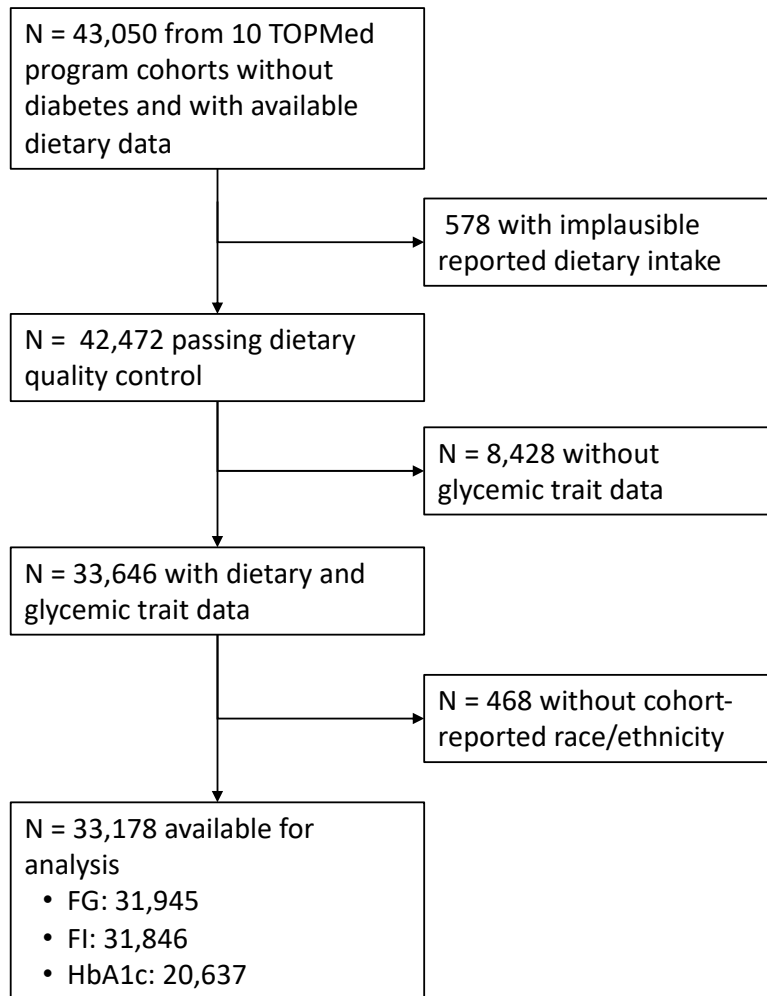
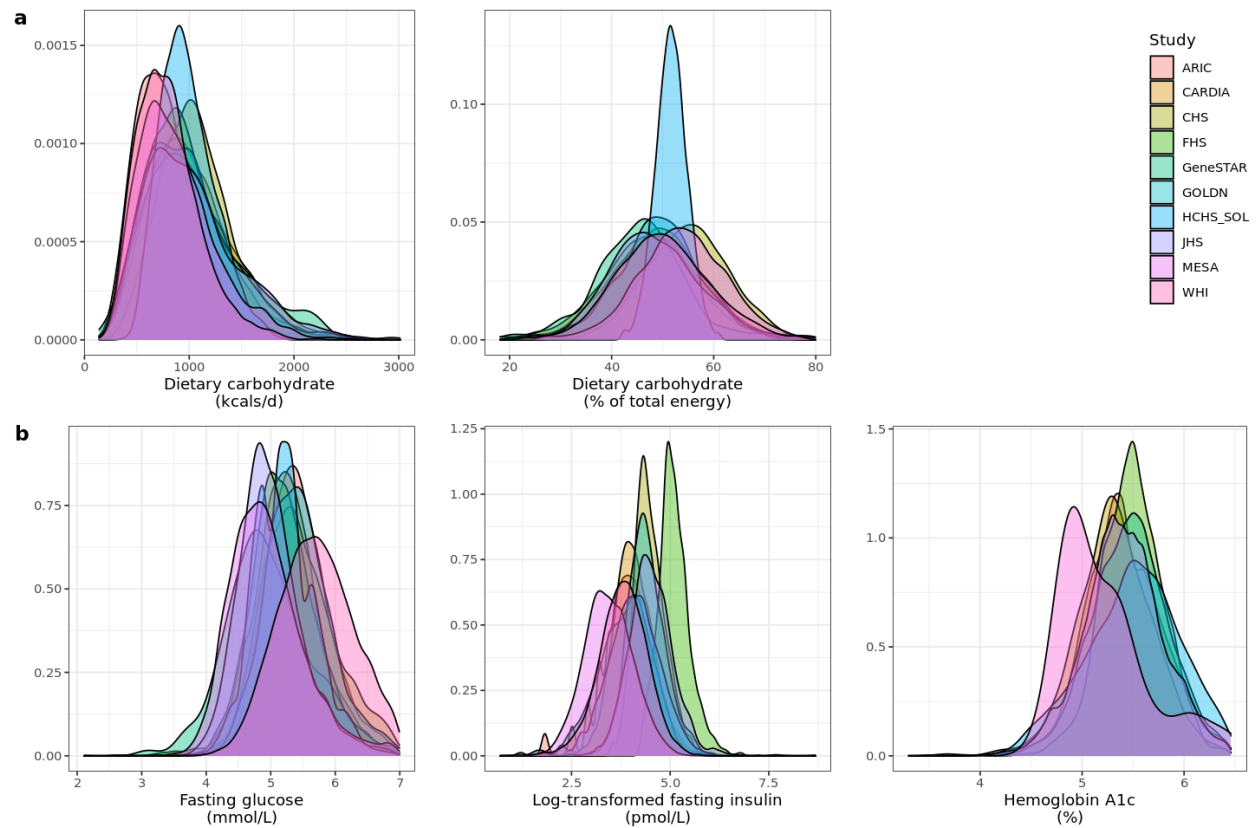


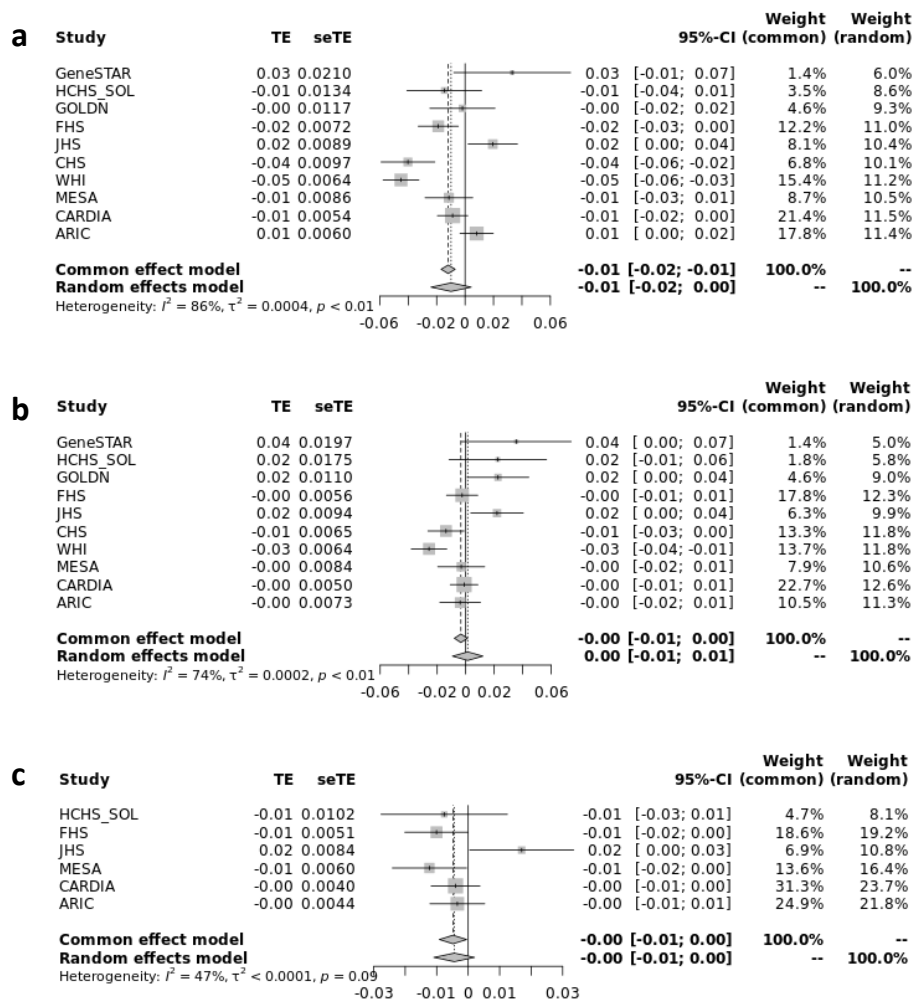
SUPPLEMENTARY FIGURES



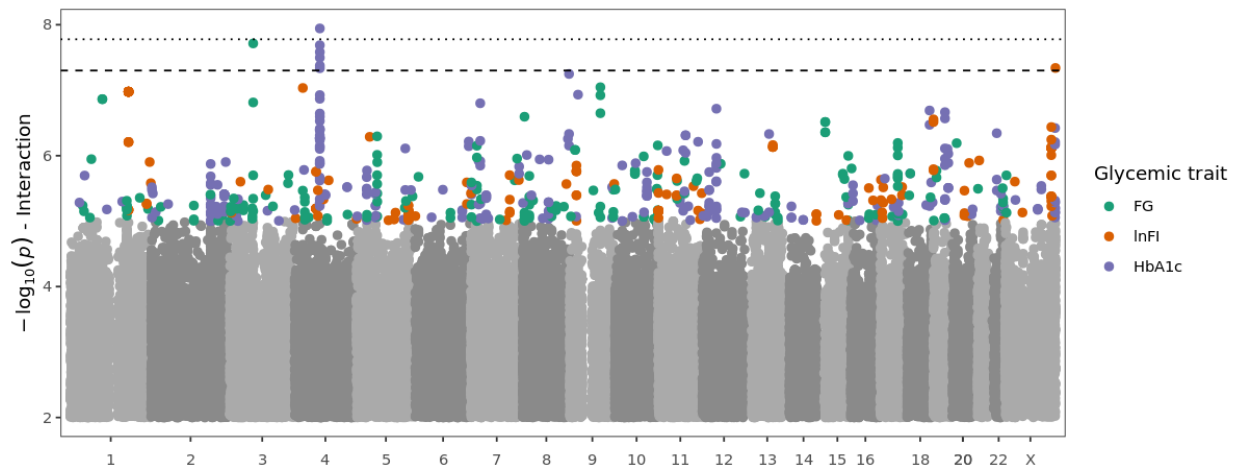
Supplementary Figure S1: Participant inclusion flowchart.



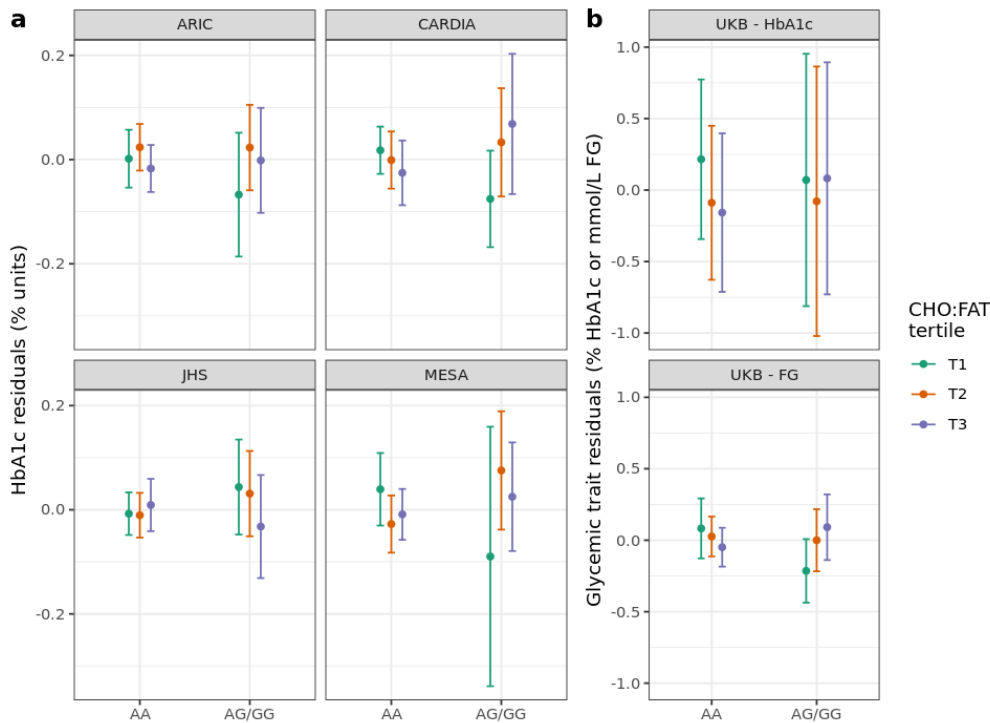
Supplementary Figure S2: Density plots illustrate the cohort-specific distributions of (a) carbohydrate intake, expressed as either kcals/day or percentage of total caloric intake, and (b) the three glycemic traits. We note that HCHS SOL was the only cohort whose dietary data were derived from 24-hour recalls rather than food frequency questionnaires.



Supplementary Figure S3: Forest plots illustrating meta-analysis results for the association of a 250 kcal carbohydrate-fat exchange with each of: FG (a), lnFI (b), and HbA1c (c).

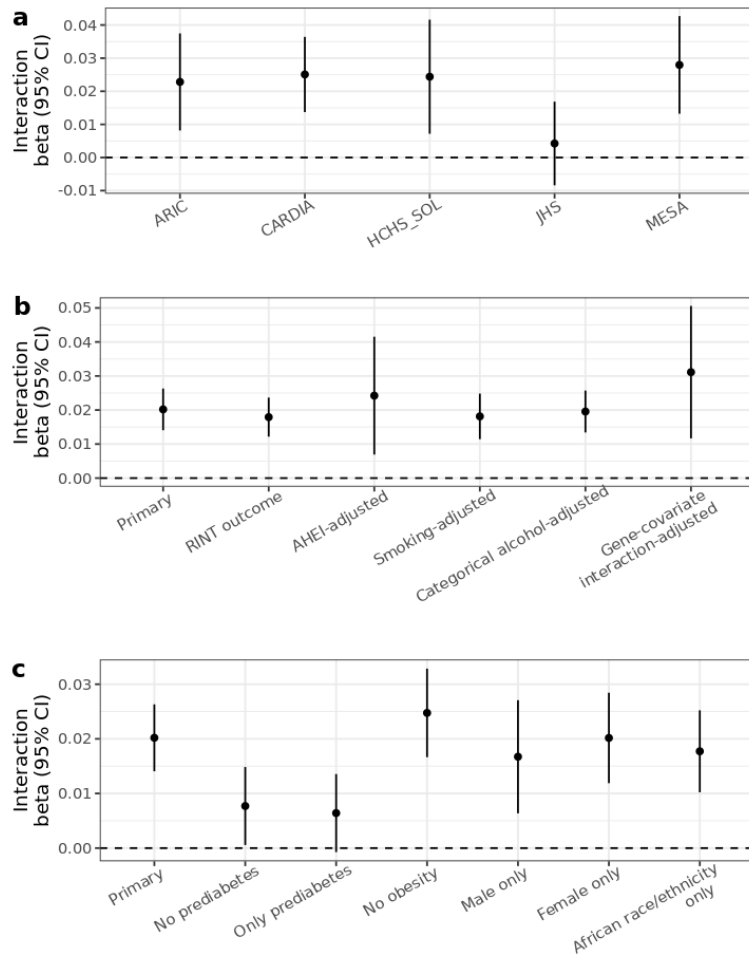


Supplementary Figure S4: Manhattan plot with single-variant interaction testing results for all glycemic traits. For each glycemic trait (colors, only shown for variants with $p < 10^{-5}$), $-\log_{10}(p\text{-values})$ (y-axis) are shown as a function of genomic position (x-axis). The dashed line denotes a standard genome-wide significance threshold of 5×10^{-8} , and the dotted line denotes a study-wide significance threshold of $5 \times 10^{-8} / 3 = 1.67 \times 10^{-8}$. Only variants with $p < 0.01$ are shown.

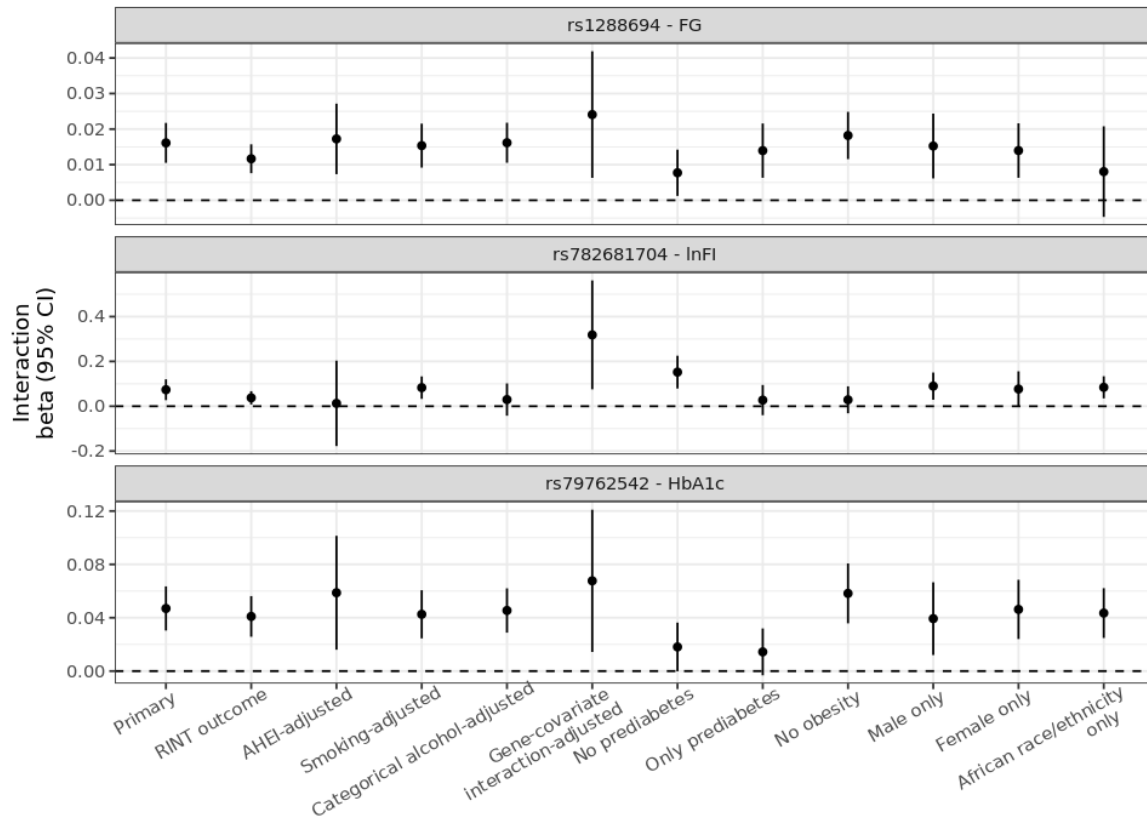


Supplementary Figure S5: Exploration of the rs79762542 interaction and replication in the population subsets with African race/ethnicity (TOPMed, [a]) and ancestry (UKB, [b]). (a) Stratified plots (one for each cohort with HbA1c available) display residualized HbA1c within strata defined by both genotype at rs79762542 (none vs. any minor alleles) and tertile of carbohydrate:fat ratio. This ratio was defined in the pooled dataset on a caloric basis and is used to provide a visual representation of the modeled macronutrient exchange. (b) Similar stratified plots for the UKB replication cohort. The y-axis displays

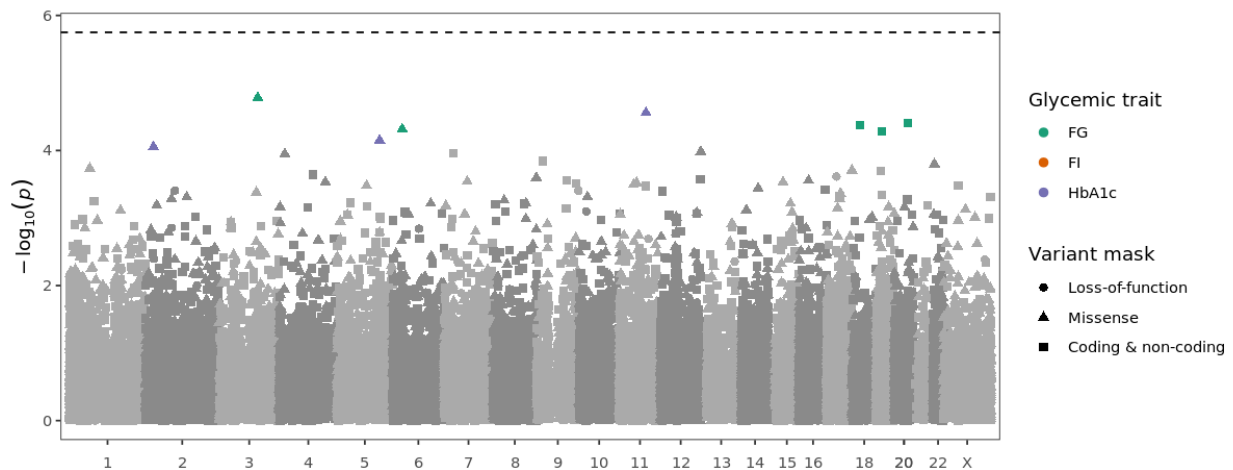
residuals after regressing the relevant trait (HbA1c or FG) on the set of covariates used in the replication analysis. Error bars indicate 95% confidence intervals for the mean residual values after stratification.



Supplementary Figure S6: Sensitivity analysis results for the study-wide significant variant rs79762542. (a) Cohort-specific interaction effect estimates for the raw HbA1c trait. (b) Interaction effect estimates from cross-cohort meta-analysis using alternative outcome transformations (RINT outcome) or additional covariate adjustments. Adjustments for AHEI, smoking, and categorical alcohol included their genotype-covariate interactions, and the “gene-covariate interaction-adjusted” model includes terms for total energy, kcals from protein, fiber intake, and alcohol intake. Categorical alcohol was coded as “none”, “moderate” (less than one drink per day for women or two for men), or “high”. (c) As in (b), but using varying subsets of the full cohorts rather than varying statistical adjustments. Prediabetes was defined as $FG > 5.6$ mmol/L or $HbA1c > 5.7\%$. Obesity was defined as $BMI > 30$ kg/m².



Supplementary Figure S7: Sensitivity analysis results for the three variants with $p < 5 \times 10^{-8}$. Panel headers indicate the tested variant and the associated glycemic trait. Adjustments and population subsets are defined as in Supp. Fig. S5.



Supplementary Figure S8: Manhattan plot with aggregate rare-variant interaction testing results for all glycemic traits. For each glycemic trait (colors, only shown for variants with $p < 10^{-4}$), gene-based $-\log_{10}(p\text{-values})$ (y-axis) are shown as a function of the average genomic position for variants included in each gene unit (x-axis). The dashed line denotes a Bonferroni significance threshold of $0.05 / 28,111 \text{ genes} = 1.78 \times 10^{-6}$.