

UPDATE 30/08/2023

Please note, that the summary statistics provided were updated on 30th August 2023 for the meta-analysis of ISI noBMI and IFC noBMI in cohorts of European ancestry due to a duplication in the summary statistic files provided caused by a formatting error. This has now been corrected. All other files remain the same.

These files include summary results for the Modified Stumvoll ISI and insulin fold change meta-analyses presented in *Williamson et al, Genome-wide association study of postprandial glucose metabolism and functional characterisation identifies candidate genes for insulin-stimulated glucose uptake. Nature Genetics (2023)*.

Brief methods:

Modified Stumvoll ISI (ISI) and Insulin Fold Change (IFC) were adjusted for age, sex, population structure (+BMI). Covariate adjustment was performed in two steps: first modelling ISI and IFC on all covariates, then inverse normal transforming the residuals, and then modelling the inverse normally transformed residuals on the covariates again.

Models adjusting for BMI (adjBMI) and without BMI adjustment (noBMI) were run.

We performed a fixed-effects inverse-variance weighted meta-analysis using METAL per ancestry and applied genomic control at the study and meta-analysis level (double genomic control). The meta-analysis of studies of participants of European ancestry (adjusted for BMI) was used as our primary analysis for both IFC and ISI. Overall individuals of European ancestry represented ~97% of the maximum sample size (25 studies), 2 studies included individuals of Hispanic American Ancestry, and 1 study individuals of East Asian ancestry.

We additionally ran multi-ancestry random effects meta-analyses of the ancestry specific results using METAL (via random-metal <https://github.com/explodecomputer/random-metal>). These included:

- Non-European – meta-analysis of Hispanic American and East Asian Ancestry results
- All - meta-analysis of European (EUR), Hispanic American (HIS-AMR) and East Asian (EAS) Ancestry results

Variants were included were:

- European only (EUR): N > 11,000, MAF > 0.005
- Non-European (HIS-AMR + EAS; NONEUR): N > 1000 (at least 2 of the 3 studies), MAF > 0.005
- All (EUR + HIS-AMR + EAS; ALL): N > 11,000, MAF > 0.005

Sample size:

A total of 55,535 and 55,172 participants without diabetes across 28 studies were included in analyses of Modified Stumvoll ISI and insulin fold change, respectively. Two of these studies included participants of Hispanic American ancestry (MACAD and HTN-IR) and 1 included participants of East Asian ancestry (TAICHI); the remaining 25 studies included individuals of European ancestry.

Meta-analysis	Number of individuals
IFC_adjBMI_EUR	53287
IFC_noBMI_EUR	53334
IFC_adjBMI_NONEUR	1837
IFC_noBMI_NONEUR	1838
IFC_adjBMI_ALL	55124
IFC_noBMI_ALL	55172
ISI_adjBMI_EUR	53657
ISI_noBMI_EUR	53710
ISI_adjBMI_NONEUR	1824

ISI_noBMI_NONEUR	1825
ISI_adjBMI_ALL	55481
ISI_noBMI_ALL	55535

For each variant, we have provided the following information:

chromosome: the chromosome that the variant is located on

base_pair_location: the base pair location of the variant in build 37

effect_allele: the effect allele of the variant

other_allele: the non-effect allele

effect_allele_frequency: frequency of the effect allele in the meta-analysis

beta: the effect size of the effect allele in the meta-analysis

standard_error: the standard error of the effect size in the meta-analysis

p_value: the p-value of the variant/trait association in the meta-analysis

n: the number of individuals after QC being tested for association at a specific variant

het_p_value: heterogeneity test p-value

variant_id – chromosome_position_EA_OA. Alleles are in order effect_allele, other_allele.