Case Studies in HIV and Cardiovascular Disease

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Learning Objectives
Upon completion of this presentation, learners should be better able to:

• Calculate 10-year cardiovascular risk and apply that risk to NCEP guidelines for prevention of cardiovascular disease.

• Account for the contribution of HIV infection and its treatment to cardiovascular risk in addition to traditional risk factors.
Faculty Disclosures

Advisory Board for Scientific Information: Bristol-Myers Squibb

Consultant for Clinical Trail Design: Abbott, Gilead Sciences, Merck, ViiV Healthcare

Grant Recipient/Research Support: Abbott Laboratories, Gilead Sciences, Merck, Pfizer, ViiV Healthcare

Other: provide disease-based lectures for Merck, ViiV Healthcare

Off-Label Disclosure

PLEASE CONFIRM OR LIST WHAT YOU INTEND TO DISCUSS OFF-LABLE
There will be no off-label/investigational uses discussed in this presentation.
Possible risk factors for atherosclerotic cardiovascular events in patients infected with HIV are:

A. Traditional cardiovascular risk factors such as diabetes, hypertension, dyslipidemia, smoking, etc.
B. Some antiretroviral agents
C. HIV infection
D. A and B
E. A and C
F. A, B, and C
CHD Risk Factors in HIV-Infected Populations

- Gender
- Family History
- Age
- Lipids
- Abdominal Obesity
- Inactivity, Diet
- Cigarette Smoking
- Hypertension
- Hyperglycemia
- Insulin Resistance
- Diabetes

HIV Infection
ART

Brown = Modifiable
Red = Nonmodifiable

*Metabolic syndrome
Case 1 – J.C.

• 56 yo male HIV+ 2/96 (40 yo) CD4=363, VL=199,000
  – Hypertension, 165 lb, 6’3”, BMI 20.1 kg/m², FBSs normal
  – SH – past smoker  FH – Father AMI < 55 yo
  – 5/96 – 9/00    AZT, 3TC, IDV
  – 10/96 – **ACUTE MYOCARDIAL INFARCTION** (41 yo)
    • Lisinopril, pravastatin, atenolol, ASA
  – 9/00 – 10/03    AZT, 3TC, IDV/r
  – 10/03 – 7/04    AZT, 3TC, ATV/r
  – 7/04 - 6/08    TDF, 3TC, fAPV/r
  – 6/08 – present    EFV/TDF/FTC
### Case 1 – J.C.  
**10/96 Acute Myocardial Infarction**

<table>
<thead>
<tr>
<th>Date</th>
<th>TC</th>
<th>HDL</th>
<th>LDL</th>
<th>TG</th>
<th>10y CVR</th>
<th>LDL goal</th>
<th>Rx</th>
<th>ARV + Cardiac Meds</th>
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<tbody>
<tr>
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<td>&gt;100 (70)</td>
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<tr>
<td>10/98</td>
<td>165</td>
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<td>93</td>
<td>158</td>
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<tr>
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<tr>
<td>10/99</td>
<td>165</td>
<td>29</td>
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<td>5%</td>
<td>&lt;100 (70)</td>
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<tr>
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<td>66</td>
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<td>&gt;100 (70)</td>
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<td>29</td>
<td>90</td>
<td>203</td>
<td>7%</td>
<td>&lt;100 (70)</td>
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<td>AZT, 3TC, IDV/r</td>
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<tr>
<td>11/00</td>
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<td>330</td>
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<td>03/01</td>
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<td>361</td>
<td>7%</td>
<td>&lt;100 (70)</td>
<td>&gt;100 (70)</td>
<td></td>
</tr>
</tbody>
</table>
What were his risk factors?

A. Dyslipidemia
B. Family History
C. HIV Infection
D. Antiretroviral Therapy
E. Hypertension
F. A, B, and C
G. A, B, and D
H. A, B, and E
CHD Risk Factors

Brown = Modifiable
Red = Nonmodifiable

*Metabolic syndrome

Gender
Family History
Age
Lipids*
Abdominal Obesity*
Inactivity, Diet
Cigarette Smoking
Hyper-tension*
Hyper-glycemia
Insulin Resistance*
Diabetes
Major CHD Risk Factors

Modifiable
- Cigarette smoking
- Diabetes*
- Hypertension: BP ≥ 140/90 mm Hg or on antihypertensive medication
- Low HDL: <40 mg/dL

Non-Modifiable
- Family history of premature CHD (1st-degree relative):
  - Male relative age <55 yrs
  - Female relative age <65 yrs
- Age
  - Male ≥45 years
  - Female ≥55 years

*Diabetes is regarded as a CHD risk equivalent

According to NCEP guidelines, which of the following lipid measurements are predictive of cardiovascular events?

A. Elevated LDL
B. Elevated non-HDL cholesterol
C. Total cholesterol
D. Elevated triglycerides
E. A, B, and D
F. A and D
G. A and B
H. A and C
Do you calculate the Framingham 10-year cardiovascular risk on your HIV-infected patients?

A. Yes. I use my computer or a portable device
B. No. I use a different calculation
C. No. I don’t know how
D. No. I don’t have time
E. None of the above
# 10-Year CHD Risk Framingham Score

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Points</th>
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<tr>
<td>20 – 34</td>
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<td>35 – 39</td>
<td>-3</td>
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<tr>
<td>40 – 44</td>
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<td>45 – 49</td>
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<td>50 – 54</td>
<td>6</td>
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<td>55 – 59</td>
<td>8</td>
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<tr>
<td>60 – 64</td>
<td>10</td>
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<td>65 – 69</td>
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<td>70 – 74</td>
<td>14</td>
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<td>75 – 79</td>
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</table>

<table>
<thead>
<tr>
<th>Total Cholesterol (mg/dL)</th>
<th>Age 20 – 39</th>
<th>Age 40 – 49</th>
<th>Age 50 – 59</th>
<th>Age 60 – 69</th>
<th>Age 70 – 79</th>
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<tbody>
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<td>0</td>
<td>0</td>
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<tr>
<td>160 – 199</td>
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<td>3</td>
<td>2</td>
<td>1</td>
<td>1</td>
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<td>200 – 239</td>
<td>8</td>
<td>6</td>
<td>4</td>
<td>2</td>
<td>1</td>
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<td>240 – 279</td>
<td>11</td>
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<td>3</td>
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<tr>
<td>≥280</td>
<td>13</td>
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<td>7</td>
<td>4</td>
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<table>
<thead>
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<th>Smoking</th>
<th>Age 20 – 39</th>
<th>Age 40 – 49</th>
<th>Age 50 – 59</th>
<th>Age 60 – 69</th>
<th>Age 70 – 79</th>
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<td>0</td>
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<td>Smoker</td>
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<td>7</td>
<td>4</td>
<td>2</td>
<td>1</td>
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</table>

<table>
<thead>
<tr>
<th>HDL (mg/dL)</th>
<th>Points</th>
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<td>≥60</td>
<td>-1</td>
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<tr>
<td>50 – 59</td>
<td>0</td>
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<tr>
<td>40 – 49</td>
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<tr>
<td>&lt;40</td>
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<table>
<thead>
<tr>
<th>Systolic BP (mm Hg)</th>
<th>If Untreated</th>
<th>If Treated</th>
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<tr>
<td>&lt;120</td>
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<td>130 – 139</td>
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<td>140 – 159</td>
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<td>5</td>
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<tr>
<td>≥160</td>
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<td>6</td>
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### 10-Year CHD Risk Framingham Score

<table>
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<tr>
<th>Point Total</th>
<th>10-Year Risk %</th>
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<tr>
<td>&lt;9</td>
<td>&lt;1</td>
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<tr>
<td>9</td>
<td>1</td>
</tr>
<tr>
<td>10</td>
<td>1</td>
</tr>
<tr>
<td>11</td>
<td>1</td>
</tr>
<tr>
<td>12</td>
<td>1</td>
</tr>
<tr>
<td>13</td>
<td>2</td>
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<tr>
<td>14</td>
<td>2</td>
</tr>
<tr>
<td>15</td>
<td>3</td>
</tr>
<tr>
<td>16</td>
<td>4</td>
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<tr>
<td>17</td>
<td>5</td>
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<tr>
<td>18</td>
<td>6</td>
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<td>23</td>
<td>22</td>
</tr>
<tr>
<td>24</td>
<td>27</td>
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<tr>
<td>≥25</td>
<td>≥30</td>
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</tbody>
</table>

10-Year Risk: ___%
CHD Risk Prediction

> 2 Risk Factors

High

Moderately High

Moderate

Estimated 10-Year Risk

< 1 Risk factor = Low Risk (<10%) – Don’t perform Framingham Risk Score

>20%, CHD, or DM

10%-20%

<10%
## LDL Cholesterol Goals

**Triglycerides <200 mg/dL**

<table>
<thead>
<tr>
<th>Risk Category</th>
<th>LDL Goal</th>
<th>LDL Level - Initiate TLC*</th>
<th>LDL Level - Consider Drug Rx</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>LR</strong></td>
<td>&lt;160 mg/dL</td>
<td>≥160 mg/dL</td>
<td>≥190 mg/dL</td>
</tr>
<tr>
<td>0-1 Risk Factor</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>MR and MHR</strong></td>
<td>&lt;130 mg/dL</td>
<td>≥130 mg/dL</td>
<td>10-20%: ≥130 mg/dL</td>
</tr>
<tr>
<td>&gt;2 Risk Factors (10 yr risk ≤20%)</td>
<td></td>
<td></td>
<td>&lt;10%: ≥160 mg/dL</td>
</tr>
<tr>
<td><strong>HR</strong></td>
<td>&lt;100** mg/dL</td>
<td>≥100 mg/dL</td>
<td>≥ 130 mg/dL</td>
</tr>
<tr>
<td>&gt;2 Risk Factors or CRE (10 yr risk &gt;20%)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Therapeutic lifestyle changes  
**Optional <70 mg/dL  

<table>
<thead>
<tr>
<th>Risk Category</th>
<th>N-HDL-C Goal</th>
<th>N-HDL-C Initiate TLC*</th>
<th>N-HDL-C Consider Drug Rx</th>
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</thead>
<tbody>
<tr>
<td>LR</td>
<td>&lt;190 mg/dL</td>
<td>≥190 mg/dL</td>
<td>≥190 mg/dL</td>
</tr>
<tr>
<td>0-1 Risk Factor</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>MR and MHR</td>
<td>&lt;160 mg/dL</td>
<td>≥160 mg/dL</td>
<td>&lt;10%:</td>
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<tr>
<td>&gt;2 Risk Factors (10 yr risk ≤20%)</td>
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<td></td>
<td>≥ 190 mg/dL</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>10-20%:</td>
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<td>≥ 160 mg/dL</td>
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<td>HR</td>
<td>&lt;130 mg/dL**</td>
<td>≥130 mg/dL</td>
<td>≥ 160 mg/dL</td>
</tr>
<tr>
<td>&gt;2 Risk Factors or CRE (10 yr risk &gt;20%)</td>
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<td></td>
<td></td>
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</tbody>
</table>

*Therapeutic lifestyle changes  **Optional <100 mg/dL  

Reduction of LDL-C Decreases Risk of CVD

LDL Cholesterol (mg/dL) vs CV Events (%)

- Secondary Prevention
- Primary Prevention

- Reduction of LDL-C Decreases Risk of CVD

Risk Factor Modifications

Cholesterol Management

- Restriction of saturated fat (<7% of total calories) and cholesterol (<200 mg/day)¹ (B Cohort Studies)

- Promotion of daily physical activity and weight management¹ (B Cohort Studies)

- Increase omega-3 fatty acid consumption² (B Cohort Studies)

- Initiation or intensification of LDL-lowering therapy in those with a baseline or on-treatment LDL level >100 mg/dL¹ (B Cohort Studies)
  - When risk is very high, LDL goal of <70 mg/dL³ (B Cohort Studies)
  - Statins, bile acid sequestrants, or nicotinic acid can be used first-line to achieve the LDL goal. Ensure there are no drug interactions with HAART or that proper dose adjustments are made¹

Risk Factor Modifications
Triglyceride Management

• If TG level 200-499 mg/dL, consider adding nicotinic acid or a fibrate to statin
  – If TG levels >200 mg/dL, non-HDL-C (Total cholesterol – HDL-C) is the target. Goal is 30 mg/dL higher than LDL-C target

• If TG level ≥500 mg/dL, consider adding nicotinic acid or a fibrate before LDL-lowering therapy
  – If TG levels > 500, TGs cannot be hydrolyzed off the apolipoprotein B matrix, trapping LDL-C in these atherogenic particles that are then deposited in the intima media of the artery.
  – TGs must be lowered (fibrates) for LDL-C to be released for utilization by LDL-receptors (increased by statins).

Risk Factor Modifications
Non-HDL and HDL Cholesterol Management

• Low HDL-C (<40 mg/dL) is a tertiary target according to NCEP/ATP III
  – Recommend weight loss, smoking cessation, regular exercise, and avoiding excessive carbohydrate calories
  – Once LDL-C and non-HDL-C goals are met, drug therapy (nicotinic acid or fibrates) may be appropriate in patients with CAD or CAD-equivalent

# Risk Factor Modifications

## Blood Pressure Control

<table>
<thead>
<tr>
<th>Modification</th>
<th>Recommendation</th>
<th>Approximate SBP Reduction Range</th>
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</thead>
<tbody>
<tr>
<td>Weight reduction</td>
<td>Maintain normal body weight (Body Mass Index = 18.5 – 24.9 kg/m²)</td>
<td>5-20 mm Hg / 10 kg weight loss</td>
</tr>
<tr>
<td>Adopt DASH diet</td>
<td>Diet rich in fruits, vegetables, low fat dairy and reduced in fat</td>
<td>8-14 mm Hg</td>
</tr>
<tr>
<td>Restrict sodium intake</td>
<td>&lt;2.4 grams of sodium/day</td>
<td>2-8 mm Hg</td>
</tr>
<tr>
<td>Physical activity</td>
<td>Regular aerobic exercise for at least 30 minutes on most days of the week</td>
<td>4-9 mm Hg</td>
</tr>
</tbody>
</table>
| Moderate alcohol consumption | <2 drinks/day for men  
<1 drink/day for women                               | 2-4 mm Hg                               |

Risk Factor Modifications
Blood Pressure Control – JNC 7
(C – Expert Consensus)

• For patients post-MI or high risk for coronary disease:
  – Use of an ACE inhibitor and/or β-blocker in those with BP >140/90 mm Hg
  – Initiate therapy when BP >130/80 mm Hg in individuals with chronic kidney disease or diabetes mellitus

ACE = angiotensin converting enzyme
BP = blood pressure

Risk Factor Modifications

• Smoking Cessation
  – Counsel the patient to quit smoking, develop a plan for smoking cessation and arrange follow-up
  – Recommend avoidance of exposure to second-hand smoke

• Maintain normal body weight
  – BMI = 18.5 – 24.9 kg/m²
  – Waist circumference
    • Men <40 inches
    • Women <35 inches

• Aspirin
  – Low-dose (75-160 mg) aspirin per day for persons at higher CHD risk, especially those with 10-year CHD risk ≥10%

Risk Factor Modifications

• EXERCISE:
  – Aerobic activity: 30 minutes, 5 days a week
    • Walking
    • Jogging
    • Cycling
  – Resistance training: 2 days a week
  – Weight machines or free weights

• DIABETES:
  – Goal Hb A1c < 7% (< 5.7%)
  – Achieve normal or near normal fasting plasma glucose with:
    • Exercise
    • Weight reduction
    • Oral hypoglycemic agents
    • Insulin

Case 2 – D.T.

- 52 yo female HIV+ 1991 (31yo–sexual transmission)
  - SH – ½ ppd X 26 years  FH – Negative for CVD
  - 110 lb.  5”8”.  BMI 16.5 kg/m²  Low to normal BP, FBS<100
  - 08/92 – 12/92     AZT  CD4 = 609,  VL = 1600
  - 12/92 – 08/96     ddI
  - 08/96 – 08/99     d4T, 3TC, IDV
  - 08/99 – 11/00     d4T, 3TC, IDV/r
  - 11/00 – 06/07     d4T, 3TC, NFV
  - 06/07 – 04/09     TDF, FTC, ATV/r
  - 04/09 – present   TDF/FTC/DRV/r
  - 03/11  ACUTE MYOCARDIAL INFARCTION (51 yo)
### Case 2 – D.T.

<table>
<thead>
<tr>
<th>Date</th>
<th>TC</th>
<th>HDL</th>
<th>LDL</th>
<th>TG</th>
<th>10y CVR</th>
<th>LDL goal</th>
<th>LDL RX</th>
<th>ARV</th>
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<tbody>
<tr>
<td>03/93</td>
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<td>44</td>
<td>115</td>
<td>133</td>
<td>4%</td>
<td>&lt;160</td>
<td>&gt;190</td>
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<tr>
<td>04/98</td>
<td>177</td>
<td>49</td>
<td>107</td>
<td>106</td>
<td>4%</td>
<td>&lt;160</td>
<td>&gt;190</td>
<td>d4T, 3TC, IDV/r</td>
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<tr>
<td>09/98</td>
<td>201</td>
<td>47</td>
<td>127</td>
<td>137</td>
<td>5%</td>
<td>&lt;160</td>
<td>&gt;190</td>
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<tr>
<td>10/00</td>
<td>287</td>
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<tr>
<td>06/03</td>
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<td>341</td>
<td>10%</td>
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<td>09/05</td>
<td>220</td>
<td>45</td>
<td>123</td>
<td>261</td>
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<td>&lt;130 (100)</td>
<td>&gt;130</td>
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<tr>
<td>03/08</td>
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<td>116</td>
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<td>TDF, FTC, DRV/r</td>
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<td>07/11</td>
<td>191</td>
<td>54</td>
<td>97</td>
<td>199</td>
<td>8%</td>
<td>&lt;100 (70)</td>
<td>&gt;100</td>
<td>AMI, ASA, NTG, atorvastatin, clopidogrel</td>
</tr>
</tbody>
</table>
What were her risk factors?

A. Elevated triglycerides
B. Smoking (13 pack year)
C. HIV infection
D. Low HDL
E. Antiretroviral drugs
F. A, B, C, and E
G. B, C, and D
H. A, B, and E
D:A:D: Prevalence of Cardiac Risk Factors in Cohort of HIV-Infected Patients

N=23,468

- Median age, yrs: 39
- Male, %: 75.9
- Median HIV-1 RNA, $\log_{10}$ c/mL: 4.6
- Median CD4 cell count, mm$^3$: 226
- Median duration of HIV, yrs: 3.5
- Previous ART, %: 80.8

FHx = family history of CHD; PHx = previous history of CHD; BMI = body mass index; HTN = hypertension; DM = diabetes mellitus; HC = hypercholesterolemia; TG = triglycerides

Modifiable Risk Factors Increased Among HIV vs General Population

- Smoking: APROCO Cohort (HIV+) vs MONICA Sample (HIV-), $P<0.0001$
- Hypertension: APROCO Cohort (HIV+) vs MONICA Sample (HIV-), $P<0.01$
- HDL <40 mg/dL: APROCO Cohort (HIV+) vs MONICA Sample (HIV-), $P<0.0001$

APROCO Cohort (N=223 HIV+ men on PI-containing regimen)
MONICA Sample (N=527 HIV- men)

**SMART: Non-AIDS Event Rates with Continuous vs Intermittent Therapy**

<table>
<thead>
<tr>
<th>Endpoint, n</th>
<th>Viral Suppression (VS) Arm (n = 2752)</th>
<th>Drug Conservation (DC) Arm (n = 2720)</th>
<th>HR (95% CI)*</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major cardiovascular, renal, or hepatic disease</td>
<td>39</td>
<td>65</td>
<td>1.7 (1.1-2.5)</td>
<td>0.009</td>
</tr>
<tr>
<td>Fatal/nonfatal cardiovascular disease</td>
<td>31</td>
<td>48</td>
<td>1.6 (1.0-2.5)</td>
<td>0.05</td>
</tr>
<tr>
<td>Fatal/nonfatal renal disease</td>
<td>2</td>
<td>9</td>
<td>4.5 (1.0-20.9)</td>
<td>0.05</td>
</tr>
<tr>
<td>Fatal/nonfatal liver disease</td>
<td>7</td>
<td>10</td>
<td>1.4 (0.6-3.8)</td>
<td>0.46</td>
</tr>
<tr>
<td>Grade 4 event or death from any cause</td>
<td>164</td>
<td>205</td>
<td>1.3 (1.0-1.6)</td>
<td>0.03</td>
</tr>
</tbody>
</table>

- Significantly more individuals in DC arm developed major CV, renal, or hepatic disease than individuals in VS arm
- Significantly more individuals in DC arm experienced grade 4 event or death from any cause than individuals in VS arm
- HIV disease itself with resultant pro-inflammatory state may be more of a predisposing factor for CV disease than HAART

*Treatment interruption group vs viral suppression group*

FRAM: The Effects of HIV on CHD/Death Results

• Comparing mortality risk in 468 HIV-infected vs 278 controls, ages 33-45: 7X higher death risk in the HIV group ($P<0.0001$)

• After adjusting for traditional CV risk factors: the death risk remained 3.4X higher in people with HIV ($P = 0.009$)

• Current smoking (but not past smoking) nearly tripled the death risk ($HR = 2.73$, $P = 0.0001$)

• Every added 10 years of age raised the risk more than 60% ($HR = 1.61$, $P<0.0001$)

• Every doubling of the baseline CD4 cell count lowered the risk 35% ($HR = 0.65$, $P<0.0001$)

FRAM = Fat Redistribution and Metabolic Change in HIV Infection Study

FRAM: Fat Redistribution and Metabolic Change in HIV Infection Study

- HIV itself emerged as a mortality risk factor as potent as:
  - Age
  - Male gender
  - Smoking
  - Diabetes

Modrich L, et al. 16th CROI 2009; Abstract 146.
HIV: A Pro-Atherogenic Virus

• HIV disease is associated with accelerated T-cell production, increased T-cell activation, and high levels of circulating inflammatory markers
  – T-lymphocytes, predominately CD4 cells, play a key role in atherogenesis
  – Activated CD4 cells generate proinflammatory cytokines, including tumor necrosis factor and interleukins, that lead to atherosclerosis

Reiss P. 16th CROI 2009; Oral 152.
CVD and SLE

Used carotid ultrasound to assess for plaque formation in SLE patients.

Odds ratio for plaque in SLE patients 4.8 (95% CI 2.8-6.7).

Cytoxan was protective?

NEJM 2003
Used CT scans to look for coronary calcification.

Found this to be more common in SLE patients and seen at younger ages.

NEJM 2003
Case 3 – P.W.

- 62 yo male HIV+ 1991 (41 yo) – CD4 404 (21.8%) VL=114,000
  - Normotensive, 158 lbs, 5’10”, BMI = 22.6 kg/m²
  - SH – Past smoker  FH – Negative for CVD  FBSs normal
  - 04/96 – 07/00  d4T, 3TC, IDV
  - 07/00 – 05/03  d4T, 3TC, IDV/r
  - 02/04 – Unstable angina, coronary artery stent (54 yo)
  - 05/03 – 03/05  d4T, 3TC, NVP
  - 03/05 – present  TDF, FTC, NVP
## Case 3 – P.W.

<table>
<thead>
<tr>
<th>Date</th>
<th>TC</th>
<th>HDL</th>
<th>LDL</th>
<th>TG</th>
<th>10y CVR</th>
<th>LDL goal</th>
<th>Rx</th>
<th>ARV</th>
</tr>
</thead>
<tbody>
<tr>
<td>07/98</td>
<td>170</td>
<td>31</td>
<td>88</td>
<td>255</td>
<td>7%</td>
<td>&lt;130</td>
<td>&gt;160</td>
<td>d4T, 3TC, IDV</td>
</tr>
<tr>
<td>07/00</td>
<td>216</td>
<td>37</td>
<td>127</td>
<td>260</td>
<td>8%</td>
<td>&lt;130</td>
<td>&gt;160</td>
<td>d4T, 3TC, IDV/r</td>
</tr>
<tr>
<td>09/01</td>
<td>257</td>
<td>45</td>
<td>157</td>
<td>273</td>
<td>8%</td>
<td>&lt;160</td>
<td>&gt;190</td>
<td></td>
</tr>
<tr>
<td>11/02</td>
<td>250</td>
<td>43</td>
<td>164</td>
<td>217</td>
<td>10%</td>
<td>&lt;160</td>
<td>&gt;190</td>
<td></td>
</tr>
<tr>
<td>08/03</td>
<td>189</td>
<td>45</td>
<td>117</td>
<td>133</td>
<td>5%</td>
<td>&lt;160</td>
<td>&gt;190</td>
<td>d4T, 3TC, NVP</td>
</tr>
<tr>
<td>02/04</td>
<td>198</td>
<td>45</td>
<td>128</td>
<td>125</td>
<td>5%</td>
<td>&lt;160</td>
<td>&gt;190</td>
<td>Cardiac Stent – Unstable Angina, ASA, simvastatin, metoprolol</td>
</tr>
<tr>
<td>11/06</td>
<td>139</td>
<td>46</td>
<td>79</td>
<td>69</td>
<td>3%</td>
<td>&lt;100 (70)</td>
<td>&gt;100</td>
<td>TDF, FTC, NVP</td>
</tr>
<tr>
<td>08/07</td>
<td>135</td>
<td>50</td>
<td>72</td>
<td>65</td>
<td>3%</td>
<td>&lt;100 (70)</td>
<td>&gt;100</td>
<td></td>
</tr>
<tr>
<td>06/08</td>
<td>118</td>
<td>51</td>
<td>55</td>
<td>62</td>
<td>3%</td>
<td>&lt;100 (70)</td>
<td>&gt;100</td>
<td></td>
</tr>
<tr>
<td>02/12</td>
<td>140</td>
<td>46</td>
<td>83</td>
<td>54</td>
<td>4%</td>
<td>&lt;100 (70)</td>
<td>&gt;100</td>
<td></td>
</tr>
</tbody>
</table>
What were his risk factors?

A. Male sex
B. HIV infection
C. Metabolic syndrome (Syndrome X)
D. Antiretroviral drugs
E. A and C
F. A and B
G. A and D
H. A, B, and D
D:A:D: Contribution to MI Risk

Relative Rate of MI* (95% CI)

- HDL cholesterol (per mmol/L): 0.72 (0.52–0.99); \( P = 0.05 \)
- Triglycerides (per log₂ mmol/L higher): 1.58 (1.43–1.75); \( P < 0.001 \)
- Total cholesterol (per mmol/L): 1.26 (1.19–1.35); \( P < 0.001 \)
- PI exposure (per additional year): 1.10 (1.01–1.18); \( P = 0.002 \)
- NNRTI exposure (per additional year): 1.00 (0.93–1.09); \( P = 0.92 \)

*Adjusted for conventional risk factors (sex, cohort, HIV transmission group, ethnicity, age, BMI, family history of CVD, smoking, previous CVD events, lipids, diabetes, and hypertension)

†Unadjusted model

D:A:D

PIs and Incidence of MI

An increase in incident CVD is associated with duration of PI-containing combination antiretroviral therapy

D:A:D conducted an analysis of the NRTI class and the risk of MI

- The primary hypothesis focused on exposure to thymidine analogues

Contrary to the hypothesis, thymidine analogues were not associated with increased risk of MI

Instead, recent use of certain NRTIs was associated with increased risk of MI

XXX Study: Drug A + Versus Drug B in HAART Regimen:

- Open-label, non-inferiority study: ART-naïve, HIV+ patients randomized to Drug A or Drug B
- Primary end points: proportion of patients achieving HIV-1 RNA <400 c/mL at Week 48 and treatment discontinuations because of an adverse event
MACS Cohort: Mean Lipid Values Before and After HIV Infection (Treated and Untreated)

- TC (Total Cholesterol)
- LDL (Low-Density Lipoprotein)
- HDL (High-Density Lipoprotein)

IDSA Recommendations for Dyslipidemia Management in HIV-Infected Patients

Obtain fasting lipid profile, prior to starting ARVS and within 3 to 6 months of starting new regimen

Count number of cardiovascular disease (CVD) risk factors and determine level of risk. If ≥2 risk factors, perform a 10-year risk calculation, based on Framingham

Intervene for modifiable nonlipid risk factors such as diet and smoking

If lipids remain above threshold based on risk group despite vigorous lifestyle interventions, consider altering ARV therapy or using lipid-lowering drugs

LIPID-LOWERING DRUG THERAPY IS NECESSARY IF:

- Serum LDL cholesterol above threshold, or
- TG 200-500 mg/dL with elevated non-HDL cholesterol:
  - STATIN

OR

- Serum TG >500 mg/dL:
  - FIBRATE

Adapted with permission from Dube MP, et al. Clin Infect Dis. 2003;37:613-627. Figure 1. Publisher: University of Chicago Press. © 2003 IDSA All rights reserved
## Goal: Reduction of CHD Risk

(C Expert Consensus)

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Untreated HIV</td>
<td>Initiate HAART</td>
</tr>
<tr>
<td>Lipid effects of HAART</td>
<td>Avoid specific antiretrovirals</td>
</tr>
<tr>
<td></td>
<td>Initiate lipid-lowering therapy</td>
</tr>
<tr>
<td>Traditional risk factors</td>
<td>Lifestyle modifications ± pharmacologic therapy</td>
</tr>
</tbody>
</table>
Summary

CHD Risk Factors in HIV-Infected Patients

• Traditional risk factors for CVD disease, such as age, smoking, and elevated lipids, increase risk in both HIV-positive and HIV-negative individuals (B Cohort Studies)

• CHD may also be linked to non-traditional factors such as HIV disease and effects of antiretrovirals (B Cohort Studies)
Summary

- Individuals with HIV/AIDS are living longer since the availability of HAART
- There may be very serious cardiovascular and metabolic consequences associated with HIV infection, as well as some ARVs
- “Aggressive treatment of HIV is the clinical priority . . . and the treatment of modifiable risk factors is prudent.”
- Crucial step in management of the HIV patient is aggressive cardiovascular risk factor modification

Mate, doesn’t HIV infection add at least some additional risk for cardiovascular disease?