**Supplemental material for "A large electronic health record-based genome-wide association study of serum lipids"**

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**Supplementary Table 1:** GERA covariate association.

(a) Mean effect size differences in Latinos (n=7,795), East Asians (n=6,855), African Americans (n=2,958), and South Asians (n=439) compared to non-Hispanic whites (n=76,627) after adjusting for age, sex, and BMI. Est, mean effect size difference from non-Hispanic whites (where each lipid trait is normalized to a standard normal distribution).

| | HDL Est | HDL P | LDL Est | LDL P | TC Est | TC P | TG Est | TG P |
|---|---|---|---|---|---|---|---|---|
| Latinos | -0.065 | 1.6e-10 | -0.008 | 0.5 | 0.011 | 0.34 | 0.127 | 1.7e-30 |
| East Asians | -0.052 | 1.7e-06 | 0.019 | 0.12 | 0.092 | 5.5e-14 | 0.280 | 5.3e-125 |
| African Americans | 0.191 | 2.6e-33 | 0.025 | 0.17 | -0.068 | 0.00016 | -0.457 | 2.3e-153 |
| South Asians | -0.330 | 3.9e-16 | -0.025 | 0.59 | -0.034 | 0.46 | 0.344 | 6.2e-15 |

(b) Covariate association within each group.

(i) Non-Hispanic whites (n=76,627). $PC_1$ represents the North-Southeast European cline. $PC_2$ Southwest-Northeast European.

| | HDL | | | LDL | | | TG | | | TC | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Sign | $r^2$ | p | Sign | $r^2$ | p | Sign | $r^2$ | p | Sign | $r^2$ | p |
| $Age_c$ | + | 0.0016 | 4e-33 | + | 0.02 | 6.2e-78 | + | 0.02 | 2.8e-210 | + | 0.035 | 3.4e-192 |
| $Age_c^2$ | - | 0.0011 | 1.4e-62 | - | 0.035 | 4.3e-202 | - | 0.022 | 2.3e-104 | - | 0.053 | 0 |
| $Age_c^3$ | - | 0.0013 | 1.4e-06 | - | 0.021 | 1.3e-29 | - | 0.014 | 1.4e-57 | - | 0.034 | 3.2e-63 |
| $\log(BMI)_c$ | - | 0.11 | 0 | + | 0.02 | 1.3e-220 | + | 0.12 | 0 | + | 0.012 | 2.2e-185 |
| $\log(BMI)_c^2$ | + | 0.00027 | 0.00036 | - | 0.0059 | 4.6e-103 | - | 6.7e-05 | 1.1e-11 | - | 0.0029 | 3e-78 |
| $\log(BMI)_c^3$ | + | 0.044 | 1.3e-32 | - | 0.0057 | 1.5e-07 | - | 0.041 | 3.4e-65 | - | 0.0027 | 7.3e-13 |
| Female | + | 0.2 | 0 | - | 0.0076 | 2.5e-30 | - | 0.014 | 2.2e-73 | + | 0.0032 | 1.5e-196 |
| $PC_1$ | + | 1.5e-05 | 0.96 | - | 0.00032 | 1.2e-11 | + | 0.00046 | 0.41 | - | 4e-05 | 2.1e-08 |
| $PC_2$ | + | 0.00045 | 0.38 | - | 0.0003 | 0.0087 | - | 7.5e-05 | 0.68 | - | 7.2e-05 | 0.068 |

(ii) Latinos (n=7,795). $PC_1$ is European-Native American, $PC_2$ African-European.

| | HDL | | | LDL | | | TG | | | TC | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Sign | $r^2$ | p | Sign | $r^2$ | p | Sign | $r^2$ | p | Sign | $r^2$ | p |
| $Age_c$ | + | 0.00078 | 0.069 | + | 0.042 | 0.00091 | + | 0.035 | 1.7e-16 | + | 0.065 | 5.5e-09 |
| $Age_c^2$ | - | 0.0013 | 0.0015 | - | 0.053 | 1.3e-18 | - | 0.033 | 5e-09 | - | 0.08 | 4.1e-28 |
| $Age_c^3$ | - | 0.0015 | 0.59 | - | 0.041 | 6.1e-06 | - | 0.024 | 3.8e-07 | - | 0.062 | 4.6e-09 |
| $\log(BMI)_c$ | - | 0.099 | 5.7e-102 | + | 0.0054 | 1.1e-05 | + | 0.085 | 9.4e-91 | + | 0.0025 | 0.00017 |
| $\log(BMI)_c^2$ | + | 0.0025 | 0.025 | - | 0.0055 | 6.8e-11 | - | 0.0008 | 0.00035 | - | 0.0056 | 2.4e-09 |
| $\log(BMI)_c^3$ | + | 0.039 | 0.00046 | + | 0.00095 | 0.2 | - | 0.031 | 0.00017 | + | 0.00014 | 0.56 |
| Female | + | 0.16 | 1.1e-294 | - | 0.02 | 2.4e-17 | - | 0.031 | 5.5e-28 | + | 0.0029 | 0.82 |
| $PC_1$ | + | 0.0068 | 1.4e-06 | + | 0.00056 | 0.027 | - | 0.011 | 2.4e-16 | + | 0.00017 | 0.46 |
| $PC_2$ | - | 0.0024 | 2.3e-05 | + | 0.00039 | 0.17 | + | 0.006 | 7.1e-09 | + | 0.00073 | 0.066 |

(iii) East Asians (n=6,855). $PC_1$ is amount of European ancestry, $PC_2$ Northern-Southern East Asian ancestry.

| | HDL | | | LDL | | | TG | | | TC | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Sign | $r^2$ | p | Sign | $r^2$ | p | Sign | $r^2$ | p | Sign | $r^2$ | p |
| $Age_c$ | + | 6.4e-07 | 0.00027 | + | 0.06 | 4.2e-07 | + | 0.049 | 9.5e-14 | + | 0.091 | 1.3e-16 |
| $Age_c^2$ | - | 0.00017 | 0.21 | - | 0.074 | 5.5e-21 | - | 0.048 | 1.3e-10 | - | 0.1 | 4.5e-30 |
| $Age_c^3$ | - | 5.2e-05 | 0.35 | - | 0.058 | 2.9e-07 | - | 0.036 | 5.5e-07 | - | 0.081 | 1.2e-11 |
| $\log(BMI)_c$ | - | 0.12 | 5.8e-84 | + | 0.032 | 2.1e-19 | + | 0.098 | 5.7e-82 | + | 0.018 | 5.7e-16 |
| $\log(BMI)_c^2$ | + | 0.059 | 1.5e-10 | - | 0.026 | 1.3e-06 | - | 0.044 | 6.9e-08 | - | 0.015 | 0.00013 |
| $\log(BMI)_c^3$ | + | 0.069 | 1.5e-07 | - | 0.018 | 0.0021 | - | 0.049 | 1.7e-08 | - | 0.0091 | 0.0013 |
| Female | + | 0.17 | 3.2e-228 | - | 0.03 | 7.8e-17 | - | 0.045 | 8.7e-26 | - | 0.0061 | 0.91 |
| $PC_1$ | - | 0.00078 | 0.054 | + | 0.0013 | 0.042 | + | 0.0005 | 1.7e-05 | + | 0.0028 | 0.0065 |
| $PC_2$ | + | 0.0099 | 1.2e-07 | - | 8.2e-07 | 0.26 | + | 0.00077 | 0.0098 | + | 0.0025 | 0.043 |

(iv) African Americans (n=2,958). $PC_1$ is African-European, $PC_2$ is amount of East Asian ancestry.

| | HDL | | | LDL | | | TG | | | TC | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Sign | $r^2$ | p | Sign | $r^2$ | p | Sign | $r^2$ | p | Sign | $r^2$ | p |
| $Age_c$ | + | 0.0059 | 8e-06 | + | 0.028 | 0.004 | + | 0.025 | 0.00015 | + | 0.047 | 2.8e-06 |
| $Age_c^2$ | - | 0.00081 | 0.64 | - | 0.04 | 1.3e-08 | - | 0.034 | 1.2e-08 | - | 0.058 | 2.6e-12 |
| $Age_c^3$ | - | 0.0017 | 0.78 | - | 0.027 | 0.0031 | - | 0.021 | 0.00018 | - | 0.04 | 0.00016 |
| $\log(BMI)_c$ | - | 0.054 | 3e-28 | + | 0.0068 | 1.9e-07 | + | 0.038 | 3.6e-24 | + | 0.00098 | 0.0009 |
| $\log(BMI)_c^2$ | + | 0.003 | 0.14 | - | 0.0014 | 0.01 | + | 0.0029 | 0.59 | - | 0.0016 | 0.21 |
| $\log(BMI)_c^3$ | + | 0.025 | 0.015 | - | 0.0011 | 0.1 | - | 0.013 | 4.1e-05 | - | 4e-05 | 0.055 |
| Female | + | 0.11 | 9e-94 | - | 0.013 | 4.6e-06 | - | 0.022 | 5.4e-15 | + | 0.001 | 0.58 |
| $PC_1$ | + | 0.0011 | 0.91 | - | 0.00017 | 0.69 | - | 0.0017 | 3.3e-05 | - | 0.00015 | 0.15 |
| $PC_2$ | - | 0.00041 | 0.033 | + | 2.2e-05 | 0.55 | + | 0.00025 | 0.14 | + | 1.2e-05 | 0.74 |

(v) South Asians (n=439). $PC_1$ is European ancestry, $PC_2$ is East Asian ancestry.

| | HDL | | | LDL | | | TG | | | TC | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Sign | $r^2$ | p | Sign | $r^2$ | p | Sign | $r^2$ | p | Sign | $r^2$ | p |
| $Age_c$ | + | 0.0001 | 0.4 | - | 0.016 | 0.059 | - | 0.025 | 0.74 | - | 0.03 | 0.14 |
| $Age_c^2$ | - | 0.00012 | 0.92 | - | 0.034 | 0.13 | - | 0.032 | 0.2 | - | 0.052 | 0.088 |
| $Age_c^3$ | + | 0.00027 | 0.97 | - | 0.032 | 0.79 | - | 0.027 | 0.38 | - | 0.049 | 0.64 |
| $\log(BMI)_c$ | - | 0.051 | 0.00012 | + | 0.027 | 0.26 | + | 0.099 | 2.3e-06 | + | 0.034 | 0.11 |
| $\log(BMI)_c^2$ | + | 0.014 | 0.79 | - | 0.022 | 0.21 | - | 0.066 | 0.0017 | - | 0.037 | 0.022 |
| $\log(BMI)_c^3$ | + | 0.019 | 0.42 | - | 0.021 | 1 | - | 0.052 | 0.059 | - | 0.026 | 0.56 |
| Female | + | 0.23 | 2.7e-25 | - | 0.033 | 0.00043 | - | 0.083 | 4e-07 | - | 0.013 | 0.083 |
| $PC_1$ | - | 0.0078 | 0.013 | + | 2.2e-05 | 0.81 | + | 0.0058 | 0.013 | + | 3e-05 | 0.78 |
| $PC_2$ | + | 0.0023 | 0.49 | + | 1.8e-05 | 0.84 | - | 2.2e-06 | 1 | + | 0.00039 | 0.7 |

**Supplementary Table 2:** Genomic inflation factors. GERA non-Hispanic whites, n=76,627; GERA Latinos, n=7,795; GERA East Asians, n=6,855; GERA African Americans, n=2,958; GERA South Asians, n=439; GERA, n=94,674; GLGC, n=94,674; GERA+GLGC, n=189,269. All tests were two-sided.

| | LDL | HDL | TC | TG |
|---|---|---|---|---|
| GERA non-Hispanic White | 1.10/1.10 | 1.15/1.15 | 1.15/1.10 | 1.15/1.15 |
| GERA Latino | 1.00/1.00 | 1.05/1.00 | 1.00/1.00 | 1.00/1.00 |
| GERA East Asian | 1.00/1.00 | 1.00/1.00 | 1.05/1.05 | 1.05/1.05 |
| GERA African American | 1.00/1.00 | 1.00/1.00 | 1.00/1.00 | 1.00/1.00 |
| GERA South Asian | 1.04/1.04 | 1.02/1.02 | 1.02/1.02 | 1.01/1.00 |
| GERA Meta | 1.07 | 1.09 | 1.07 | 1.09 |
| GERA+GLGC Meta | 1.07 | 1.10 | 1.07 | 1.09 |

**Supplementary Table 10:** Top candidate *ABO* SNPs at *FUT2* secretors. Discovery was done in the meta-analysis (n=94,674) of GERA non-Hispanic whites (n=76,627), Latinos (7,795), East Asians (n=6,855), African Americans (2,958), and South Asians (n=439), each using linear regression, two-sided test.

| | | | | non-Hispanic White | | Latino | | East Asian | | African American | | Meta-analysis | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| SNP | Chr | Pos | Allele | Eff | P | Eff | P | Eff | P | Eff | P | Eff | P | $I^2$ | Het. P |
| chr9:136138765:D | 9 | 136138765 | G/GCGCCCACCACTA | 0.127 | 1.2e-50 | 0.141 | 9.2e-08 | 0.070 | 0.12 | 0.123 | 0.033 | 0.126 | 5e-58 | 0 | 0.52 |
| chr9:136139907:D | 9 | 136139907 | G/GAAACTGCC | 0.113 | 2.5e-48 | 0.189 | 2.2e-15 | 0.098 | 2.4e-05 | 0.097 | 0.027 | 0.118 | 9.2e-65 | 73 | 0.012 |
| rs2519093 | 9 | 136141870 | T/C | 0.131 | 2e-59 | 0.184 | 1.6e-13 | 0.109 | 2.9e-06 | 0.064 | 0.2 | 0.132 | 5.5e-75 | 59 | 0.061 |
| chr9:136145424:D | 9 | 136145424 | A/AC | 0.111 | 2.7e-46 | 0.189 | 3.2e-15 | 0.080 | 0.00071 | 0.092 | 0.033 | 0.114 | 1.3e-60 | 77 | 0.0044 |
| rs9411378 | 9 | 136145425 | A/C | 0.112 | 9.1e-47 | 0.188 | 4e-15 | 0.080 | 0.00071 | 0.093 | 0.032 | 0.115 | 4.7e-61 | 77 | 0.0049 |
| rs550057 | 9 | 136146597 | T/C | 0.111 | 2.1e-46 | 0.188 | 2.5e-15 | 0.103 | 8e-06 | 0.100 | 0.023 | 0.116 | 2.6e-63 | 72 | 0.012 |
| rs507666 | 9 | 136149399 | A/G | 0.132 | 6.4e-60 | 0.185 | 1.1e-13 | 0.105 | 5.9e-06 | 0.068 | 0.17 | 0.132 | 2.6e-75 | 61 | 0.051 |
| chr9:136149709:D | 9 | 136149709 | A/AC | 0.132 | 2.4e-59 | 0.176 | 8e-12 | 0.082 | 0.056 | 0.076 | 0.22 | 0.133 | 1.1e-69 | 43 | 0.16 |
| rs532436 | 9 | 136149830 | A/G | 0.132 | 3.6e-60 | 0.185 | 1.3e-13 | 0.109 | 2.7e-06 | 0.068 | 0.18 | 0.133 | 6.4e-76 | 59 | 0.065 |
| rs600038 | 9 | 136151806 | C/T | 0.122 | 6.9e-53 | 0.173 | 1.2e-12 | 0.109 | 2.7e-06 | 0.066 | 0.15 | 0.123 | 6.8e-68 | 52 | 0.099 |
| rs651007 | 9 | 136153875 | T/C | 0.120 | 8.8e-52 | 0.174 | 1e-12 | 0.108 | 3e-06 | 0.066 | 0.15 | 0.122 | 8.5e-67 | 54 | 0.09 |
| rs579459 | 9 | 136154168 | C/T | 0.121 | 9.6e-53 | 0.173 | 1.4e-12 | 0.113 | 1e-06 | 0.067 | 0.15 | 0.123 | 3.1e-68 | 50 | 0.11 |
| rs649129 | 9 | 136154304 | T/C | 0.121 | 9.1e-53 | 0.173 | 1.4e-12 | 0.110 | 2.2e-06 | 0.067 | 0.15 | 0.123 | 6.4e-68 | 51 | 0.11 |
| rs495828 | 9 | 136154867 | T/G | 0.121 | 9.1e-53 | 0.173 | 1.6e-12 | 0.110 | 2.2e-06 | 0.062 | 0.18 | 0.123 | 9.2e-68 | 52 | 0.1 |
| rs635634 | 9 | 136155000 | T/C | 0.133 | 7.2e-61 | 0.181 | 4e-13 | 0.111 | 1.5e-06 | 0.066 | 0.19 | 0.133 | 1.6e-76 | 53 | 0.092 |

**Supplementary Table 11:** *ABO* haplotype analysis. Haplotype pairs with at least 50 individuals present are included, for the SNPs rs2519093 / rs507666 / chr9:136149709:D / rs532436 / rs635634. Discovery was done in the meta-analysis (n=94,674) of GERA non-Hispanic whites (n=76,627), Latinos (7,795), East Asians (n=6,855), African Americans (2,958), and South Asians (n=439), each using linear regression, two-sided test. Mean, mean residual LDL for each group; SE, standard error. All tests two-sided.

| | | | | | | Compare to non-Hispanic white by t-test | | | | Compare to all by t-test | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | C/G/AC/G/C+ C/G/AC/G/C | | C/G/AC/G/C T/A/A/A/T | | C/G/AC/G/C T/A/A/A/T | | C/G/AC/G/C T/A/A/A/T | |
| Haplotype 1 | Haplotype 2 | Pop | N | Mean | SE | t | P | t | P | t | P | | |
| C/G/AC/G/C | C/G/AC/G/C | non-Hispanic white | 38177 | 0.017 | 0.005 | | | | | | | | |
| | | Latino | 4499 | 0.024 | 0.014 | | | | | | | | |
| | | East Asian | 4264 | 0.035 | 0.014 | | | | | | | | |
| | | African American | 1775 | 0.116 | 0.025 | | | | | | | | |
| | | All | 48715 | 0.023 | 0.004 | | | | | | | | |
| C/G/AC/G/C | T/A/A/A/T | non-Hispanic white | 17891 | 0.149 | 0.007 | | | | | | | | |
| | | Latino | 1661 | 0.197 | 0.025 | | | | | | | | |
| | | East Asian | 401 | 0.059 | 0.046 | | | | | | | | |
| | | African American | 236 | 0.194 | 0.065 | | | | | | | | |
| | | All | 20189 | 0.152 | 0.007 | | | | | | | | |
| C/G/AC/G/C | T/A/A/A/C | non-Hispanic white | 90 | -0.035 | 0.082 | 0.53 | 0.59 | 1.83 | 0.067 | 0.59 | 0.55 | 1.85 | 0.065 |
| C/G/AC/G/C | C/G/AC/G/T | non-Hispanic white | 100 | 0.103 | 0.091 | 0.93 | 0.35 | 0.48 | 0.63 | 0.86 | 0.39 | 0.50 | 0.61 |
| C/G/AC/G/C | T/A/AC/A/T | non-Hispanic white | 1772 | 0.137 | 0.021 | | | | | | | | |
| | | Latino | 303 | 0.124 | 0.054 | | | | | | | | |
| | | East Asian | 193 | 0.180 | 0.078 | | | | | | | | |
| | | African American | 176 | 0.223 | 0.072 | | | | | | | | |
| | | All | 2444 | 0.145 | 0.019 | | | | | | | | |
| T/A/A/A/T | T/A/A/A/T | non-Hispanic white | 2129 | 0.153 | 0.020 | | | | | | | | |
| T/A/A/A/T | T/A/A/A/T | Latino | 148 | 0.405 | 0.091 | | | | | | | | |
| T/A/A/A/T | T/A/A/A/T | All | 2288 | 0.170 | 0.020 | | | | | | | | |
| T/A/A/A/T | T/A/AC/A/T | non-Hispanic white | 87 | 0.307 | 0.099 | | | | | | | | |
| T/A/AC/A/T | T/G/AC/A/T | East Asian | 124 | 0.112 | 0.083 | | | | | | | | |
| C/G/AC/G/C | T/G/AC/G/C | non-Hispanic white | 92 | 0.024 | 0.099 | | | | | | | | |

**Supplementary Table 13:** Pearson's correlation between lipid trait GRS (using all previously-reported and newly-reported lead and conditional SNPs with $R^2 < 0.3$). GERA non-Hispanic whites (n=76,627), Latinos (7,795), East Asians (n=6,855), and African Americans (2,958).

**non-Hispanic white females**:

| | HDL | LDL | TC | TG |
|---|---|---|---|---|
| HDL | 1.000 (1.000, 1.000) | -0.162 (-0.171, -0.153) | 0.083 (0.074, 0.092) | -0.481 (-0.488, -0.473) |
| LDL | -0.162 (-0.171, -0.153) | 1.000 (1.000, 1.000) | 0.935 (0.934, 0.936) | 0.259 (0.250, 0.267) |
| TC | 0.083 (0.074, 0.092) | 0.935 (0.934, 0.936) | 1.000 (1.000, 1.000) | 0.359 (0.351, 0.367) |
| TG | -0.481 (-0.488, -0.473) | 0.259 (0.250, 0.267) | 0.359 (0.351, 0.367) | 1.000 (1.000, 1.000) |

**non-Hispanic white males**:

| | HDL | LDL | TC | TG |
|---|---|---|---|---|
| HDL | 1.000 (1.000, 1.000) | 0.021 (0.010, 0.032) | 0.136 (0.125, 0.147) | -0.504 (-0.512, -0.495) |
| LDL | 0.021 (0.010, 0.032) | 1.000 (1.000, 1.000) | 0.933 (0.932, 0.935) | 0.107 (0.097, 0.118) |
| TC | 0.136 (0.125, 0.147) | 0.933 (0.932, 0.935) | 1.000 (1.000, 1.000) | 0.328 (0.319, 0.338) |
| TG | -0.504 (-0.512, -0.495) | 0.107 (0.097, 0.118) | 0.328 (0.319, 0.338) | 1.000 (1.000, 1.000) |

**Latino females**:

| | HDL | LDL | TC | TG |
|---|---|---|---|---|
| HDL | 1.000 (1.000, 1.000) | -0.120 (-0.148, -0.092) | 0.127 (0.099, 0.155) | -0.471 (-0.493, -0.448) |
| LDL | -0.120 (-0.148, -0.092) | 1.000 (1.000, 1.000) | 0.930 (0.926, 0.934) | 0.272 (0.245, 0.298) |
| TC | 0.127 (0.099, 0.155) | 0.930 (0.926, 0.934) | 1.000 (1.000, 1.000) | 0.382 (0.357, 0.406) |
| TG | -0.471 (-0.493, -0.448) | 0.272 (0.245, 0.298) | 0.382 (0.357, 0.406) | 1.000 (1.000, 1.000) |

**Latino males**:

| | HDL | LDL | TC | TG |
|---|---|---|---|---|
| HDL | 1.000 (1.000, 1.000) | 0.053 (0.017, 0.088) | 0.173 (0.139, 0.207) | -0.486 (-0.512, -0.458) |
| LDL | 0.053 (0.017, 0.088) | 1.000 (1.000, 1.000) | 0.928 (0.923, 0.932) | 0.121 (0.086, 0.156) |
| TC | 0.173 (0.139, 0.207) | 0.928 (0.923, 0.932) | 1.000 (1.000, 1.000) | 0.350 (0.319, 0.381) |
| TG | -0.486 (-0.512, -0.458) | 0.121 (0.086, 0.156) | 0.350 (0.319, 0.381) | 1.000 (1.000, 1.000) |

**East Asian females**:

| | HDL | LDL | TC | TG |
|---|---|---|---|---|
| HDL | 1.000 (1.000, 1.000) | -0.000 (-0.031, 0.031) | 0.254 (0.225, 0.283) | -0.454 (-0.479, -0.429) |
| LDL | -0.000 (-0.031, 0.031) | 1.000 (1.000, 1.000) | 0.911 (0.905, 0.916) | 0.293 (0.265, 0.321) |
| TC | 0.254 (0.225, 0.283) | 0.911 (0.905, 0.916) | 1.000 (1.000, 1.000) | 0.421 (0.396, 0.446) |
| TG | -0.454 (-0.479, -0.429) | 0.293 (0.265, 0.321) | 0.421 (0.396, 0.446) | 1.000 (1.000, 1.000) |

**East Asian males**:

| | HDL | LDL | TC | TG |
|---|---|---|---|---|
| HDL | 1.000 (1.000, 1.000) | 0.125 (0.088, 0.161) | 0.229 (0.194, 0.264) | -0.462 (-0.490, -0.433) |
| LDL | 0.125 (0.088, 0.161) | 1.000 (1.000, 1.000) | 0.908 (0.901, 0.914) | 0.162 (0.126, 0.198) |
| TC | 0.229 (0.194, 0.264) | 0.908 (0.901, 0.914) | 1.000 (1.000, 1.000) | 0.433 (0.402, 0.462) |
| TG | -0.462 (-0.490, -0.433) | 0.162 (0.126, 0.198) | 0.433 (0.402, 0.462) | 1.000 (1.000, 1.000) |

**African American females**:

| | HDL | LDL | TC | TG |
|---|---|---|---|---|
| HDL | 1.000 (1.000, 1.000) | -0.178 (-0.223, -0.132) | 0.059 (0.013, 0.106) | -0.524 (-0.557, -0.489) |
| LDL | -0.178 (-0.223, -0.132) | 1.000 (1.000, 1.000) | 0.940 (0.934, 0.945) | 0.239 (0.195, 0.283) |
| TC | 0.059 (0.013, 0.106) | 0.940 (0.934, 0.945) | 1.000 (1.000, 1.000) | 0.320 (0.277, 0.361) |
| TG | -0.524 (-0.557, -0.489) | 0.239 (0.195, 0.283) | 0.320 (0.277, 0.361) | 1.000 (1.000, 1.000) |

**African American males**:

| | HDL | LDL | TC | TG |
|---|---|---|---|---|
| HDL | 1.000 (1.000, 1.000) | -0.072 (-0.128, -0.015) | 0.070 (0.013, 0.126) | -0.429 (-0.474, -0.381) |
| LDL | -0.072 (-0.128, -0.015) | 1.000 (1.000, 1.000) | 0.940 (0.933, 0.947) | 0.208 (0.153, 0.261) |
| TC | 0.070 (0.013, 0.126) | 0.940 (0.933, 0.947) | 1.000 (1.000, 1.000) | 0.407 (0.359, 0.453) |
| TG | -0.429 (-0.474, -0.381) | 0.208 (0.153, 0.261) | 0.407 (0.359, 0.453) | 1.000 (1.000, 1.000) |

**Supplementary Table 14:** Increase in variance explained with a greater number of repeated independent measures in GERA non-Hispanic whites (for a fixed sample size of 34,936 only individuals with 5 or more measures were included). Variance explained was calculated using a risk score of the previously-described hits with previous effect sizes.

| # Measurements | HDL | LDL | TG | TC |
|---|---|---|---|---|
| 1 | 0.076 | 0.073 | 0.059 | 0.066 |
| 2 | 0.089 | 0.086 | 0.071 | 0.078 |
| 3 | 0.095 | 0.091 | 0.075 | 0.083 |
| 4 | 0.098 | 0.095 | 0.079 | 0.087 |
| $\geq 5$ (all available) | 0.101 | 0.099 | 0.084 | 0.088 |
| Infinite (no measurement error) | 0.108 | 0.105 | 0.088 | 0.097 |

**Supplementary Table 15:** GERA array heritability estimates. The method using GCTA required PC adjustment, whereas the REAP method does not. Adj PC, Adjusted for PCs; Y, yes; N, no; GRM, genotype relationship matrix calculated with GCTA (does not account for population structure) or PC-Relate (which accounts for population structure).

| Trait | Adj PC | GRM | Method | Genotypes | $h^2$ | N |
|---|---|---|---|---|---|---|
| LDL | N | GCTA | GCTA | Genotyped | 23.3 (21.4, 25.2) | 55163 |
| LDL | N | GCTA | GCTA | Imputed | 30.1 (27.7, 32.5) | 55163 |
| LDL | N | GCTA | GEAR | Genotyped | 19.8 (17.8, 21.7) | 55163 |
| LDL | N | GCTA | GEAR | Imputed | 21.1 (19.3, 22.9) | 55163 |
| LDL | N | PC-Relate | GEAR | Genotyped | 17.2 (15.4, 19.0) | 59327 |
| LDL | N | PC-Relate | GEAR | Imputed | 19.3 (17.6, 21.0) | 59327 |
| LDL | Y | GCTA | GCTA | Genotyped | 23.3 (21.4, 25.2) | 55163 |
| LDL | Y | GCTA | GCTA | Imputed | 30.1 (27.7, 32.5) | 55163 |
| LDL | Y | GCTA | GEAR | Genotyped | 19.8 (17.8, 21.7) | 55163 |
| LDL | Y | GCTA | GEAR | Imputed | 20.7 (18.9, 22.5) | 55163 |
| LDL | Y | PC-Relate | GEAR | Genotyped | 16.9 (15.0, 18.7) | 59327 |
| LDL | Y | PC-Relate | GEAR | Imputed | 18.8 (17.1, 20.4) | 59327 |
| HDL | N | GCTA | GCTA | Genotyped | 33.2 (31.3, 35.1) | 55163 |
| HDL | N | GCTA | GCTA | Imputed | 36.2 (33.8, 38.6) | 55163 |
| HDL | N | GCTA | GEAR | Genotyped | 25.6 (23.6, 27.5) | 55163 |
| HDL | N | GCTA | GEAR | Imputed | 27.6 (25.9, 29.4) | 55163 |
| HDL | N | PC-Relate | GEAR | Genotyped | 27.1 (25.3, 28.9) | 59327 |
| HDL | N | PC-Relate | GEAR | Imputed | 28.1 (26.5, 29.7) | 59327 |
| HDL | Y | GCTA | GCTA | Genotyped | 32.8 (31.0, 34.7) | 55163 |
| HDL | Y | GCTA | GCTA | Imputed | 35.8 (33.4, 38.2) | 55163 |
| HDL | Y | GCTA | GEAR | Genotyped | 26.2 (24.3, 28.1) | 55163 |
| HDL | Y | GCTA | GEAR | Imputed | 24.1 (22.3, 25.9) | 55163 |
| HDL | Y | PC-Relate | GEAR | Genotyped | 27.8 (26.0, 29.5) | 59327 |
| HDL | Y | PC-Relate | GEAR | Imputed | 24.8 (23.2, 26.5) | 59327 |
| TG | N | GCTA | GCTA | Genotyped | 30.6 (28.8, 32.5) | 55163 |
| TG | N | GCTA | GCTA | Imputed | 36.8 (34.4, 39.2) | 55163 |
| TG | N | GCTA | GEAR | Genotyped | 26.3 (24.4, 28.1) | 55163 |
| TG | N | GCTA | GEAR | Imputed | 28.4 (26.7, 30.1) | 55163 |
| TG | N | PC-Relate | GEAR | Genotyped | 24.4 (22.6, 26.1) | 59327 |
| TG | N | PC-Relate | GEAR | Imputed | 26.6 (25.0, 28.2) | 59327 |
| TG | Y | GCTA | GCTA | Genotyped | 30.5 (28.7, 32.4) | 55163 |
| TG | Y | GCTA | GCTA | Imputed | 36.7 (34.3, 39.1) | 55163 |
| TG | Y | GCTA | GEAR | Genotyped | 26.3 (24.5, 28.2) | 55163 |
| TG | Y | GCTA | GEAR | Imputed | 27.8 (26.1, 29.5) | 55163 |
| TG | Y | PC-Relate | GEAR | Genotyped | 24.4 (22.7, 26.1) | 59327 |
| TG | Y | PC-Relate | GEAR | Imputed | 26.2 (24.6, 27.8) | 59327 |
| TC | N | GCTA | GCTA | Genotyped | 25.3 (23.4, 27.1) | 55163 |
| TC | N | GCTA | GCTA | Imputed | 33.0 (30.6, 35.5) | 55163 |
| TC | N | GCTA | GEAR | Genotyped | 23.1 (21.1, 25.0) | 55163 |
| TC | N | GCTA | GEAR | Imputed | 25.6 (23.8, 27.3) | 55163 |
| TC | N | PC-Relate | GEAR | Genotyped | 20.9 (19.1, 22.7) | 59327 |
| TC | N | PC-Relate | GEAR | Imputed | 24.0 (22.3, 25.6) | 59327 |
| TC | Y | GCTA | GCTA | Genotyped | 25.3 (23.4, 27.1) | 55163 |
| TC | Y | GCTA | GCTA | Imputed | 33.0 (30.6, 35.4) | 55163 |
| TC | Y | GCTA | GEAR | Genotyped | 23.2 (21.2, 25.1) | 55163 |
| TC | Y | GCTA | GEAR | Imputed | 25.0 (23.2, 26.8) | 55163 |
| TC | Y | PC-Relate | GEAR | Genotyped | 20.7 (18.9, 22.5) | 59327 |
| TC | Y | PC-Relate | GEAR | Imputed | 23.2 (21.6, 24.9) | 59327 |

**Supplementary Table 16:** Time to lipidemia treatment onset using a Cox proporotional hazards model. Non-hispanic white females, n=44,856; non-Hispanic white males, n=31,771; Latino females, n=4,708; Latino males, n=3,087; East Asian females, n=4,013; East Asian moles, n=2,842; African American males, n=1,761; African American females, n=1,197.

**LDL GRS**:

| Group | Sex | HR GRS LDL | SE GRS LDL | P GRS LDL | Concordance |
|---|---|---|---|---|---|
| non-Hispanic white | Female | 2.504 | 0.018 | $10^{-550}$ | 0.610 |
| non-Hispanic white | Male | 2.198 | 0.020 | $10^{-345}$ | 0.590 |
| Latino | Female | 2.399 | 0.061 | $10^{-46}$ | 0.604 |
| Latino | Male | 2.227 | 0.068 | $10^{-31}$ | 0.584 |
| East Asian | Female | 1.848 | 0.095 | 1.3e-10 | 0.548 |
| East Asian | Male | 1.967 | 0.091 | $10^{-13}$ | 0.553 |
| African American | Female | 1.881 | 0.081 | $10^{-14}$ | 0.584 |
| African American | Male | 1.841 | 0.088 | $10^{-11}$ | 0.577 |
| Meta | Female | 2.442 | 0.017 | $10^{-612}$ | — |
| Meta | Male | 2.174 | 0.018 | $10^{-397}$ | — |

**HDL GRS**:

| Group | Sex | HR GRS HDL | SE GRS HDL | P GRS HDL | Concordance |
|---|---|---|---|---|---|
| non-Hispanic white | Female | 0.717 | 0.021 | $10^{-54}$ | 0.534 |
| non-Hispanic white | Male | 0.787 | 0.024 | $10^{-22}$ | 0.522 |
| Latino | Female | 0.716 | 0.069 | 1.6e-06 | 0.536 |
| Latino | Male | 0.823 | 0.078 | 0.013 | 0.517 |
| East Asian | Female | 0.916 | 0.088 | 0.32 | 0.514 |
| East Asian | Male | 0.818 | 0.096 | 0.035 | 0.520 |
| African American | Female | 0.834 | 0.096 | 0.058 | 0.513 |
| African American | Male | 0.870 | 0.119 | 0.24 | 0.512 |
| Meta | Female | 0.730 | 0.019 | $10^{-58}$ | — |
| Meta | Male | 0.794 | 0.022 | $10^{-25}$ | — |

**TG GRS**:

| Group | Sex | HR GRS TG | SE GRS TG | P GRS TG | Concordance |
|---|---|---|---|---|---|
| non-Hispanic white | Female | 1.784 | 0.023 | $10^{-135}$ | 0.556 |
| non-Hispanic white | Male | 1.511 | 0.021 | $10^{-82}$ | 0.543 |
| Latino | Female | 1.738 | 0.074 | $10^{-13}$ | 0.557 |
| Latino | Male | 1.583 | 0.070 | $10^{-10}$ | 0.547 |
| East Asian | Female | 1.563 | 0.090 | 7.1e-07 | 0.545 |
| East Asian | Male | 1.533 | 0.077 | 3.2e-08 | 0.543 |
| African American | Female | 1.373 | 0.110 | 0.0039 | 0.528 |
| African American | Male | 1.555 | 0.111 | 6.5e-05 | 0.540 |
| Meta | Female | 1.750 | 0.021 | $10^{-153}$ | — |
| Meta | Male | 1.519 | 0.019 | $10^{-101}$ | — |

**LDL and TG GRS**:

| Group | Sex | HR GRS LDL | SE GRS LDL | P GRS LDL | HR GRS TG | SE GRS TG | P GRS TG | Concordance |
|---|---|---|---|---|---|---|---|---|
| non-Hispanic white | Female | 2.353 | 0.019 | $10^{-448}$ | 1.340 | 0.024 | $10^{-33}$ | 0.614 |
| non-Hispanic white | Male | 2.128 | 0.020 | $10^{-317}$ | 1.396 | 0.022 | $10^{-53}$ | 0.596 |
| Latino | Female | 2.250 | 0.063 | $10^{-37}$ | 1.334 | 0.077 | 0.00017 | 0.608 |
| Latino | Male | 2.132 | 0.069 | $10^{-28}$ | 1.440 | 0.070 | 2.3e-07 | 0.591 |
| East Asian | Female | 1.689 | 0.099 | 1.3e-07 | 1.366 | 0.094 | 0.00087 | 0.558 |
| East Asian | Male | 1.832 | 0.093 | $10^{-10}$ | 1.398 | 0.079 | 2e-05 | 0.562 |
| African American | Female | 1.843 | 0.084 | $10^{-13}$ | 1.116 | 0.114 | 0.34 | 0.584 |
| African American | Male | 1.760 | 0.089 | 2.4e-10 | 1.352 | 0.112 | 0.0073 | 0.579 |
| Meta | Female | 2.297 | 0.017 | $10^{-497}$ | 1.332 | 0.022 | $10^{-38}$ | — |
| Meta | Male | 2.099 | 0.018 | $10^{-360}$ | 1.398 | 0.020 | $10^{-64}$ | — |

**LDL and HDL GRS**:

| Group | Sex | HR GRS LDL SE | GRS LDL P | GRS LDL HR | GRS HDL SE | GRS HDL P | GRS HDL Concordance |
|---|---|---|---|---|---|---|---|
| non-Hispanic white | Female | 2.452 | 0.018 | $10^{-514}$ | 0.841 | 0.022 | $10^{-15}$ | 0.612 |
| non-Hispanic white | Male | 2.215 | 0.020 | $10^{-350}$ | 0.765 | 0.024 | $10^{-28}$ | 0.593 |
| Latino | Female | 2.351 | 0.062 | $10^{-43}$ | 0.802 | 0.070 | 0.0017 | 0.606 |
| Latino | Male | 2.246 | 0.068 | $10^{-32}$ | 0.791 | 0.078 | 0.0026 | 0.586 |
| East Asian | Female | 1.850 | 0.095 | 1.2e-10 | 0.909 | 0.088 | 0.28 | 0.549 |
| East Asian | Male | 2.025 | 0.092 | $10^{-14}$ | 0.753 | 0.096 | 0.0032 | 0.558 |
| African American | Female | 1.869 | 0.082 | $10^{-14}$ | 0.962 | 0.098 | 0.69 | 0.584 |
| African American | Male | 1.836 | 0.088 | $10^{-11}$ | 0.914 | 0.119 | 0.45 | 0.577 |
| Meta | Female | 2.394 | 0.017 | $10^{-573}$ | 0.845 | 0.020 | $10^{-17}$ | — |
| Meta | Male | 2.191 | 0.018 | $10^{-403}$ | 0.771 | 0.022 | $10^{-31}$ | — |

**LDL, TG, and HDL GRS**:

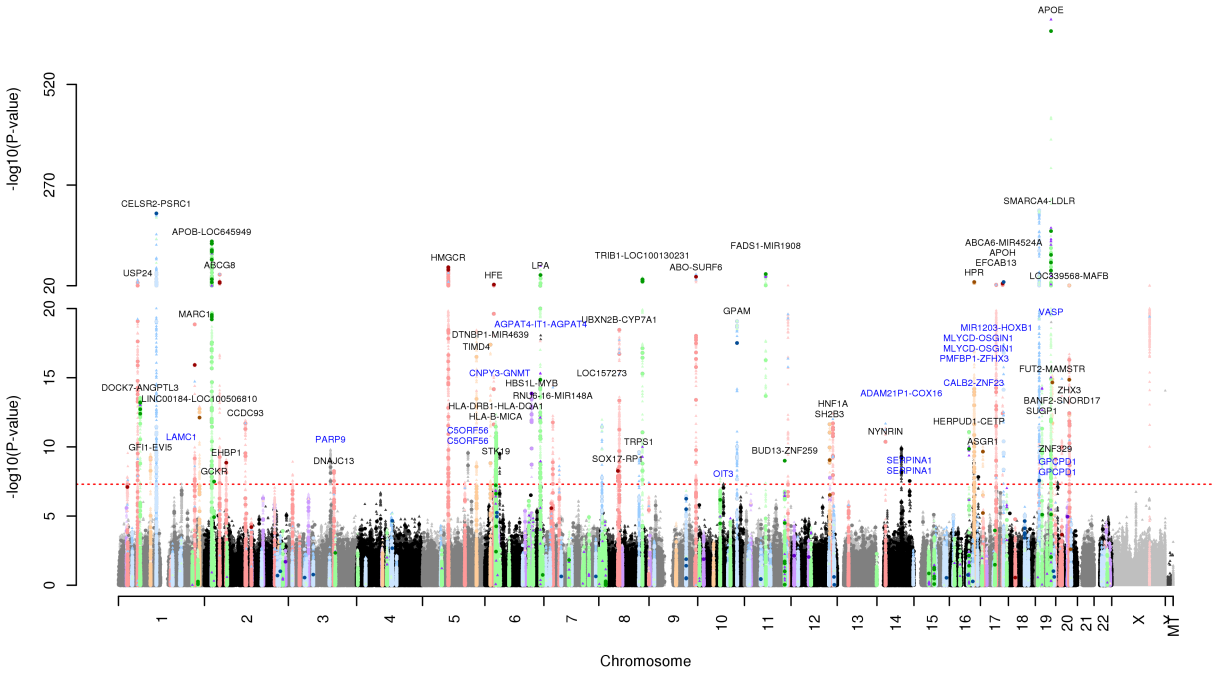
| Group | Sex | HR GRS LDL SE | GRS LDL P | GRS LDL HR | GRS TG SE | GRS TG P | GRS TG HR | GRS HDL SE | GRS HDL P | GRS HDL Concordance |
|---|---|---|---|---|---|---|---|---|---|---|
| non-Hispanic white | Female | 2.351 | 0.019 | $10^{-446}$ | 1.294 | 0.027 | $10^{-20}$ | 0.935 | 0.024 | 0.006 | 0.614 |
| non-Hispanic white | Male | 2.144 | 0.020 | $10^{-319}$ | 1.332 | 0.025 | $10^{-29}$ | 0.903 | 0.028 | 0.00033 | 0.596 |
| Latino | Female | 2.256 | 0.063 | $10^{-37}$ | 1.252 | 0.087 | 0.0098 | 0.884 | 0.080 | 0.12 | 0.608 |
| Latino | Male | 2.140 | 0.069 | $10^{-27}$ | 1.412 | 0.081 | 2.3e-05 | 0.958 | 0.090 | 0.64 | 0.591 |
| East Asian | Female | 1.673 | 0.100 | 3e-07 | 1.409 | 0.107 | 0.0013 | 1.063 | 0.101 | 0.55 | 0.558 |
| East Asian | Male | 1.871 | 0.095 | $10^{-10}$ | 1.338 | 0.090 | 0.0012 | 0.895 | 0.110 | 0.32 | 0.563 |
| African American | Female | 1.843 | 0.084 | $10^{-13}$ | 1.122 | 0.130 | 0.38 | 1.009 | 0.112 | 0.94 | 0.584 |
| African American | Male | 1.757 | 0.089 | 2.7e-10 | 1.382 | 0.124 | 0.009 | 1.057 | 0.131 | 0.67 | 0.579 |
| Meta | Female | 2.295 | 0.017 | $10^{-495}$ | 1.290 | 0.025 | $10^{-24}$ | 0.940 | 0.022 | 0.0052 | — |
| Meta | Male | 2.115 | 0.018 | $10^{-362}$ | 1.340 | 0.023 | $10^{-37}$ | 0.913 | 0.026 | 0.00038 | — |

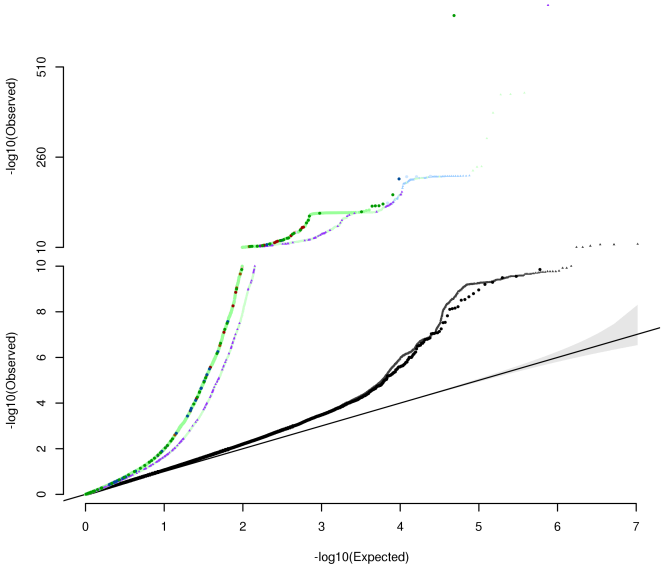
**Supplementary Table 17:** Mendelian lipid disorders.

| Defect | Disease | Gene | Location |
|---|---|---|---|
| Low HDL | Apo A-1 Deficiency | APOA1 | 11q23 |
| | LCAT Deficiency | LCAT | 16q22 |
| | Tangier Disease | ABCA1 | 9q31 |
| High HDL | CETP Deficiency | CETP | 16q13 |
| Low LDL | Abetalipoproteinemia | MTTP | 4q24 |
| | Familial hypobetalip. | APOB | 2p24 |
| | PCSK9 Deficiency | PCSK9 | 1p32 |
| High LDL | AD hypercholest. | PCSK9 | 1p32 |
| | AR hypercholest. | LDLRAP | 1 1p36 |
| | Fam. Defec. APOB-100 | APOB | 2p24 |
| | Fam. Hypercholest. | LDLR | 19p13 |
| | Sitosterolemia | ABCG5 | 2p21 |
| | Sitosterolemia | ABCG8 | 2p21 |
| High TG | Combined lipase def. | LMF1 | 16p13 |
| | Hypertrig. Type 1 | LPL | 8p21 |

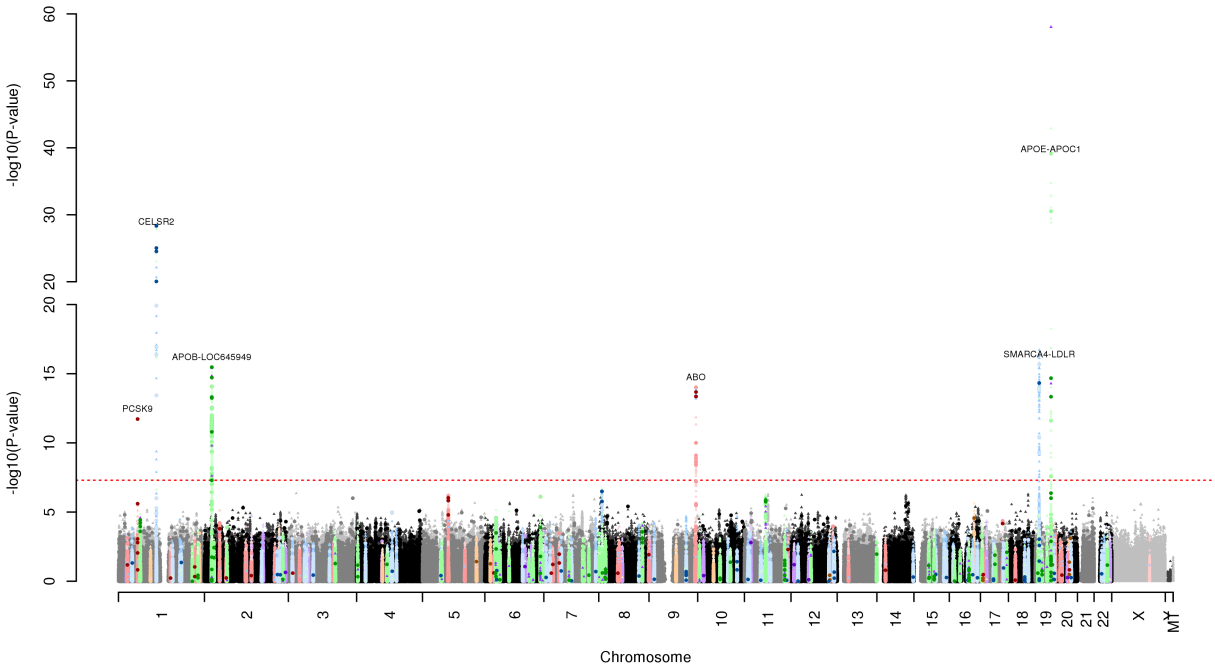
**Supplementary Figure 1:** Manhattan plots and Q-Q plots of each ancestry/ethnicity, and of the meta-analysis, for each of the four lipids traits. In each plot, the triangles are imputed SNPs, whereas the circles are based on the genotyped SNPs; in the meta-analysis all points are imputed. The color coding of the plot is described in the legend, where "<0.5Mb prev. known" indicates that a SNP was previously identified to be a particular lipids risk variant, and that the current SNP is within 0.5 megabases of that SNP (a 1 megabase window). Tests were done using linear regression in GERA non-Hispanic whites (n=76,627), GERA Latinos (7,795), GERA East Asians (n=6,855), GERA African Americans (2,958), and GERA South Asians (n=439), and GLGC (n=94,595), and a fixed effects meta-analysis.

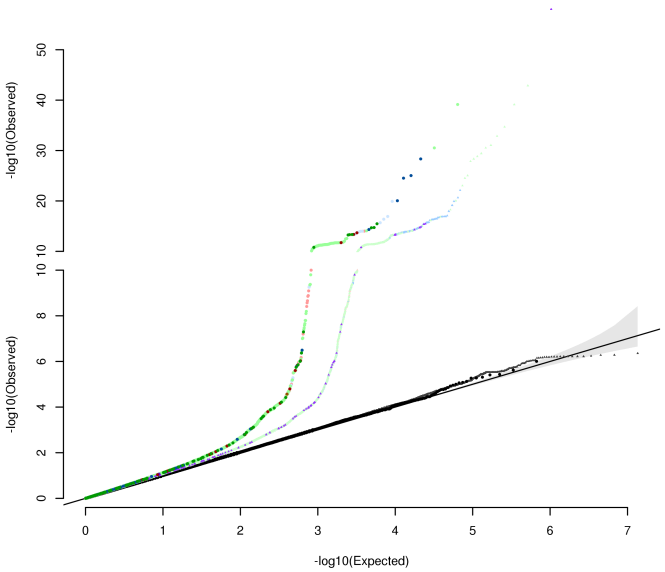
LDL non-Hispanic whites. $\lambda_{\text{typed}} = 1.10$, $\lambda_{\text{imputed}} = 1.10$.



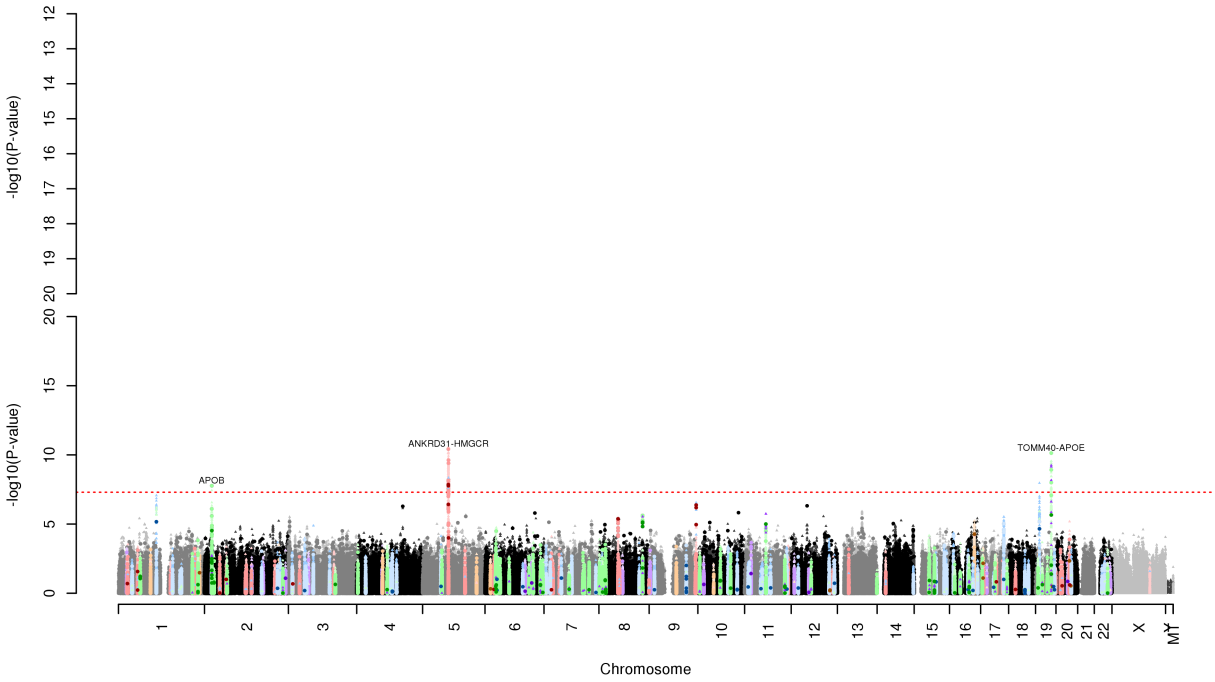



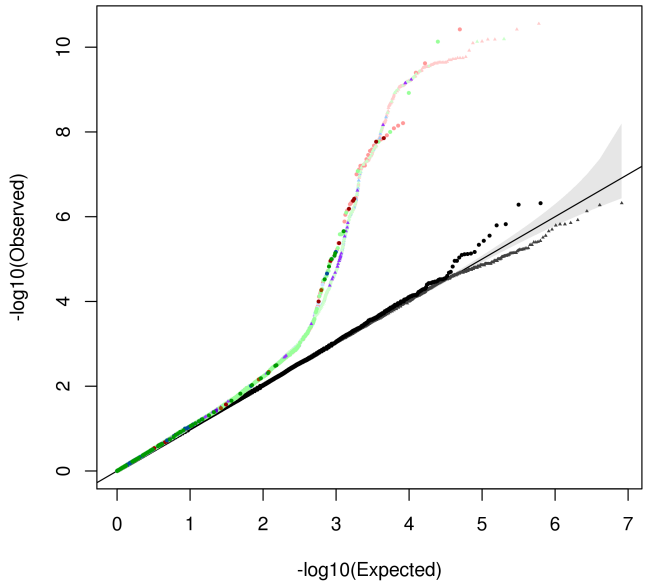
LDL Latinos. $\lambda_{\text{typed}} = 1.00$, $\lambda_{\text{imputed}} = 1.00$.



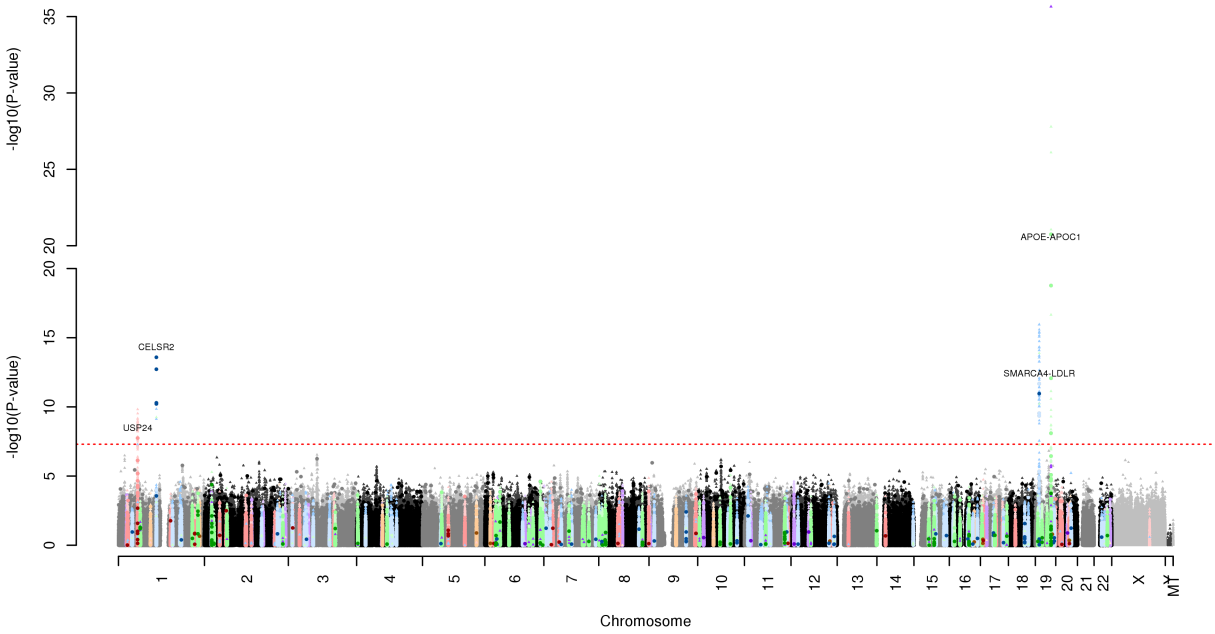



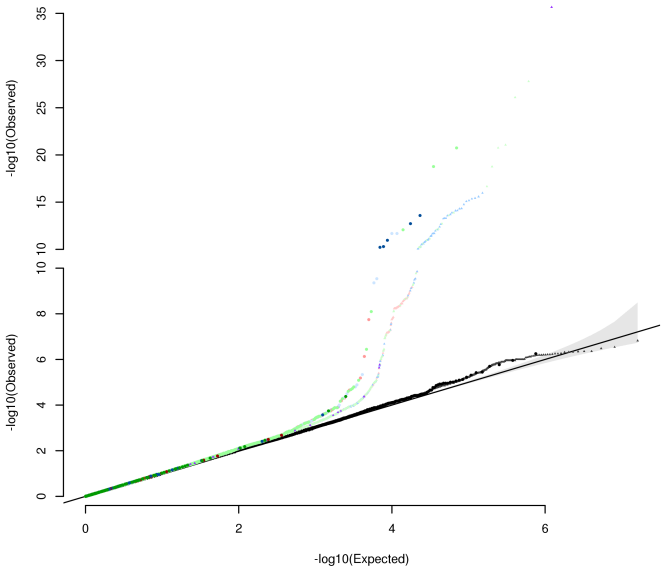
LDL East Asians. $\lambda_{\text{typed}} = 1.00$, $\lambda_{\text{imputed}} = 1.00$.



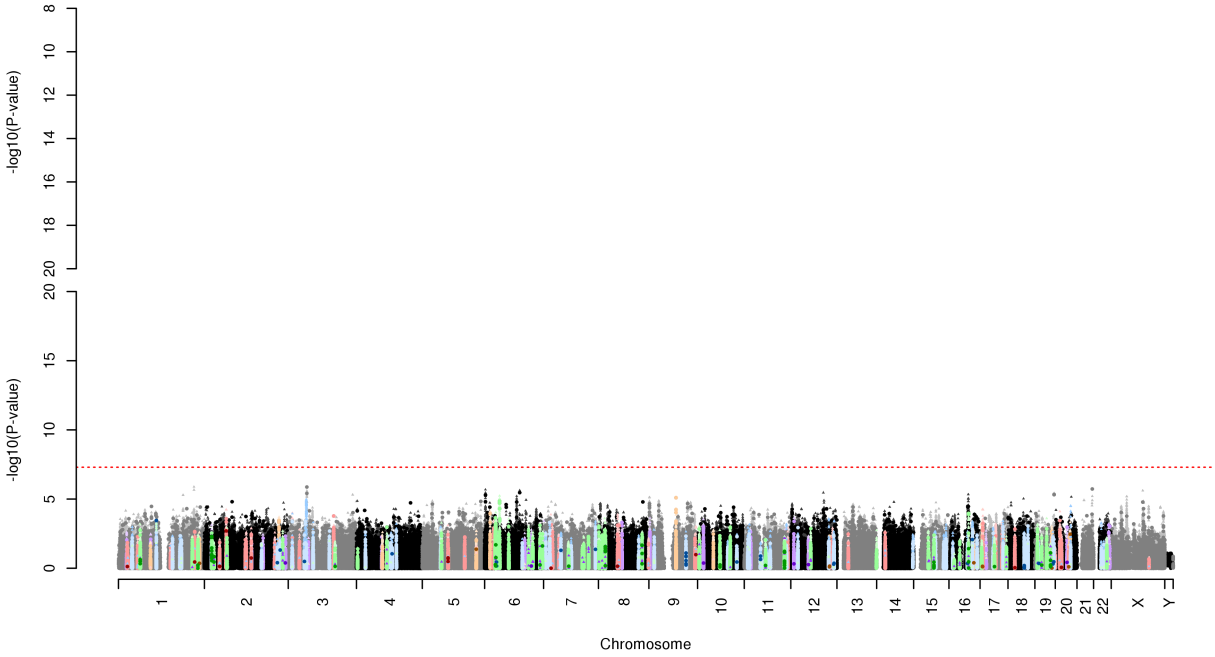



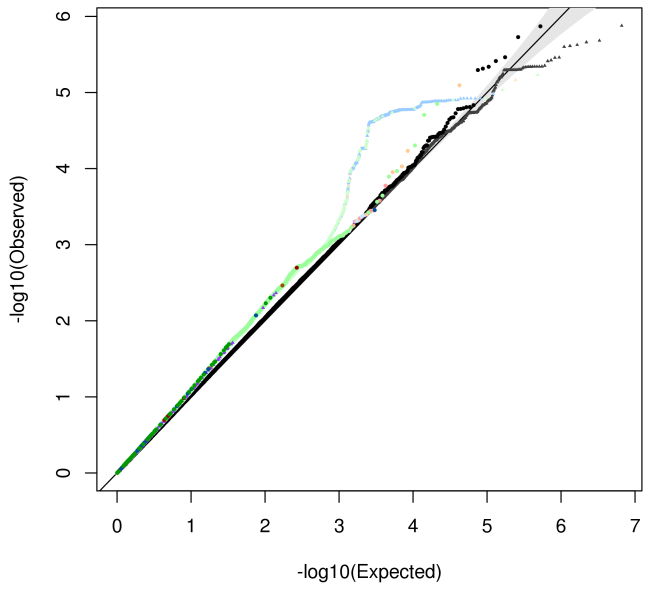
LDL African Americans. $\lambda_{\text{typed}} = 1.00$, $\lambda_{\text{imputed}} = 1.00$.



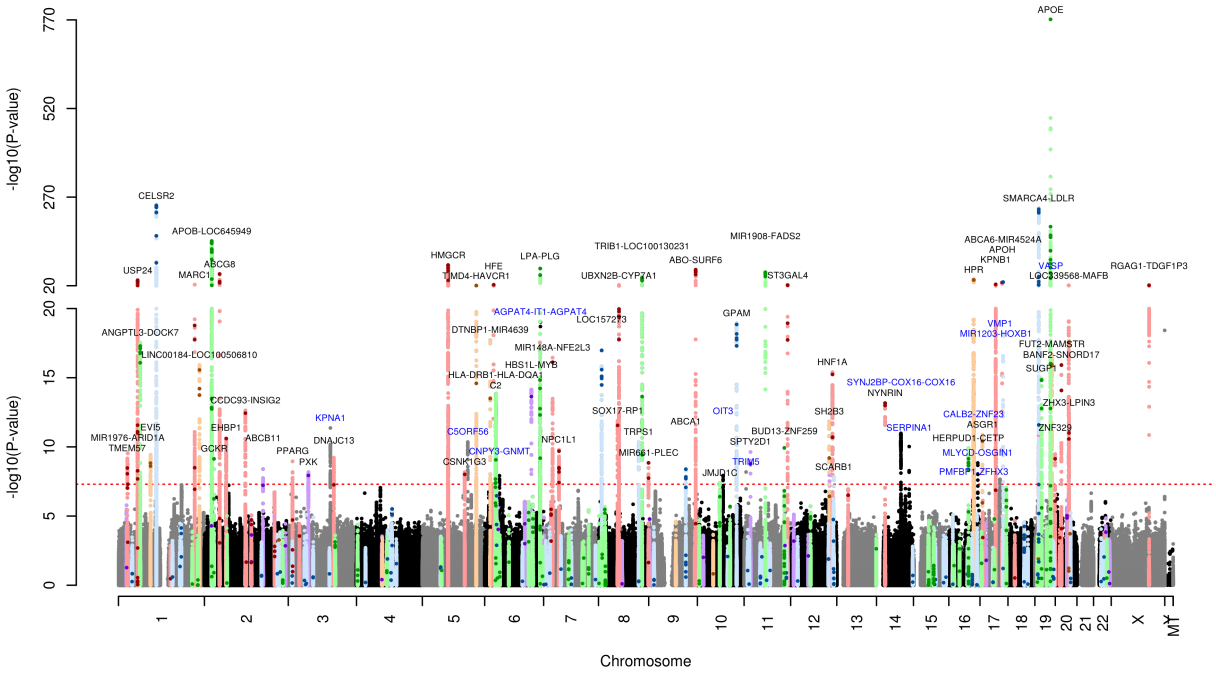



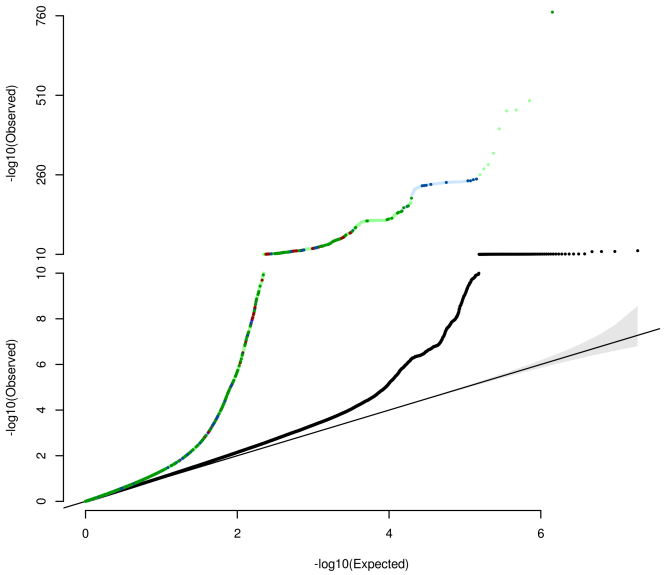
LDL South Asians. $\lambda_{\text{typed}} = 1.04$, $\lambda_{\text{imputed}} = 1.04$.



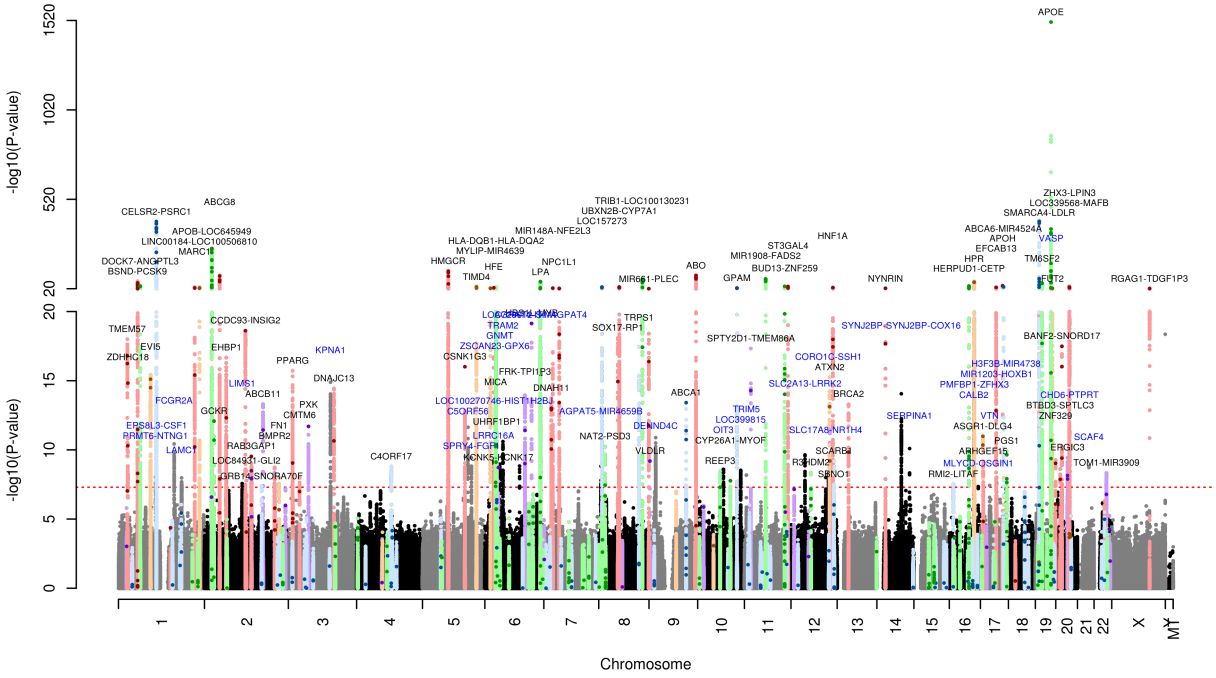



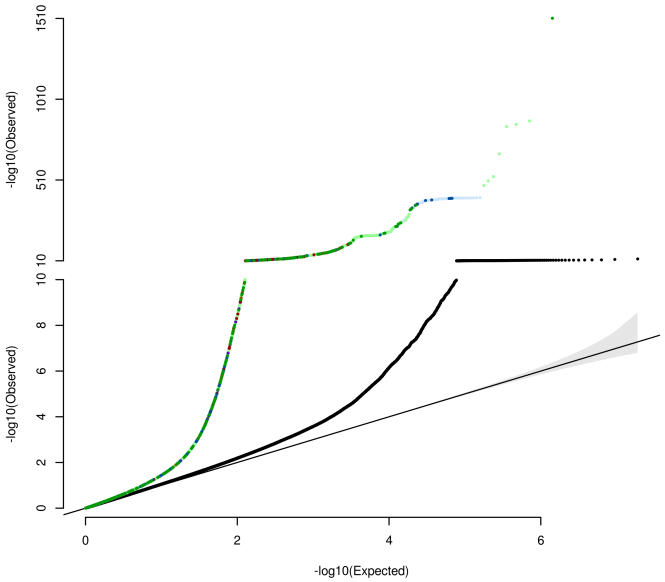
LDL GERA. $\lambda = 1.07$.



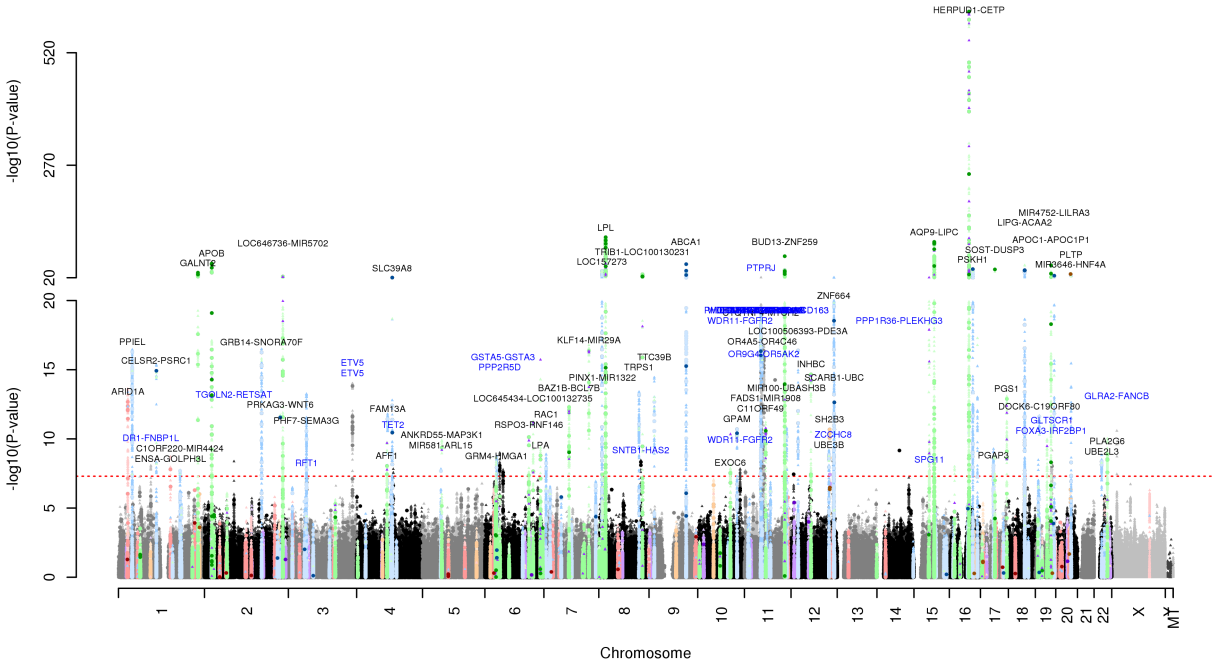



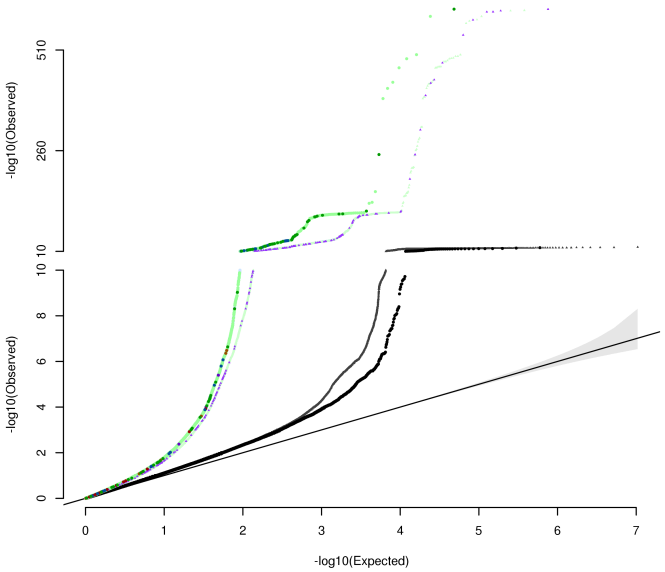
LDL GERA+GLGC. $\lambda = 1.07$.



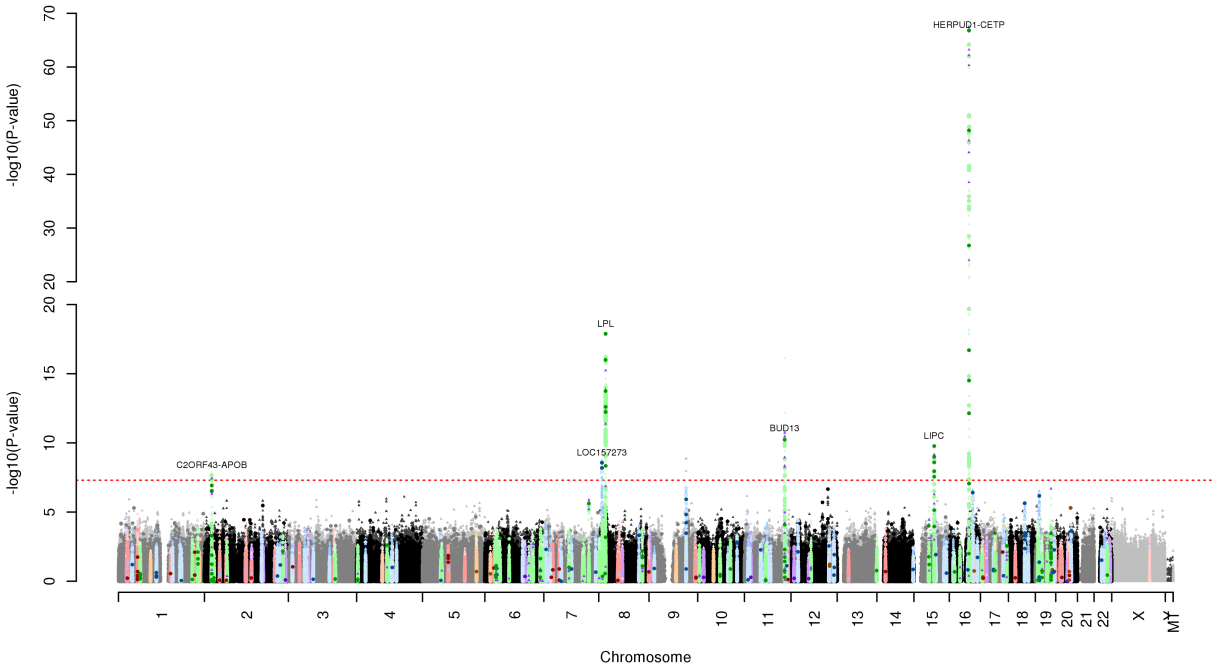



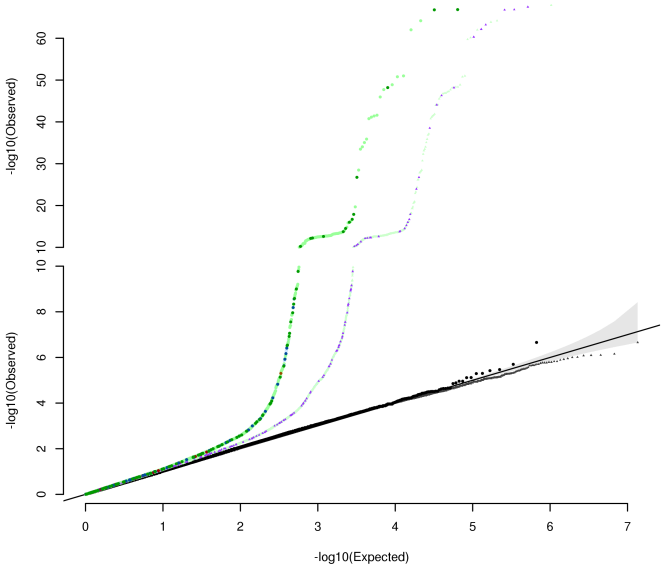
HDL non-Hispanic whites. $\lambda_{\text{typed}} = 1.15$, $\lambda_{\text{imputed}} = 1.15$.



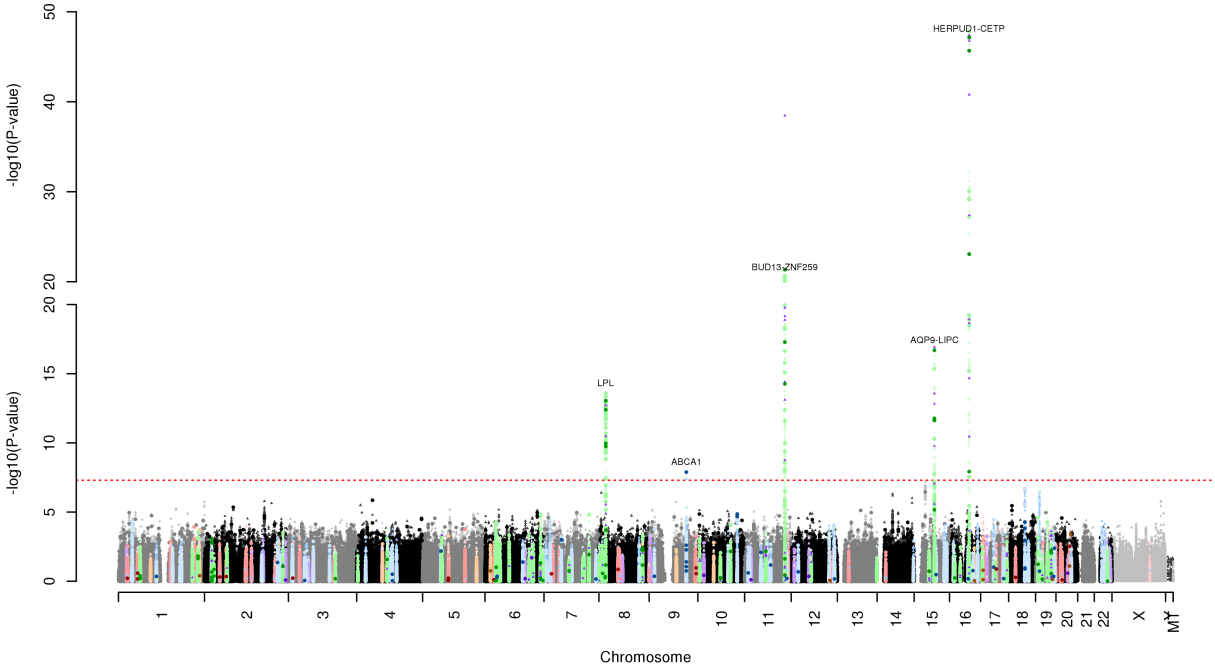



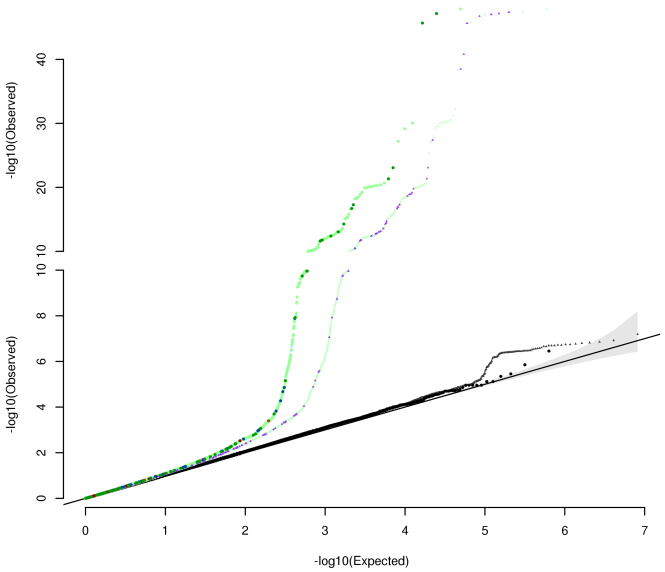
HDL Latinos. $\lambda_{\text{typed}} = 1.05$, $\lambda_{\text{imputed}} = 1.00$.



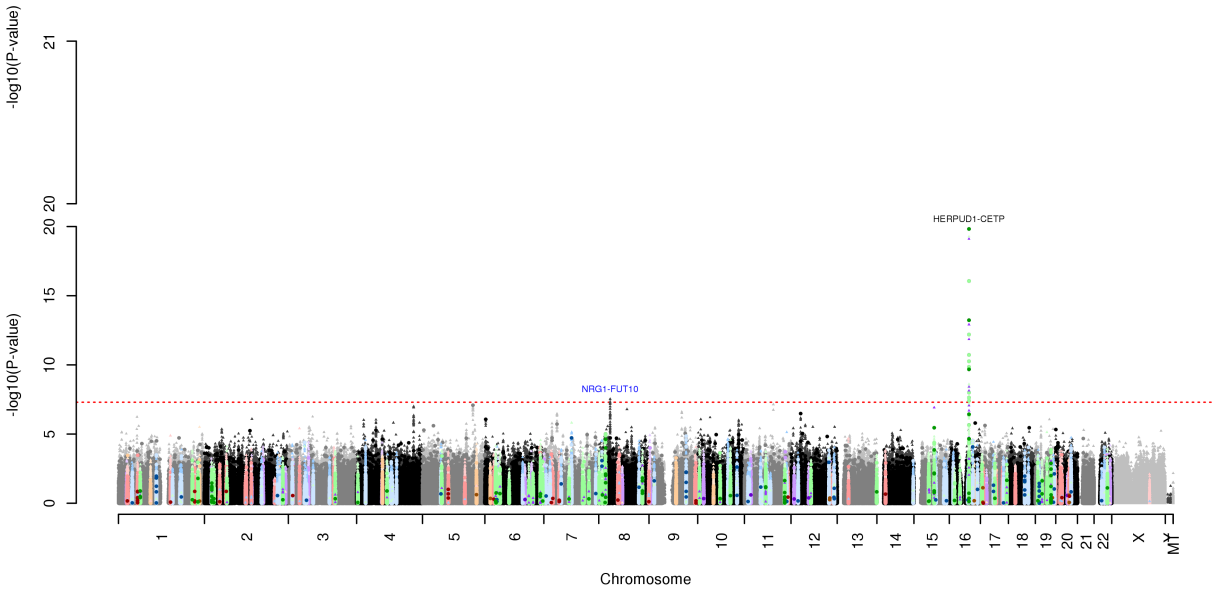



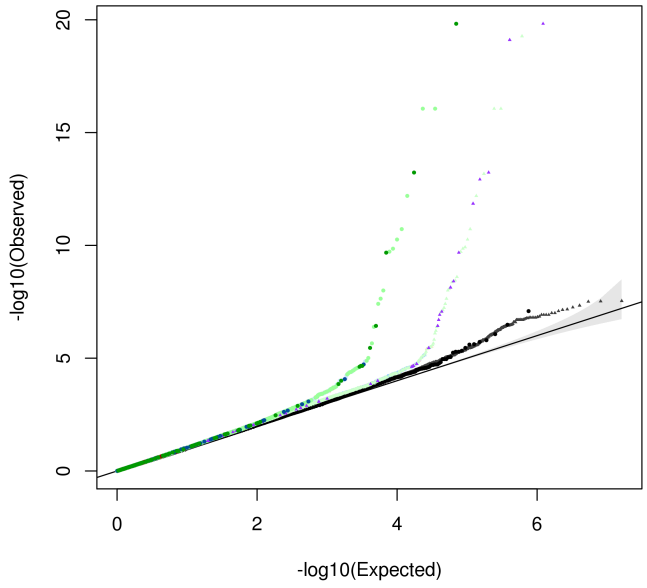
HDL East Asians. $\lambda_{\text{typed}} = 1.00$, $\lambda_{\text{imputed}} = 1.00$.



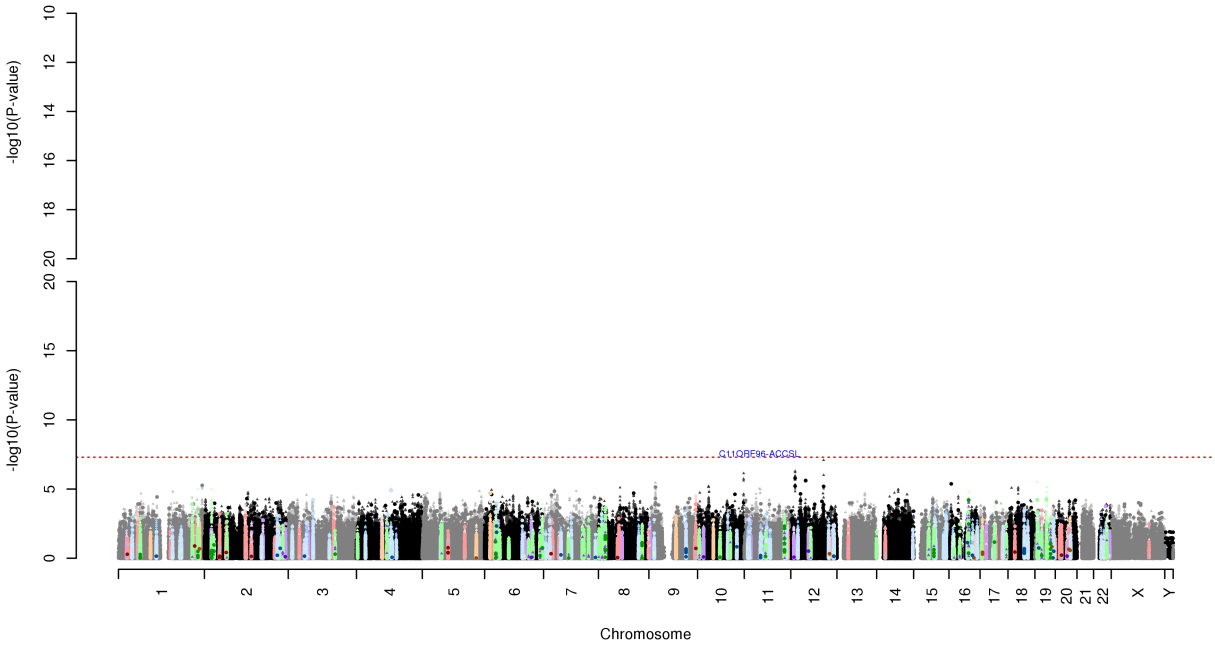



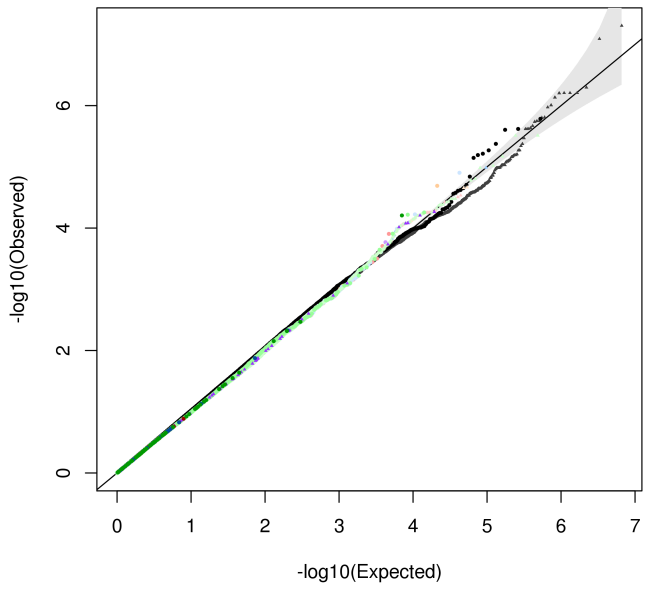
HDL African Americans. $\lambda_{\text{typed}} = 1.00$, $\lambda_{\text{imputed}} = 1.00$.



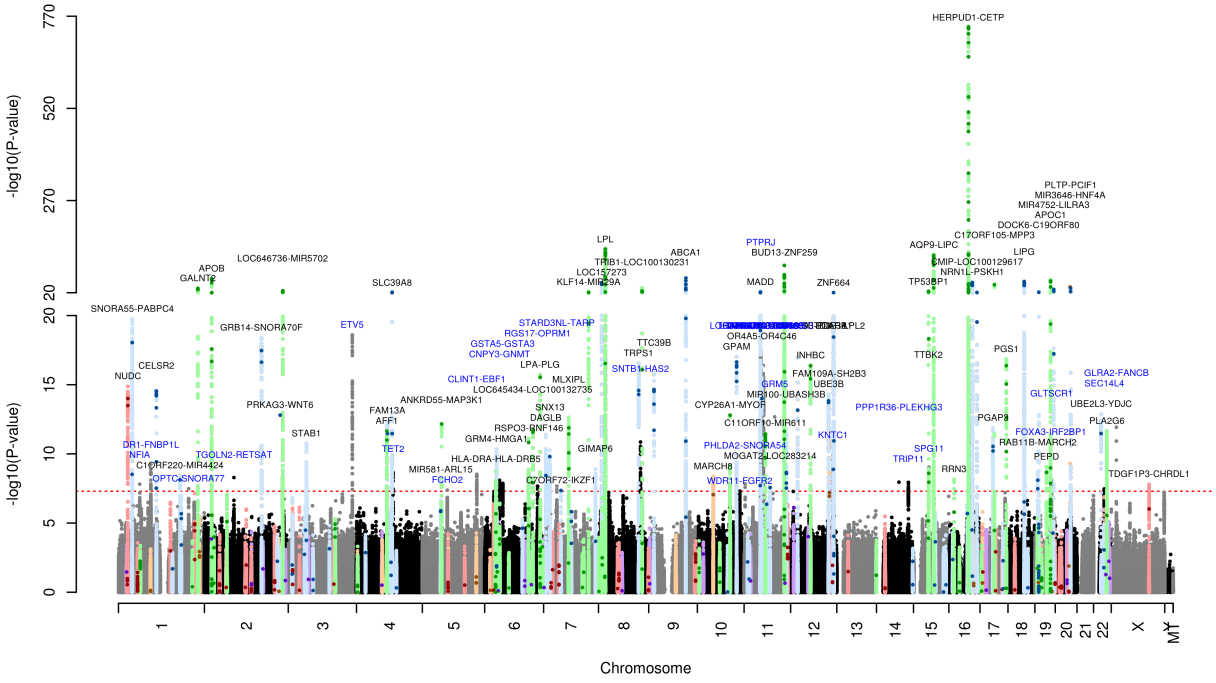



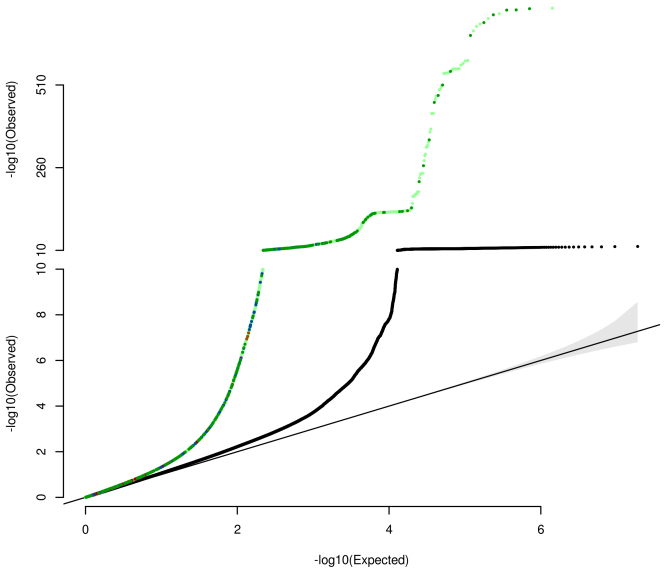
HDL South Asians. $\lambda_{\text{typed}} = 1.02$, $\lambda_{\text{imputed}} = 1.02$.



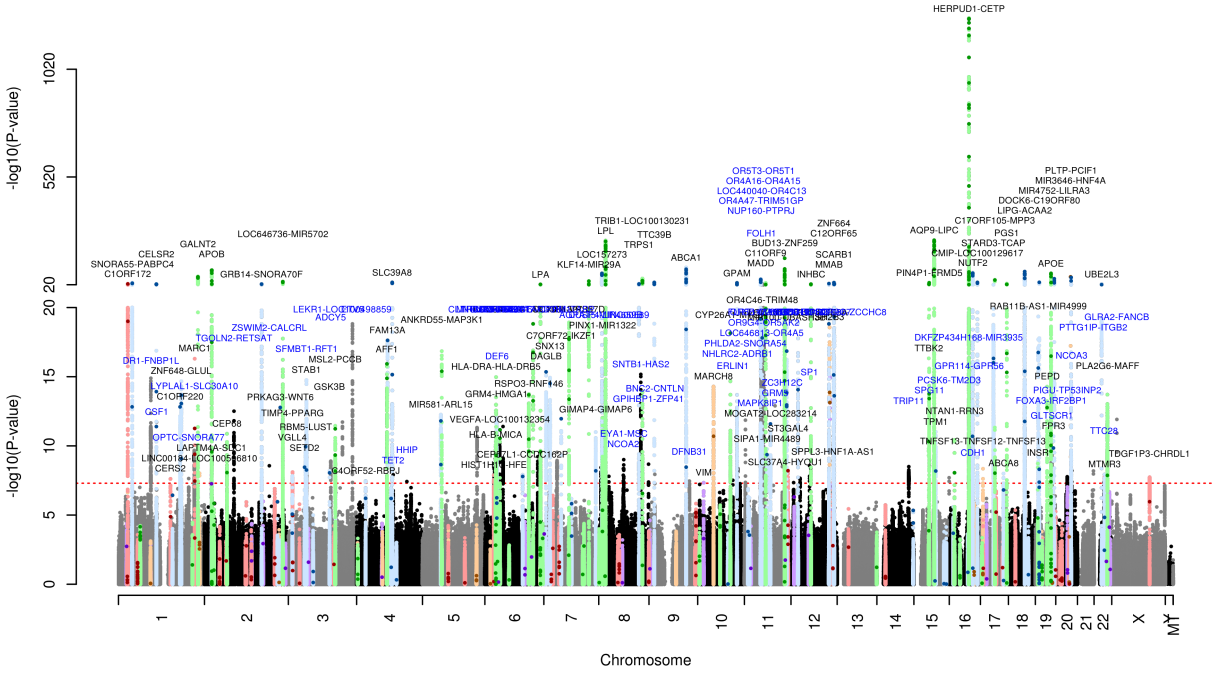



HDL GERA. $\lambda = 1.09$.

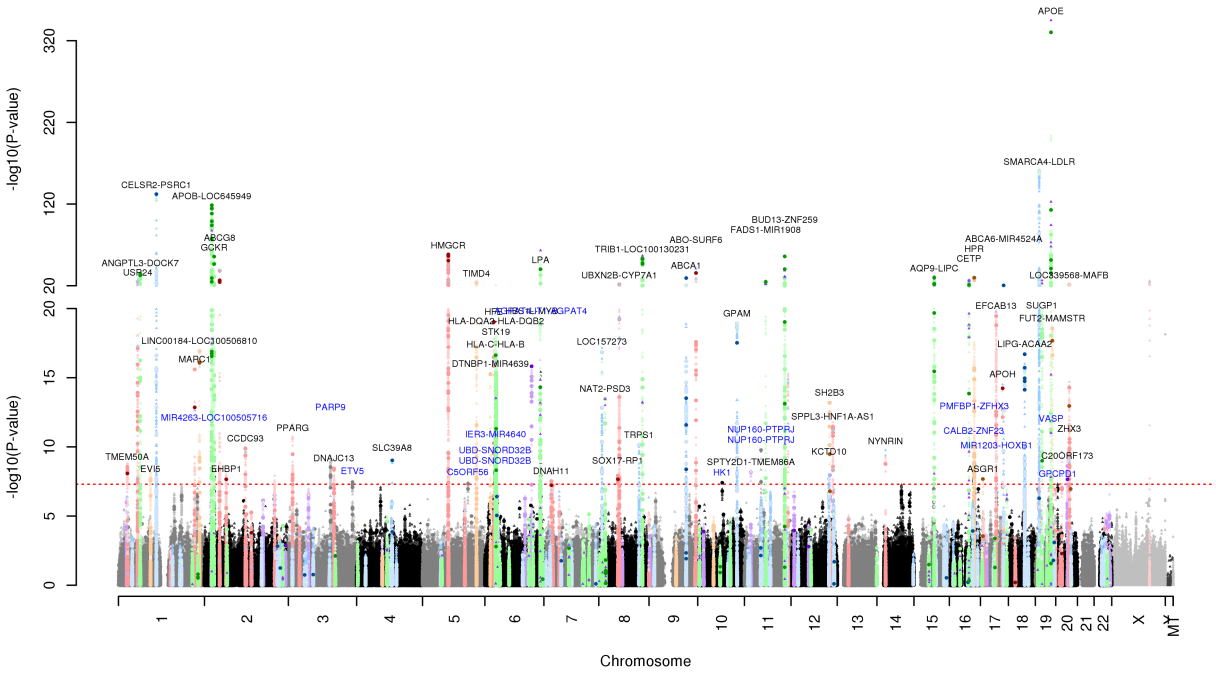


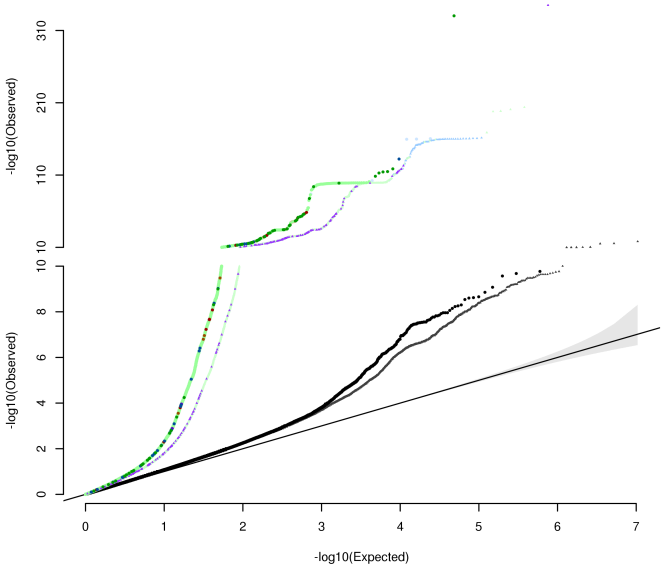



HDL GERA+GLGC. $\lambda = 1.10$.

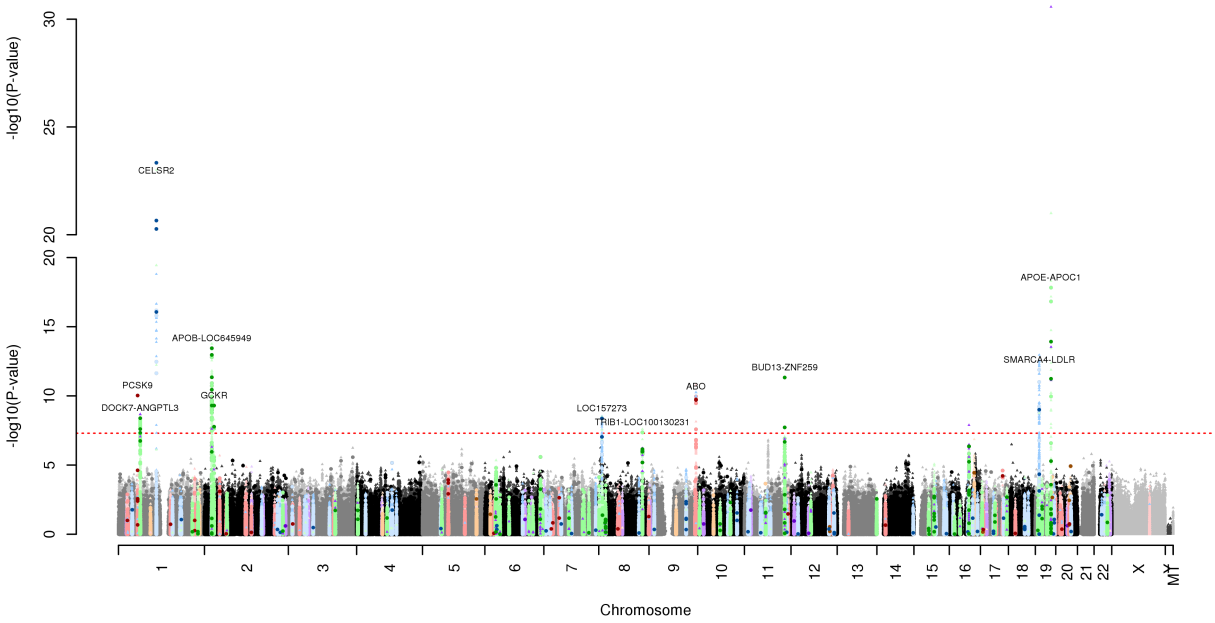


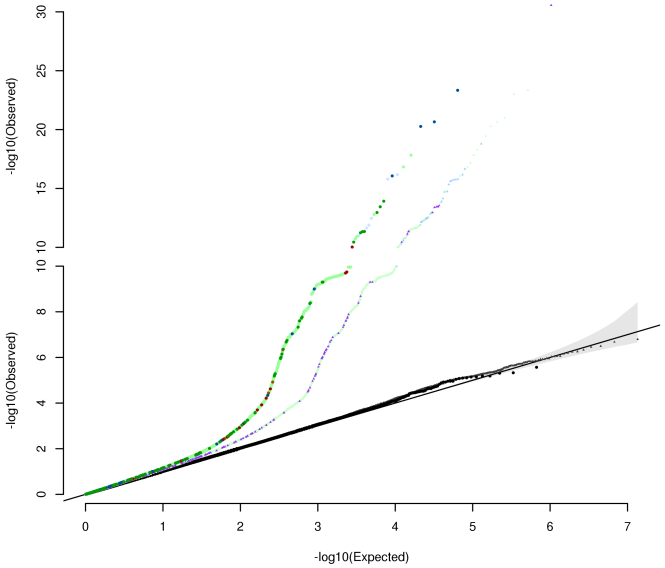
TC non-Hispanic whites. $\lambda_{\text{typed}} = 1.15$, $\lambda_{\text{imputed}} = 1.10$.



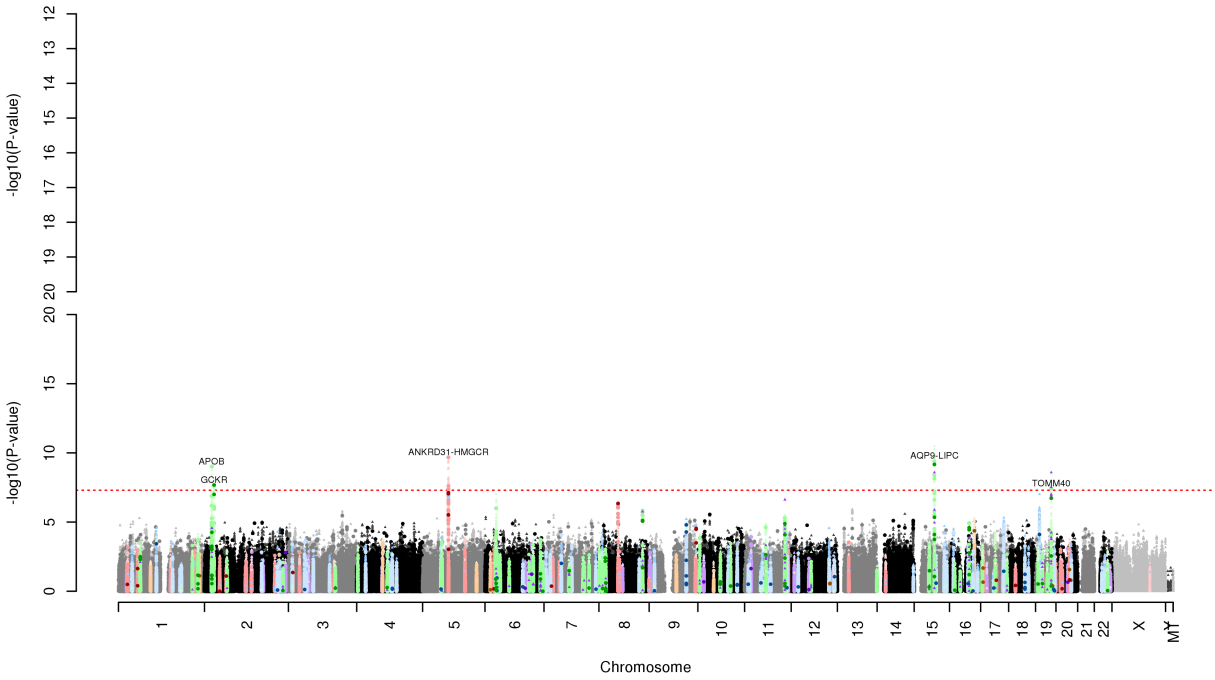



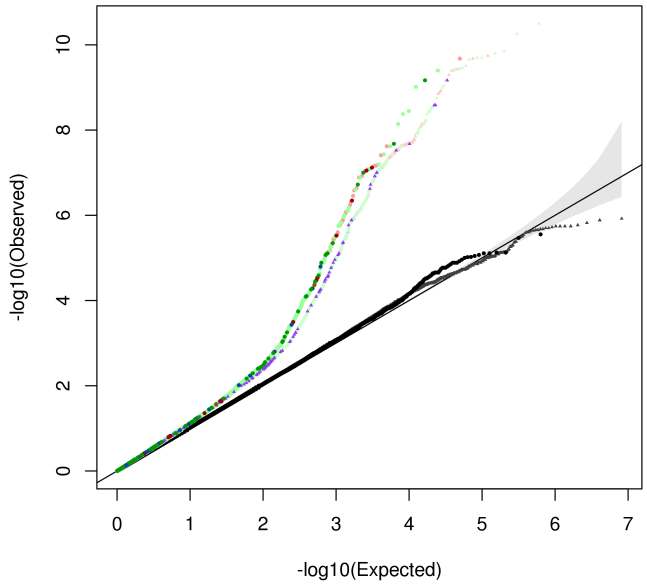
TC Latinos. $\lambda_{\text{typed}} = 1.00$, $\lambda_{\text{imputed}} = 1.00$.



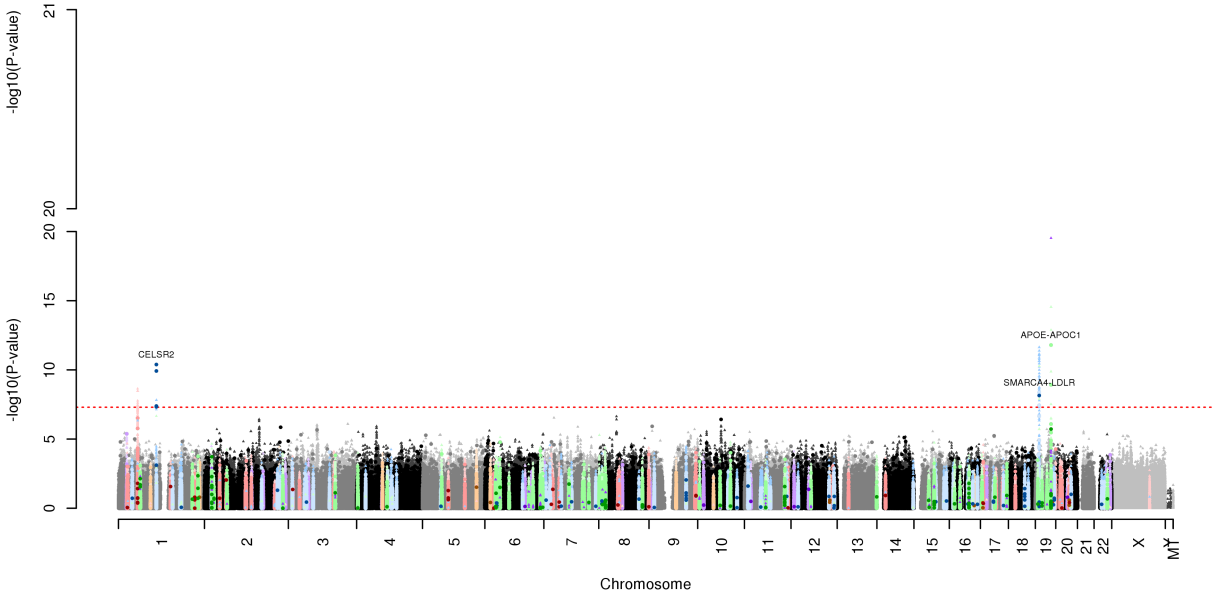



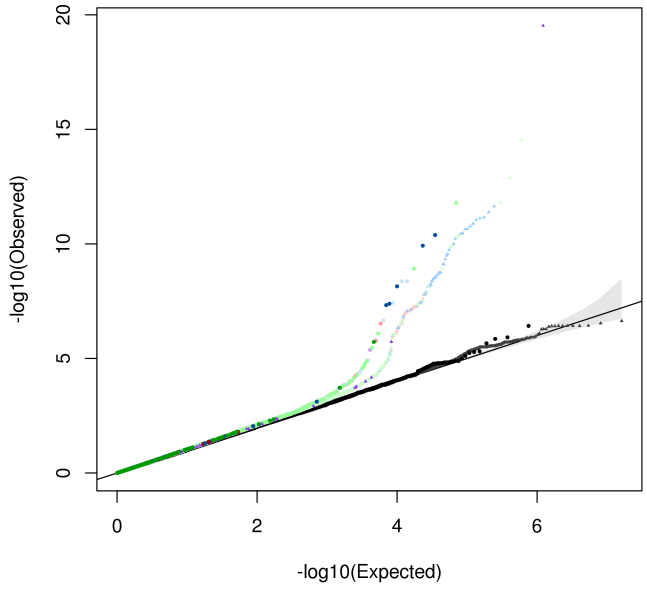
TC East Asians. $\lambda_{\text{typed}} = 1.05$, $\lambda_{\text{imputed}} = 1.05$.



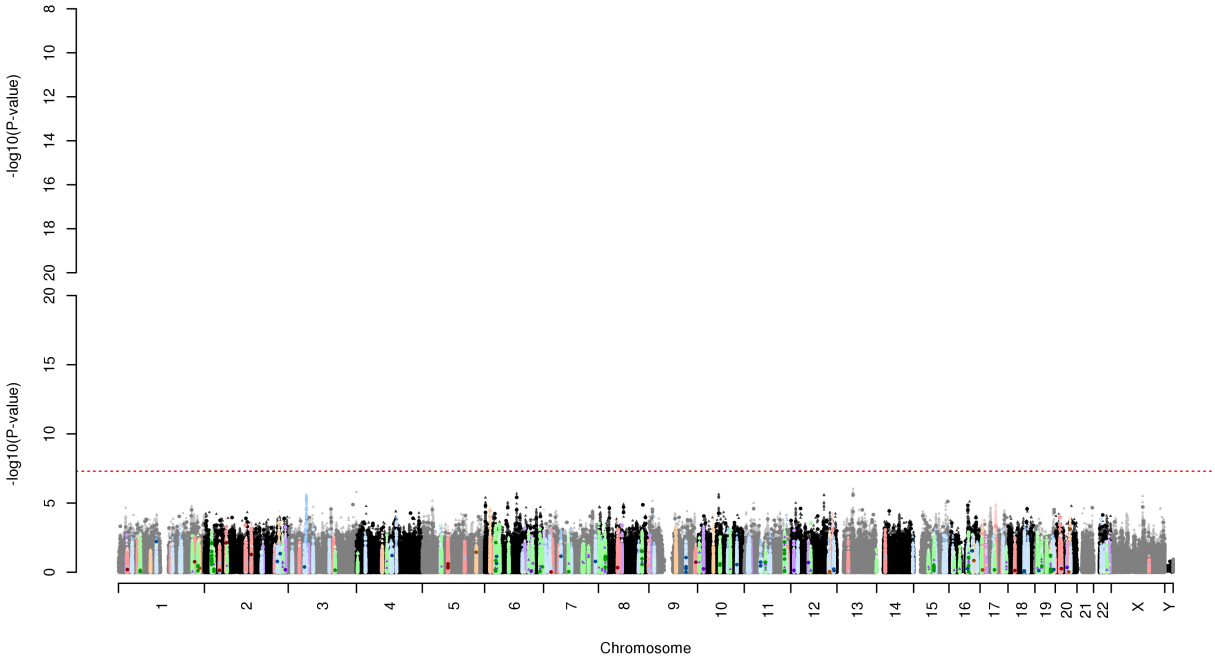



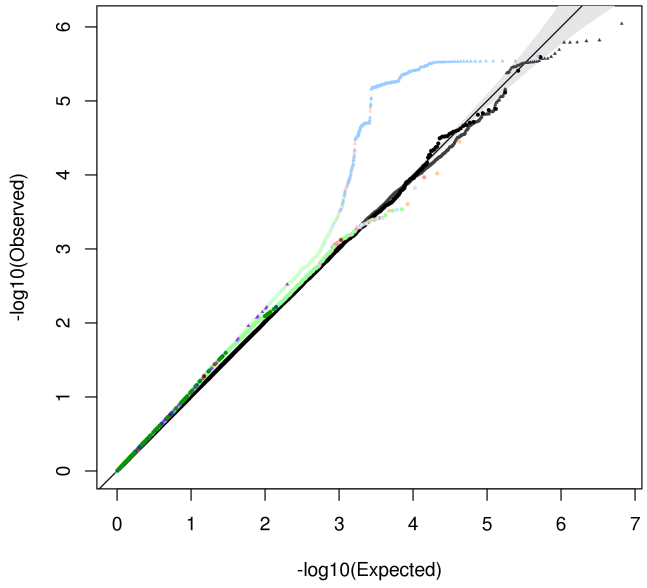
TC African Americans. $\lambda_{\text{typed}} = 1.00$, $\lambda_{\text{imputed}} = 1.00$.



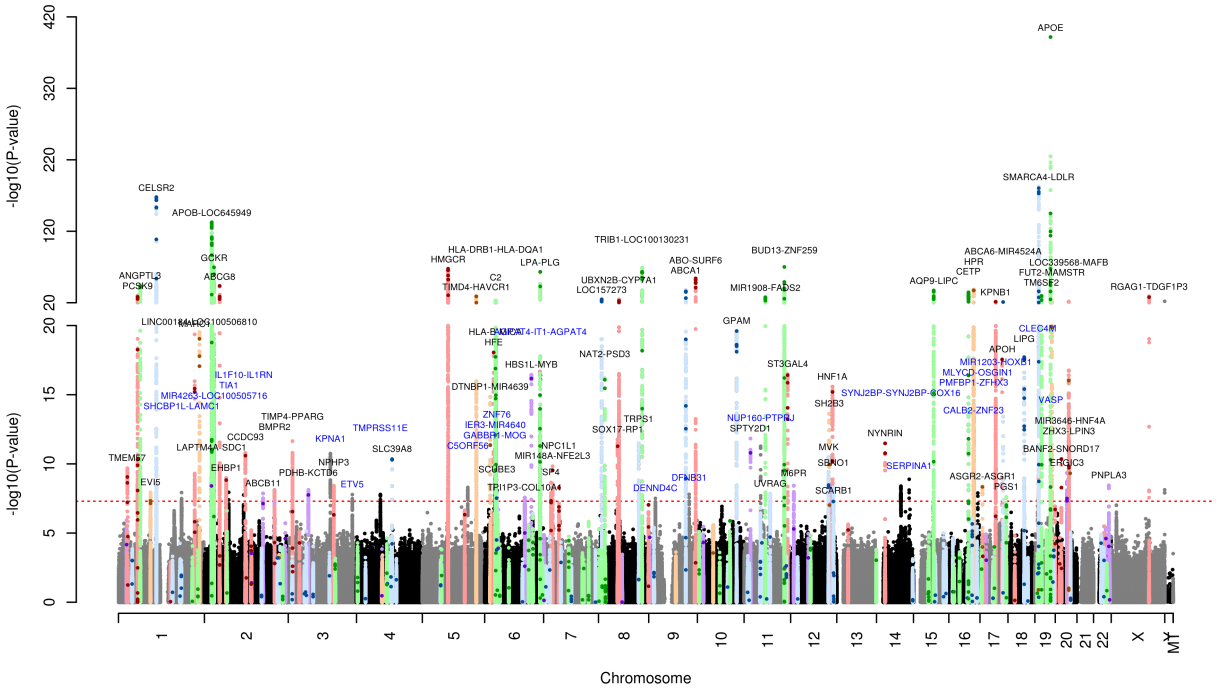



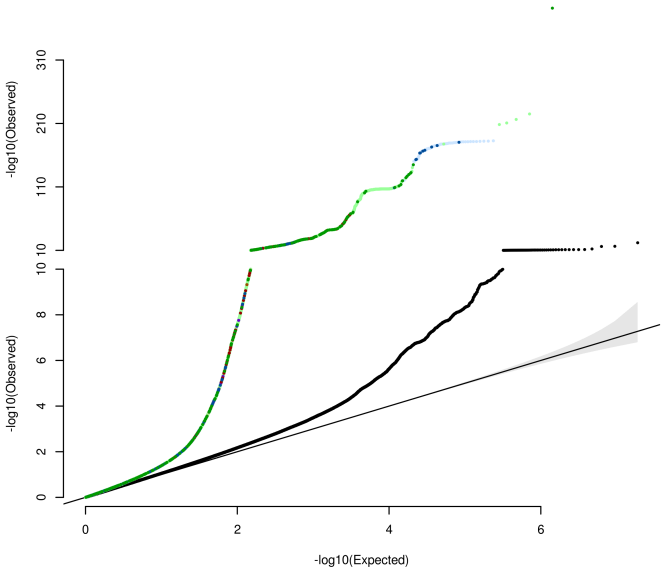
TC South Asians. $\lambda_{\text{typed}} = 1.02$, $\lambda_{\text{imputed}} = 1.02$.



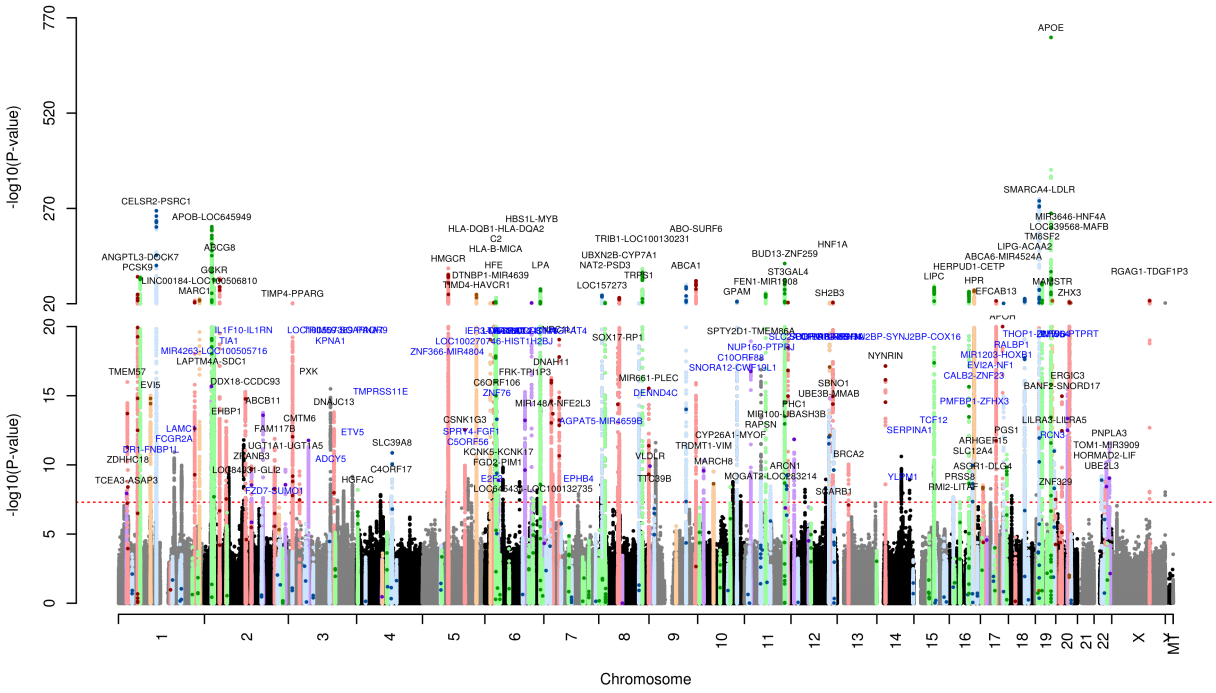



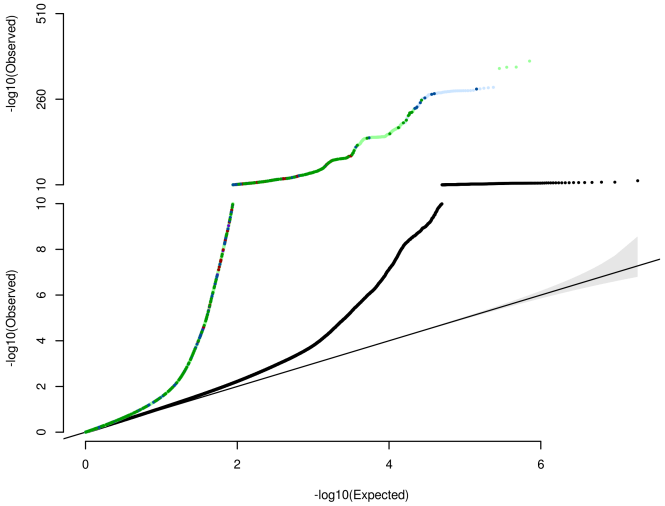
TC GERA. $\lambda = 1.07$.



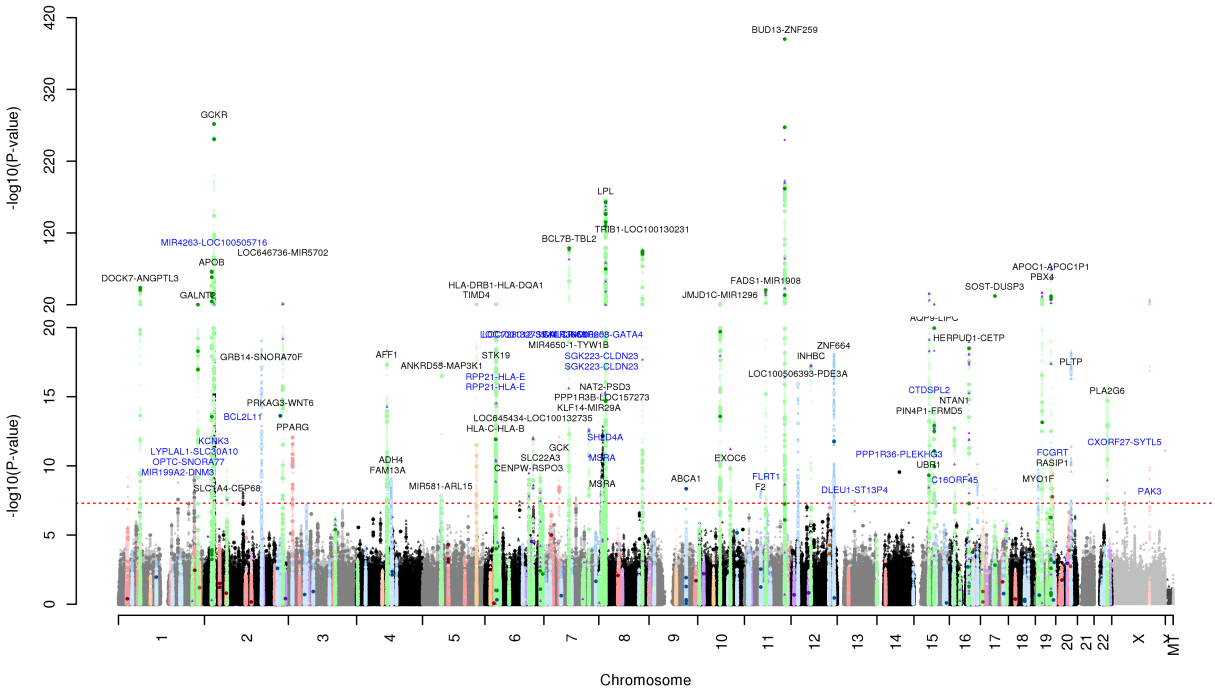



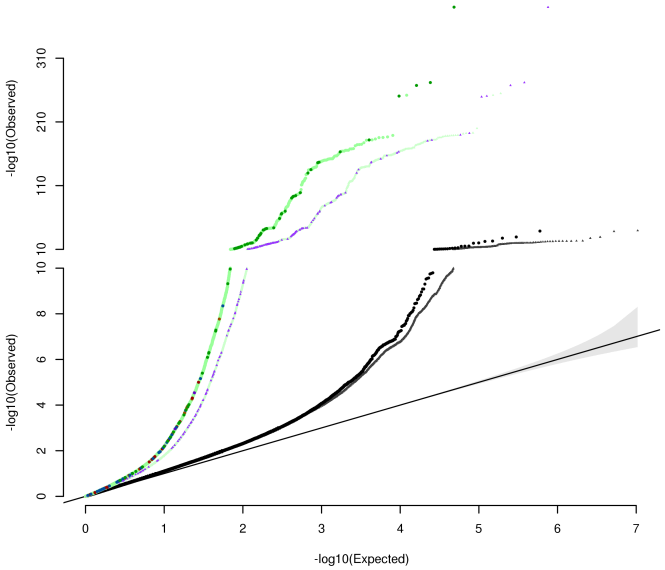
TC GERA+GLGC. $\lambda = 1.07$.



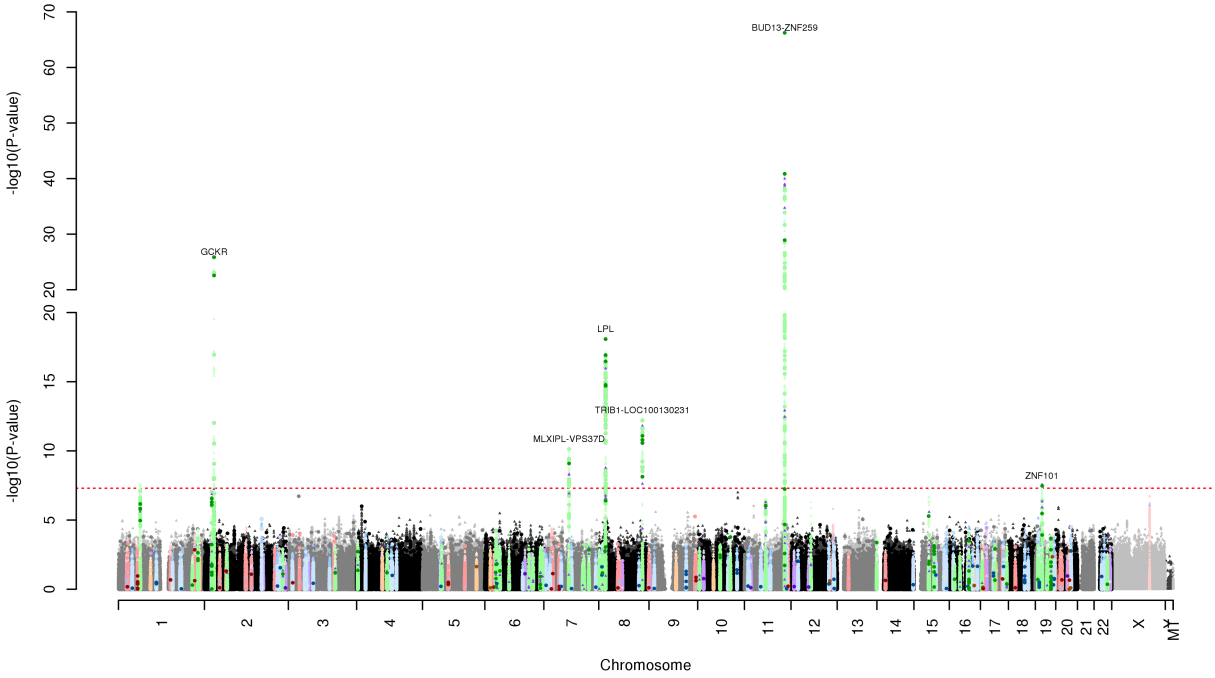



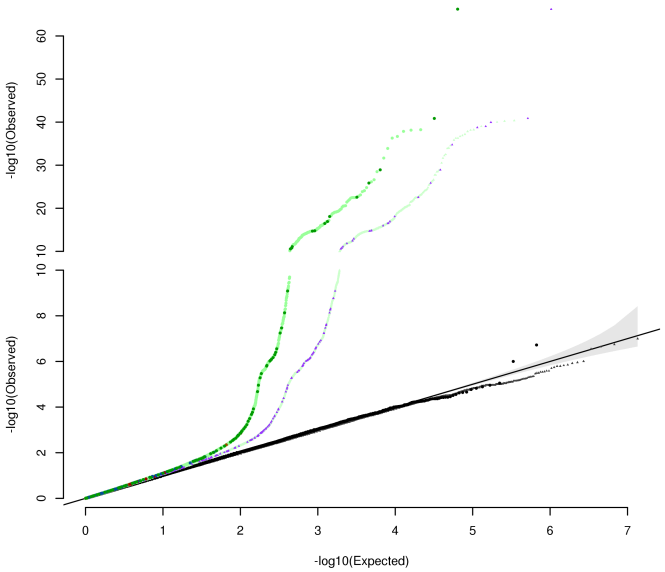
TG non-Hispanic whites. $\lambda_{\text{typed}} = 1.15$, $\lambda_{\text{imputed}} = 1.15$.



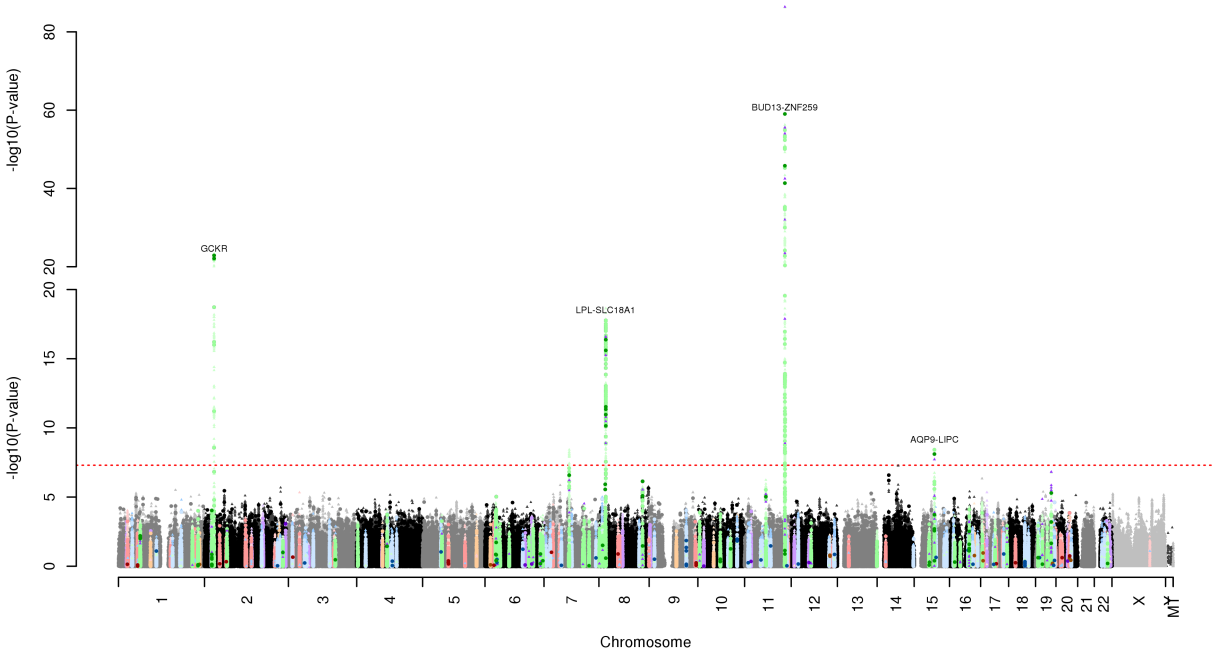



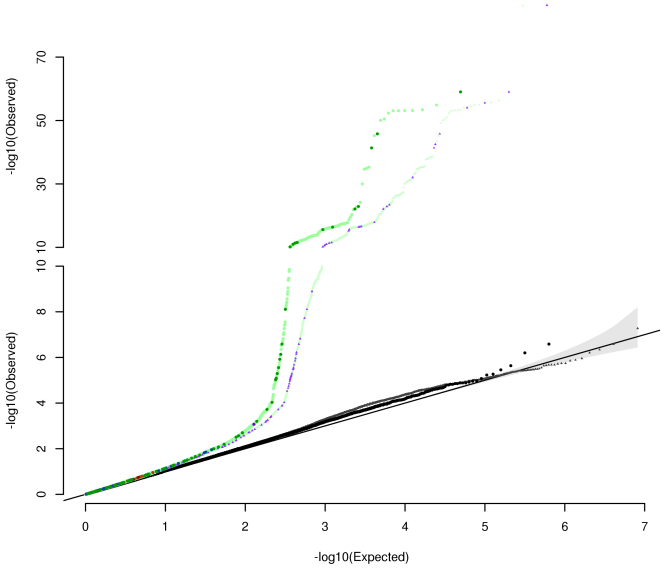
TG Latinos. $\lambda_{\text{typed}} = 1.00$, $\lambda_{\text{imputed}} = 1.00$.



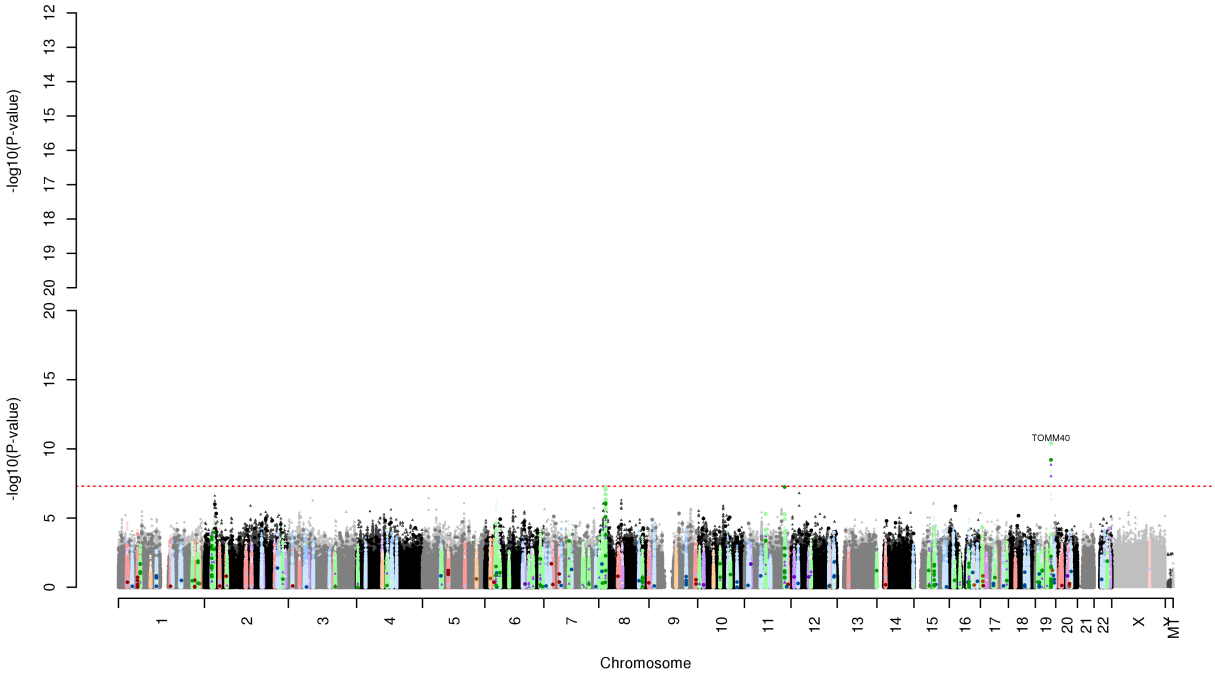



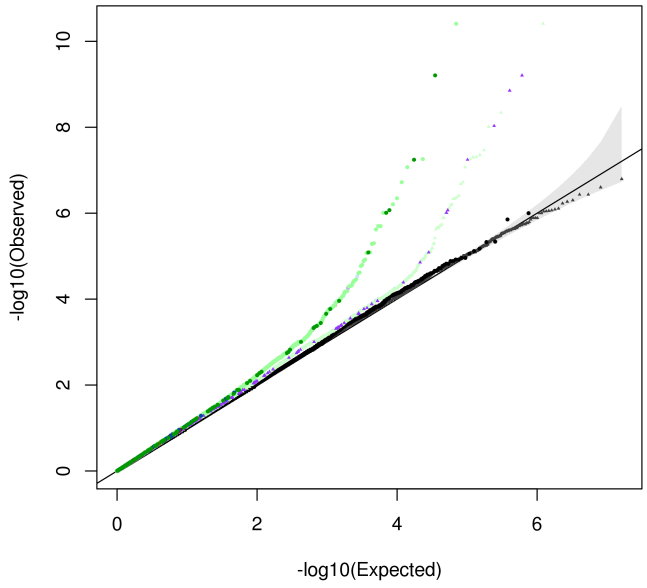
TG East Asians. $\lambda_{\text{typed}} = 1.05$, $\lambda_{\text{imputed}} = 1.05$.



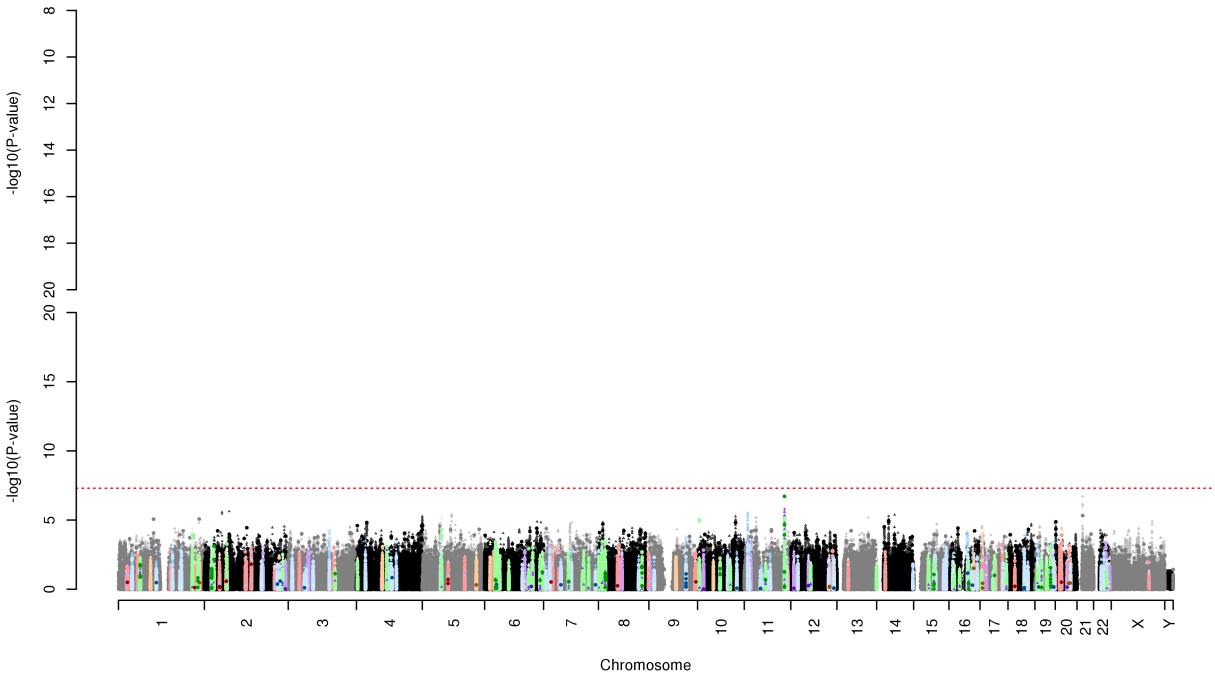



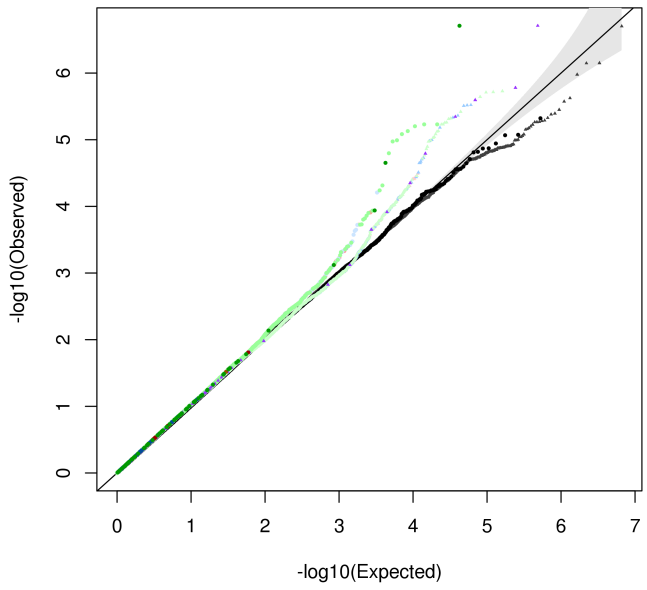
TG African Americans. $\lambda_{\text{typed}} = 1.00$, $\lambda_{\text{imputed}} = 1.00$.



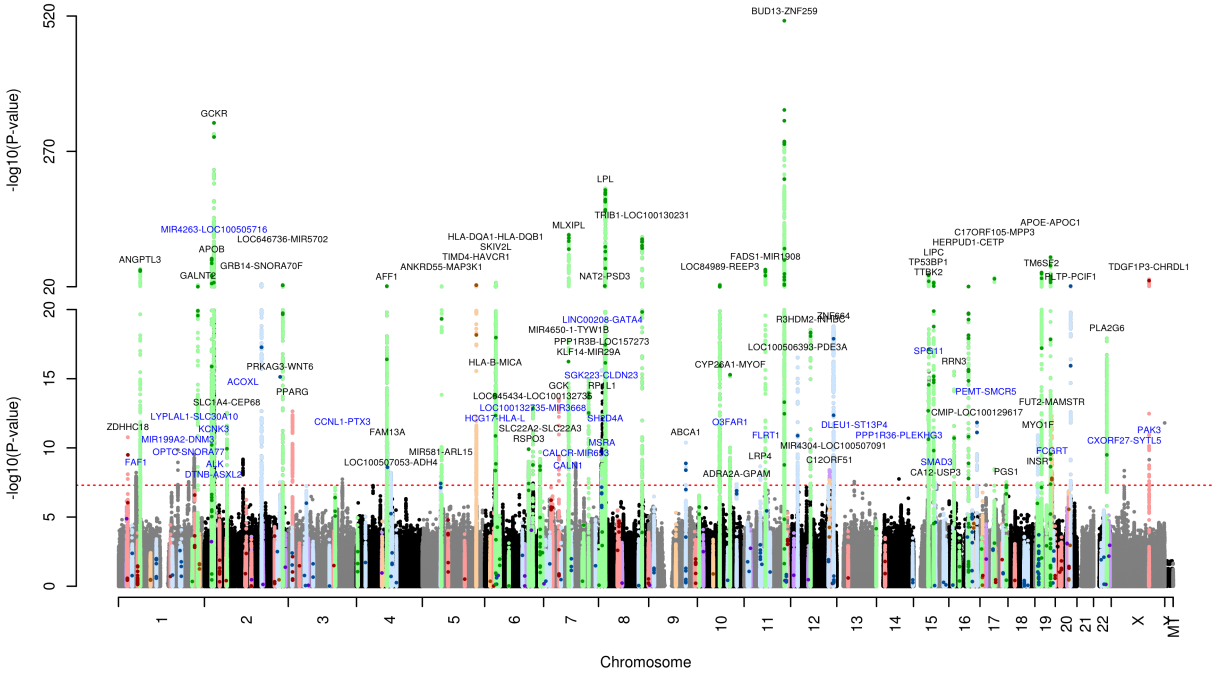



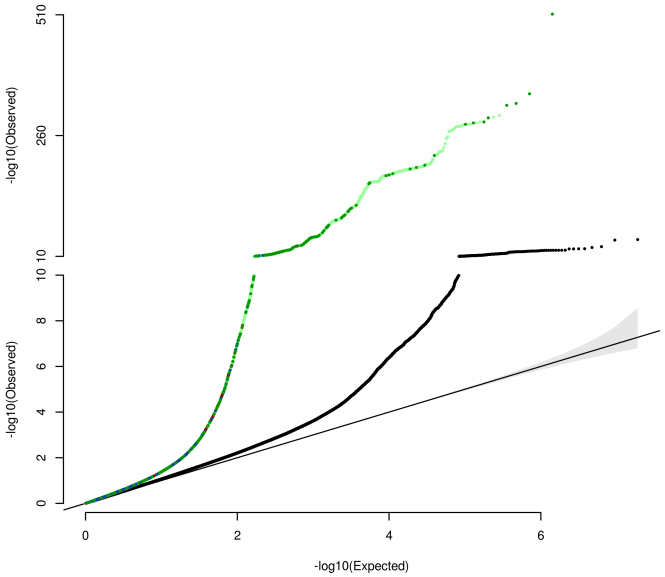
TG South Asians. $\lambda_{\text{typed}} = 1.01$, $\lambda_{\text{imputed}} = 1.00$.



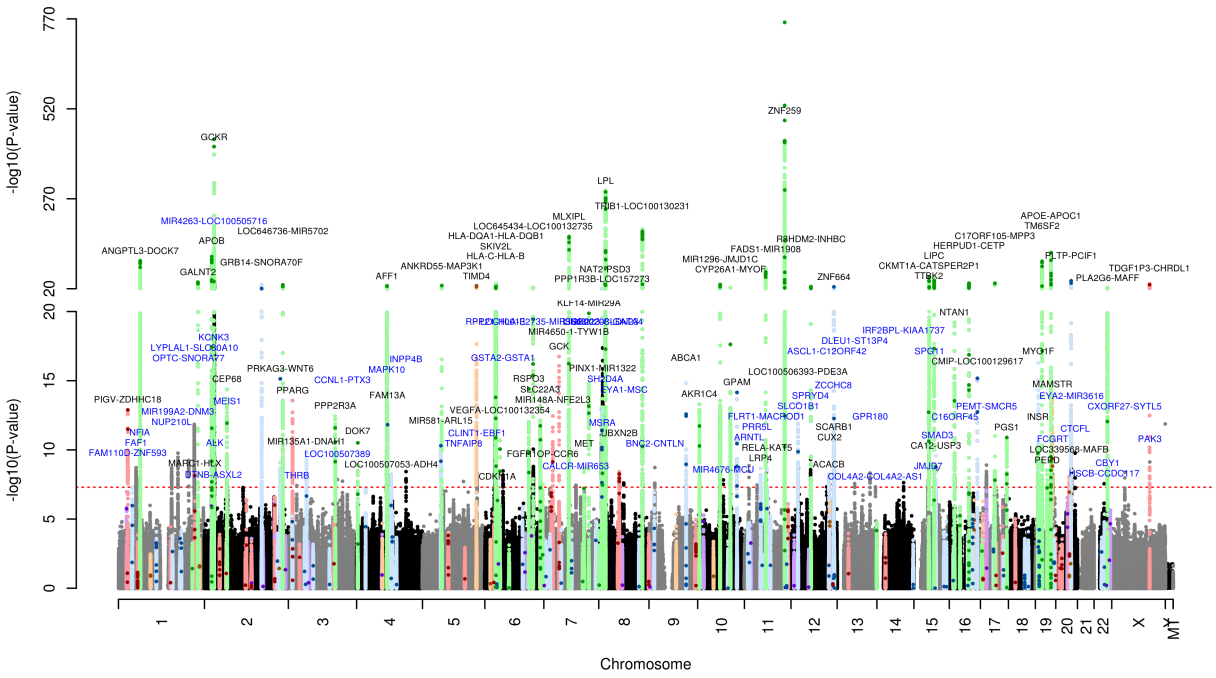



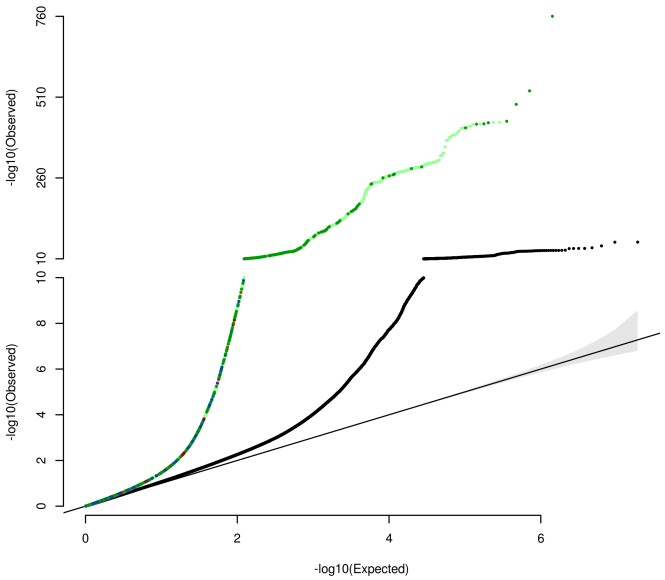
TG GERA. $\lambda = 1.09$.



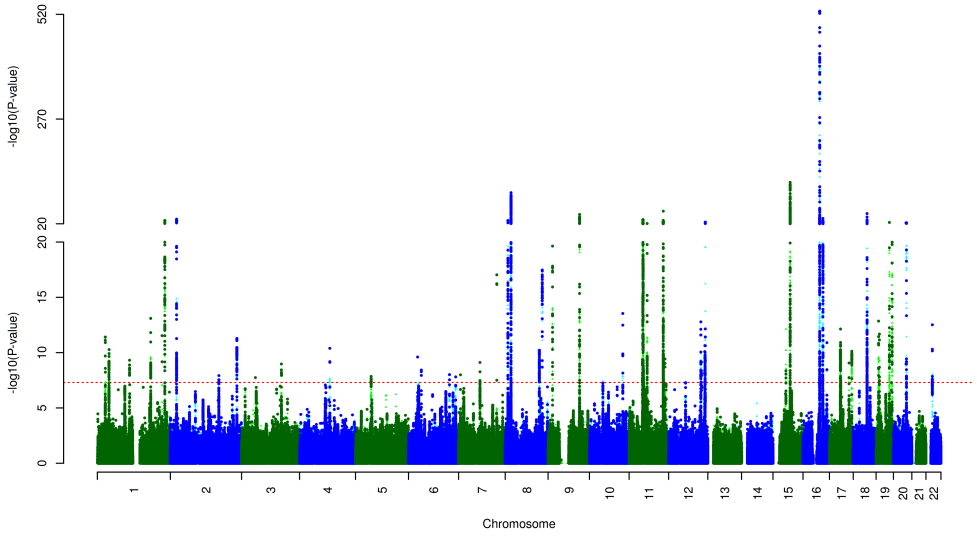
TG GERA+GLGC. $\lambda = 1.09$.



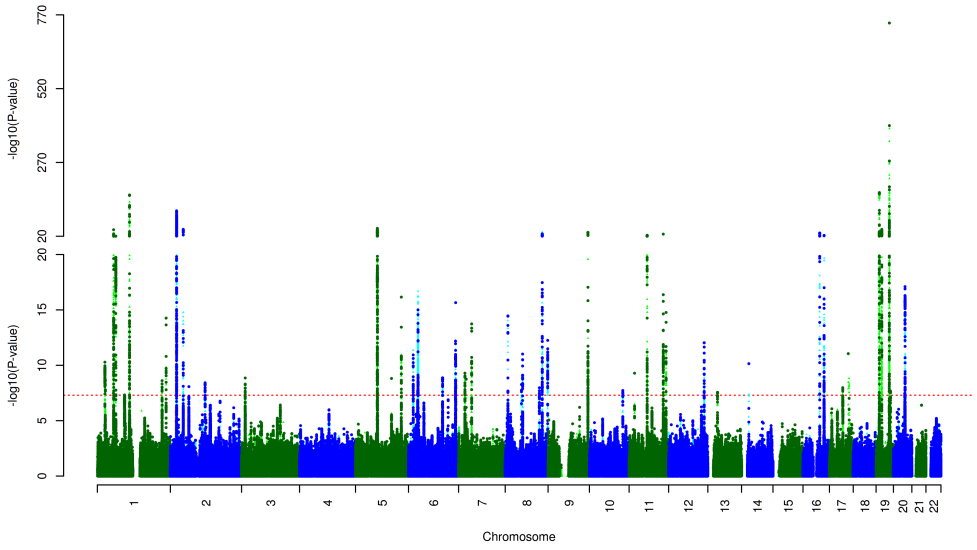



**Supplementary Figure 3:** Extending the GLGC (n=94,595) summary statistics (linear regression) from HapMap to 1000 Genomes.

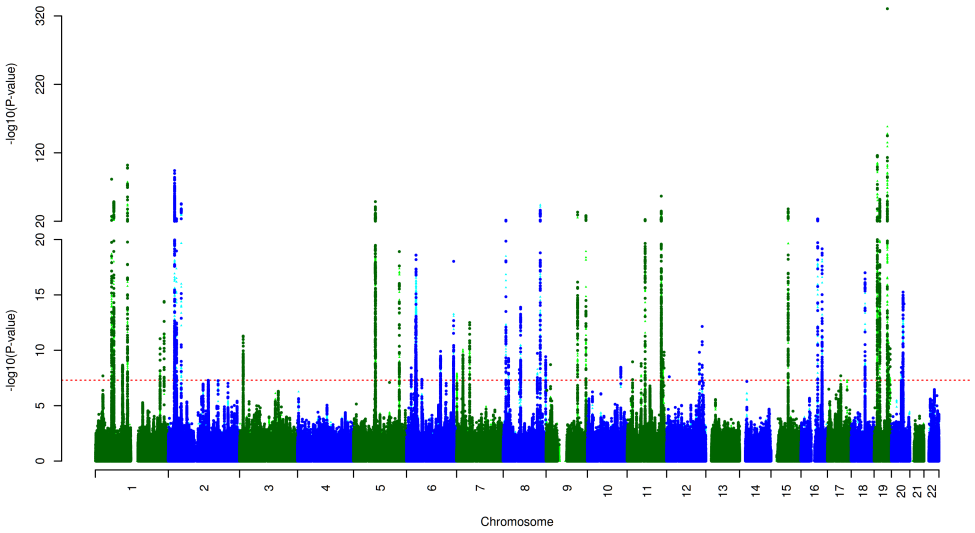
HDL.



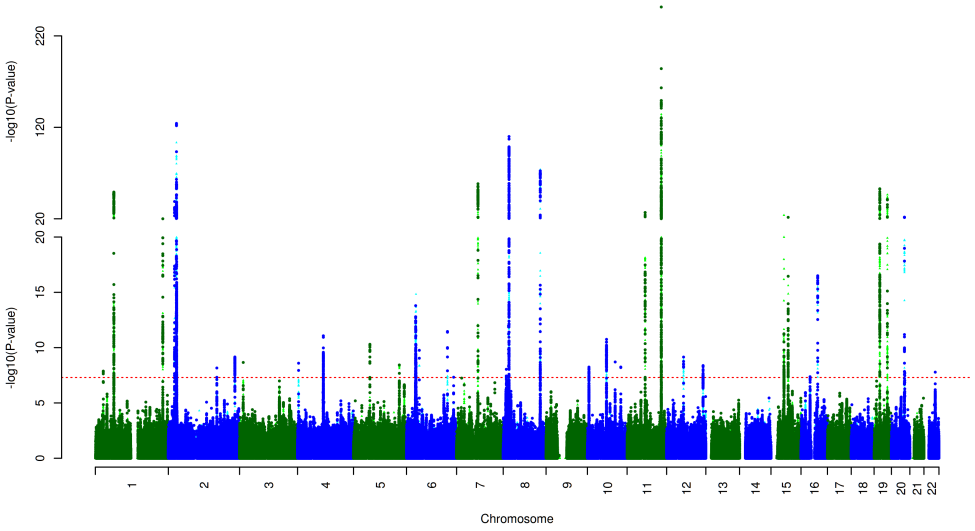

LDL.



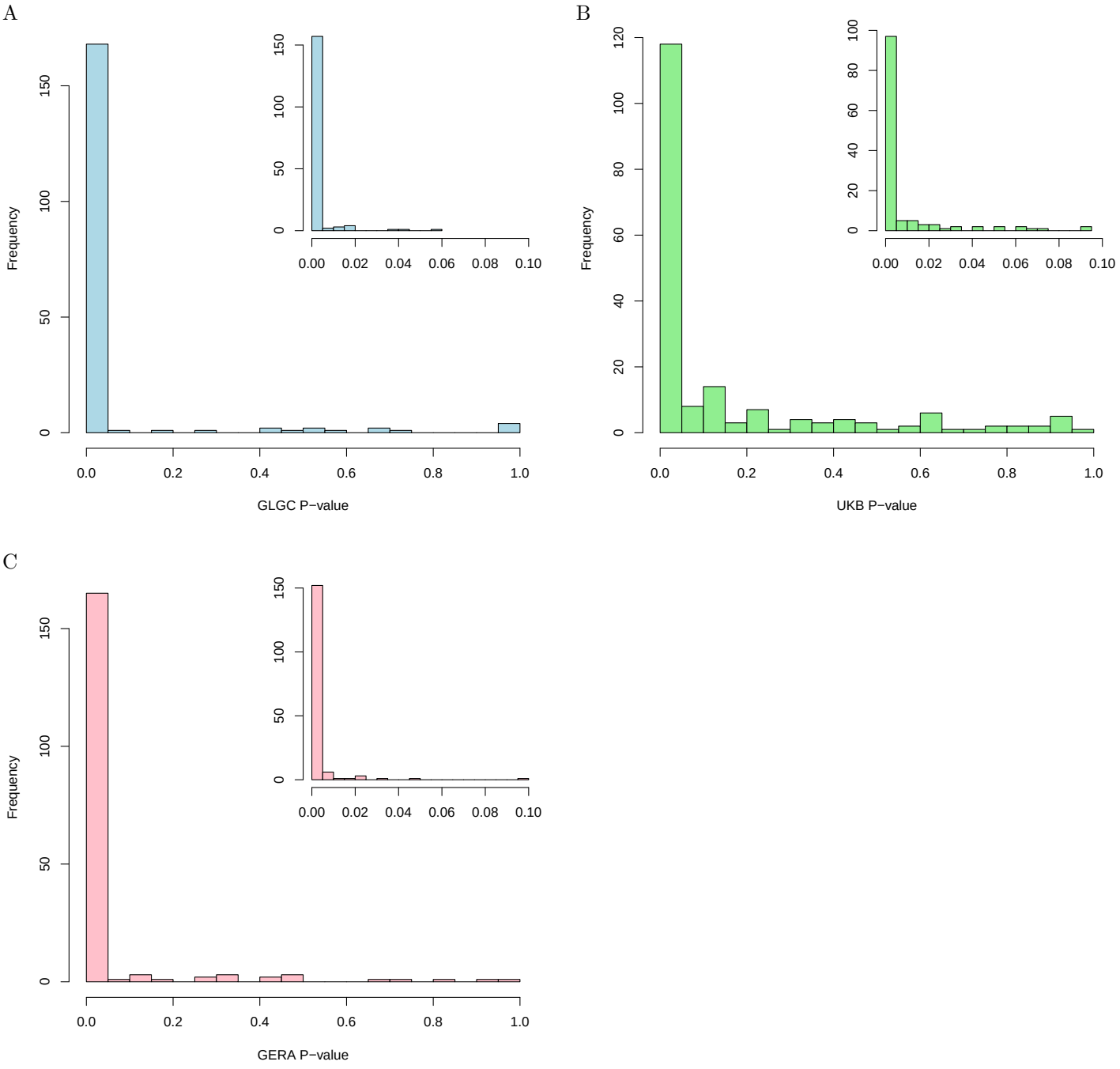
TC.


-log10(P-value)
0
5
10
15
20
20
120
220
320
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
Chromosome

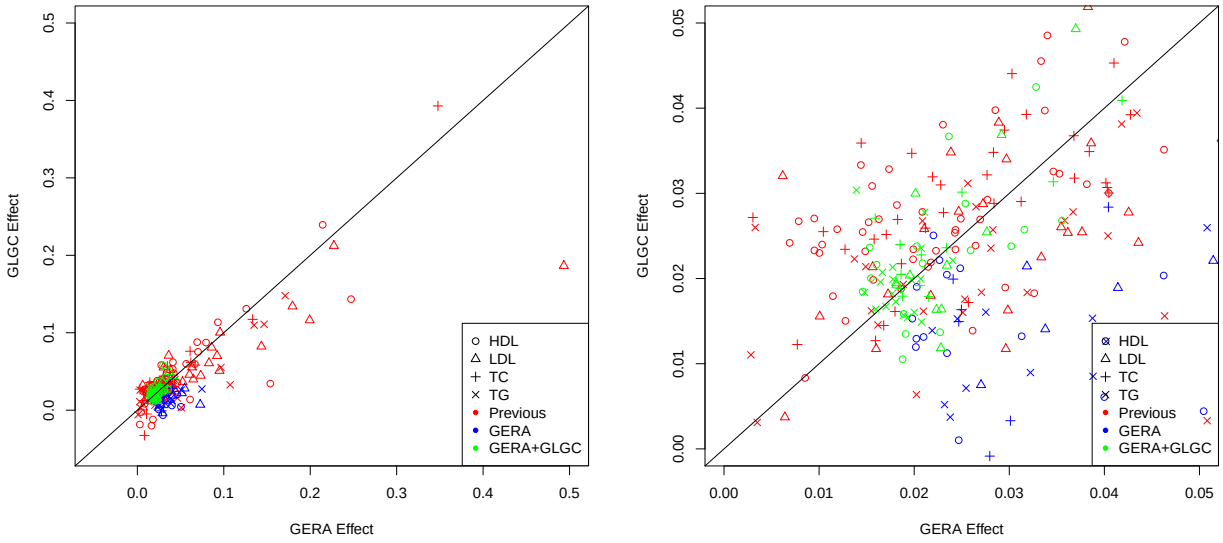
TG.


-log10(P-value)
0
5
10
15
20
20
120
220
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
Chromosome

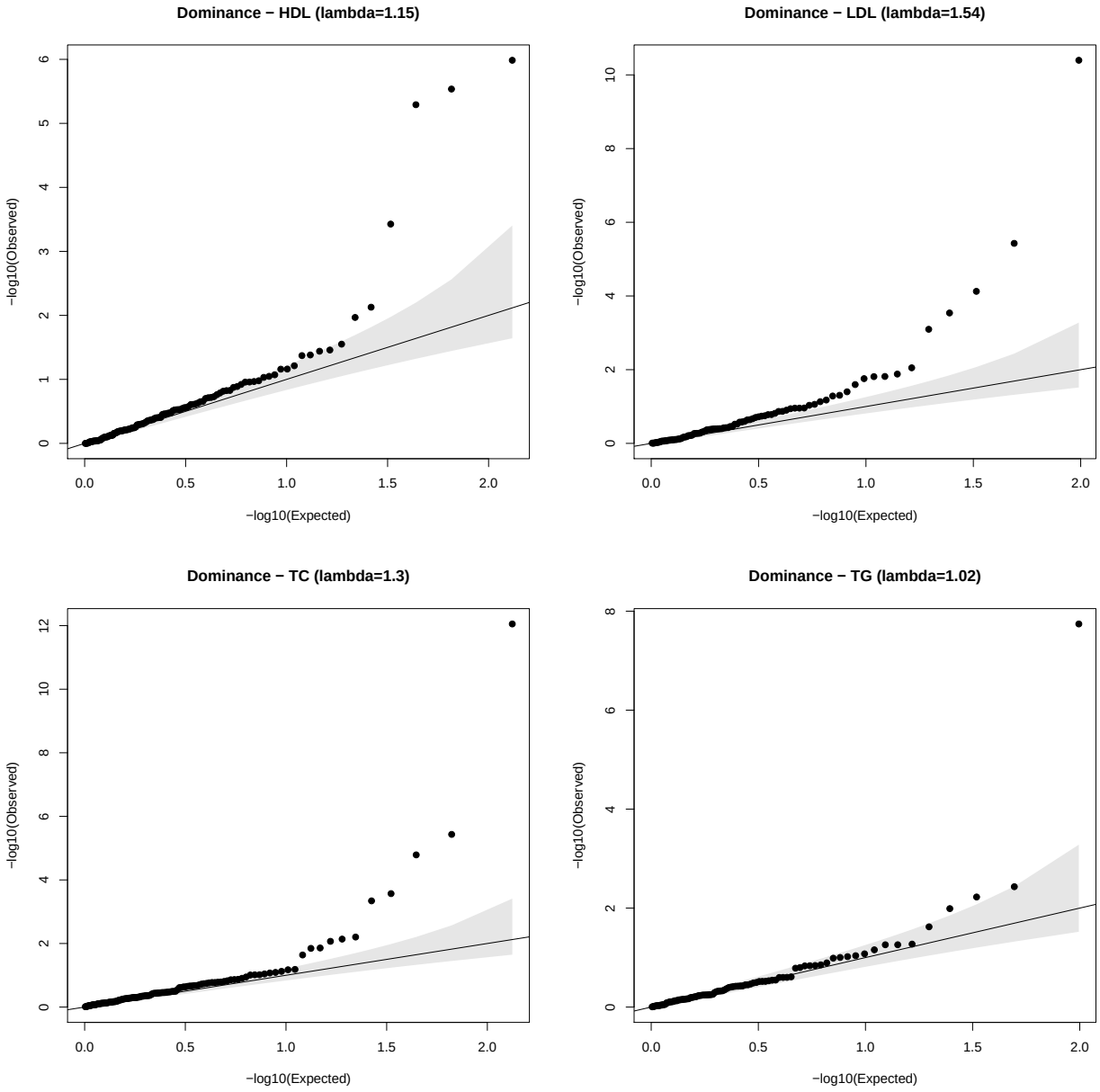
**Supplementary Figure 4:** Replication p-value distribution. Replication of SNPs (A) discovered in GERA (n=94,674) using GLGC (n=94,595), (B) discovered in GERA using UKB (n=460,088), and (C) all previously-identified SNPs using GERA (n=94,674). All tests two-sided via linear regression.



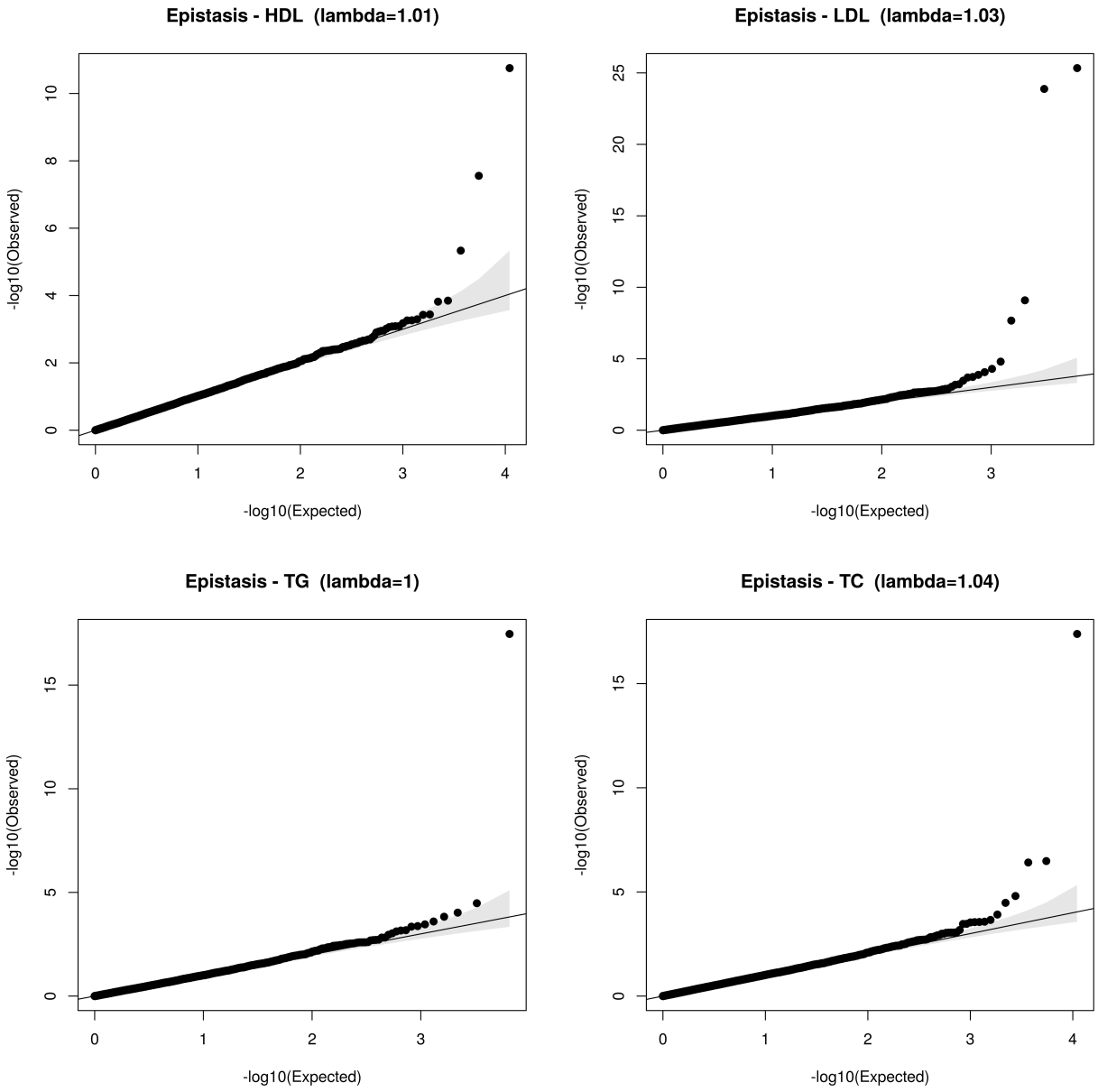
**Supplementary Figure 5:** Effect size estimates in the RPGEH GERA (n=94,674) cohort vs. previously-reported GLGC (n=94,595) effect size estimates. All tests two-sided via linear regression.



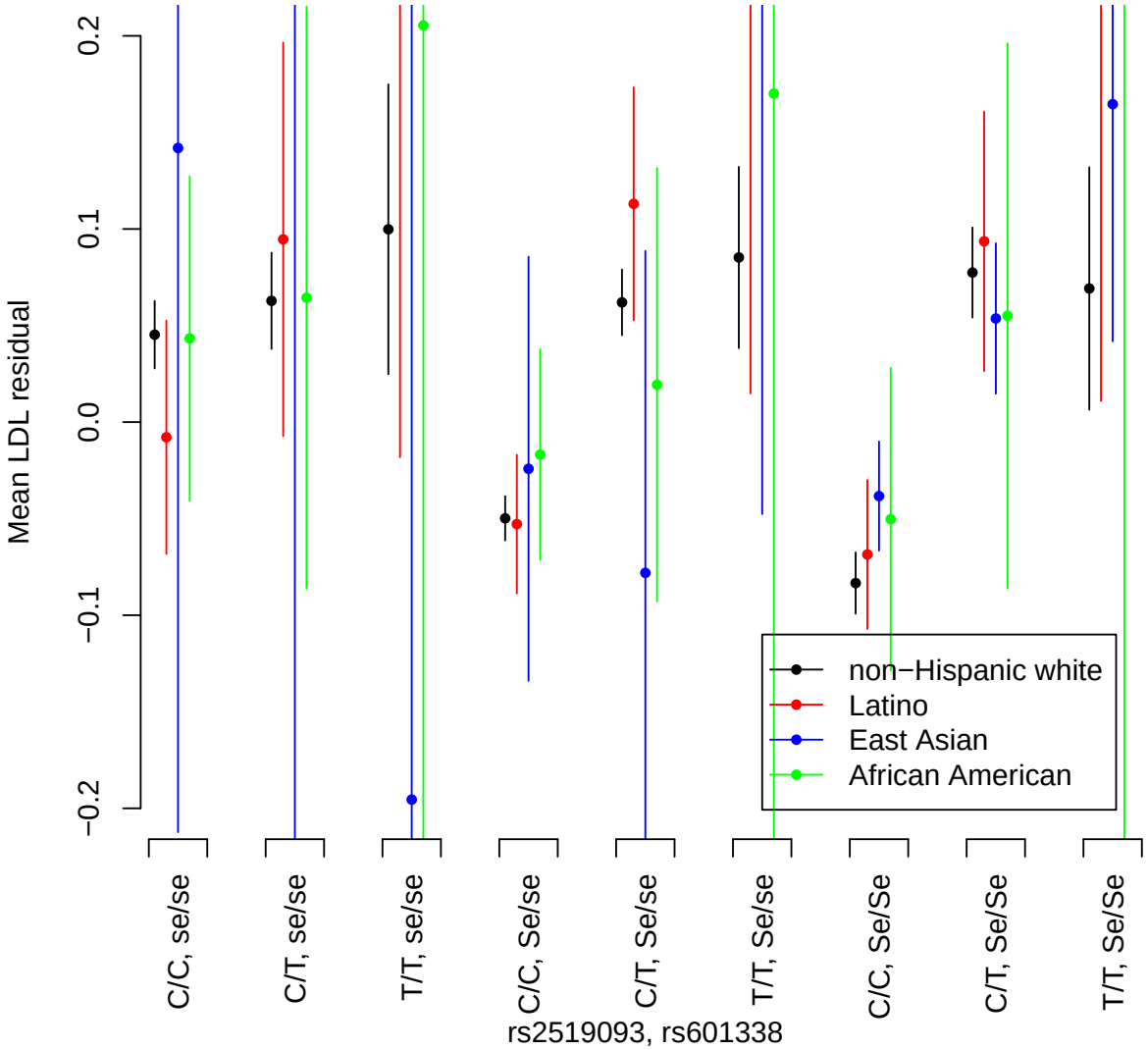
**Supplementary Figure 6:** Dominance Q-Q plots in RPGEH GERA (n=94,674) of all previously-, GERA-, and GERA+GLGC-identified lead SNPs. All tests two-sided via linear regression.



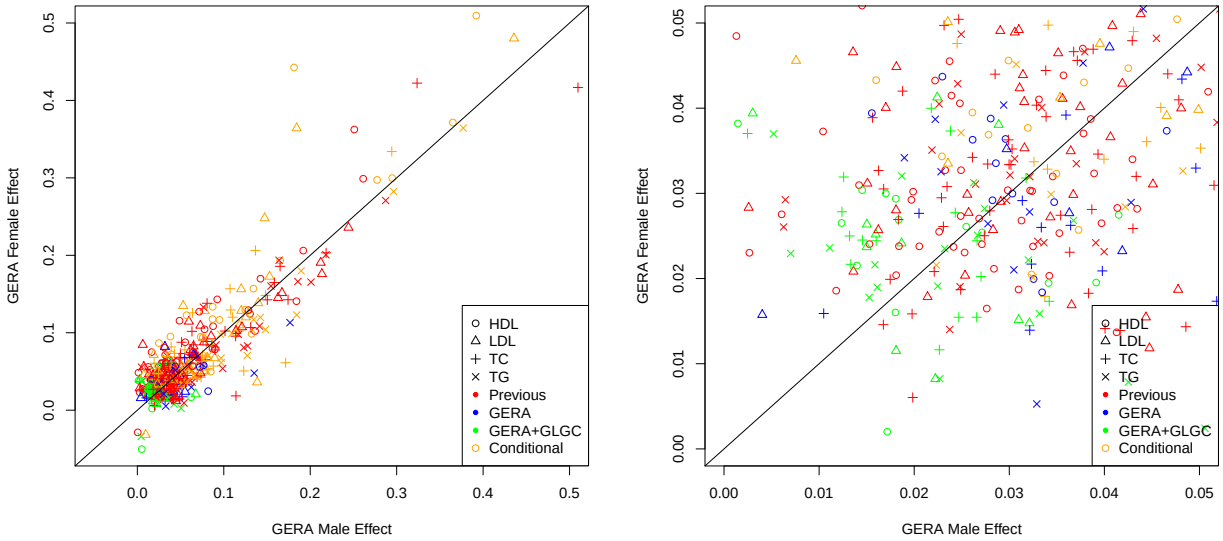
**Supplementary Figure 7:** Epistasis Q-Q plots in RPGEH GERA (n=94,674) of all pairwise tests of previously-, GERA-, and GERA+GLGC-identified lead SNPs. All tests two-sided via linear regression.



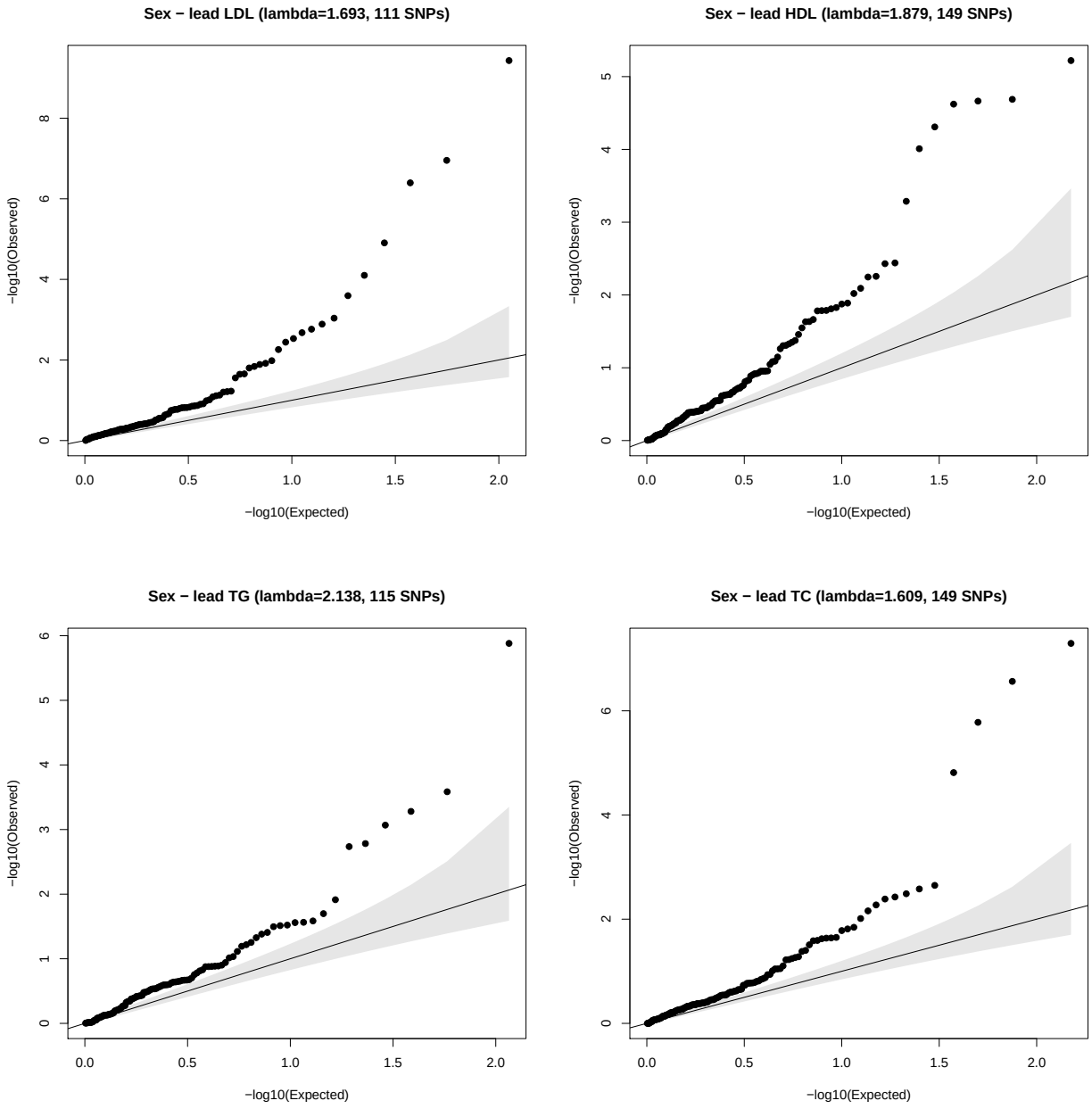
**Supplementary Figure 8:** Interaction of rs2519093 (*FUT2*) and rs601338 (*ABO*) in GERA (n=94,674). The rs601338 allele determines secretor status; Se/Se and Se/se are secretors (dominant) and se/se are nonsecretors. The vertical lines represents 95% confidence intervals. All tests two-sided via linear regression.



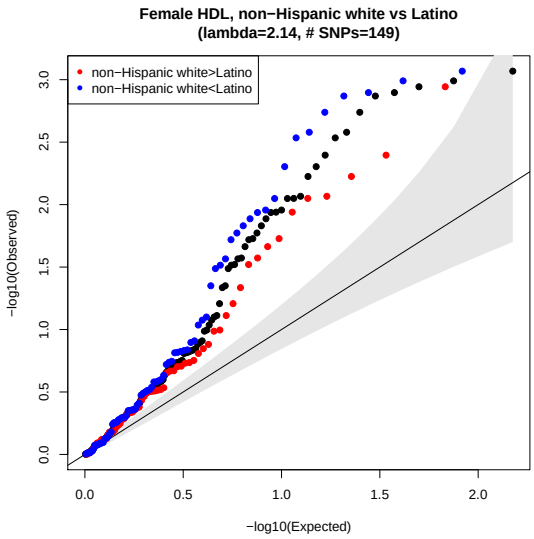
**Supplementary Figure 9:** Effect size estimates in RPGEH GERA (n=94,674) males (n=39,159) vs. females (n=55,515). All tests are two-sided via linear regression

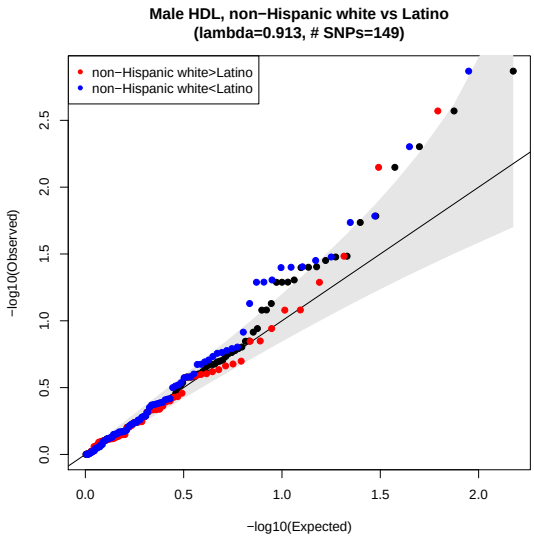


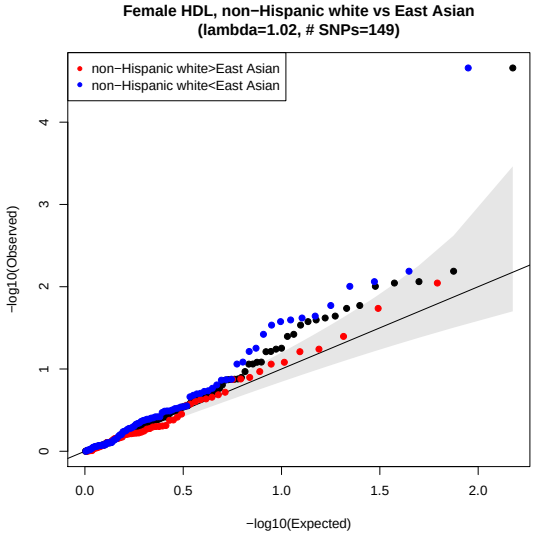
**Supplementary Figure 10:** Sex Q-Q plots in RPGEH GERA (n=94,674) of all previously-, GERA-, and GERA+GLGC-identified lead SNPs, comparing the effect sizes of females (n=55,515) to males (n=39,159). All tests are two-sided via linear regression.

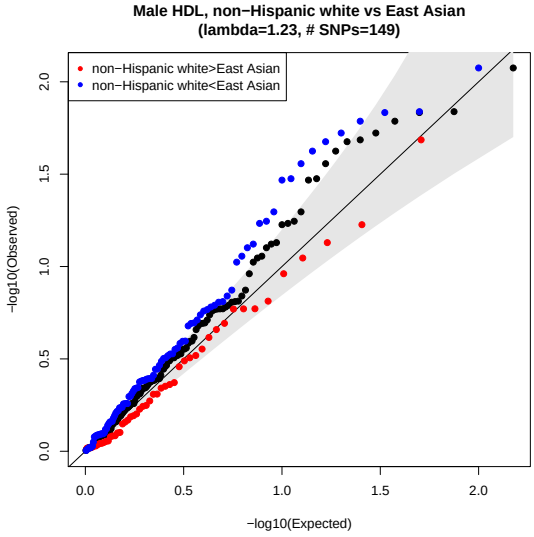


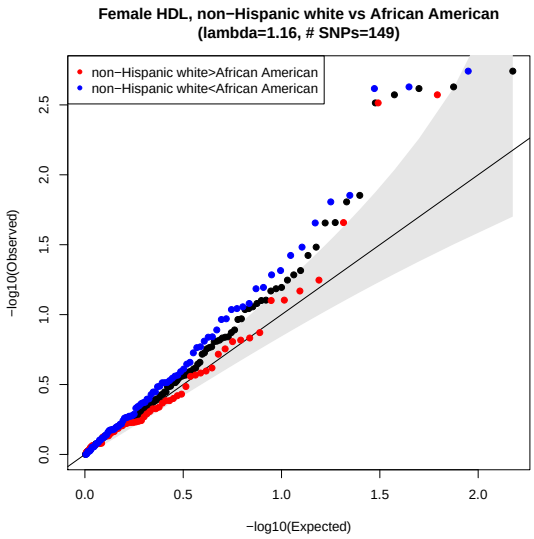

**Supplementary Figure 11:** Heterogeneity of GERA non-Hispanic whites (n=76,627) vs. other groups (Latinos, n=7,795; East Asians, n=6,855; African Americans, n=2,958; South Asians, n=439).

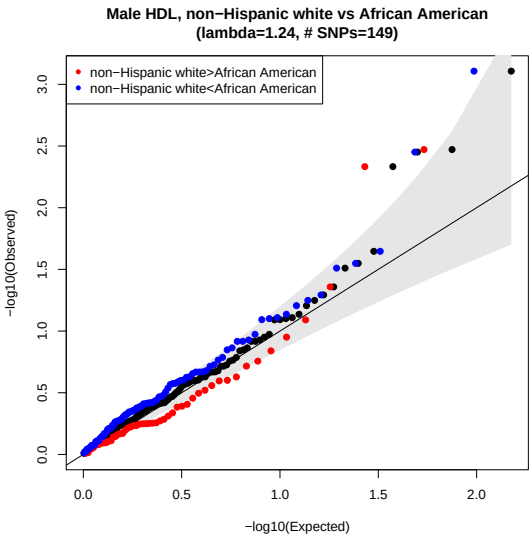

Female HDL, non−Hispanic white vs Latino
(lambda=2.14, # SNPs=149)
non−Hispanic white>Latino
non−Hispanic white<Latino
−log10(Observed)
−log10(Expected)

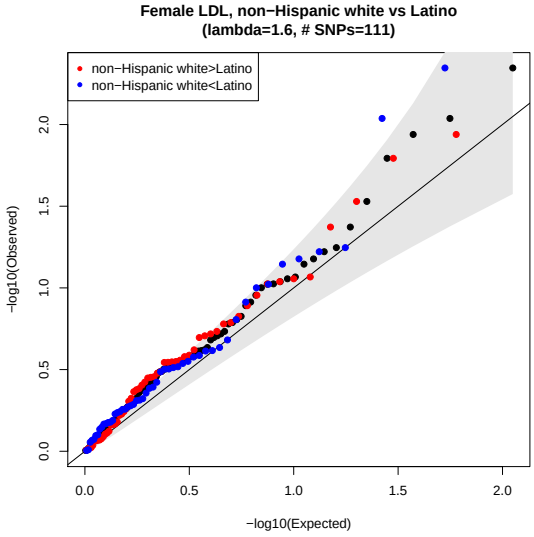

Male HDL, non−Hispanic white vs Latino
(lambda=0.913, # SNPs=149)
non−Hispanic white>Latino
non−Hispanic white<Latino
−log10(Observed)
−log10(Expected)

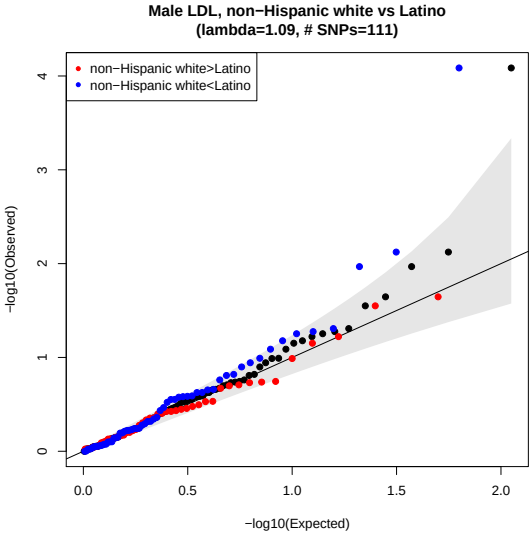

Female HDL, non−Hispanic white vs East Asian
(lambda=1.02, # SNPs=149)
non−Hispanic white>East Asian
non−Hispanic white<East Asian
−log10(Observed)
−log10(Expected)

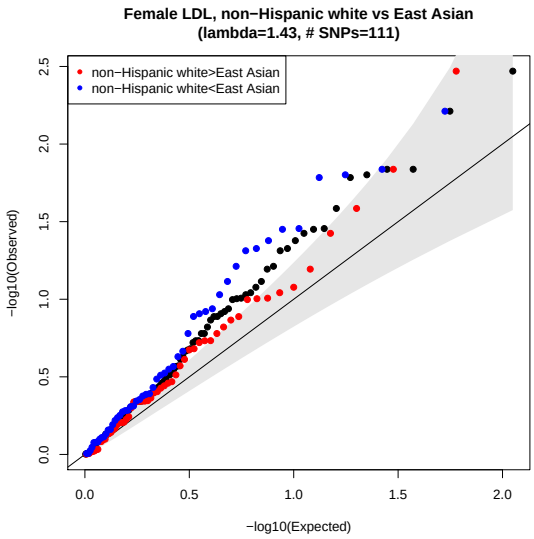

Male HDL, non−Hispanic white vs East Asian
(lambda=1.23, # SNPs=149)
non−Hispanic white>East Asian
non−Hispanic white<East Asian
−log10(Observed)
−log10(Expected)

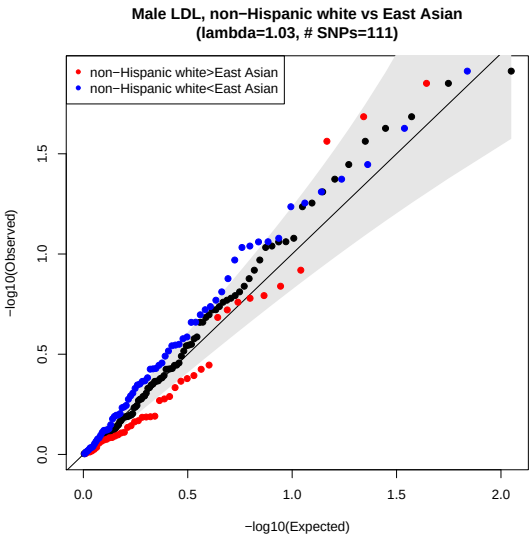

Female HDL, non−Hispanic white vs African American
(lambda=1.16, # SNPs=149)
non−Hispanic white>African American
non−Hispanic white<African American
−log10(Observed)
−log10(Expected)

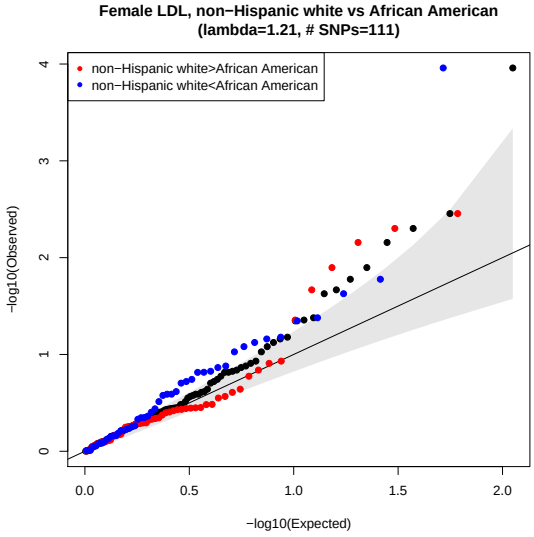

Male HDL, non−Hispanic white vs African American
(lambda=1.24, # SNPs=149)
non−Hispanic white>African American
non−Hispanic white<African American
−log10(Observed)
−log10(Expected)

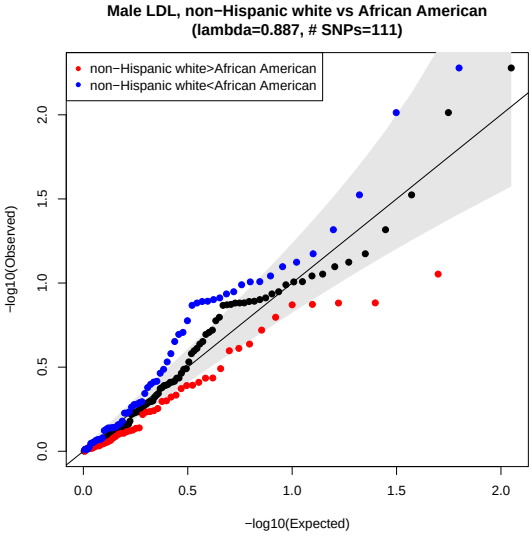

Female LDL, non−Hispanic white vs Latino
(lambda=1.6, # SNPs=111)
non−Hispanic white>Latino
non−Hispanic white<Latino
−log10(Observed)
−log10(Expected)

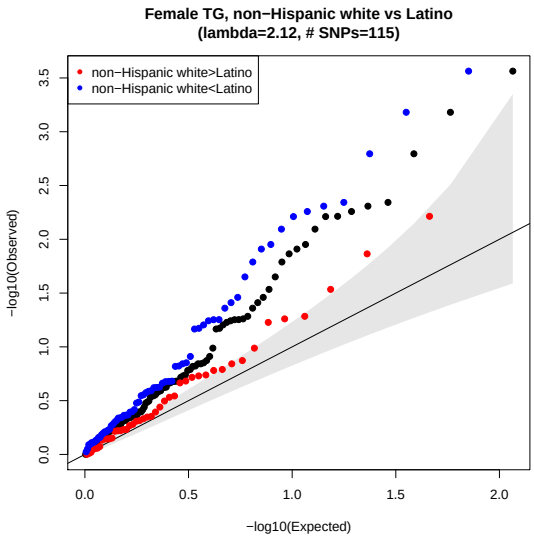

Male LDL, non−Hispanic white vs Latino
(lambda=1.09, # SNPs=111)
non−Hispanic white>Latino
non−Hispanic white<Latino
−log10(Observed)
−log10(Expected)

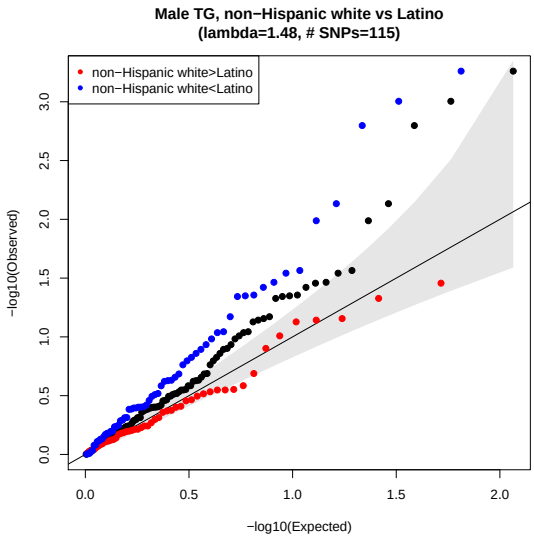

Female LDL, non−Hispanic white vs East Asian
(lambda=1.43, # SNPs=111)
non−Hispanic white>East Asian
non−Hispanic white<East Asian
−log10(Observed)
−log10(Expected)

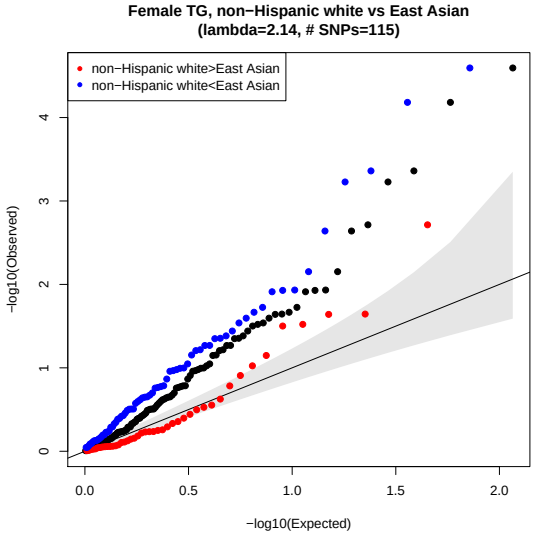

Male LDL, non−Hispanic white vs East Asian
(lambda=1.03, # SNPs=111)
non−Hispanic white>East Asian
non−Hispanic white<East Asian
−log10(Observed)
−log10(Expected)

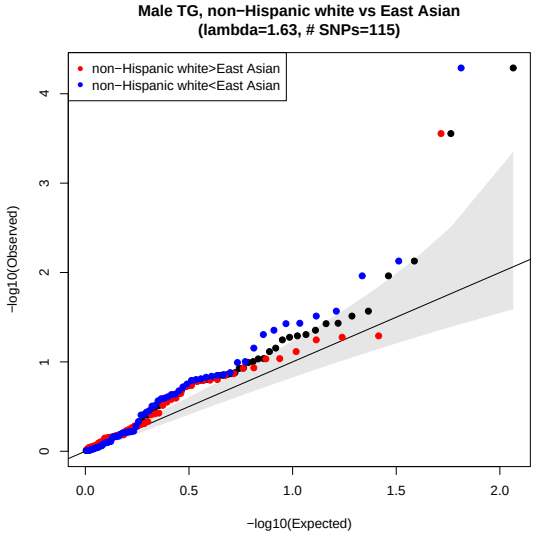

Female LDL, non−Hispanic white vs African American
(lambda=1.21, # SNPs=111)
non−Hispanic white>African American
non−Hispanic white<African American
−log10(Observed)
−log10(Expected)

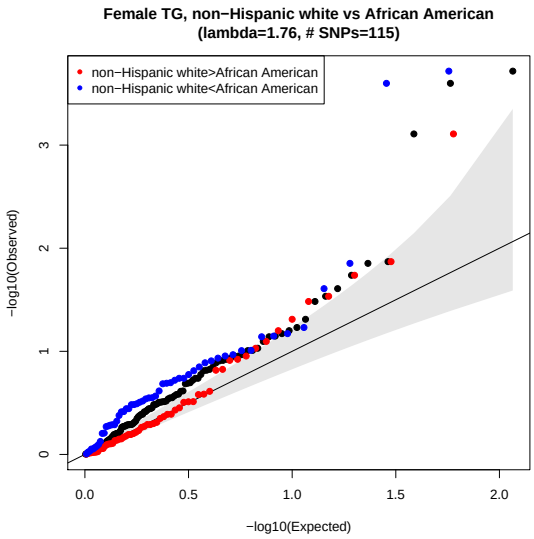

Male LDL, non−Hispanic white vs African American
(lambda=0.887, # SNPs=111)
non−Hispanic white>African American
non−Hispanic white<African American
−log10(Observed)
−log10(Expected)

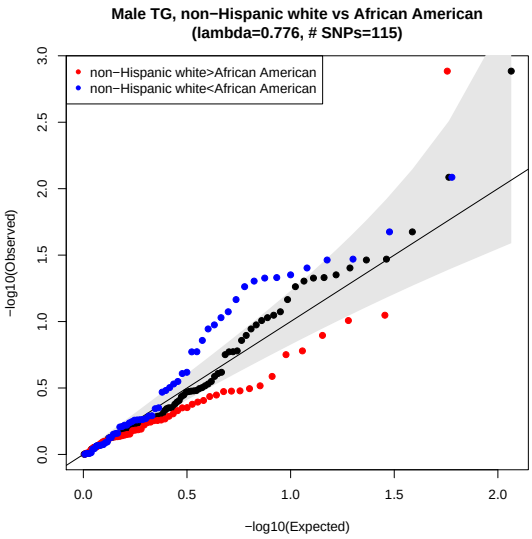

Female TG, non−Hispanic white vs Latino
(lambda=2.12, # SNPs=115)
non−Hispanic white>Latino
non−Hispanic white<Latino
−log10(Observed)
−log10(Expected)

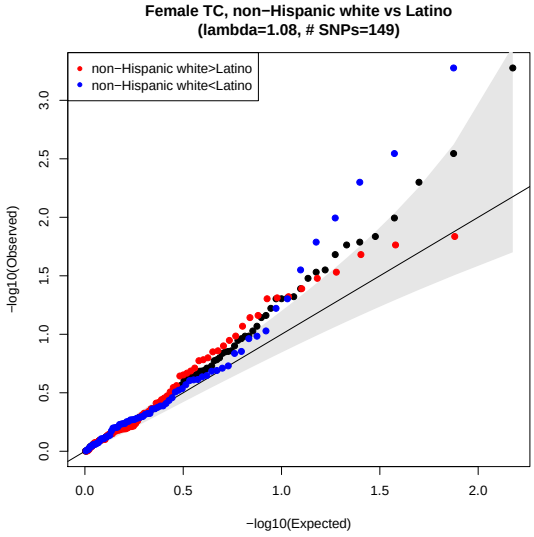

Male TG, non−Hispanic white vs Latino
(lambda=1.48, # SNPs=115)
non−Hispanic white>Latino
non−Hispanic white<Latino
−log10(Observed)
−log10(Expected)

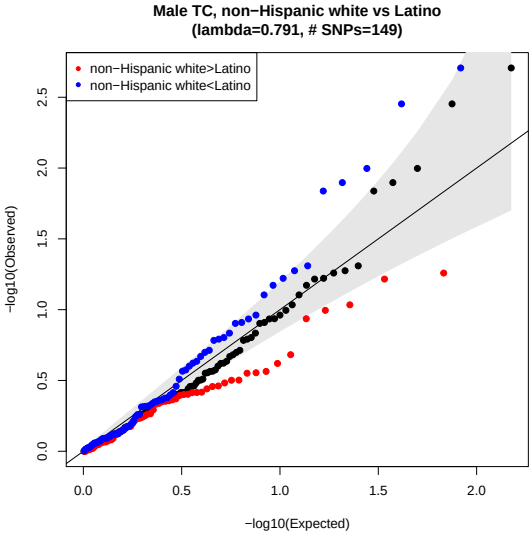

Female TG, non−Hispanic white vs East Asian
(lambda=2.14, # SNPs=115)
non−Hispanic white>East Asian
non−Hispanic white<East Asian
−log10(Observed)
−log10(Expected)

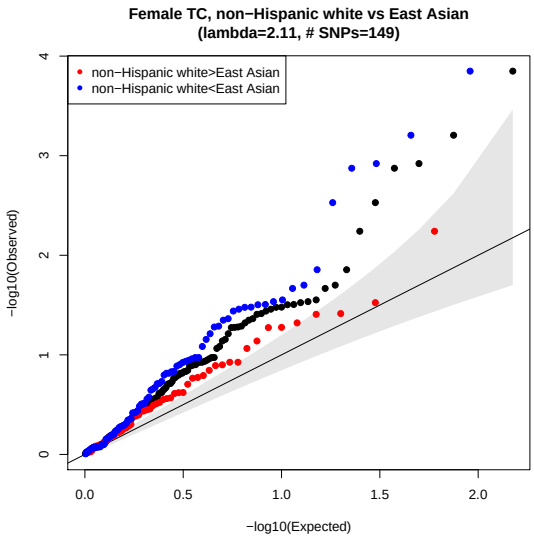

Male TG, non−Hispanic white vs East Asian
(lambda=1.63, # SNPs=115)
non−Hispanic white>East Asian
non−Hispanic white<East Asian
−log10(Observed)
−log10(Expected)

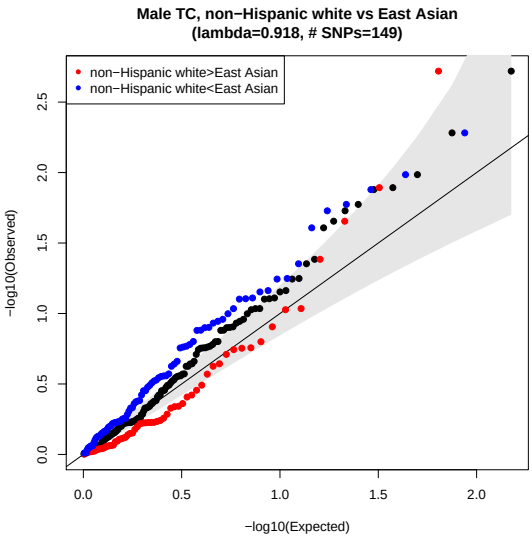

Female TG, non−Hispanic white vs African American
(lambda=1.76, # SNPs=115)
non−Hispanic white>African American
non−Hispanic white<African American
−log10(Observed)
−log10(Expected)

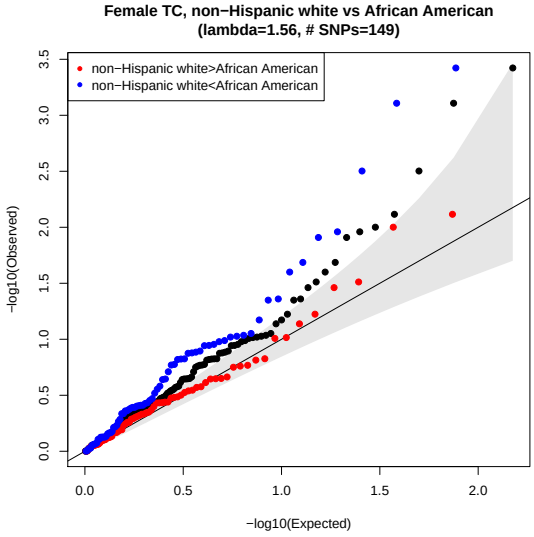

Male TG, non−Hispanic white vs African American
(lambda=0.776, # SNPs=115)
non−Hispanic white>African American
non−Hispanic white<African American
−log10(Observed)
−log10(Expected)

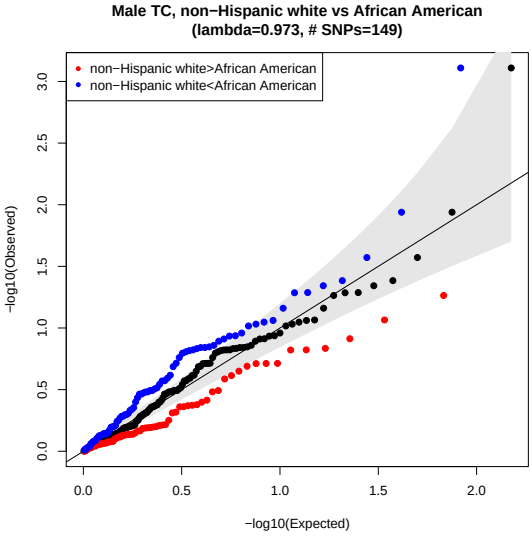

Female TC, non−Hispanic white vs Latino
(lambda=1.08, # SNPs=149)
non−Hispanic white>Latino
non−Hispanic white<Latino
−log10(Observed)
−log10(Expected)


Male TC, non−Hispanic white vs Latino
(lambda=0.791, # SNPs=149)
non−Hispanic white>Latino
non−Hispanic white<Latino
−log10(Observed)
−log10(Expected)

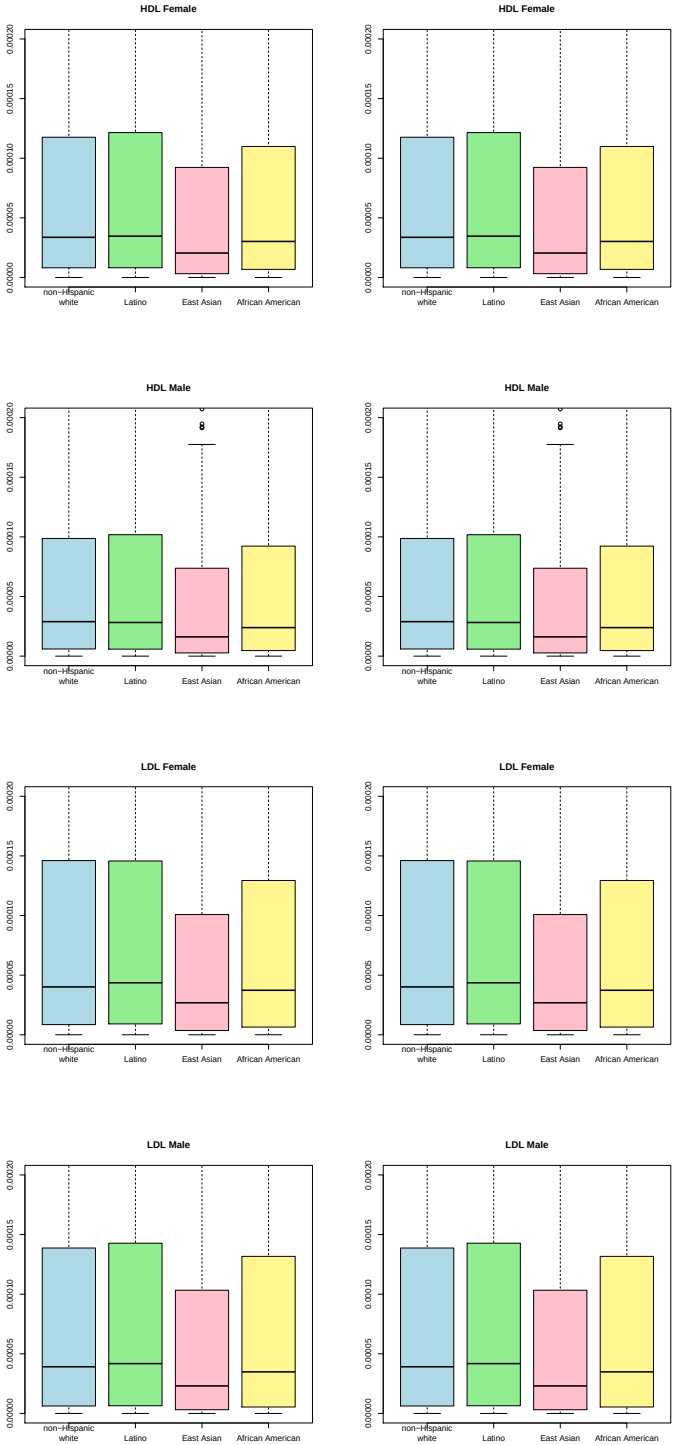

Female TC, non−Hispanic white vs East Asian
(lambda=2.11, # SNPs=149)
non−Hispanic white>East Asian
non−Hispanic white<East Asian
−log10(Observed)
−log10(Expected)


Male TC, non−Hispanic white vs East Asian
(lambda=0.918, # SNPs=149)
non−Hispanic white>East Asian
non−Hispanic white<East Asian
−log10(Observed)
−log10(Expected)

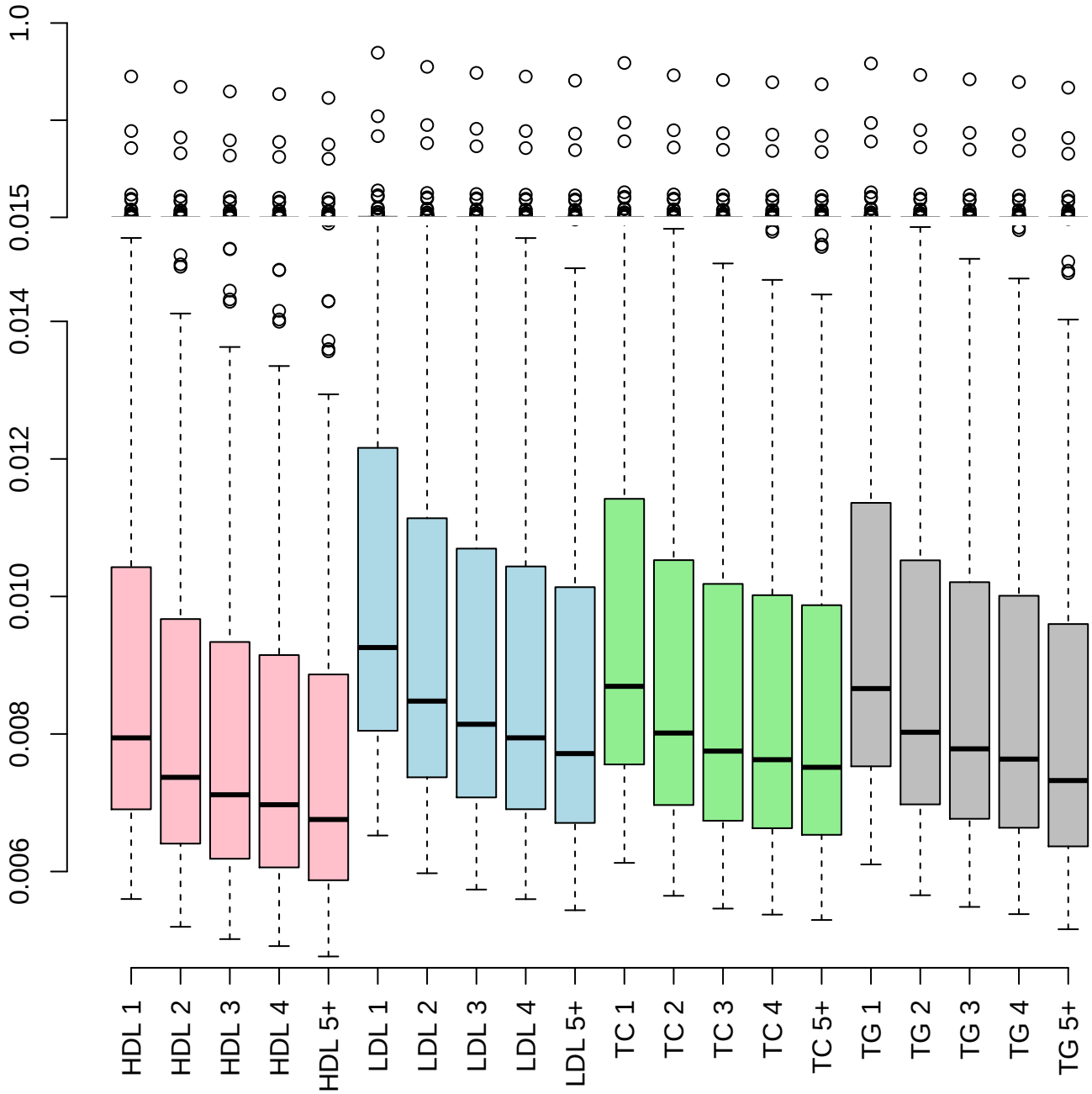

Female TC, non−Hispanic white vs African American
(lambda=1.56, # SNPs=149)
non−Hispanic white>African American
non−Hispanic white<African American
−log10(Observed)
−log10(Expected)


Male TC, non−Hispanic white vs African American
(lambda=0.973, # SNPs=149)
non−Hispanic white>African American
non−Hispanic white<African American
−log10(Observed)
−log10(Expected)

**Supplementary Figure 12:** Boxplots of $p(1-p)\beta^2$ minor allele frequency distributions in GERA (non-Hispanic whites, n=76,627; Latinos, 7,795; East Asians, n=6,855; African Americans, n=2,958; South Asians, n=439). In the boxplot, each box represents the interquartile range, split by the median, with the whiskers extending to the upper and lower extremes, excluding outliers. The y-axis range was in order to view the interquartile range better.



**Supplementary Figure 13:** Benefit of repeated measures on SNP SEs. Boxplots of the previously-identified SNPs SEs using increasing numbers of measurements per individual (for a fixed sample size; only individuals with five or move measurements were included; n=34,936 non-Hispanic whites). The x-axis indicates the number of measurements for each of the three phenotypes. In the boxplot, each box represents the interquartile range, split by the median, with the whiskers extending to the upper and lower extremes, excluding outliers.



**Supplementary Figure 14:** Lipidemia treatment time-to-onset Kaplan Meier curves by LDL quintiles (lower, middle, and upper only for clarity) and TG GRS upper/lower halves. (A) Latino females (n=4,708), (B) Latino males (n=3,087), (C) East Asian females (n=4,013), (D) East Asian males (n=2,842), (E) African American females (n=1,761), (F) African American males (n=1,197). The shaded areas represent the 95% confidence intervals around the estimated curves. All tests are two-sided.