

Table S1. Characteristics of the study samples

| A. Study Characteristics | | | | | | | | | | | |
|---|---|---|---|---|---|--|--|---|---|---|---|
| Study | ARIC | MEC | WHI Batch1 | WHI Batch2 | HyperGEN | CLHNS | TAICHI | Finnish T2D patients ^a | Finnish unaffected ^a | Norwegian T2D ^b | Norwegian unaffected ^b |
| Study design | population-based | population-based | population-based | population-based | family-based | population-based | population-based | Selected T2D cases from population-based studies | Selected controls from population-based studies | Selected T2D cases from population-based studies | Selected controls from population-based studies |
| Ethnicity of study participants | African American | African American | African American | African American | African American | East Asian | East Asian | European | European | European | European |
| B. Phenotypes | | | | | | | | | | | |
| Total sample size (% female) | 3,180 (62.4) | 380 (17.1) | 1,387 (100) | 646 (100) | 1,230 (66.9) | 1,716 (47.6) | 7,733 (38.7) | 1,970 (30.7) | 6,066 (45.3) | 1,298 (50.0) | 1,495 (49.6) |
| Age (mean±SD, yrs) | 53.6±5.9 | ---- ^c | 61.7±7.2 | 60.7±6.6 | 47.0±12.6 | 21.5±0.3 | 65.46 ± 11.44 | 60.3 ± 8.1 | 58.4 ± 8.4 | 64.2 ± 12.8 | 63.3 ± 13.9 |
| Fasting status | ≥ 8 hours | ≥ 8 hours | ≥ 8 hours | ≥ 8 hours | ≥ 8 hours | ≥ 8 hours | various | overnight or >8 hours fast | overnight or >8 hours fast | non-fasting | non-fasting |
| Use of lipid-lowering medication & exclusion | NO exclusion ^d | NO exclusion ^d | NO exclusion ^d | NO exclusion ^d | NO exclusion ^d | NO exclusion ^d | NO exclusion ^d | Exclude when known to be on lipid-lowering medication | Exclude when known to be on lipid-lowering medication | NO relevant information available | NO relevant information available |
| Methods/reagents of triglycerides measurement | Standard enzymatic methods | Standard enzymatic methods | Standard enzymatic methods | Standard enzymatic methods | Standard enzymatic methods | Standard enzymatic methods | varied across study sites | Standard enzymatic methods | Standard enzymatic methods | Standard enzymatic methods | Standard enzymatic methods |
| Methods/reagents of HDL-C measurement | Standard enzymatic methods | Standard enzymatic methods | Standard enzymatic methods | Standard enzymatic methods | Standard enzymatic methods | Standard enzymatic methods | Homogenous assay direct HDL-C (Equal Diagnostics, Exton, PA) | Standard enzymatic methods | Standard enzymatic methods | Standard enzymatic methods | Standard enzymatic methods |
| Methods/reagents of LDL-C measurement | Calculated using Friedewald equation | Calculated using Friedewald equation | Calculated using Friedewald equation | Calculated using Friedewald equation | Calculated using Friedewald equation | Calculated using Friedewald equation | Homogenous assay direct LDL-C (Equal Diagnostics, Exton, PA) | Calculated using Friedewald equation | Calculated using Friedewald equation | Calculated using Friedewald equation | Calculated using Friedewald equation |
| Triglycerides (median [interquartile]) | 1.10 (0.81-1.51) | 1.30 (0.82-1.53) | 1.35 (0.93-1.59) | 1.08 (0.81-1.46) | 1.04 (0.75-1.50) | 1.04 (0.75-1.50) | 1.19 (0.74-1.41) | 1.33 (0.94 - 1.95) | 1.83 (1.14-2.17) | 2.60 (1.53-3.19) | 1.87 (1.13-2.34) |
| HDL-C (mean±SD, mmol/L) | 1.42 ± 0.45 | 1.37 ± 0.38 | 1.51 ± 0.39 | 1.47 ± 0.38 | 1.38 ± 0.41 | 1.38 ± 0.41 | 1.09 ± 0.29 | 1.21 ± 0.36 | 1.33 ± 0.39 | 1.26 ± 0.39 | 1.42 ± 0.41 |
| LDL-C (mean±SD, mmol/L) | 3.57 ± 1.12 | 3.20 ± 1.13 | 3.40 ± 0.99 | 3.69 ± 1.02 | 3.08 ± 0.97 | 3.08 ± 0.97 | 2.44 ± 0.75 | 2.93 ± 0.91 | 3.32 ± 0.94 | 4.16 ± 1.11 | 4.27 ± 1.14 |
| C. Genotyping | | | | | | | | | | | |
| Metabochip genotype calling | GenCall | GenCall | GenCall | GenCall | BeadStudio | BeadStudio | BeadStudio | GenomeStudio | GenomeStudio | GenomeStudio | GenomeStudio |
| HWE P value threshold | > 1E-06 | > 1E-06 | > 1E-06 | > 1E-06 | > 1E-06 | > 1E-06 | > 0.001 | n.a. | n.a. | n.a. | n.a. |
| SNP call rate | 95% | 95% | 95% | 95% | 95% | 97% | 95% | 95% | 95% | 95% | 95% |
| SNP MAF threshold | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. | n.a. |
| Other SNP QC | Mendelian errors in YRI > 1 (out of 30 trios); Discordant calls on YRI > 3 (out of 90 samples); Discordant calls from GenoSNP > 3.3%; PAGE consensus vs HapMap database > 3 (out of 90 samples) | Mendelian errors in YRI > 1 (out of 30 trios); Discordant calls on YRI > 3 (out of 90 samples); Discordant calls from GenoSNP > 3.3%; PAGE consensus vs HapMap database > 3 (out of 90 samples) | Mendelian errors in YRI > 1 (out of 30 trios); Discordant calls on YRI > 3 (out of 90 samples); Discordant calls from GenoSNP > 3.3%; PAGE consensus vs HapMap database > 3 (out of 90 samples) | Mendelian errors in YRI > 1 (out of 30 trios); Discordant calls on YRI > 3 (out of 90 samples); Discordant calls from GenoSNP > 3.3%; PAGE consensus vs HapMap database > 3 (out of 90 samples) | GenTrain score <0.7; Cluster Separation Score < 0.45 (both GenTrain and CSS were selected at 5% percentile) | poor genotyping cluster; MI errors in ≥ 3 samples; SNPs with ≥ 3 discrepancies with known HapMap genotypes among 14 CEU samples; SNPs with primers that do not map > 97% to genome or map to multiple places in genome | replication errors (1 or more) | Cluster Separation score less than 0.2 or which had more than 1 replicate error as defined with the HapMap control samples. Additional hand editing was done for X, Y and Mitochondrial loci. | Cluster Separation score less than 0.2 or which had more than 1 replicate error as defined with the HapMap control samples. Additional hand editing was done for X, Y and Mitochondrial loci. | Cluster Separation score less than 0.2 or which had more than 1 replicate error as defined with the HapMap control samples. Additional hand editing was done for X, Y and Mitochondrial loci. | Cluster Separation score less than 0.2 or which had more than 1 replicate error as defined with the HapMap control samples. Additional hand editing was done for X, Y and Mitochondrial loci. |
| Sample success rate | ≥98.98% | ≥97.74% | ≥97.70% | ≥97.70% | ≥98.5% | ≥ 98.6% | ≥ 98.49% | ≥ 98.15% | ≥ 98.15% | ≥ 98.15% | ≥ 98.15% |
| Concordance rate for duplicate pairs | 99.51% | 99.99% | 99.99% | 99.99% | 99.98% | 99.99% | ---- | Across all our Metabochip samples, 99.9978% reproducibility among 163 blind duplicate pairs; 99.52% concordance with HapMap genotypes (326 HapMap controls) | Across all our Metabochip samples, 99.9978% reproducibility among 163 blind duplicate pairs; 99.52% concordance with HapMap genotypes (326 HapMap controls) | Across all our Metabochip samples, 99.9978% reproducibility among 163 blind duplicate pairs; 99.52% concordance with HapMap genotypes (326 HapMap controls) | Across all our Metabochip samples, 99.9978% reproducibility among 163 blind duplicate pairs; 99.52% concordance with HapMap genotypes (326 HapMap controls) |
| D. Statistical analysis | | | | | | | | | | | |
| Software for association analyses | PLINK | PLINK | PLINK | PLINK | GWAF | PLINK | PLINK | EMMAX | EMMAX | EMMAX | EMMAX |
| Statistical model | multiple linear | multiple linear | multiple linear | multiple linear | linear mixed effect | multiple linear | multiple linear | mixed model | mixed model | mixed model | mixed model |
| Covariates used | age, sex, PC1-10 | age, sex, PC1-10 | age, PC1-10 | age, PC1-10 | age, sex, PC1-10 | age, sex, household assets, household income, PC1 | age, sex, PC1-PC5, study cohort | sex, age, age ² , study | sex, age, age ² , study | sex, age, age ² , study | sex, age, age ² , study |

^a Finnish T2D patients and unaffected individuals were from the Finland-United States Investigation of NIDDM Genetics (FUSION), Dehko 2D 2007 (D2D2007), Diabetes Prevention Study (DPS), Dose-Responses to Exercise Training (DR's EXTRA), and Metabolic Syndrome in Men (METSIM)

^b Norwegian T2D patients and unaffected individuals were from the cohorts of Nord-Trøndelag Health Study (HUNT 2) and the Tromsø Study (TROMSO)

^c The mean and SD were not provided for MEC because the ages of MEC subjects were provided as a categorical value with seven 5-year age groups due to confidentiality

^d Sensitivity analyses that excluded individuals on lipid lowering medication did not appreciably alter the association results