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

Ann Von Holle, Anne Justice, Misa Graff, Kari North, UNC, Chapel Hill, NC; Estela Blanco, Sheila Gahagan, UCSD, San Diego, CA; Bárbara Angel, Unidad de Nutrición Pública INTA, Univ de Chile, Santiago, Chile; José Luis Santos, Pontificia Univ Católica de Chile, Santiago, Chile

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.
- Sparse research in younger age groups motivates further investigation.

Aims

1. To estimate association between:
   - Lipid risk variants first identified in adults and adolescent traits.
   - Lipid traits of adolescents from a Chilean infancy cohort.
2. Compare results across Chilean and Finnish cohorts.

Sample

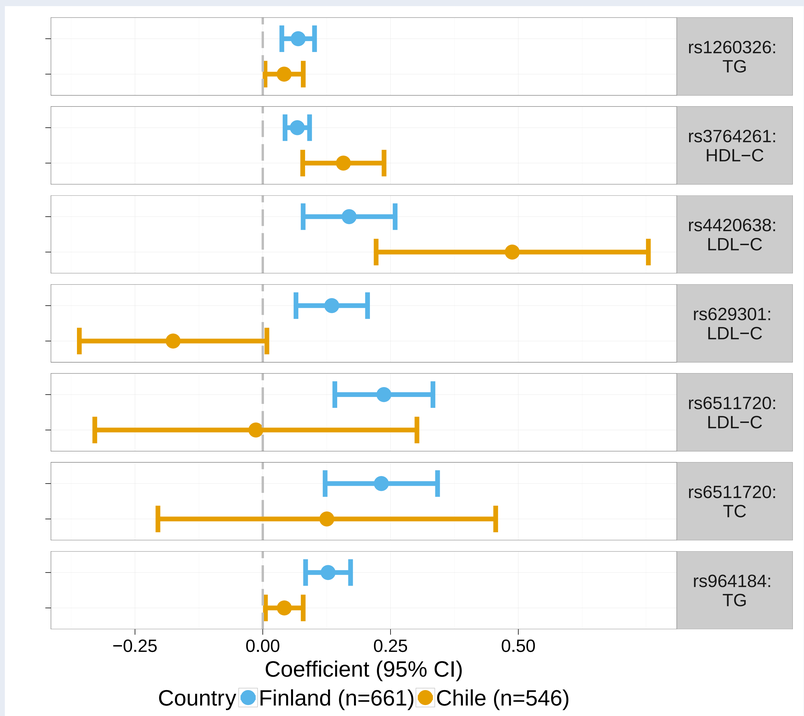
- Santiago Longitudinal Cohort Study (n=1645), 1991-1996
- Current sample recruited from n=888, which were 2/3 RCT groups
- n=677 with infancy and adolescent data (average age = 17 years) and of those n=546 with genotyped data in analyses that follow
- Low to middle income
- Ethnically mixed American Indian and Spanish descent families
- Lipid traits measured after overnight fasting

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 **single variants** with *a priori* power > 0.80.
2. Assess the association of weighted polygenic risk scores (wPRS) on lipid traits using additive linear regression model.
   - **Coefficients** for wPRS and power calculations based on European adult association studies (4).
3. Characterize proportion of variance explained by lipid variants.

Results

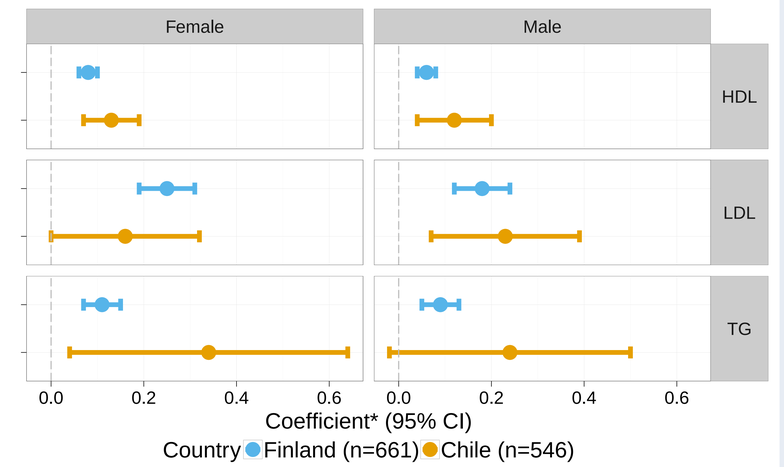
Figure 1. Candidate single variant tests of association by variant and sample



- Majority of single variants tested in Chilean sample have concordant direction of associations.
  - Two LDL-C variants in opposite direction.

Results, cont...

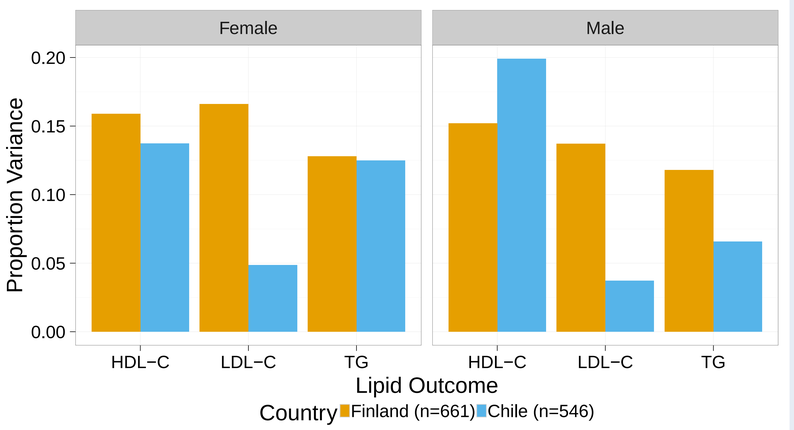
Figure 2. wPRS regression coefficients by sample and sex



*Coefficients represent change in outcome per 1 SD change in wPRS, adjusted for first five principal components representing ancestry but NOT BMI.

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

Figure 3. Proportion of lipid traits variance explained by lipid-related variants, by sex



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

Summary

- This study provides evidence that genetic architecture underlying lipid traits in a Chilean cohort is similar to that previously found in a Finnish cohort.
  - LDL-C traits are an exception.

vonholle@unc.edu