

SUPPLEMENTAL MATERIAL

Supplemental Table 1. Quality control pipeline*

| Individuals with phenotypes | 51,186 | | | | | | | | |
|---|-------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|-------------------|
| 7,305 individuals' samples not sent to Broad due to lack of patient consent, lack of DNA, or DNA quality issues | | | | | | | | | |
| Total DNA samples sent to Broad Institute for genotyping (including controls and duplicates) | 46,560 | | | | | | | | |
| 2,679 control samples or duplicates removed | | | | | | | | | |
| Study | ARIC | CARDIA | CFS | CHS | CSSCD | FHS | JHS | MESA | Total |
| Samples genotyped (not including controls or duplicates) | 14,996 | 3,520 | 1,481 | 5,485 | 1,707 | 7,992 | 2,156 | 6,544 | 43,881 |
| Twins removed | | | | | | 23 | | | 23 |
| Removed for incomplete family information | | | | | | 436 | | | 436 |
| Removed for Mendel errors | | | 7 | | | 26 | | | 33 |
| Removed for low genotyping rate | 287 | 124 | 48 | 183 | 57 | 130 | 36 | 249 | 1,114 |
| Final number of genotyped unique individuals (% of samples genotyped) | 14,709 (98.1%) | 3,396 (96.5%) | 1,426 (96.3%) | 5,302 (96.7%) | 1,650 (96.7%) | 7,377 (92.3%) | 2,120 (98.3%) | 6,295 (96.2%) | 42,275 (96.3%) |
| Self-identified solely as AA, with available pilot phenotypes | 3,435 | 1,613 | 693 | 794 | | 2,118 | 1,713 | | 10,366 |
| Self-identified solely as EA, with available pilot phenotypes | 10,504 | 1,743 | 691 | 4,362 | | 6,914 | 2,433 | | 26,647 |
| Self-identified solely as HIS, with available pilot phenotypes | | | | | | | 1,410 | | 1,410 |
| Self-identified solely as CHI, with available pilot phenotypes | | | | | | | 717 | | 717 |
| Total analyzed[†] (% of final number of genotyped individuals) | 13,939 (94.8%) | 3,356 (98.8%) | 1,384 (97.1%) | 5,156 (97.2%) | | 6,914 (93.7%) | 2,118 (99.9%) | 6,273 (99.7%) | 39,140 (92.6%) |

AA = African American; EA = European American or Caucasian; HIS = Hispanic; CHI = Chinese American.

* The Sleep Heart Health Study (SHHS)¹¹ is not represented in this table because the subgroup of the SHHS cohort with genotype data comprises individuals originally recruited from ARIC, CHS, and FHS (and who are included in this table under these other cohorts).

[†] Because no lipid phenotypes were available for the CSSCD cohort, no analyses were performed for this cohort in the Pilot Study.

Supplemental Table 2. Genotype-phenotype associations for lipid traits

| Trait | Gene | SNP (minor/major alleles) | African American | | | | | | | European American | | | | | | | Hispanic | Chinese American |
|-------|--------------|---------------------------------|--|--|--|--|--|--|--|--|--|--|--|---|---|--|---|--|
| | | | ARIC N=3435 | JHS N=2118 | MESA N=1713 | CARDIA N=1613 | CHS N=794 | CFS N=693 | Meta- analysis N=10366 | ARIC N=10504 | FHS N=6914 | CHS N=4362 | MESA N=2433 | CARDIA N=1743 | CFS N=691 | Meta- analysis N=26647 | MESA N=1410 | MESA N=717 |
| HDL | <i>CETP</i> | rs4783961 A/G | 0.24 (0.02) 4.2E-22 (43%) 0.49 | 0.21 (0.03) 8.5E-12 (44%) 0.12 | 0.21 (0.04) 9.6E-10 (44%) 0.59 | 0.16 (0.05) 6.8E-06 (44%) 0.84 | 0.22 (0.06) 1.2E-05 (45%) 0.94 | 0.22 (0.01) 5.7E-05 (41%) 0.16 | 0.21 (0.01) 1.8E-52 (49.8%) 0.41 | 0.11 (0.01) 1.6E-16 (49.8%) 0.34 | 0.11 (0.02) 4.1E-10 (49.8%) 0.49 | 0.15 (0.02) 4.6E-12 (49%) 0.44 | 0.09 (0.03) 1.9E-04 (49.7%) 0.67 | 0.13 (0.03) 0.10 (0.06) 0.59 | 0.10 (0.01) 1.6E-40 (49.5%) 1.0 | 0.12 (0.04) 0.001 (24%) 0.18 | 0.12 (0.05) 0.001 (24%) 1.0 | 0.12 (0.04) 0.001 (24%) 0.18 |
| HDL | <i>CETP</i> | rs17231506 T/C | 0.16 (0.04) 6.9E-06 (14%) 1.0 | 0.07 (0.04) 0.11 (0.05) 0.34 | 0.10 (0.05) 0.04 (0.05) 0.85 | 0.06 (0.07) 0.18 (0.07) 0.35 | 0.13 (0.07) 0.06 (0.07) 0.30 | 0.26 (0.08) 0.001 2.5E-09 1.0 | 0.12 (0.02) 0.001 2.5E-09 30% | 0.24 (0.01) 1.7E-60 9.8E-33 0.71 | 0.23 (0.02) 0.001 1.0E-35 0.83 | 0.28 (0.02) 0.001 5.1E-11 0.70 | 0.21 (0.03) 0.001 4.1E-05 0.74 | 0.24 (0.04) 0.001 2.0E-148 0.86 | 0.26 (0.06) 0.001 4.1E-05 0.42 | 0.24 (0.01) 2.0E-148 0.40 | 0.24 (0.04) 0.001 4.7E-09 1.0 | 0.35 (0.07) 3.9E-07 0.40 |
| HDL | <i>LIPC</i> | rs1800588 T/C | 0.09 (0.02) 5.9E-04 (48%) 1.0 | 0.07 (0.03) 0.03 (0.03) 0.93 | 0.11 (0.03) 0.002 (0.03) 0.81 | 0.11 (0.05) 0.002 (0.05) 0.40 | 0.18 (0.06) 0.002 (0.06) 0.22 | 0.11 (0.06) 0.001 2.1E-04 0.86 | 0.10 (0.01) 0.001 2.3E-12 0.86 | 0.13 (0.02) 0.001 2.3E-14 0.03 | 0.12 (0.02) 0.001 5.7E-08 0.93 | 0.13 (0.03) 0.001 2.0E-06 0.21 | 0.24 (0.04) 0.001 0.001 0.14 | 0.08 (0.07) 0.001 0.31 0.31 | 0.12 (0.01) 0.001 2.8E-29 0.01 | 0.14 (0.04) 0.001 1.3E-04 0.01 | 0.05 (0.06) 0.35 (35%) 0.12 | |
| HDL | <i>LPL</i> | rs328 G/C | 0.17 (0.05) 5.0E-04 (7%) 0.68 | 0.20 (0.06) 5.2E-04 (8%) 0.44 | 0.10 (0.07) 0.13 (0.07) 1.0 | 0.04 (0.07) 0.50 (0.07) 0.86 | 0.06 (0.10) 0.55 (0.07) 0.79 | 0.12 (0.11) 0.28 (0.11) 0.48 | 0.13 (0.03) 0.1E-06 1.1E-06 0% | 0.18 (0.02) 0.001 2.9E-15 0.26 | 0.19 (0.03) 0.001 1.1E-09 0.16 | 0.16 (0.03) 0.001 8.9E-06 0.38 | 0.06 (0.05) 0.001 2.0E-08 0.46 | 0.13 (0.06) 0.001 0.27 0.31 | 0.08 (0.07) 0.001 0.13 0.13 | 0.12 (0.01) 0.001 1.8E-33 0.48 | 0.14 (0.04) 0.001 0.001 0.12 | |
| LDL | <i>PCSK9</i> | rs505151 G/A | 0.09 (0.03) 0.002 (25%) 0.26 | 0.15 (0.04) 3.7E-05 (26%) 0.86 | 0.09 (0.04) 0.02 (24%) 0.52 | 0.15 (0.04) 0.06 (25%) 0.01 | 0.08 (0.06) 0.17 (24%) 0.01 | -0.08 (0.09) 0.37 (28%) 1.0 | 0.11 (0.02) 0.001 1.1E-10 0.35% | 0.09 (0.04) 0.02 0.17 0.11 | 0.05 (0.05) 0.36 0.17 0.07 | 0.07 (0.05) 0.17 0.17 1.0 | -0.03 (0.07) 0.001 0.001 0.07 | 0.12 (0.09) 0.17 0.17 1.0 | 0.12 (0.09) 0.49 0.49 0.0% | 0.07 (0.02) 0.004 0.004 0.22 | 0.23 (0.08) 0.03 0.03 0.76 | |
| LDL | <i>PCSK9</i> | rs11591147 T/G | -0.52 (0.17) 0.002 (0.5%) 0.07 | -0.14 (0.21) 0.50 (0.5%) 1.0 | -0.27 (0.26) 0.30 (0.4%) 1.0 | -0.38 (0.21) 0.08 (0.6%) 0.06 | -0.70 (0.45) 0.12 (0.3%) 1.0 | — — — — | -0.38 (0.10) 0.62 0% | -0.47 (0.06) 0.53 | -0.47 (0.08) 1.0 | -0.50 (0.09) 0.60 | -0.25 (0.12) 0.10 | -0.61 (0.14) 0.10 | -0.50 (0.26) 0.50 | -0.46 (0.04) 0.50 | -0.21 (0.20) 0.30 — | |
| TG | <i>LPL</i> | rs328 G/C | -0.21 (0.05) 3.5E-05 (7%) 0.68 | -0.18 (0.06) 0.003 (8%) 0.44 | -0.13 (0.07) 0.07 (7%) 1.0 | -0.18 (0.07) 0.007 (8%) 0.86 | 0.00 (0.10) 0.99 (7%) 0.79 | -0.36 (0.16) 0.02 0.35 0.48 | -0.17 (0.03) 1.3E-09 0.10% | -0.20 (0.02) 1.1E-17 0.26 | -0.19 (0.03) 8.5E-09 0.16% | -0.22 (0.03) 2.8E-10 0.38 | -0.23 (0.05) 4.9E-07 0.46 | -0.09 (0.05) 0.10 0.46 | -0.25 (0.06) 0.14 0.44 | -0.20 (0.07) 0.14 0.63 | 0.27 (0.08) 0.59 0.48 | |
| TG | <i>APOA5</i> | rs3135506 C/G | 0.22 (0.05) 2.3E-05 (6%) 0.37 | 0.31 (0.06) 1.6E-06 (6%) 0.57 | 0.29 (0.07) 4.0E-08 (6%) 1.0 | 0.14 (0.08) 1.2E-04 (6%) 0.70 | 0.23 (0.10) 0.16 0.09 | 0.27 (0.14) 0.09 2.6E-20 | 0.27 (0.03) 0.09 2.6E-24 | 0.28 (0.04) 0.09 1.1E-08 | 0.22 (0.04) 0.09 1.1E-08 | 0.26 (0.05) 0.002 1.1E-08 | 0.18 (0.06) 0.002 0.19 | 0.29 (0.07) 0.002 0.61 | 0.48 (0.14) 0.07 0.38 | 0.26 (0.02) 0.002 0.59 | 0.37 (0.05) 0.59 0.09 | |

For each study cohort/ethnicity with each phenotype, the five numbers are (1) effect size (beta-coefficient), (2) standard error for the effect size, (3) P value for genotype-phenotype association, (4) allele frequency for the allele designated in the SNP column as the minor allele, and (5) the Hardy-Weinberg P value for the SNP. For the meta-analyses, the five numbers are (1) the overall effect size, (2) the overall standard error, (3) the overall P value for the ethnicity, (4) the Cochran's Q P value for heterogeneity among the cohorts for the ethnicity, and (5) the I² inconsistency metric for heterogeneity. The numbers of DNA samples successfully genotyped and passing QC criteria for each cohort are indicated in the top row. HDL = high-density lipoprotein cholesterol; LDL = low-density lipoprotein cholesterol; TG = triglyceride

SUPPLEMENTAL FIGURE LEGENDS

Supplemental Figure 1. Governance structure of CARe.

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