Infant growth trajectories and high density lipoprotein cholesterol levels in adolescence.

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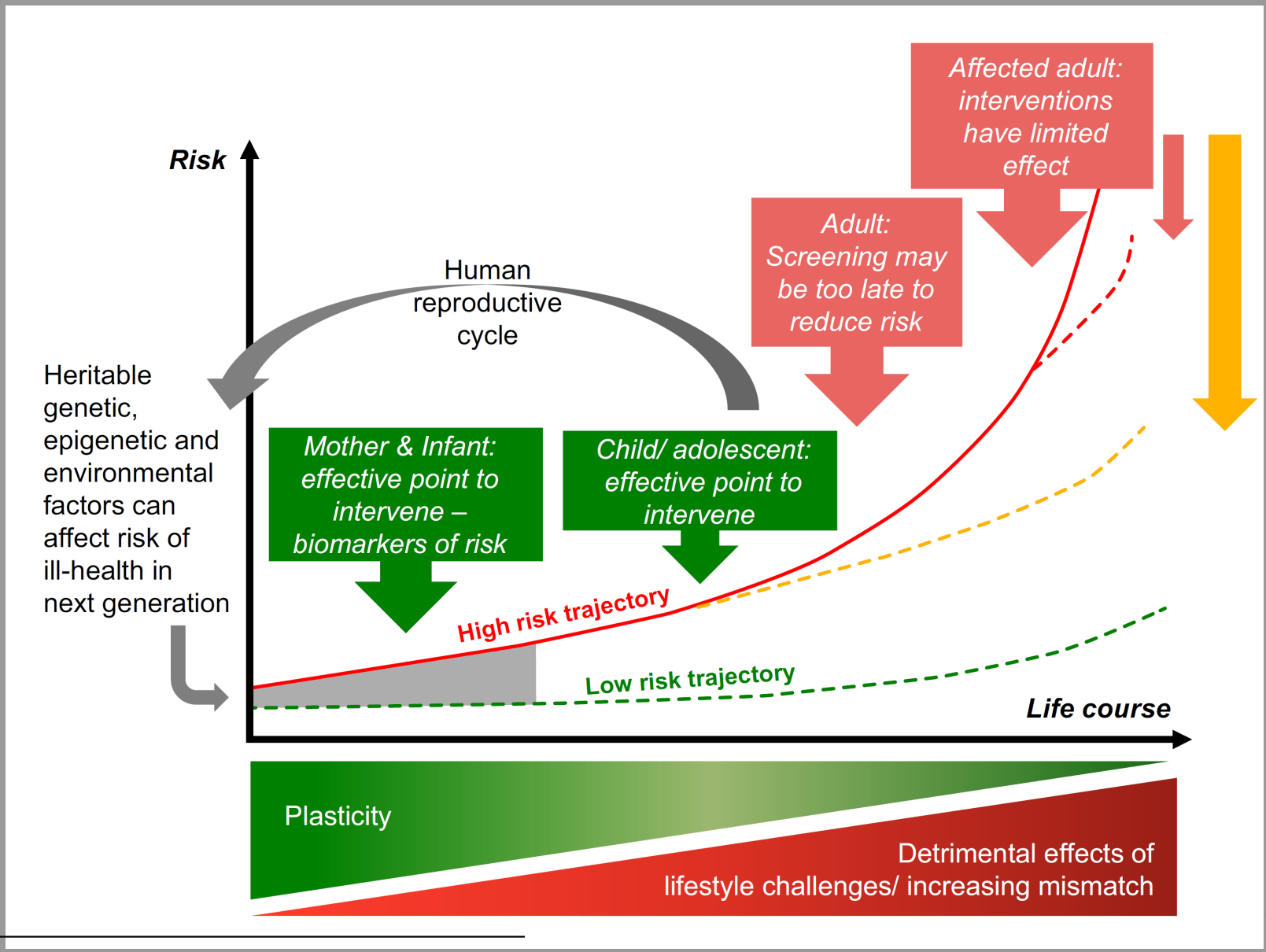
Cardiovascular disease (CVD) and high density lipoprotein cholesterol (HDL-C)

- Cardiovascular disease (CVD) is a chronic disease responsible for one out of every three deaths in the United States.
- Primary and modifiable risk factors including blood pressure, smoking, physical inactivity, obesity, and blood cholesterol.
- High density lipoprotein cholesterol (HDL-C) is one of the blood cholesterols.
  - A strong risk factor for CVD.
  - Function in the development of CVD remains unknown.
  - Investigation remains active to determine both HDL function in atherosclerosis and potential areas for intervention such as pharmacotherapy.

Developmental Origins of Health and Disease



[1]

[1] M. A. Hanson and P. D. Gluckman. "Early Developmental Conditioning of Later Health and Disease: Physiology or Pathophysiology?" In: *Physiological Reviews* 94.4 (Oct. 1, 2014), pp. 1027–1076. DOI: 10.1152/physrev.00029.2013.

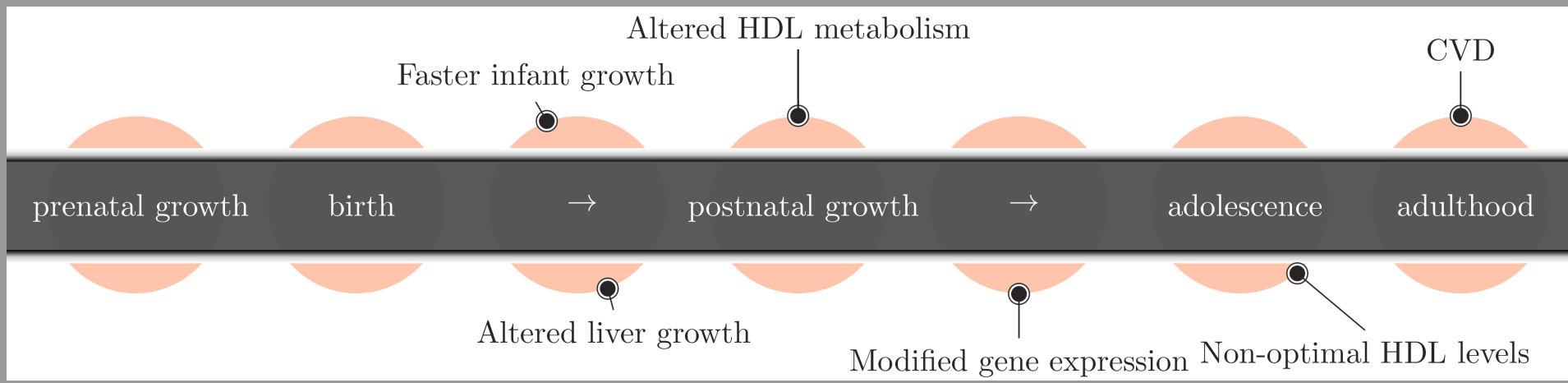
Postnatal growth and HDL-C

- Repeated animal and human studies have shown that postnatal growth is associated with the later development of adverse cardiovascular risk factors like low HDL-C levels.

	Author	Year published	Direction of growth with increase in HDL-C	2+ observations in change measure	Non-European sample?
1	Corvalan	2009	+		✔
2	Ekelund	2007	+		
3	Howe	2010	–		
4	Kajantie	2008	+		
5	Leunissen	2009	–		
6	Oostvogels	2014	–		
7	Tzoulaki	2010	+	✔	

Postnatal growth as an environmental cue

- Abnormal postnatal growth hypothesized to alter liver growth and subsequent HDL metabolism[2].



[2] E. Kajantie et al. "Growth before 2 years of age and serum lipids 60 years later: The Helsinki Birth Cohort Study". In: *International Journal of Epidemiology* 37.2 (Apr. 1, 2008), pp. 280–289. DOI: 10.1093/ije/dyn012; M.-M. Perl and J. G. Eriksson. "Early growth and postprandial glucose, insulin, lipid and inflammatory responses in adulthood:" in: *Current Opinion in Lipidology* 23.4 (Aug. 2012), pp. 327–333. DOI: 10.1097/MOL.0b013e3283541da6.

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Aims

Overall:

- Investigate the association between postnatal growth trajectories and HDL-C levels in adolescence
  - Contemporary Chilean birth cohort with monthly measures of weight in the first year of life
  - High quality clinical measures of cardiovascular disease risk factors.

Note: Unless otherwise indicated, postnatal growth trajectories are in terms of a weight-for-length outcome.

Aim 1

What do growth trajectories look like for infants from 0 to 12 months and what are some significant predictors?

Aim 1 Characterize individual growth trajectories in the first year of life and replicate predictors of growth using external validation with an independent sample.

- We expect to replicate previous findings[3] indicating a positive association between:
  1. Maternal characteristics such as pre-pregnancy BMI, height and age with trajectory size.
  2. Maternal education and trajectory velocity.

[3] C. Pizzi et al. "Prenatal Influences on Size, Velocity and Tempo of Infant Growth: Findings from Three Contemporary Cohorts". In: *PLoS ONE* 9.2 (Feb. 27, 2014). Ed. by G. Wang, e90291. DOI: 10.1371/journal.pone.0090291.

Aim 2

Are there any specific types of postnatal growth trajectories associated with adverse levels of HDL-C?

Aim 2 Examine the association between postnatal growth trajectories and HDL-C levels.

- Based on prior evidence we expect
  1. Infants with steeper growth trajectories to associate with adverse HDL-C levels in adolescence.
  2. Males will show a stronger association between size, tempo and velocity measures than females.

Aim 3

Do growth trajectories modify the association between genetic variants related to HDL metabolism and HDL-C levels in adolescence?

Aim 3 Assess gene-environment interaction between growth trajectory characteristics and genetic variants of HDL metabolism with HDL-C at 17 years of age as an outcome.

- We expect that
  1. The selected genetic variants will associate with HDL-C levels in adolescence.
  2. A gene-environment interaction exists in which extreme and less favorable growth characteristics will exhibit stronger, deleterious associations between the genetic variants and HDL-C levels.

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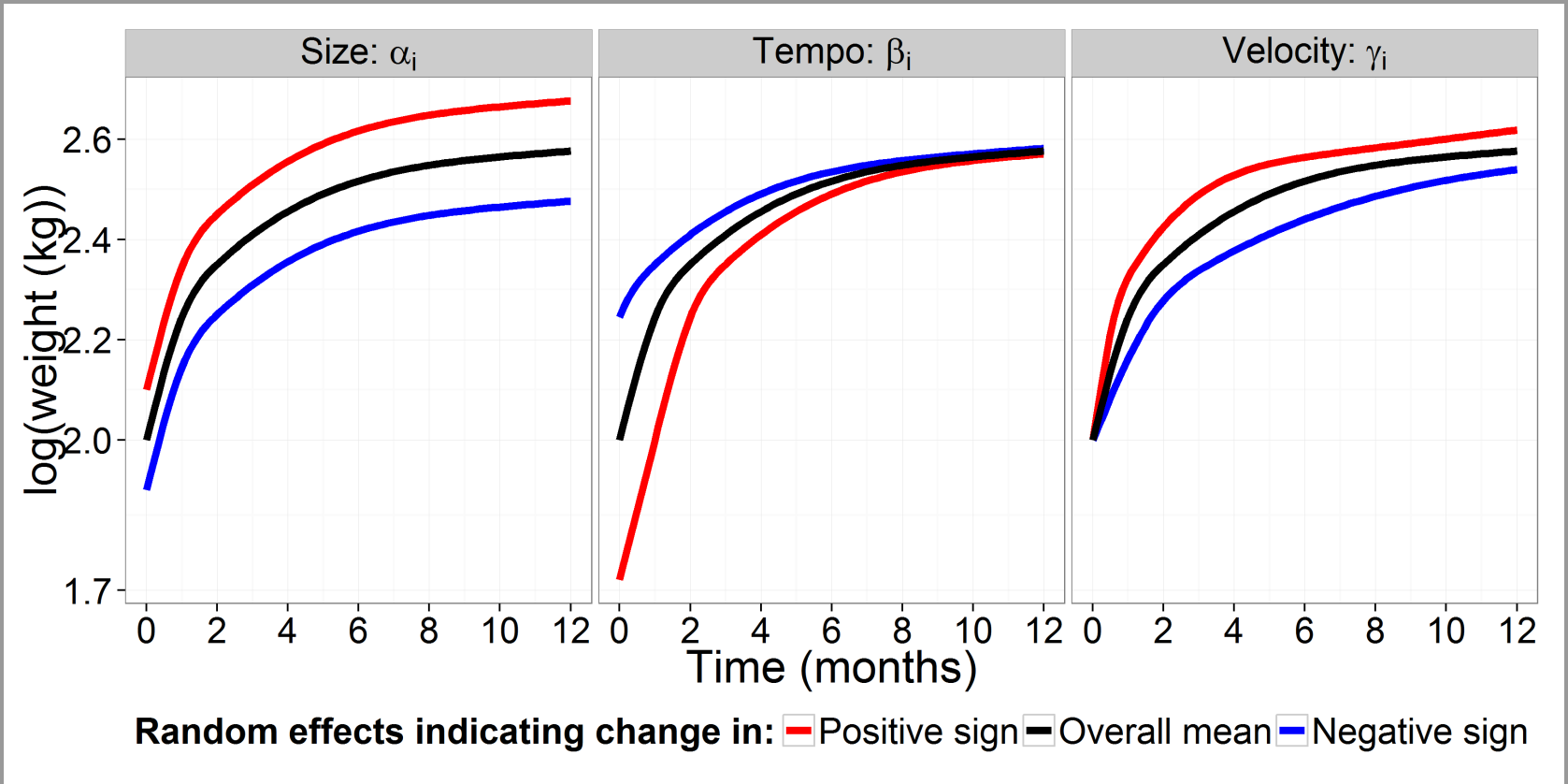
SITAR method

SITAR: SuperImposition by Translation And Rotation[4].

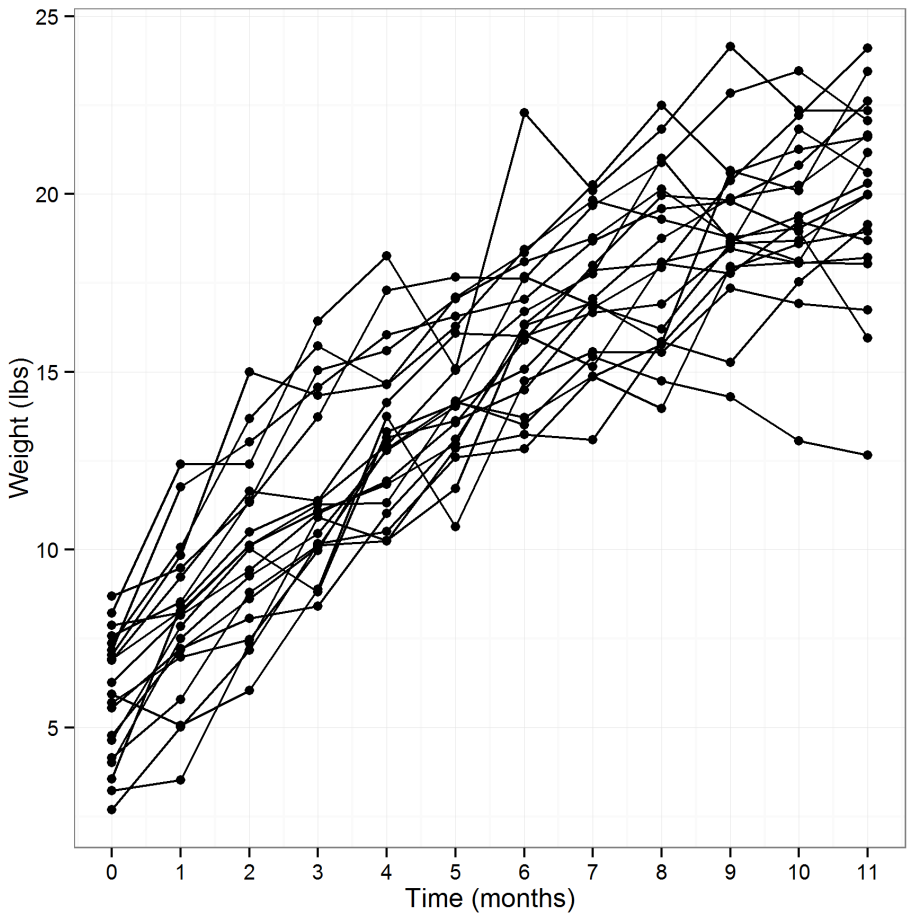
Use SITAR to measure three measures of postnatal growth: size, tempo and velocity.

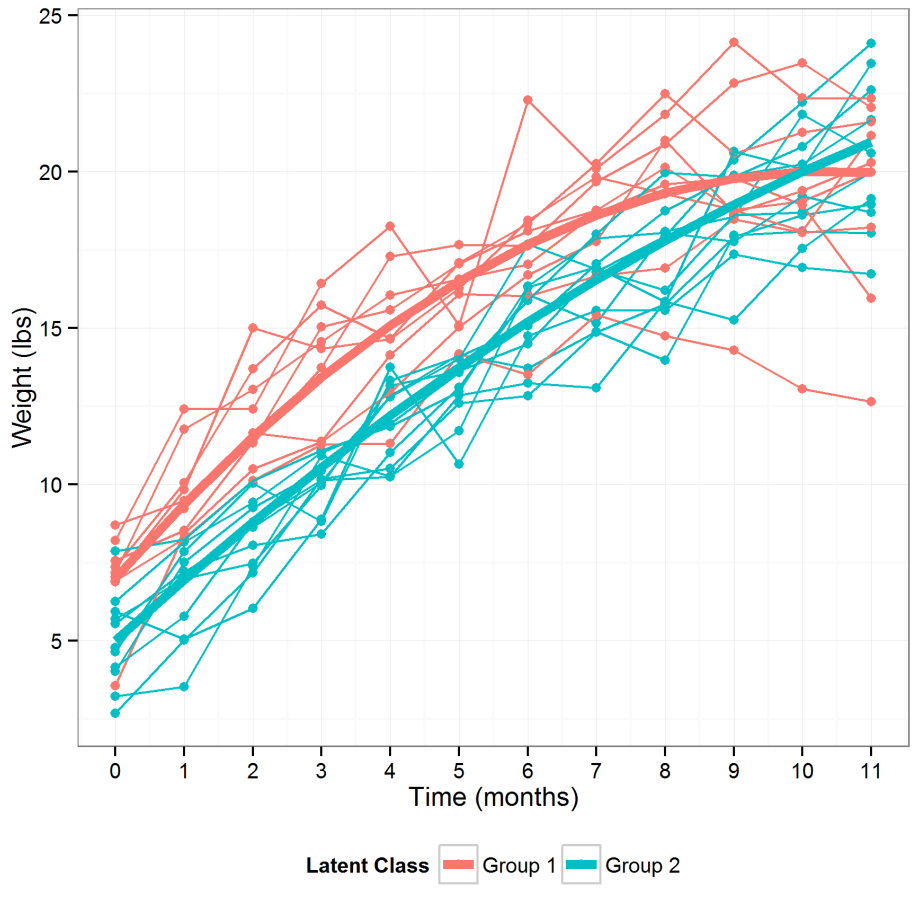


[4] K. J. Beath. "Infant growth modelling using a shape invariant model with random effects". In: *Statistics in Medicine* 26.12 (May 30, 2007), pp. 2547–2564. DOI: 10.1002/sim.2718; T. J. Cole et al. "SITAR–a useful instrument for growth curve analysis". In: *International Journal of Epidemiology* 39.6 (July 20, 2010), pp. 1558–1566. DOI: 10.1093/ije/dyq115.

Latent growth mixture models (LGMM)

Use LGMM to identify underlying patterns in infant growth and regress HDL-C levels on these latent groups.





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Strengths:

Underepresented sample The majority of studies on this topic to date involve European populations.

Detail This project uses methods unavailable to most prior studies due to limited number of postnatal growth observations.

Limitations:

Outcome a proxy Many factors contribute to postnatal growth trajectories. Infants with similar trajectories could experience different prior exposures and different risk later in life[5].

Washout Cumulative exposures to adverse life circumstances over the life course wash out any effect present in infancy[6].

[5] M. A. Hanson and P. D. Gluckman. "Early Developmental Conditioning of Later Health and Disease: Physiology or Pathophysiology?" In: *Physiological Reviews* 94.4 (Oct. 1, 2014), pp. 1027–1076. DOI: 10.1152/physrev.00029.2013.

[6] M. H. Valente et al. "Relation between Birth Weight, Growth, and Subclinical Atherosclerosis in Adulthood". In: *BioMed Research International* 2015 (2015), pp. 1–10. DOI: 10.1155/2015/926912.

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Results from this research can:

- Inform efforts to identify predictors of HDL-C and its accompanying risk of CVD
- Support of postnatal growth as an environmental cue inducing permanent change of HDL metabolism.

Further attention would be warranted to investigate the composition of optimal postnatal growth. These interventions would have the potential for modification of CVD later in life.

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