Large scale genome-wide association meta-analyses of lipid, glycaemic and obesity-related traits

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Within the European Network for Genetic and Genomic Epidemiology (ENGAGE) Consortium (http://www.euengage.org/index.html), we undertook large-scale meta-analysis of genome-wide association studies (GWAS) supplemented by 1000 Genomes imputation for eight quantitative (lipid, glycaemic and obesity-related) traits in individuals of European ancestry.

Summary statistics from the meta-analyses of GWAS is available as a tab-separated table, enclosed in a zip file. This document is available in PDF format here.

Individuals were assayed with a range of genotyping arrays, with sample and SNP quality control (QC) undertaken within each individual study. Each GWAS scaffold was imputed up to the 1000 Genomes "all ancestries" reference panel (Phase 1 interim release, June 2011).

Obesity-related traits. The meta-analysis consists of 87,048 individuals for BMI, and 54,572 individuals for WHR adjusted for BMI from 22 studies of European ancestry as described in Horikoshi *et al*. (submitted). Within each study, BMI was inverse normal transformed separately in males and females, and then tested for sex-stratified association in a linear regression framework under an additive model after adjustment for age, age^2 and study-specific covariates. WHR_{adjBMI} was obtained as residuals after adjustment for age, age^2, BMI, and study-specific covariates, separately in males and females, and were subsequently inverse-rank normalised. WHR_{adjBMI} was then tested for sex-stratified association in a linear regression framework under an additive model. Association summary statistics passing QC in each GWAS were corrected for population structure with genomic control and then combined across studies using sex-combined fixed-effect meta-analyses (single GC correction). The files containing association summary statistics are available for download here (**BMI**) and here (**WHR_{adjBMI}**).

Glycaemic traits. The meta-analysis consists of 46,694 individuals for Fasting glucose (FG), and 24,245 individuals for FI adjusted for BMI from 13 studies of European ancestry as described in Horikoshi *et al*. (submitted). Within each study, FG was measured in mmol/L. FI was measured in pmol/L with subsequent natural log transformation. FG and FI traits were tested for association in a linear regression framework under an additive model after adjustment for age, age^2 and study-specific covariates (for FG) or age, age^2, BMI and study-specific covariates (for FI_{adjBMI}), separately in males and females. Association summary statistics passing QC in each GWAS were corrected for population structure with genomic control and then combined across studies using sex-combined fixed-effect meta-analyses (single GC correction). The files containing association summary statistics are available for download here (**FG**) and here (**FI_{adjBMI}**).

Lipids. The meta-analysis consists of up to 62,166 individuals across 22 studies of European ancestry as described in Surakka *et al*. (accepted). Within each study, residuals of high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), triglycerides (TG) and total cholesterol (TC), were obtained after adjustment for age, age^2, and study-specific covariates, separately in males and females, and were subsequently inverse-rank normalised.

Each trait was tested for sex-stratified association in a linear regression framework under an additive model. Association summary statistics passing QC in each GWAS were corrected for population structure with genomic control and then combined across studies using sex-combined fixed-effect meta-analyses (single GC correction). The files containing association summary statistics are available for download here (**HDL-C**), here (**LDL-C**), here (**TG**) and here (**TC**).

File format. For each SNP, we have provided the following information:

1. Chromosome and position (build 37, base-pairs)

2. Effect and other allele (aligned to the forward strand)

3. Effect size and standard error for effect allele

4. P-value for association

5. Total sample size reported

The sample size and precision of the statistics presented should preclude identification of any individual subject. However, in downloading these data, you undertake not to attempt to de-identify individual subjects.

References.

For glycaemic and obesity-related traits.

Horikoshi M *et al*. Discovery and fine-mapping of glycaemic and obesity-related trait loci using high-density imputation (submitted).

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For lipid traits.

Surakka I *et al*. The impact of low-frequency and rare variants on lipid levels. Nat Genet 2015 (accepted).

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