

Childhood Risk Factors and Cardiovascular Disease Outcomes in Adulthood. Preliminary Findings from The International Childhood Cardiovascular Cohort (i3C) Consortium.

Terry Dwyer , David Jacobs, Jessica G. Woo, Elaine M. Urbina, Lydia Bazzano, Markus Juonala, Jorma Viikari, Wei Chen, Ronald Prineas, Julia Steinberger, Stephen Daniels, Alan Sinaiko, Alison Venn, Trudy L. Burns, Tian Hu, Olli T. Raitakari

Background: Atherosclerosis develops decades before clinical cardiovascular disease (cCVD) occurs. Longitudinally, childhood risk factors predict adult pre-clinical atherosclerosis. There is currently no evidence directly linking childhood risk factors to cCVD.

Purpose: To provide the first direct evidence of any association between known risk factors for CVD when measured in childhood and adult CVD incidence and death.

Methods: Using i3C Consortium data, we linked childhood risk factors to adult cCVD. cCVD events were ascertained by participant re-contact in the US and Australia, medically adjudicated hospital records; and using the Finnish national health registry. Of 16,964 adult participants (mean age 49 years) examined during ages 3-19, 201 people with any cCVD event (70% coronary artery, 25% cerebrovascular, and 5% peripheral artery disease) have been determined. The analysis included Cox proportional hazard models. Each model was adjusted for childhood age, age at followup, sex and cohort/race. Continuous childhood variables were z-scored for each participant's last repeated measure during childhood.

Results: Childhood body mass index (BMI), serum total cholesterol (TC) and triglycerides, and systolic blood pressure were positively associated with adult cCVD events ($P < 0.0001$). Smoking in childhood was associated with nearly 50% increased risk of adult cCVD ($P = 0.08$). BMI; TC remained significant in the simultaneous risk factor model. The adjudication pipeline suggests that over 500 hospitalized cCVD events will be found on completion. Regression using the full set of imputed events yielded similar findings. Analysis of deaths is in process.

Conclusion: Childhood CVD risk factors predicts adult cCVD with implications for primordial CVD prevention.

Table: Childhood risk factor link to adult CVD

| Childhood risk variable | Single risk factor models | | Simultaneous risk factor model | |
|--------------------------------|-----------------------------|---|--------------------------------|---|
| | n cCVD events/ N at risk | Hazard ratio (95% Confidence limits), p | n cCVD events/ N at risk | Hazard ratio (95% Confidence limits), p |
| Body Mass Index | 201/16964 | 1.52 (1.33-1.73), <0.0001 | 142/11124 | 1.37 (1.14-1.64), 0.0008 |
| Total cholesterol | 191/13778 | 1.32 (1.14-1.52), 0.0001 | " | 1.21 (1.02-1.43), 0.03 |
| Triglycerides | 191/13654 | 1.17 (1.04-1.33), 0.01 | " | 1.04 (0.88-1.24), 0.6 |
| Systolic blood pressure | 190/14883 | 1.28 (1.11-1.48), 0.0007 | " | 1.18 (0.99-1.42), 0.07 |
| Regular smoking ≥ 1 / day | 151/13436 | 1.44 (0.96-2.16), 0.08 | " | 1.43 (0.94-2.17), 0.10 |

Hazard ratios = increased risk per one standard deviation increase in continuous risk variables. E.g. every ~0.9 mmol/L or ~33 mg/dL increase in childhood total cholesterol is associated with a ~32% and 21% increase in adult CVD risk in single and simultaneous risk factor models respectively. "Simultaneous risk factor model" recognizes that the risk factors are causally connected.