PREDICTION OF GLOBAL CVD RISK IN HIV-POSITIVE PERSONS

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for the D:A:D Study Group
Background

• With the aging of the population living with HIV, the absolute risk of cardiovascular disease (CVD) is increasing

• There is a need to further facilitate the identification of HIV-positive persons at increased risk of CVD

Purpose of study:

• Updated CVD prediction models
  • Global CVD risk *
  • Baseline CVD risk factors
  • Full and reduced D:A:D models (+/- ARVs)

Methods – participants and outcome

• 32,663 HIV-positive persons from 20 countries in Europe and Australia, who
  ✓ were free of CVD at entry into the D:A:D Study
  ✓ had complete information on CVD risk factors

• Outcome: A composite CVD endpoint that included
  • Myocardial infarction
  • Stroke
  • Invasive coronary artery procedure (including coronary artery bypass or angioplasty)
  • Carotid artery endarterectomy
  • Death from other CVD

• All CVD outcomes are reported real time, and are centrally validated
Methods – Participant follow-up

• Predictive risk equations based on Cox regression models
• Individuals were followed from D:A:D entry to the first of:
  • CVD
  • Six months after last clinic visit
  • 1st February 2011
• Full and reduced D:A:D models (+/- ARVs)
  • Estimated 5-year risk of CVD
• Comparison: Recent Framingham model re-calibrated to the D:A:D dataset
There were 1,010 CVD in 32,663 individuals followed for 186,364.5 person-years

Rate: 5.42 per 1,000 person-years

95% CI: 5.09-5.76
Components of Composite CVD Outcome

- MI: 493
- Bypass: 44
- Angioplasty: 129
- Carotid endarterectomy: 13
- Stroke: 36
- Other CVD death: 1010

$n=1010$
### Baseline Characteristics

<table>
<thead>
<tr>
<th></th>
<th>No CVD (n=31,653)</th>
<th>CVD (n=1,010)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>years</td>
<td></td>
</tr>
<tr>
<td></td>
<td>39 (33-46)</td>
<td>47 (41-57)</td>
</tr>
<tr>
<td><strong>Female</strong></td>
<td>%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>26.0</td>
<td>12.5</td>
</tr>
<tr>
<td><strong>Smoking current / former</strong></td>
<td>%</td>
<td>51.9 / 16.7</td>
</tr>
<tr>
<td><strong>Diabetes</strong></td>
<td>%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2.8</td>
<td>10.4</td>
</tr>
<tr>
<td><strong>Systolic BP</strong></td>
<td>mmHg</td>
<td></td>
</tr>
<tr>
<td></td>
<td>120 (110-130)</td>
<td>130 (120-140)</td>
</tr>
<tr>
<td><strong>Total cholesterol</strong></td>
<td>mmol/L</td>
<td>4.8 (4.1-5.7)</td>
</tr>
<tr>
<td><strong>HDL cholesterol</strong></td>
<td>mmol/L</td>
<td>1.14 (0.91-1.42)</td>
</tr>
<tr>
<td><strong>cART/PI/ NRTI</strong></td>
<td>years</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.75 / 0.68 / 2.42</td>
<td>3.19 / 1.44 / 4.34</td>
</tr>
<tr>
<td><strong>CD4 count</strong></td>
<td>cells/µL</td>
<td></td>
</tr>
<tr>
<td></td>
<td>440 (290-630)</td>
<td>402(260-611)</td>
</tr>
<tr>
<td><strong>HIV RNA &lt;50 copies/mL</strong></td>
<td>%</td>
<td>53.8</td>
</tr>
</tbody>
</table>
Risk Factors Considered

- Age
- Sex
- Blood pressure (systolic and diastolic)
- Smoking (current, former)
- Diabetes
- Family history of CVD
- Serum values of
  - Total (TC) and HDL cholesterol (TC:HDL ratio)
  - Triglycerides
  - CD4 / HIV-RNA
- HIV-exposure category
- cART
  - IDV/r, LPV/r, PI, NRTI as cumulative exposure
  - Abacavir as current exposure
- Body-mass index (BMI)
- Lipodystrophy
Risk Factors Included

- Age
- Sex
- Blood pressure (systolic) and diastolic
- Smoking (current, former)
- Diabetes
- Family history of CVD
- Serum values of
  - Total (TC) and HDL cholesterol (TC:HDL ratio)
  - Triglycerides
  - CD4 / HIV-RNA
- HIV-exposure category
- cART
  - IDV/r, LPV/r, PI, NRTI as cumulative exposure
  - Abacavir as current exposure
- Body-mass index (BMI)
- Lipodystrophy
# Three Models

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>D:A:D Full</th>
<th>D:A:D Reduced</th>
<th>Framingham</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Sex</td>
<td>+</td>
<td>+</td>
<td>Seperate models by sex</td>
</tr>
<tr>
<td>Diabetes</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Smoking Current and former</td>
<td>Current and former</td>
<td>Current and former</td>
<td>Current</td>
</tr>
<tr>
<td>Total and HDL cholesterol</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Systolic BP</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Family History CVD</td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>CD₄ cell count</td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Abacavir - current</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PI - cum. exposure</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NRTI – cum. exposure</td>
<td>+</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
## Three Models – Hazard Ratios from Cox Models

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Per unit</th>
<th>D:A:D Full</th>
<th>D:A:D Reduced</th>
<th>Framingham (men)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>ln</td>
<td>22.0</td>
<td>24.0</td>
<td>21.4</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td>1.37</td>
<td>1.41</td>
<td>-</td>
</tr>
<tr>
<td>Diabetes</td>
<td></td>
<td>1.96</td>
<td>2.08</td>
<td>1.78</td>
</tr>
<tr>
<td>Smoking current / former</td>
<td></td>
<td>2.25 / 1.24</td>
<td>2.26 / 1.27</td>
<td>1.92 / -</td>
</tr>
<tr>
<td>Total and HDL cholesterol</td>
<td>ln</td>
<td>2.58 / 0.61</td>
<td>2.98 / 0.59</td>
<td>3.08 / 0.39</td>
</tr>
<tr>
<td>Systolic BP (#: if treated)</td>
<td>ln</td>
<td>4.59</td>
<td>4.56</td>
<td>6.91 / 7.38 #</td>
</tr>
<tr>
<td>Family History CVD</td>
<td></td>
<td>1.37</td>
<td>1.39</td>
<td></td>
</tr>
<tr>
<td>CD4 cell count</td>
<td></td>
<td>0.89</td>
<td>0.89</td>
<td></td>
</tr>
<tr>
<td>Abacavir - current</td>
<td></td>
<td>1.47</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PI - cum. exposure</td>
<td>year</td>
<td>1.05</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NRTI – cum.exposure</td>
<td>year</td>
<td>1.03</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
5-year CVD risk – Age and Diabetes

- Framingham model
- D:A:D reduced model
- D:A:D Full model
- Observed Kaplan-Meier
Summary (I)

D:A:D models tailored to HIV-positive persons
  • based on observed data in HIV-positive persons

What’s new:
  • Additional 80,000 PY of follow-up (total of 186,000 PY)
  • One outcome only: Global CVD risk
  • Based on baseline rather than time-updated risk parameters (Cox model)
  • Full and reduced D:A:D models (+/- ARVs)
    • CD4 count included
Summary (II)

- The recent Framingham model for global CVD risk can be re-calibrated to predict well in HIV-positive persons in the D:A:D Study population.
- However, our analyses suggest that risk equations developed from the D:A:D dataset are superior in HIV-positive persons, in particular for the accuracy of prediction in subgroups.
- Generalizability of the D:A:D prediction models require external independent validation in cohorts of HIV positive persons.
Perspectives

Holistic approach

• Assessment of global CVD risk

• Individual level: In the clinical context to inform doctor patient discussions on CVD risks and interventions
  • Moderate-high CVD risk: more targeted interventions to reduce this risk

• Population level: for research purposes of estimations of predicted risk at population levels

*Updated D:A:D models will become available at:*

Acknowledgements

Steering Committee: Members indicated w/ *, ¢ chair;
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