

Supplementary Information

A two-sample Mendelian randomization study explores metabolic profiling of different glycemic traits

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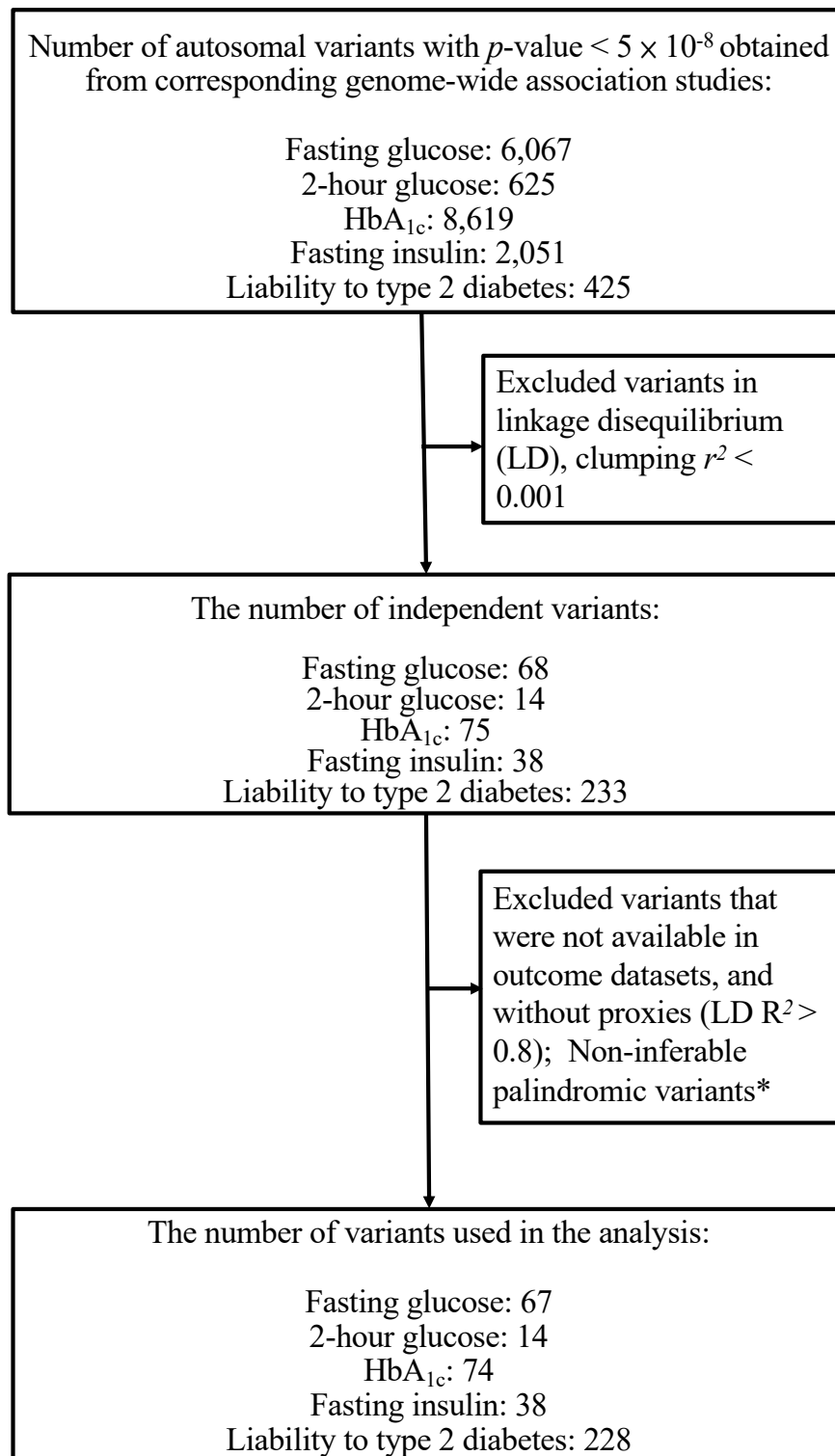
Supplementary Figure 1. Flowchart for genetic instrument selection for glycemic traits (fasting glucose, 2-hour glucose, HbA_{1c} and fasting insulin) and liability to type 2 diabetes

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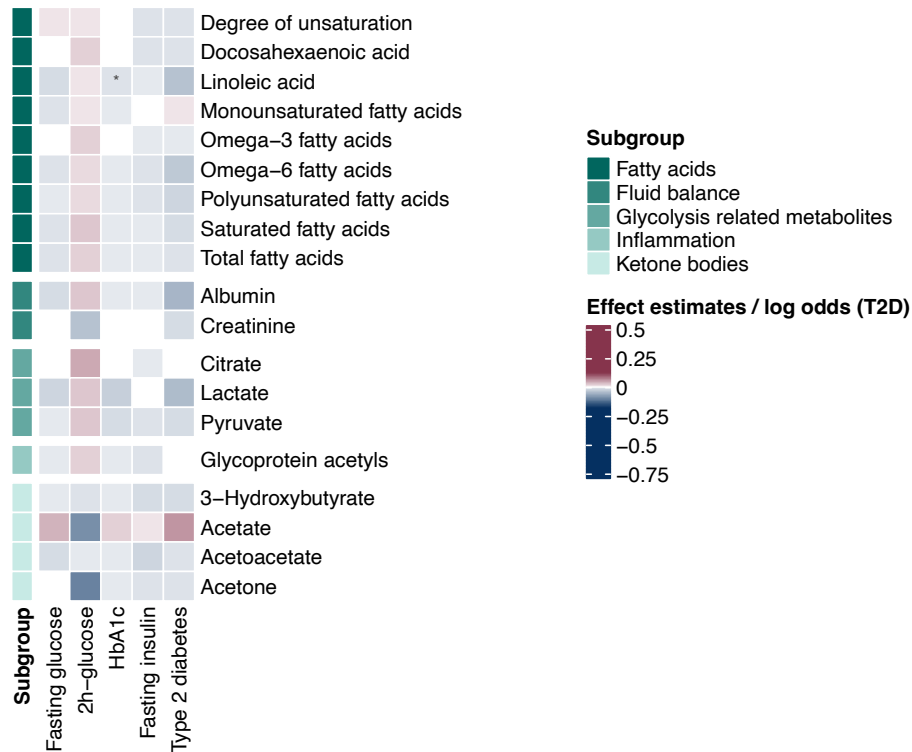
Supplementary Figure 4. Heatmap of associations of 14 genetically predicted lipoprotein subclasses on glycemic traits (fasting glucose, 2-hour glucose, f HbA_{1c} and fasting insulin) and type 2 diabetes risk

Supplementary Figure 1. Flowchart for genetic instrument selection for glycemic traits and liability to type 2 diabetes



Non-inferable palindromic variants, with effect allele frequencies between 0.42 and 0.58.

Supplementary Figure 2. Heatmap of associations of genetically predicted circulating fatty acids and various low-molecular weight metabolites on glycemic traits (fasting glucose, 2-hour glucose, HbA_{1c} and fasting insulin) and type 2 diabetes risk



Circulating metabolites include: fatty acids, biomarkers of fluid balance, glycolysis related metabolites, inflammation, and ketone bodies. The estimates were obtained from Mendelian randomization analyses using the inverse variance weighted method. Asterisks depict statistical significance ($p < 0.0004$).

Supplementary Figure 3. Heatmap of associations of genetically predicted circulating cholesterol metabolites on glycemic traits (fasting glucose, 2-hour glucose, HbA_{1c} and fasting insulin) and type 2 diabetes risk



Measures of cholesterol metabolites include: apolipoproteins, cholesterol, cholesteryl esters, free cholesterol, lipoprotein particle concentrations, lipoprotein particle sizes, other lipids, phospholipids, total lipids, and triglycerides. The estimates were obtained from Mendelian randomization analyses using the inverse variance weighted method. Asterisks depict statistical significance ($p < 0.0004$). LDL, low-density lipoprotein. HDL, high-density lipoprotein. VLDL, very low-density lipoprotein.

Supplementary Figure 4. Heatmap of associations of 14 genetically predicted lipoprotein subclasses on glycemic traits (fasting glucose, 2-hour glucose, f HbA_{1c} and fasting insulin) and type 2 diabetes risk

a)



b)



Lipoprotein subclasses in panel a): lipoprotein subfractions in very small, small, medium, large, very large VLDL, and chylomicrons and extremely large VLDL; and panel b): lipoprotein subfractions in small, medium, and large LDL, in small, medium, large, and very large HDL and those in IDL. The estimates were obtained from Mendelian randomization analyses using the inverse variance weighted method. Asterisks depict statistical significance ($p < 0.0004$). HDL, high-density lipoprotein. IDL, intermediate-density lipoprotein. LDL, low-density lipoprotein. VLDL, very low-density lipoprotein.