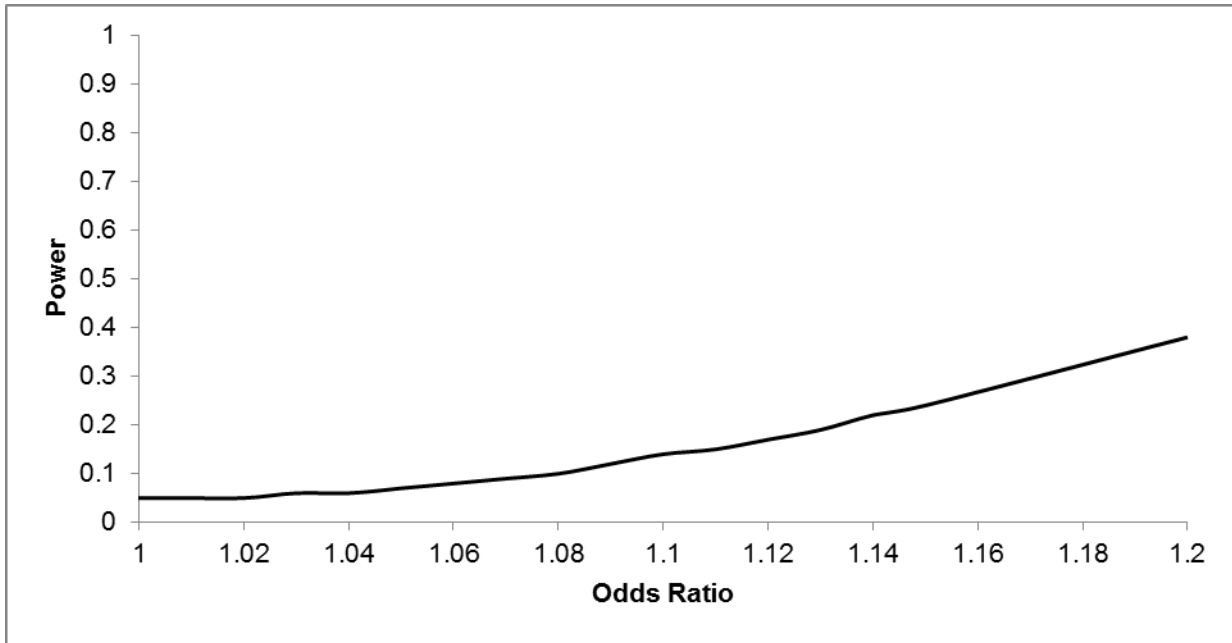
Supplementary Fig. 11 TGCT and WHRadjBMI (male specific) effect sizes (and 95% CI) for seven WHRadjBMI (male specific) risk SNPs.



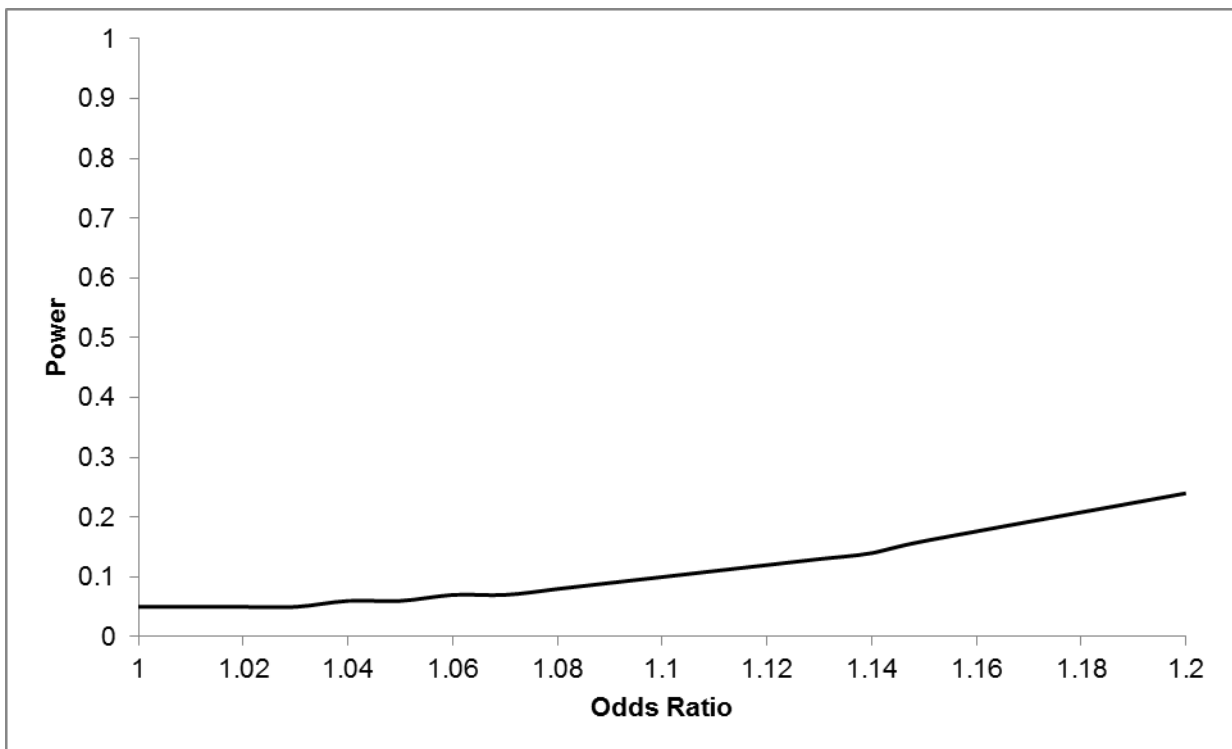
Supplementary Fig. 12 Estimated power of the present study to detect a range of odds ratios of height and TGCT risk. SNPs used here are estimated to explain ~20% of the phenotypic variation in height (Wood *et al.* 2014).



Supplementary Fig. 13 Estimated power of the present study to detect a range of odds ratios of BMI and TGCT risk. SNPs used here are estimated to explain ~3% of the phenotypic variation in BMI (Locke *et al.* 2015).



Supplementary Fig. 14 Estimated power of the present study to detect a range of odds ratios of WHRadjBMI and TGCT risk. SNPs used here are estimated to explain ~1.36% of the phenotypic variation of WHRadjBMI (Shungin *et al.* 2015).



Supplementary Fig. 15 Estimated power of the present study to detect a range of odds ratios of birth weight and TGCT risk. SNPs used here are estimated to explain ~0.76% of the phenotypic variation of birth weight (Horikoshi *et al.* 2013).

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Horikoshi M, Yaghooskar H, Mook-Kanamori D O, Sovio U, Taal H R, Hennig B J, *et al.* (2013) New loci associated with birth weight identify genetic links between intrauterine growth and adult height and metabolism. *Nat Genet* **45**, 76-82.

Locke A E, Kahali B, Berndt S I, Justice A E, Pers T H, Day F R, *et al.* (2015) Genetic studies of body mass index yield new insights for obesity biology. *Nature* **518**, 197-206.

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