Abstract: 1447

Childhood risk factors and cardiovascular disease outcomes in adulthood. Preliminary findings from the International Childhood Cardiovascular Cohort (i3C) Consortium

Authors:
T Dwyer¹, DR Jacobs², JG Woo³, EM Urbina⁴, M Juonala⁵, JS Viikari⁵, W Chen⁴, RJ Prineas⁶, J Steinberger², S Daniels⁷, A Sinaiko², A Venn⁸, T Burns⁹, OT Raitakari⁵, ¹University of Oxford, The George Institute for Global Health, Nuffield Department of Women's & Reproductive Health - Oxford - United Kingdom of Great Britain & Northern Ireland, ²University of Minnesota - Minneapolis - United States of America, ³Cincinnati Children's Hospital Medical Center - Cincinnati - United States of America, ⁴Tulane University - New Orleans - United States of America, ⁵University of Turku - Turku - Finland, ⁶Wake Forest University - Winston-Salem - United States of America, ⁷Children’s Hospital Colorado - Aurora - United States of America, ⁸University of Tasmania - Hobart - Australia, ⁹University of Iowa - Iowa - United States of America,

On behalf: The International Childhood Cardiovascular Cohort (i3C) Consortium

Topic(s):
Risk Factors and Prevention – Epidemiology

Citation:

Funding Acknowledgements:
National Heart, Lung, and Blood Institute (NHLBI)

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>
<thead>
<tr>
<th>Childhood Risk Factor</th>
<th>Hazard Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI</td>
<td>1.52 (1.33-1.73), &lt;0.0001</td>
</tr>
<tr>
<td>Total Cholesterol</td>
<td>1.32 (1.14-1.52), 0.0001</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>1.17 (1.04-1.33), 0.01</td>
</tr>
<tr>
<td>Systolic Blood Pressure</td>
<td>1.28 (1.11-1.48), 0.0007</td>
</tr>
<tr>
<td>Smoking</td>
<td>1.44 (0.96-2.16), 0.08</td>
</tr>
</tbody>
</table>

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.
Childhood risk factor and cardiovascular disease outcomes in adulthood. Preliminary findings from the International Childhood Cardiovascular Cohort (i3C) Consortium

Authors:
T Dwyer, DR Jacobs, JG Woo, EM Urbina, L Bazzano, M Juonala, JS Viikari, W Chen, RJ Prineas, J Steinberger, S Daniels, A Sinaiko, A Venn, T Burns, OT Raitakari

University of Oxford, The George Institute for Global Health, Nuffield Department of Women’s & Reproductive Health – Oxford – United Kingdom of Great Britain & Northern Ireland,

University of Minnesota – Minneapolis – United States of America,

Cincinnati Children's Hospital Medical Center – Cincinnati – United States of America,

Tulane University – New Orleans – United States of America,

University of Turku – Turku – Finland,

Wake Forest University – Winston-Salem – United States of America,

Children’s Hospital Colorado – Aurora – United States of America,

University of Tasmania – Hobart – Australia,

University of Iowa – Iowa – United States of America,

On behalf: The International Childhood Cardiovascular Cohort (i3C) Consortium

Topic(s): Risk Factors and Prevention – Epidemiology

Citation:

Funding Acknowledgements:
National Heart, Lung, and Blood Institute (NHLBI)

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 cCVD 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 predict adult cCVD with implications for primordial CVD prevention.

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

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.