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

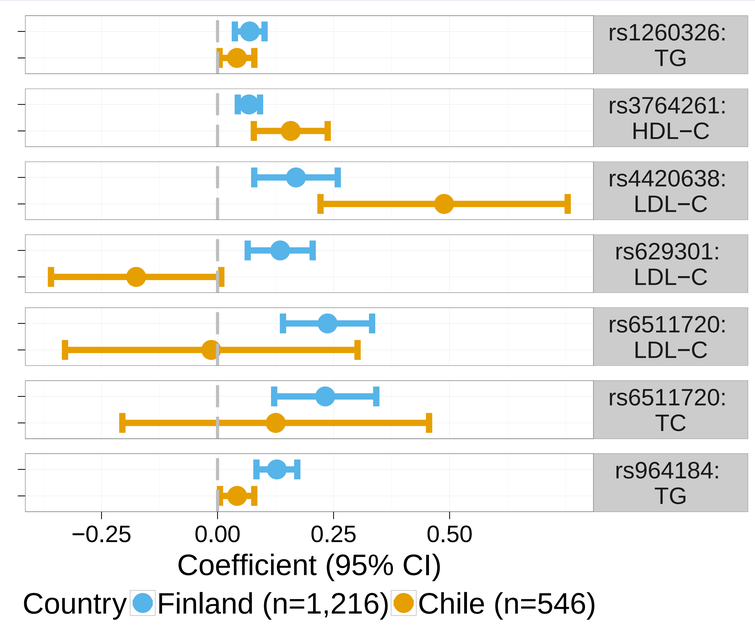
1. Test additive association between lipid traits and adequately powered single risk variants.
   - 76 common lipid variants selected from a European genome-wide meta-analysis with strongest independent signal.
   - Association tests include 6 single variants with *a priori* power > 0.80.
2. Assess the 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

	Chile		Finland	
Measure	**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)

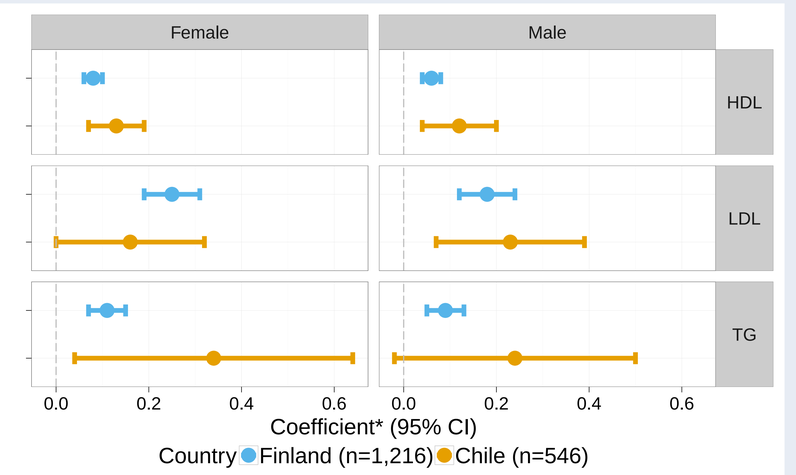
Figure 1. Association tests by variant and sample



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

Results, cont...

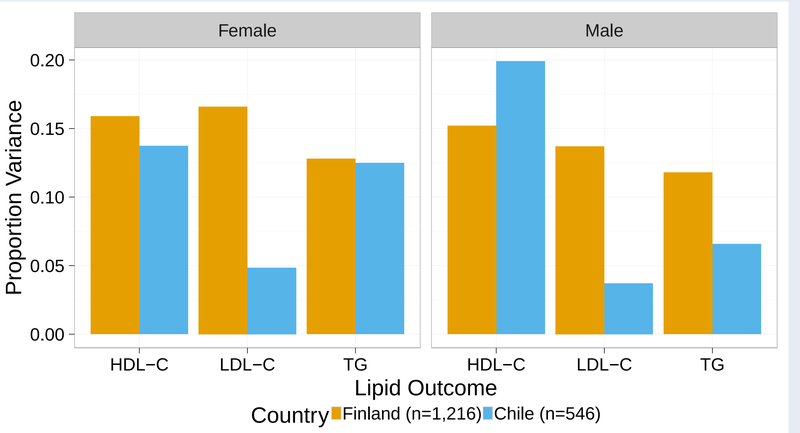
Figure 2. wGRS regression coefficients by sample and sex



*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.

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