Cardiovascular disease screening in HIV-infected patients
A cost-effectiveness analysis

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Context – Relevance of cardiovascular disease in HIV-infected patients

HIV-positive patients at increased risk for cardiovascular disease (CVD)...
- Lo and colleagues observed an increased prevalence of subclinical atherosclerosis in HIV-positive men.
- The D:A:D study group reported HIV-infected patients to be at an elevated risk for myocardial infarction.
- Reinach et al found the prevalence of asymptomatic left ventricular diastolic dysfunction (ALVDD) to be 45% in the HIV-HEART cohort as compared to 6% in a non-infected population of similar age.

Thus, the American Heart Association encourages the screening of HIV-infected patients for cardiac diseases.

Objective – Evaluation of CVD screening interventions in HIV-positive men

- Assessment of effectiveness, costs, and cost-effectiveness of screening HIV-positive men without known CVD for coronary artery disease (CAD) and cardiac dysfunction using a Markov microsimulation model.
- Base case: One-time screening of HIV-positive men at intermediate risk of CVD (10-year Framingham CAD risk ≥ 7.5%).
- Secondary analysis: Screening at different 10-year CAD risk thresholds.
- Secondary analysis: Screening at regular time intervals, i.e., every 5 or 3 years.
- Probabilistic sensitivity analysis applied to the base case.
- Estimation of main outcome measures.
- Probabilistic sensitivity analysis applied to the base case.
- Lifetime outcomes: Discounted quality-adjusted life years (QALYs), discounted direct costs, incremental cost-effectiveness ratios (ICERs).

Diagnostic outcomes: Number of patients correctly diagnosed with CVD, screening costs per patient.

Methods – Overview of CVD screening strategies

- No screening
  - Disease progression under current HIV treatment guidelines, i.e., no CVD screening.
- "Outpatient" screening
  - Electrocardiogram (ECG) and brain natriuretic peptide (BNP) measurement for all patients.
  - Additional echocardiography and stress-testing if indicated.
- "Cardiologist" screening
  - ECG, BNP measurement, echocardiography, and stress-testing for all patients.

Methods – State transition diagram of the Markov model

- CAD screening in HIV-positive men.
- CAD: Cardiac artery disease.
- ALVDD: Asymptomatic left ventricular diastolic dysfunction.
- ALVSD: Asymptomatic left ventricular systolic dysfunction.
- CHF: Congestive heart failure.
Note: HAART = highly active antiretroviral therapy.

* ICERs reported in the original paper were inflated to the year 2007 using the medical care component of the consumer price index for the US.

| Note: Deviations in numbers due to rounding. WTP = willingness-to-pay. |

Screening HIV-positive men without known CVD for cardiac diseases increases quality-adjusted life expectancy and is associated with additional health care expenditure.

Conclusions

- Screening HIV-positive men without known CVD for cardiac diseases increases quality-adjusted life expectancy and is associated with additional health care expenditure.
- “Cardiologist” screening (65,552 €/QALY, 78,976 US$/QALY in 2007 US$) comes at an ICER comparable to that of: Breast cancer screening in women aged 50 to 74 years compared to no screening (69,750 US$/QALY in 2007 US$)
- In the context of recommended screenings, it comes at an ICER comparable to those of other interventions recommended in HIV-infected individuals:
  
  - Fusion inhibitor enfuvirtide (89,436 US$/QALY in 2007 US$)
  - Genotypic resistance testing for HAART optimization (92,410 US$/QALY in 2007 US$)

Thus, the incorporation of routine CVD screening into HIV treatment guidelines could improve health outcomes and be cost-effective.

Results – One-time CVD screening of HIV-positive men at intermediate risk for cardiac diseases

<table>
<thead>
<tr>
<th>Diagnostic outcomes</th>
<th>No screening</th>
<th>“Outpatient”</th>
<th>“Cardiologist”</th>
</tr>
</thead>
<tbody>
<tr>
<td># patients w/ CAD per 1,000</td>
<td>129</td>
<td>129</td>
<td>129</td>
</tr>
<tr>
<td>€ / patient screened</td>
<td>0</td>
<td>1,707</td>
<td>93</td>
</tr>
</tbody>
</table>

Note: CAD risk denotes Framingham 10-year CAD risk; only non-dominated CVD screening strategies are shown. WTP = willingness-to-pay.

Key limitations

- Due to the lack of angiographic data, the prevalence of CAD in the HIV-HEART cohort was estimated using an Framingham risk-based algorithm.
- Given the high degree of uncertainty associated with selected input parameters, we intend to complement the cost-effectiveness analysis by an expected value of information analysis.
- Based on the results of the expected value of information analysis, we plan to give recommendations for future research priorities.

Next steps

- Due to insufficient data on incidence and progression of CVD in HIV-infected patients, we applied adjusted values derived from the general population.
- Due to the lack of data on CVD prevalence in HIV-infected women, we chose to evaluate CVD screening strategies in HIV-positive men only.

Limitations and next steps

<table>
<thead>
<tr>
<th>Cost (€)</th>
<th>∆ Cost (€)</th>
<th>QALYs</th>
<th>∆ QALYs</th>
<th>ICER (€/QALY)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Screening</td>
<td>195,389</td>
<td>0</td>
<td>10.522</td>
<td>-</td>
</tr>
<tr>
<td>“Outpatient” – one-time</td>
<td>195,389</td>
<td>0</td>
<td>10.522</td>
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</tr>
<tr>
<td>“Outpatient” – every 5 years</td>
<td>195,546</td>
<td>0</td>
<td>10.543</td>
<td>0.009</td>
</tr>
<tr>
<td>“Outpatient”– every 2 years</td>
<td>195,546</td>
<td>0</td>
<td>10.543</td>
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<tr>
<td>“Cardiologist” – one-time</td>
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At a WTP of 100,000 US$/QALY, screening HIV-infected men is cost-effective with a probability of greater 80%.

Results – Cost-effectiveness of CVD screening strategies at different screening levels

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<th>Screening threshold</th>
<th>% Sensitive CAD</th>
<th>ICER (€/QALY)</th>
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<tbody>
<tr>
<td>All</td>
<td>198,541</td>
<td>65,552</td>
</tr>
<tr>
<td>CAD risk ≤ 5%</td>
<td>196,024</td>
<td>54,815</td>
</tr>
<tr>
<td>CAD risk ≤ 10%</td>
<td>195,389</td>
<td>53,878</td>
</tr>
<tr>
<td>CAD risk ≤ 15%</td>
<td>194,464</td>
<td>52,085</td>
</tr>
</tbody>
</table>

Screening most cost-effective in a high-risk population: screening all HIV-positive men stays below the WTP threshold of 100,000 US$/QALY.

Results – Cost-effectiveness of CVD screening strategies at different screening intervals

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Results – Probabilistic sensitivity analysis

Cost-effectiveness acceptability curve

- “No screening”
- “Outpatient”
- “Cardiologist”

At a WTP of 100,000 US$/QALY, screening HIV-infected men is cost-effective with a probability of greater 80%.

Screening at five year intervals extended dominated: “Cardiologist” every 3 years marginally exceeds the threshold of 100,000 US$/QALY

Results – One-time CVD screening of HIV-positive men at intermediate risk for cardiac diseases

Conclusions

- Screening HIV-positive men without known CVD for cardiac diseases increases quality-adjusted life expectancy and is associated with additional health care expenditure.
- “Cardiologist” screening (65,552 €/QALY, 78,976 US$/QALY in 2007 US$) comes at an ICER comparable to those of other interventions recommended in HIV-infected individuals:
  
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  - Genotypic resistance testing for HAART optimization (92,410 US$/QALY in 2007 US$)

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References


Appendix – “Cardiologist plus” screening strategy

Appendix – Lifetime outcomes including “Cardiologist plus” screening

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<th>QALYs</th>
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</thead>
<tbody>
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<td>No Screening</td>
<td>195,389</td>
<td>-</td>
<td>10,532</td>
<td>-</td>
</tr>
<tr>
<td>&quot;Outpatient&quot;</td>
<td>196,024</td>
<td>635</td>
<td>10,534</td>
<td>0.012</td>
</tr>
<tr>
<td>&quot;Cardiologist&quot;</td>
<td>198,541</td>
<td>2,517</td>
<td>10,572</td>
<td>0.038</td>
</tr>
<tr>
<td>&quot;Cardiologist plus&quot;</td>
<td>198,377</td>
<td>-</td>
<td>10,574</td>
<td>0.001</td>
</tr>
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"Cardiologist plus" identifies more patients in early disease states leading to better health outcomes