ACTHIV
THE AMERICAN CONFERENCE FOR THE TREATMENT OF HIV

ACTHIV 2016: A State-of-the-Science Conference for Frontline Health Professionals
Cardiovascular Issues in HIV

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Disclosures

• None
Learning Objectives

As a result of participating in this activity, participants will be able to:

• Review the epidemiology of HIV-related cardiovascular disease

• Develop an approach to modifying traditional and nontraditional cardiovascular risk factors in HIV

• Apply recommended best practices for reducing cardiovascular risk in HIV-infected individuals
Outline

• Epidemiology of HIV and CVD

• Pathophysiology of HIV and CVD
  – Role of traditional risk factors and ART
  – Role of inflammation/immune activation

• Management of CVD in HIV
  – CVD risk prediction
  – CVD prevention
    • Novel risk factors
    • Traditional risk factors
HIV Patients are Aging

- Projected age distribution of HIV patients on ART 2010-2030
- National Dutch ATHENA cohort with data between 1996 and 2010
- Median age will increase from 43.9 years in 2010 to 56.6 in 2030
- Proportion of HIV patients over 50 will increase from 28% in 2010 to 73% in 2030

HIV Patients will Face Increased Rates of NCDs as they Age

- Predicted burden of non-communicable diseases (NCDs) in HIV patients modeled for 2010-2030
- NCDs include:
  - Cardiovascular disease (hypertension, hypercholesterolemia, myocardial infarction, stroke)
  - Diabetes
  - Chronic kidney disease
  - Osteoporosis
  - Non-AIDS malignancies

Aging-associated noncommunicable comorbidities (AANCC) include: HTN, MI, PAD, CVA, angina, DM2, COPD, CKD, non-AIDS cancer, fracture/osteoporosis.

Schouten CID 2014.
Heart Trouble Early and Often in H.I.V. Patients

By DONALD G. MCNEIL JR.  JUNE 18, 2012

Mike Godfrey was 19 when he found out he had H.I.V.
He was 29 when he began antiretroviral therapy.
He was 43 when he had a heart attack.

“I felt fluttery,” he said. “Weird and flustered.” He ignored it. A week later, it got worse, and this time he felt something in his chest, too. He was too stupid to call an ambulance. He walked a few blocks and went to the hospital.

Mr. Godfrey’s experience exemplifies what AIDS specialists have long suspected: People infected with H.I.V. have heart attacks and have them earlier in life than do patients whose infection is well suppressed and whose AIDS drugs are at higher risk.
# HIV and Risk of Acute Myocardial Infarction

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Population</th>
<th>N (HIV)</th>
<th>Primary Result</th>
<th>Effect Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Klein</td>
<td>2002</td>
<td>Kaiser</td>
<td>4159</td>
<td>↑ MI and CHD in HIV vs. control</td>
<td>1.5 (MI) 1.7 (CHD)</td>
</tr>
<tr>
<td>Currier</td>
<td>2003</td>
<td>CA Medicaid</td>
<td>28513</td>
<td>↑ CHD in HIV (age 18-33) vs. control</td>
<td>2.06</td>
</tr>
<tr>
<td>Triant</td>
<td>2007</td>
<td>Partners</td>
<td>3851</td>
<td>↑ MI in HIV vs. control</td>
<td>1.75</td>
</tr>
<tr>
<td>Obel</td>
<td>2007</td>
<td>Danish cohort</td>
<td>3953</td>
<td>↑ CHD in HIV (on ART) vs. control</td>
<td>2.12</td>
</tr>
<tr>
<td>Lang</td>
<td>2010</td>
<td>FHDH</td>
<td>74958</td>
<td>↑ MI in HIV vs. 3 population registries</td>
<td>1.5</td>
</tr>
<tr>
<td>Durand</td>
<td>2011</td>
<td>Quebec</td>
<td>7053</td>
<td>↑ MI in HIV vs. 4:1 matched control</td>
<td>2.11</td>
</tr>
<tr>
<td>Freiberg</td>
<td>2013</td>
<td>VA</td>
<td>27350</td>
<td>↑ MI in HIV vs. 2:1 matched control</td>
<td>1.48</td>
</tr>
<tr>
<td>Silverberg</td>
<td>2014</td>
<td>Kaiser</td>
<td>22081</td>
<td>↑ MI and CHD in HIV vs. 10:1 matched control</td>
<td>1.4</td>
</tr>
</tbody>
</table>

CVD Incidence by Gender and Age

- Increased relative risk in patients traditionally considered low risk
- May reflect the different distribution of CVD risk factors in HIV

Triant CROI 2014, abstract 738.
Hospitalization Rates by Diagnosis

- CVD admissions surpassed AIDS-defining illnesses in 4 U.S. clinics
- In military cohort, higher nadir/recent CD4 count associated with decreased risk all-cause hospitalization
CVD Mortality in HIV

Morlat AIDS 2014.
Outline

• Epidemiology of HIV and CVD
• Pathophysiology of HIV and CVD
  – Role of traditional risk factors and ART
  – Role of inflammation/immune activation
• Management of CVD in HIV
  – CVD risk prediction
  – CVD prevention
    • Novel risk factors
    • Traditional risk factors
Pathophysiology of HIV-Associated CVD

- Early (1990s-early/mid 2000s) understanding of heightened CVD risk
- Traditional CVD risk factors
  - Elevated rates observed in HIV
- ART
  - Select PIs
  - Abacavir (debated)
  - Effects on CVD risk factors versus other effects

Diagram:
- ART
  - CVD
    - GENETICS
  - DYSLIPIDEMIA
  - DIABETES
  - HYPERTENSION
  - SMOKING
Traditional CVD Risk Factors in HIV

Smoking in HIV

- Heightened rates
  - 56% (D:A:D)
  - 54% (SFGH)
  - 47% (US cohort)
  - 69% (French cohort)
- 85% lifetime history
- Significantly higher than non-HIV patients

Impact of Smoking in HIV

- Treated HIV patients may lose more life years through smoking than HIV
- Excess mortality with smoking increases with age
- Increased incidence rate ratio for AMI for smokers
- Quitting smoking decreases AMI event rates
  - IRR 3.73 <1 year since quitting
  - IRR 2.07 >3 years since quitting

AMI Incidence Increased with ART/Pis

- D:A:D - prospective observational cohort of 33,347 patients
- Relative risk of AMI 1.16 per year ART exposure
- PIs but not NNRTIs conferred increased risk

Traditional Risk Factors Do Not Explain CVD Risk in HIV

- **Increased AMI risk persists despite accounting for established CVD risk factors and ART use**
  - Traditional risk factors only account for 10-25% of risk in large cohorts
  - Persistent 40-80% increased risk in HIV-infected patients

- **Persistently increased risk thought to be driven by HIV-specific inflammation and immune activation, supported by extensive data**
  - SMART study
  - Biomarkers of inflammation linked to surrogate markers of CVD
  - Vulnerable plaque and arterial inflammation linked to monocyte activation
  - Low CD4 and high viral load linked to CVD events

- **In treated and suppressed HIV patients:**
  - Reduced but persistent inflammation/immune activation and CVD risk
SMART, Inflammation and CVD

- SMART study showed increased CVD event rates in drug conservation (episodic treatment) vs. viral suppression (continuous treatment) group
  - HR=1.57, P=0.05
  - Primary endpoint recurrent OI/death

- Inflammatory markers IL-6 and d-dimer increased 1 month after treatment interruption in SMART
- Baseline hsCRP, IL-6, and d-dimer strongly correlated to overall mortality

Immune Activation Linked to Vascular Lesions

- Increased immune activation in HIV women vs. controls
- Higher frequencies of activated T cells associated with carotid artery lesions within HIV patients
- Effect present even among virologically suppressed patients

Kaplan JID 2011.
Decreased CD4 Count Linked to CVD

- CD4 <500 associated with CVD events independent of CVD risk factors or ART
- CD4 <200 independently associated with AMI with OR of 1.74

Lichtenstein CID 2010; Triant JAIDS 2010.
Increased HIV RNA Linked to CVD

- Increased HIV viral load linked to ischemic stroke events
- Detectable viral load (>50) associated with increased risk of myocardial infarction with odds ratio of 1.51

Chow JAIDS 2014; Lang CID 2012.
Decreased CD4 Count and HIV Viremia Independently Increase CVD Risk

- AMI risk in recent VA study by CD4 and HIV RNA status
- HIV RNA $\geq 500$ and CD4 $< 200$ associated with increased AMI risk
- AMI risk persists in patients achieving virologic suppression

**Table 4. Time-Updated Analyses Assessing the Association of HIV-1 RNA and CD4 Cell Count Values and the Risk of AMI in Separate Models**

<table>
<thead>
<tr>
<th>Category</th>
<th>HR (95% CI)</th>
<th>P Value $^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV-1 RNA Uninfected</td>
<td>1 [Reference]</td>
<td></td>
</tr>
<tr>
<td>$\geq 500$</td>
<td>1.75 (1.40-2.18)</td>
<td>.05</td>
</tr>
<tr>
<td>$&lt; 500$</td>
<td>1.39 (1.17-1.66)</td>
<td></td>
</tr>
<tr>
<td>CD4 cell count Uninfected</td>
<td>1 [Reference]</td>
<td></td>
</tr>
<tr>
<td>$&lt; 200$</td>
<td>1.88 (1.46-2.40)</td>
<td>.04</td>
</tr>
<tr>
<td>$\geq 200$</td>
<td>1.43 (1.21-1.69)</td>
<td></td>
</tr>
</tbody>
</table>

Freiberg JAMA IM 2013.
Pathophysiology of HIV-Associated CVD
Outline

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    • Traditional risk factors
HIV-Specific CVD Guidelines

Guidelines for the Evaluation and Management of Dyslipidemia in Human Immunodeficiency Virus (HIV)–Infected Adults Receiving Antiretroviral Therapy: Recommendations of the HIV Medicine Association of the Infectious Disease Society of America and the Adult AIDS Clinical Trials Group

European AIDS Clinical Society (EACS) guidelines on the prevention and management of metabolic diseases in HIV*

Primary Care Guidelines for the Management of Persons Infected With HIV: 2013 Update by the HIV Medicine Association of the Infectious Diseases Society of America

New Cardiovascular Risk Guidelines Add Complexity to HIV-Specific Risk Prediction

- New ACC/AHA guidelines on CVD risk estimation released in 2013
- New CVD risk prediction equation employed (Pooled cohorts equation)
- Reports of overestimation of risk in the general population

Goff Circulation 2014.
2013 ACC/AHA Calculator Overestimates Risk

- Primary prevention cohorts
- ACC/AHA risk prediction algorithm systematically overestimated observed risk in general population
- Degree of risk overestimation 75-150%
- Overestimation observed by guideline developers in 2 additional external validation cohorts
- Studies from Women’s Health Study and MESA also observed overestimation of risk

CVD Risk Prediction in HIV

- CVD risk prediction tools designed for the general population may underestimate risk in HIV
  - Novel HIV-specific risk factors not accounted for
- Framingham Risk Score underestimates risk in HIV (AMI and stroke)
- HIV-specific risk prediction tool developed but not externally validated

FRS and ACC/AHA Underestimate CVD Risk in HIV

- Partners HIV longitudinal cohort, 2239 patients
- ACC/AHA risk score and FRS underestimate CVD risk in HIV
  - 5-year observed versus predicted event rates

Regan CROI 2015, abstract 751.
CVD Risk Prediction in HIV: Strategies

• Unknown accuracy of FRS and new ACC/AHA calculator in HIV
• New ACC/AHA risk score overestimates risk in general population but may underestimate risk in HIV
• In HIV, risk scores discordant in approximately 19%
  – FRS assigns low risk and ACC/AHA high risk in 99% of discordant cases

Clinical strategy
• Consider calculating both Framingham Risk Score and ACC/AHA risk score
• Patients in high-risk category by at least one score (>10% for FRS and >7.5% for ACC/AHA) merit:
  – Suppressive ART if not already treated
  – Strong consideration of statin
  – Aggressive CVD risk factor reduction

Preliminary data, Partners HIV cohort.
ART and CVD Risk

• Paradigm shift in role of ART in relation to CVD risk in HIV

• 2010 IAS-USA HIV treatment guidelines
  – Recommended initiation of ART specifically for patients with high cardiovascular risk regardless of CD4 count
  – Endorse aggressive management of modifiable CVD risk factors

• 2012 DHHS HIV treatment guidelines
  – Recommend antiretroviral therapy for all HIV-infected individuals
  – The recommendation to initiate therapy at CD4 count >500 cells/mm3 (BIII) is based on growing awareness that untreated HIV infection or uncontrolled viremia may be associated with development of many non-AIDS defining diseases, including cardiovascular disease (CVD), kidney disease, liver disease, neurologic complications, and malignancy

ART and CVD Risk: Strategies

• Treat HIV to reduce CVD risk

• CVD-related benefit from virologic suppression and immune reconstitution achieved by treating HIV thought to outweigh possible proatherogenic effects of individual medications

• START trial was first RCT to assess rates of comorbidities including CVD by early versus deferred ART initiation

Clinical strategy

• Treat HIV to reduce inflammation, immune activation, and associated cardiovascular risk

• Consider underlying CVD risk when selecting specific drugs, as individual ART medications may have varying risk

Thompson JAMA 2010; clinicaltrials.gov NCT00867048.
Statins in HIV

- **Dyslipidemia in HIV:**
  - Prevalent, with higher rates than control patients
  - Distinctive pattern of low HDL and high TG
  - May be more difficult to treat with statins
  - Drug interactions with ARVs important

- **Statins are mainstay of treatment and may reduce both traditional and non-traditional risk factors**

- **Statins in HIV:**
  - Effectively lower LDL
  - Decrease immune activation (T cell and monocyte)
  - Contribute to immune reconstitution independent of ART
  - Decreased mortality in HIV observational cohort

Paradigm Shift in Cholesterol Treatment for General Population

- New cholesterol/statin guidelines released November 2013
- Replaced NCEP ATP-III
- Controversial new approach to treating cholesterol

Stone Circulation 2014.
2013 ACC/AHA Cholesterol Treatment Guidelines

• Statin initiation: 4 major benefit groups
  – Clinical ASCVD
  – LDL ≥ 190 mg/dL
  – DM age 40-75
  – Estimated 10-year ASCVD risk ≥ 7.5%

• No LDL treatment targets

• No non-statin therapies

• New risk calculator to estimate 10-yr ASCVD risk

• Recommend increased statin treatment in general population
Increased Statin Use in the General Population with New Guidelines

- 12.8 million additional adults eligible for statin therapy
  - 43 → 56 million US adults
- Increase driven by 10-year predicted risk
- Greatest increase in men and older patients

Pencina NEJM 2014.
2013 ACC/AHA Cholesterol Treatment Guidelines

Focused on fixed dose statin RCTs to reduce atherosclerotic CVD risk
3 years deliberation

Why treat-to-target was abandoned
- Inadequate RCT data on what target
- Unknown magnitude of ASCVD risk reduction
- Potential adverse effects from multidrug therapy

Critique
- Scope limited to RCTs
- Abandonment of LDL targets
- Increase in patients eligible for statins
- Discordance of risk calculators

Figure 2. Major recommendations for statin therapy for ASCVD prevention

Stone Circulation 2014.
Limitations of New Cholesterol Guidelines in HIV

Future Updates to the Blood Cholesterol Guideline

CQs for future guidelines could examine:

1. the treatment of hypertriglyceridemia;
2. use of non-HDL-C in treatment decision-making;
3. whether on-treatment markers such as Apo B, Lp(a), or LDL particles are useful for guiding treatment decisions;
4. the best approaches to using noninvasive imaging for refining risk estimates to guide treatment decisions;
5. how lifetime ASCVD risk should be used to inform treatment decisions and the optimal age for initiating statin therapy to reduce lifetime risk of ASCVD;
6. subgroups of individuals with heart failure or undergoing hemodialysis that might benefit from statin therapy;
7. **long-term effects of statin-associated new onset diabetes and management**
8. **efficacy and safety of statins in patient groups excluded from RCTs to date (e.g., HIV positive or solid organ transplant); and**
9. role of pharmacogenetic testing.

8. Limitations

Exceeding the risk of adverse events or drug-drug interactions. Clinician judgment is especially important for several patient groups for whom the RCT evidence is insufficient for guiding clinical recommendations. These patient groups include younger adults (<40 years of age) who have a low estimated 10-year ASCVD risk, but a high lifetime ASCVD risk based on single strong factors or multiple risk factors. Other groups include those with serious comorbidities and increased ASCVD risk (e.g., individuals with HIV, rheumatologic or inflammatory diseases, or who have undergone a solid organ transplant). This guideline encourages clinicians to use clinical judgment in these situations weighing potential benefits, adverse effects, drug-drug interactions and patient preferences.
Further Challenges in Applying New Cholesterol Guidelines to HIV

Table 5. High- Moderate- and Low-Intensity Statin Therapy (Used in the RCTs reviewed by the Expert Panel)*

<table>
<thead>
<tr>
<th>High-Intensity Statin Therapy</th>
<th>Moderate-Intensity Statin Therapy</th>
<th>Low-Intensity Statin Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily dose lowers LDL–C on average, by approximately ≥50%</td>
<td>Daily dose lowers LDL–C on average, by approximately 30% to &lt;50%</td>
<td>Daily dose lowers LDL–C on average, by &lt;30%</td>
</tr>
<tr>
<td><strong>Atorvastatin (40†)–80 mg</strong></td>
<td><strong>Atorvastatin 10 (20) mg</strong></td>
<td><strong>Simvastatin 10 mg</strong></td>
</tr>
<tr>
<td><strong>Kosuvastatin 20 (40) mg</strong></td>
<td><strong>Kosuvastatin (5) 10 mg</strong></td>
<td><strong>Pravastatin 10–20 mg</strong></td>
</tr>
<tr>
<td><strong>Simvastatin 20–40 mg†</strong></td>
<td><strong>Pravastatin 40 (80) mg</strong></td>
<td><strong>Lovastatin 20 mg</strong></td>
</tr>
<tr>
<td><strong>Lovastatin 40 mg</strong></td>
<td></td>
<td><strong>Fluvastatin 20–40 mg</strong></td>
</tr>
<tr>
<td><strong>Fluvastatin XL 80 mg</strong></td>
<td></td>
<td><strong>Pitavastatin 1 mg</strong></td>
</tr>
<tr>
<td><strong>Fluvastatin 40 mg bid</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Pitavastatin 2–4 mg</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Dose-adjustment in HIV (with PIs)

Contraindicated in HIV (with PIs)

Awaiting further study in HIV

Stone Circulation 2014.
Statins in HIV: Strategies

• HIV patients excluded from RCTs
• Different mechanism of CVD
• Different typical cholesterol profile
• Unclear role of new ACC/AHA risk calculator
• Statin intensity definition not directly applicable

Clinical strategy
• In HIV, still likely that statins will be effective in risk groups outlined by guidelines
  – Traditional risk factors remain important in HIV
  – Risk scores may underestimate risk in HIV

Clinical strategy based on expert opinion.
Dyslipidemia in HIV: Strategies

Clinical strategy
• Check fasting lipids
  – At HIV diagnosis
  – Prior to and within 1-3 months after starting or changing ART
  – Every 6-12 months
• Consider starting statin based on ACC/AHA cholesterol guidelines
• Consider therapy with:
  – Statin if LDL above ATPIII goal or TG 200-500 with elevated non-HDL
  – Fibrate if TG>500
• 2013 HIV primary care guidelines includes detailed statin-ARV interaction chart
• Await REPRIEVE results

<table>
<thead>
<tr>
<th>Statin</th>
<th>Level w/ PI</th>
<th>Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pravastatin</td>
<td>--</td>
<td>Can use safely</td>
</tr>
<tr>
<td>Atorvastatin</td>
<td>↑</td>
<td>Use with caution/low dose</td>
</tr>
<tr>
<td>Simvastatin</td>
<td>↑↑</td>
<td>Contraindicated</td>
</tr>
<tr>
<td>Lovastatin</td>
<td>↑↑</td>
<td>Contraindicated</td>
</tr>
<tr>
<td>Rosuvastatin</td>
<td>↑</td>
<td>Use with caution/low dose</td>
</tr>
<tr>
<td>Pitavastatin</td>
<td>?</td>
<td>Accruing data</td>
</tr>
</tbody>
</table>

## Aspirin for Primary Prevention of CVD

<table>
<thead>
<tr>
<th>Population</th>
<th>Men Age 45–79 Years</th>
<th>Women Age 55–79 Years</th>
<th>Men Age &lt;45 Years</th>
<th>Women Age &lt;55 Years</th>
<th>Men and Women Age ≥80 Years</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Recommendation</strong></td>
<td>Encourage aspirin use when potential CVD benefit (MIs prevented) outweighs potential harm of GI hemorrhage</td>
<td>Encourage aspirin use when potential CVD benefit (strokes prevented) outweighs potential harm of GI hemorrhage</td>
<td>Do not encourage aspirin use for MI prevention</td>
<td>Do not encourage aspirin use for stroke prevention</td>
<td>No Recommendation</td>
</tr>
<tr>
<td><strong>Grade</strong></td>
<td>Grade: A</td>
<td>Grade: D</td>
<td></td>
<td></td>
<td>Grade: I (insufficient evidence)</td>
</tr>
</tbody>
</table>

Shared decision making is strongly encouraged with individuals whose risk is close to (either above or below) the estimates of 10-year risk levels indicated below. As the potential CVD benefit increases above harms, the recommendation to take aspirin should become stronger.

To determine whether the potential benefit of MIs prevented (men) and strokes prevented (women) outweighs the potential harm of increased GI hemorrhage, both 10-year CVD risk and age must be considered.

<table>
<thead>
<tr>
<th>Risk Level at Which CVD Events Prevented (Benefit) Exceeds GI Harms</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td><strong>10-Year CHD Risk</strong></td>
<td><strong>Age</strong></td>
</tr>
<tr>
<td>45–59 years</td>
<td>≥4%</td>
<td>55–59 years</td>
</tr>
<tr>
<td>60–69 years</td>
<td>≥9%</td>
<td>60–69 years</td>
</tr>
<tr>
<td>70–79 years</td>
<td>≥12%</td>
<td>70–79 years</td>
</tr>
</tbody>
</table>

The table above applies to adults who are not taking NSAIDs and who do not have upper GI pain or a history of GI ulcers. NSAID use and history of GI ulcers increase the risk for serious GI bleeding events considerably and should be considered in determining the balance of benefits and harms.

NSAID use combined with aspirin use approximately quadruples the risk for serious GI bleeding events compared with the risk with aspirin use alone. The rate of serious bleeding in aspirin users is approximately 2 to 3 times greater in patients with a history of GI ulcers.

Rates of ASA Use in HIV versus Controls by CVD Risk Group

Prevalence of ASA Use in Low CHD Risk

Prevalence of ASA Use in High CHD Risk*

Suchindran OFID 2014.
ASA Does Not Improve Immune Activation or Endothelial Function

- Can antiplatelet agents decrease immune activation in HIV patients?
- Preliminary data showed ASA for 1 week decreased immune activation
- ACTG A5331
- RCT of 12 weeks ASA (300 vs 100 vs placebo)
- N ~ 40 per arm
- No effect of ASA on decreasing:
  - sCD14, marker of monocyte activation (primary outcome)
  - sCD163 (increase in 300mg arm)
  - endothelial function by FMD
  - Additional markers of inflammation and immune activation

Data do not support use of ASA as anti-inflammatory in HIV
Additional investigation of platelet activation planned

Aspirin in HIV: Strategies

- ASA may modulate traditional and novel CVD risk factors
- ASA significantly underused in HIV patients meeting criteria for its use
  - 31% met criteria yet 1.6% received ASA
  - Less than 1 in 5 received ASA in US clinic
- ASA use rates lower in HIV versus non-HIV
- Unclear role of ASA in primary prevention of AMI or stroke for HIV patients

Clinical strategy
- Reasonable to use ASA if known CVD or high predicted CVD risk (ATPIII or ACC/AHA) and low bleeding risk
- Should be used in combination with other CVD risk reduction methods
- Interventions targeted at HIV-specific inflammation and immune activation may better reflect pathogenesis and reduce CVD

Novel Interventions Targeting Inflammation and Immune Activation

- ART treatment intensification
- Methotrexate
- CCR5 antagonists
- Rifaximin
- Sevelamer
- Mesalamine
- Pentoxifylline
- Hydroxychloroquine

Smoking Cessation in HIV: Strategies

• Priority for all HIV-infected patients
• HIV patients cited as priority in 2008 clinical practice guideline *Treating Tobacco Use and Dependence*
• HIV-specific smoking cessation interventions differ in efficacy

Clinical strategy
• Apply guidelines for general population to all HIV smokers
  – Routine screening integrated into HIV primary care
  – Strong, brief, intensive repeated counseling
  – Pharmacologic interventions (varenicline safe and effective in HIV)
• Consider systematic approaches to identify HIV smokers and ensure smoking cessation interventions applied

DM and HTN Management in HIV: Strategies

• Check fasting glucose or HbA1C at HIV diagnosis, 1-3 months after starting or changing ART, and every 6-12 months
• HbA1C may be used for screening
  – Consider cutoff 5.8%
  – HbA1C may underestimate glycemia in HIV
• Check HbA1C every 6 months in DM
• Lifestyle intervention recommended
  – Shown to decrease HbA1C for HIV patients

• Check blood pressure annually
• Follow existing JNC8 (2014 Hypertension Guideline) for general population
  – No HIV-specific guidelines
• Consider drug interactions
  – Use of some calcium-channel blockers contraindicated with protease inhibitors

Prevention of HIV-Associated CVD

ART

ANTIBOODY RESPONSE TO IMMUNE ACTIVATION

VIRAL REPLICATION

INFLAMMATION

MICROBIAL TRANSLOCATION

DYSLIPIDEMIA

DIABETES

HYPERTENSION

SMOKING

GENETICS

PREVENT CVD

ANTI-INFLAMMATORIES AND IMMUNE MODULATORS

STATINS

TRADITIONAL RISK FACTOR MODIFICATION

STATINS

SMOKING CESSATION

LIFESTYLE

COUNSEL
Management of CVD in HIV: Key Questions

• Are the new ACC/AHA risk calculator and cholesterol guidelines applicable and accurate in HIV?
• What is the role for statins in HIV?
• Will tailored immunomodulatory agents further decrease CVD risk in HIV?
• Are CVD prevention strategies similar in key subgroups, including HIV-infected women and patients in resource-limited settings?
• Should HIV be considered a cardiovascular risk equivalent?
• Should ART be considered an intervention to reduce cardiovascular risk?
Management of CVD in HIV: Key Principles

• Significant impact of CVD in HIV populations anticipated
• Pathophysiology driven in large part by HIV-related immunologic and inflammatory changes
• Current treatment paradigms do not reflect this pathophysiology
• Recommended strategies
  – Build CVD risk assessment into practice
  – Manage traditional CVD risk factors aggressively (e.g. smoking)
  – Start appropriate statin if candidate by general population guidelines
  – Low threshold for diagnostic workup in traditionally low-risk groups
  – Treat HIV to reduce CVD risk
• Intensity and consistency of HIV care provide opportunity to prevent and manage chronic disease complications
Case

• 46 year old man diagnosed with HIV 3 years ago
• CD4 800 and HIV RNA undetectable on abacavir/lamivudine/darunavir/ritonavir
• No other significant medical history
• Smokes one pack per day despite numerous quit attempts
• BP 126/74
• TC 211, LDL 147, HDL 35, TG 234
Information about your risk score:

Age: 46
Gender: male
Total Cholesterol: 211 mg/dL
HDL Cholesterol: 35 mg/dL
Smoker: Yes
Systolic Blood Pressure: 126 mm/Hg
On medication for HBP: No
Risk Score*: 14%

* Means 14 of 100 people with this level of risk will have a heart attack in the next 10 years.

* Your risk score was calculated using an equation. Other NCEP products, such as printed ATP III materials, use a point system to determine a risk score that is close to the equation score.
## ACC/AHA Risk Score

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Units</th>
<th>Value</th>
<th>Acceptable range of values</th>
<th>Optimal values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>M (for males) or F (for females)</td>
<td>M</td>
<td>M or F</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>years</td>
<td>40</td>
<td>20-75</td>
<td></td>
</tr>
<tr>
<td>Race</td>
<td>AA (for African Americans) or WH (for whites or others)</td>
<td>Y/R</td>
<td>AA or WH</td>
<td></td>
</tr>
<tr>
<td>Total Cholesterol</td>
<td>mg/dL</td>
<td>211</td>
<td>130-220</td>
<td>170</td>
</tr>
<tr>
<td>HDL-Cholesterol</td>
<td>mg/dL</td>
<td>36</td>
<td>20-100</td>
<td>50</td>
</tr>
<tr>
<td>Systolic Blood Pressure</td>
<td>mm Hg</td>
<td>125</td>
<td>90-200</td>
<td>110</td>
</tr>
<tr>
<td>Treatment for High Blood Pressure</td>
<td>Y (for yes) or N (for no)</td>
<td>N</td>
<td>Y or N</td>
<td>N</td>
</tr>
<tr>
<td>Diabetes</td>
<td>Y (for yes) or N (for no)</td>
<td>N</td>
<td>Y or N</td>
<td>N</td>
</tr>
<tr>
<td>Smoker</td>
<td>Y (for yes) or N (for no)</td>
<td>Y</td>
<td>Y or N</td>
<td>N</td>
</tr>
</tbody>
</table>

**Your 10-Year ASCVD Risk (%)**

- 6.4%

**10-Year ASCVD Risk (%) for Someone Your Age with Optimal Risk Factor Levels (shown above in column E)**

- 1.3%

**Your Lifetime ASCVD Risk* (%)**

- 50.0%

**Lifetime ASCVD Risk (%) for Someone at Age 50 with Optimal Risk Factor Levels (shown above in column E)**

- 5.0%

*This is the lifetime ASCVD risk for an individual at age 50 years with your risk factor levels. In rare cases, 10-year risks may exceed lifetime risks given that the estimates come from different approaches. While 10-year risk estimates are derived from methods and data using continuous variables, the reported estimate of lifetime risk is based on assigning each person into one of 5 mutually exclusive sex-specific groups, as per Lloyd-Jones et al., Circulation 2010.*

*For patients and the public:* This is the 10-Year and Lifetime ASCVD Risks
Case

• Which intervention would you prioritize to reduce his cardiovascular risk?
  A. Switch off abacavir
  B. Assist in quitting smoking
  C. Start a statin
  D. Switch off ritonavir
  E. Start ASA
• View results in your browser: https://api.cvent.com/polling/v1/api/polls/sp-b6v7t9
Case

- He starts to exercise and quits smoking.
- TG 201, LDL 127, HDL 35, TG 194
Information about your risk score:

| Age:       | 46          |
| Gender:    | male        |
| Total Cholesterol: | 201 mg/dL |
| HDL Cholesterol: | 35 mg/dL |
| Smoker:    | No          |
| Systolic Blood Pressure: | 126 mm/Hg |
| On medication for HBP: | No |

Risk Score*: 4%

*Means 4 of 100 people with this level of risk will have a heart attack in the next 10 years.

* Your risk score was calculated using an equation. Other NCEP products, such as printed ATP III materials, use a point system to determine a risk score that is close to the equation score.
# ACC/AHA Risk Score

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Units</th>
<th>Value</th>
<th>Acceptable range of values</th>
<th>Optimal values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td>M or F</td>
<td>M or F</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>years</td>
<td>45</td>
<td>20-79</td>
<td></td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td>AA or WH</td>
<td>AA or WH</td>
<td></td>
</tr>
<tr>
<td>Total Cholesterol</td>
<td>mg/dL</td>
<td>261</td>
<td>130-220</td>
<td>170</td>
</tr>
<tr>
<td>HDL-Cholesterol</td>
<td>mg/dL</td>
<td>35</td>
<td>20-100</td>
<td>50</td>
</tr>
<tr>
<td>Systolic Blood Pressure</td>
<td>mm Hg</td>
<td>126</td>
<td>90-140</td>
<td>110</td>
</tr>
<tr>
<td>Treatment for High Blood Pressure</td>
<td>Y or N</td>
<td>N</td>
<td>Y or N</td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td></td>
<td>Y or N</td>
<td>Y or N</td>
<td></td>
</tr>
<tr>
<td>Smoker</td>
<td></td>
<td>Y or N</td>
<td>Y or N</td>
<td></td>
</tr>
</tbody>
</table>

Accepted ranges for non-Asian women: 201 mg/dL for cholesterol, 35 mg/dL for HDL cholesterol, 126 mm Hg for systolic blood pressure.

- **Your 10-Year ASCVD Risk (%)**
  - 3.4

- **10-Year ASCVD Risk (%) for Someone Your Age with Optimal Risk Factor Levels (shown above in column E)**
  - 1.3

- **Your Lifetime ASCVD Risk (%)**
  - 46.0

- **Lifetime ASCVD Risk (%) for Someone at Age 50 with Optimal Risk Factor Levels (shown above in column E)**
  - 5.0

*This is the lifetime ASCVD risk for an individual at age 50 years with your risk factor levels. In rare cases, 10-year risks may exceed lifetime risks given that the estimates come from different approaches. While 10-year risk estimates are derived from methods and data using continuous variables, the reported estimate of lifetime risk is based on assigning each person into one of 5 mutually exclusive sex-specific groups, as per Lloyd-Jones et al., Circulation.*

**For patients and the public:**
*This is the model.*
Case

Which intervention would you prioritize now to reduce his cardiovascular risk?

A. Switch off abacavir
B. Start a statin
D. Switch off ritonavir
E. Start ASA
• View results in your browser: https://api.cvent.com/polling/v1/api/polls/splhpga