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\(^1\)
- The D:A:D study group reported HIV-infected patients to be at an elevated risk for myocardial infarction\(^2\)
- Reinsch et al found the prevalence of asymptomatic left ventricular diastolic dysfunction (ALVDD) to be 48% in the HIV-HEART cohort as compared to 6% in a non-infected population of similar age\(^3,4\)

... due to behavioral, virus, and HAART factors\(^5,6\)

- Increased prevalence of traditional CVD risk factors in the HIV-infected population, e.g., > 50% current smokers in the HIV-HEART cohort\(^3\)
- Development of traditional CVD risk factors due to HIV or HAART, e.g., lipid-altering effect of protease inhibitors
- Effects of HIV or HAART on the pathogenetic process leading to CVD through other mechanisms, e.g., inflammation

Thus, the American Heart Association encourages the screening of HIV-infected patients for cardiac diseases\(^7\)

Note: HAART = highly active antiretroviral therapy.
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
  – Diagnostic outcomes: Number of patients correctly diagnosed with CVD, screening costs per patient
  – Lifetime outcomes: Discounted quality-adjusted life years (QALYs), discounted direct costs, incremental cost-effectiveness ratios (ICERs)\(^a\)

Input parameters derived from patient-level data of the HIV-HEART cohort (558 men, age 44.3 ±10.0 years) and the published literature

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\(^a\): Annual discounting rate of 3%, costs reported in 2007 Euros.
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

Patients can have (1) neither cardiac disease, (2) CAD or cardiac dysfunction, or (3) both

a. 1-49% coronary luminal stenosis for left main or 1-69% for any other coronary artery.  
b. ≥ 50% coronary luminal stenosis for left main or ≥ 70% for any other coronary artery. 
Note: ALVDD = asymptomatic left ventricular diastolic dysfunction, ALVSD = asymptomatic left ventricular systolic dysfunction, CHF = congestive heart failure.
# Results – One-time CVD screening of HIV-positive men at intermediate risk for cardiac diseases

## Diagnostic outcomes

<table>
<thead>
<tr>
<th></th>
<th>No screening</th>
<th>&quot;Outpatient&quot;</th>
<th>&quot;Cardiologist&quot;</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># true positives per 1,000</td>
<td>0</td>
<td>17</td>
<td>93</td>
</tr>
<tr>
<td>€ / patient screened</td>
<td>0</td>
<td>126</td>
<td>618</td>
</tr>
</tbody>
</table>

## Lifetime outcomes

<table>
<thead>
<tr>
<th></th>
<th>Cost (€)</th>
<th>Δ Cost (€)</th>
<th>QALYs</th>
<th>Δ QALYs</th>
<th>ICER (€/QALY)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Screening</td>
<td>195,389</td>
<td>-</td>
<td>10.522</td>
<td>-</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>
<td>54,815</td>
</tr>
<tr>
<td>&quot;Cardiologist&quot;</td>
<td>198,541</td>
<td>2,517</td>
<td>10.572</td>
<td>0.038</td>
<td>65,552</td>
</tr>
</tbody>
</table>

At a WTP of 100,000 US$/QALY (83,000 €/QALY), screening HIV-infected men using the "Cardiologist" approach is cost-effective.

Note: Deviations in numbers due to rounding. WTP = willingness-to-pay.
Results – Cost-effectiveness of CVD screening strategies at different screening thresholds

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

Note: CAD risk denotes Framingham 10-year CAD risk; only non-dominated CVD screening strategies are shown. WTP = willingness-to-pay.
Results – Probabilistic sensitivity analysis
Cost-effectiveness acceptability curve

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

Note: WTP = willingness-to-pay.
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:
  - Fusion inhibitor enfuvirtide (89,436 US$/QALY in 2007 US$)*
  - Genotypic resistance testing for HAART optimization (92,410 US$/QALY in 2007 US$)*

- In the context of recommended screenings, it 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$/QALY in 2007 US$)*

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

* 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: HAART = highly active antiretroviral therapy.
Limitations and next steps

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

- 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

Next steps

- 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
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References


