

Lipid-related Genetic Variants and Lipid Outcomes in a Cohort of Chilean Children

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Introduction

- Lipid concentrations:
- Are a recognized heritable risk factor for cardiovascular disease (CVD)
 - Associate with >150 loci in adults
 - Vary across ancestral groups
 - Include high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C) and triglycerides (TG).
- Genetic architecture underlying lipid traits is similar across ancestral groups for adults.
 - Unclear if lipid-related loci associations found in adults extend to younger age groups.
 - One European study establishes continuity of associations across the age spectrum, but no evidence exists in Hispanic/Latino (HL) populations.

Aims

- Aim 1** Estimate association between lipid risk variants first identified in adults and adolescent lipid traits from Santiago Longitudinal Cohort Study (SLCS), a Chilean infancy cohort.
- Aim 2** Compare results between SLCS and Cardiovascular Risk in Young Finns Study Cohort.

Sample

- 1,645 infants began SLCS between 1991-1996
- Current sample recruited from 2 of 3 randomized control trial groups (n=888)
- n=677 with infancy and adolescent data and of those n=546 with genotyped data (platform: Multi-Ethnic Global Array (MEGA))
- Low to middle income status in Chile.
- Ancestrally mixed American Indian and Spanish descent families
- Lipid traits measured after overnight fasting at mean age 17 years.



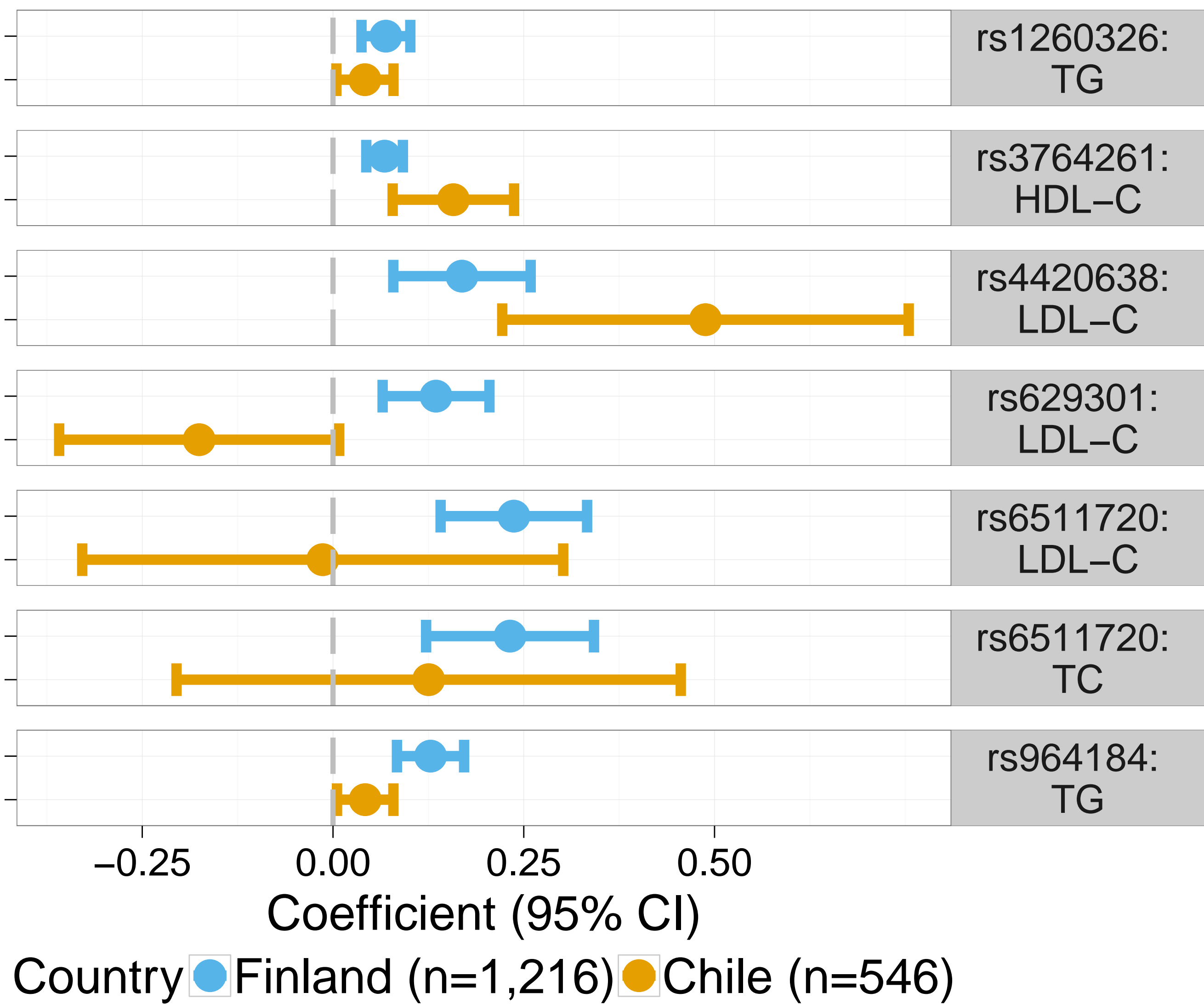
Methods

1. Test additive association between lipid traits and adequately powered single risk variants.
 - 76 common lipid variants selected from a European genome-wide meta-analysis with strongest independent signal.
 - Association tests include 6 single variants with *a priori* power > 0.80.
2. Assess the association of weighted genetic risk scores (wGRS) on lipid traits using linear regression model.
 - Coefficients for wGRS and power calculations based on European adult association studies.
3. Characterize proportion of variance explained by lipid variants.

Results

| Table. Sample descriptive statistics | | | | |
|--------------------------------------|----------------|----------------|----------------|----------------|
| Measure | Chile | | Finland | |
| | n=263 | n=283 | n=661 | n=555 |
| log(TG (mmol/l)) | 1.44 (0.53) | 1.38 (0.6) | 0.900 (0.37) | 0.911 (0.39) |
| LDL-C (mmol/l) | 5.26 (1.55) | 5.02 (1.53) | 3.07 (0.79) | 2.91 (0.79) |
| HDL-C (mmol/l) | 2.3 (0.77) | 2.05 (0.66) | 1.55 (0.29) | 1.34 (0.24) |
| TC (mmol/l) | 8.55 (1.79) | 7.96 (1.65) | 5.02 (0.89) | 4.67 (0.84) |
| Age (years) | 16.77 (0.3) | 16.76 (0.31) | 18 | 18 |
| BMI (kg/m2) | 23.25 (5.33) | 22.31 (5.12) | — | — |
| HDL wGRS | 33.13 (3.47) | 33.20 (3.42) | 32.46 (3.36) | 32.62 (3.41) |
| LDL wGRS | 39.96 (6.38) | 39.81 (6.40) | 42.1 (6.60) | 41.9 (6.90) |
| TG wGRS | 138.84 (17.33) | 138.32 (17.40) | 132.71 (16.81) | 131.91 (15.72) |

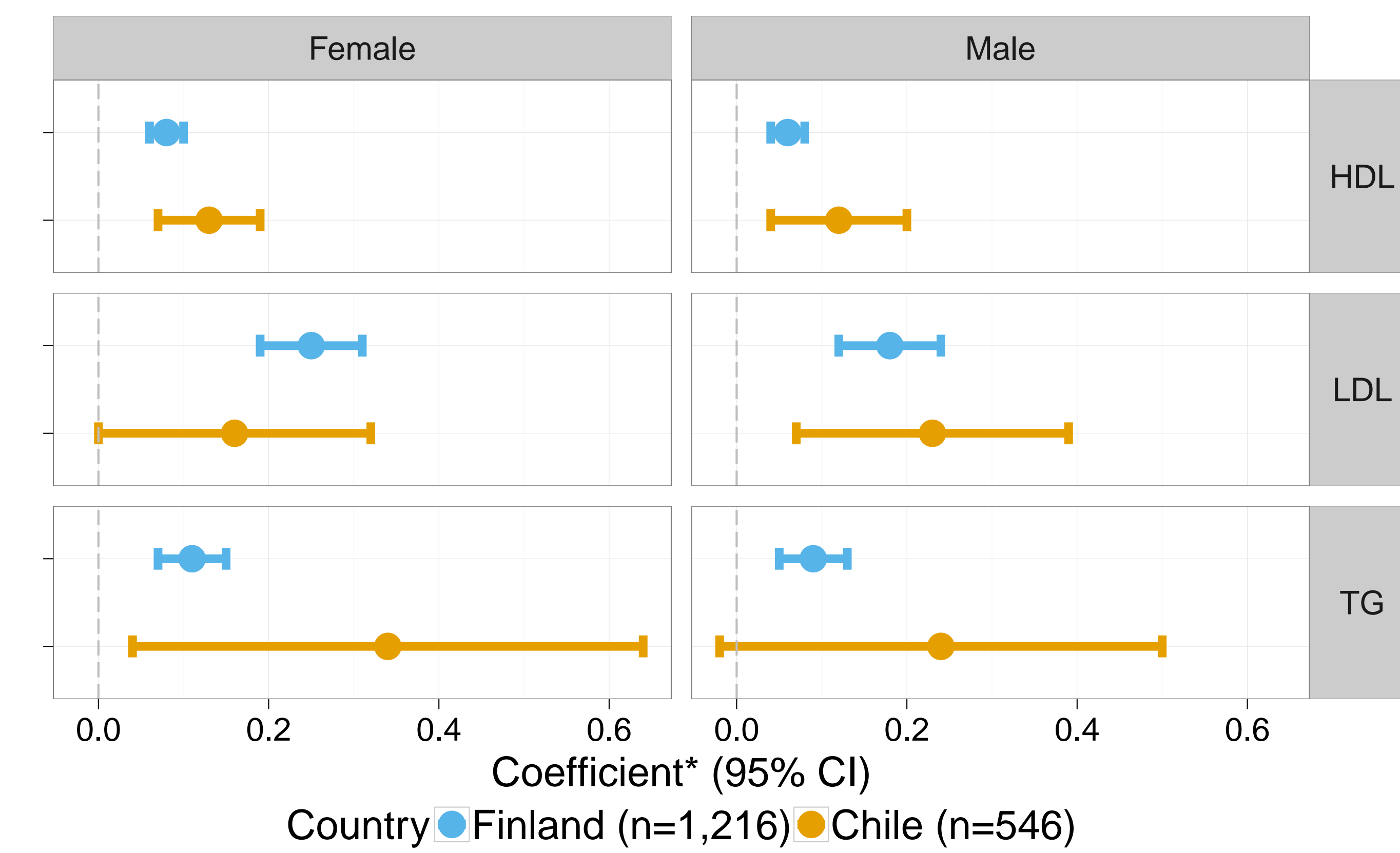
Figure 1. Association tests by variant and sample



- Four of the seven association tests were nominally statistically significant.

Results, cont...

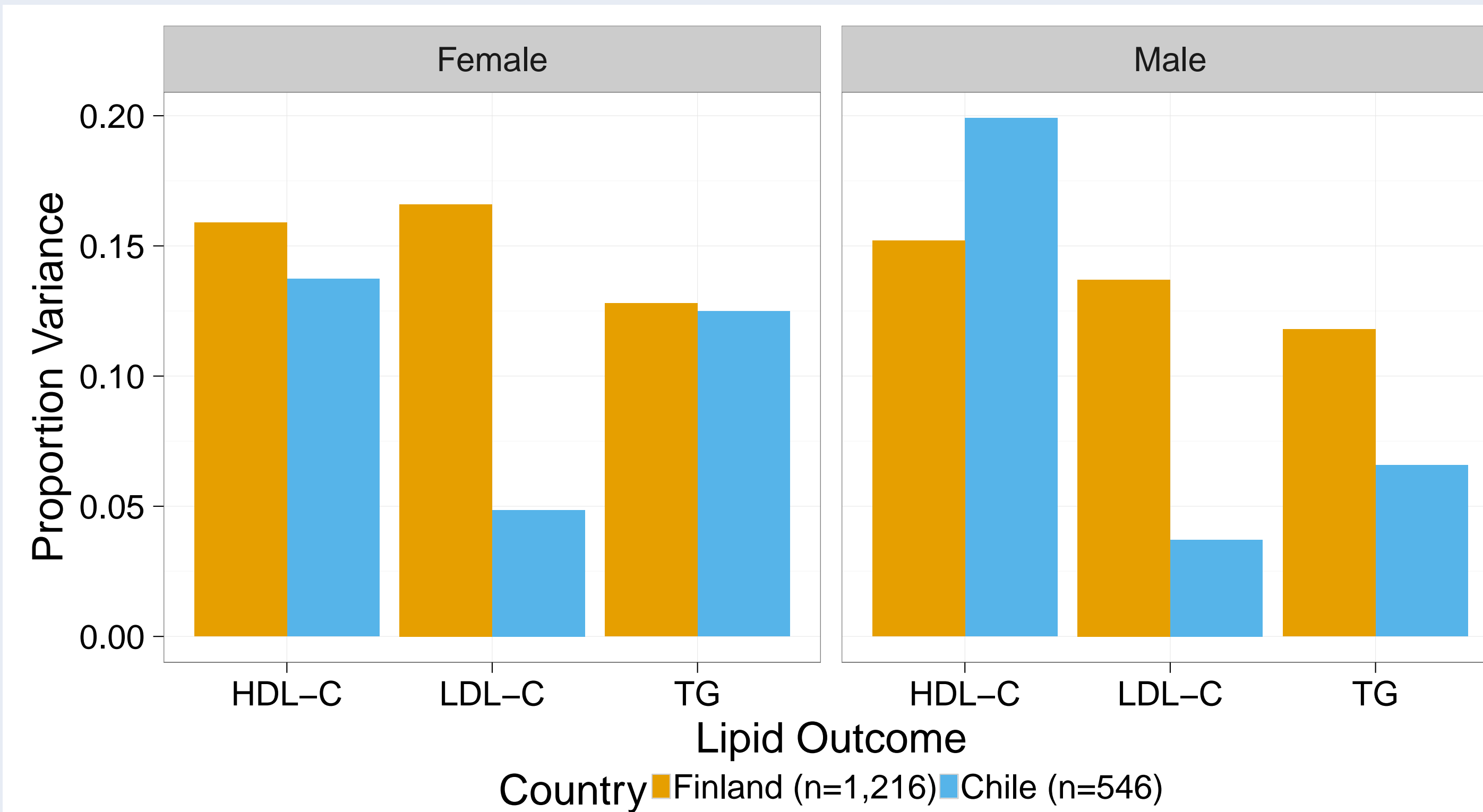
Figure 2. wGRS regression coefficients by sample and sex



*Coefficients represent change in outcome per 1 SD change in wGRS, adjusted for first five principal components representing ancestry.

- wGRS has stronger association for each lipid outcome in Chilean versus Finnish sample except LDL-C for females.

Figure 3. Proportion of variance explained by genetic variants, by sex



- LDL-C-related variants explain much less variance in Chilean sample.

Summary

- Significant associations support concordance of effects across European and HL populations first found in adults for these loci.
- Genetic risk evident in childhood presents across different populations, emphasizing younger ages as a point for intervention.

