ASCVD Risk Prediction to Guide Initial Statin Therapy for People with HIV

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Disclosures

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All relevant financial relationships have been mitigated.
50 years old
AIDS in 2002; on ART since
Nadir/Current CD4+ 20/600
BP 140/70 on amlodipine 10mg daily
LDL 100mg/dl on atorvastatin 40mg daily

50 years old
HIV-negative
BP 150/90
LDL 160mg/dl

50 years old
HIV+ 2010; on ART since
Nadir/Current CD4+ 600/1000
BP 120/70
LDL 100mg/dl on atorvastatin 40mg daily
Clinical case

- 59 yo man with HIV (CD4 800, VL UD on DTG/TDF/FTC) and avid smoker seen initially for palpitations. Work-up (echo, holter monitor) of his symptoms was unrevealing. He returns to clinic after a low-dose chest CT for lung cancer showed 3 vessel coronary calcification.

- Class II dyspnea on exertion, modest decrease in exercise tolerance

- Risk factors:
  - smoker (50 pack years, currently 1ppd) and
  - high cholesterol (Total 178, LDL 95, HDL 38)
  - Father had coronary bypass @ 60 (not technically “early”)

- Meds: DTG/TDF/FTC, atorvastatin 20, IM testosterone, albuterol

- BP 142/80

- Other Labs: nl chemistries, LFTs

- What to do next?
2018 ACC/AHA Cholesterol Guidelines

1. Clinical ASCVD
2. LDL > 190mg/dL
3. Diabetes Age 40-75
4. >7.5% estimated risk Age 40-75

- Very High Risk
- High Risk
- High dose statin
- Mod-high dose statin
- Consider additional risk factors and calcium score

Grundy et al, Circulation 2018
** ASCVD event defined as:
- Non-fatal MI
- coronary heart disease death
- stroke

<table>
<thead>
<tr>
<th>Current Age</th>
<th>59</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic Blood Pressure (mm Hg)</td>
<td>142</td>
</tr>
<tr>
<td>Diastolic Blood Pressure (mm Hg)</td>
<td>80</td>
</tr>
<tr>
<td>Total Cholesterol (mg/dL)</td>
<td>178</td>
</tr>
<tr>
<td>HDL Cholesterol (mg/dL)</td>
<td>38</td>
</tr>
<tr>
<td>LDL Cholesterol (mg/dL)</td>
<td>95</td>
</tr>
<tr>
<td>History of Diabetes?</td>
<td>✅ No</td>
</tr>
<tr>
<td>Smoker</td>
<td>✅ Yes</td>
</tr>
<tr>
<td>On Hypertension Treatment?</td>
<td>✅ Yes</td>
</tr>
<tr>
<td>On a Statin?</td>
<td>✅ Yes</td>
</tr>
<tr>
<td>On Aspirin Therapy?</td>
<td>✅ Yes</td>
</tr>
</tbody>
</table>
The ACC/AHA calculator may underestimate risk in Blacks despite including a race/ethnicity term.
5-yr risk of CVD = **8.24%**

CVD defined as:
Myocardial infarction, stroke, invasive coronary artery procedure (including coronary artery by-pass or angioplasty and carotid artery endarterectomy) or death from coronary heart disease

** The D:A:D (F) model is valid for HIV infected individuals aged 18-75 years, with cumulative NRTI exposure up to about 8-10 years, and PI exposure up to around 5-6 years.
5-yr risk of CVD = 8.07%

CVD defined as:
Myocardial infarction, stroke, invasive coronary artery procedure (including coronary artery by-pass or angioplasty and carotid artery endarterectomy) or death from coronary heart disease
Primary Prevention: Assess ASCVD Risk in Each Age Group
Emphasize Adherence to Healthy Lifestyle

Age 0-19 y
Lifestyle to prevent or reduce ASCVD risk
Diagnosis of familial hypercholesterolemia → statin

Age 20-39 y
Estimate lifetime risk to encourage lifestyle to reduce ASCVD risk
Consider statin if family history premature ASCVD and LDL-C ≥160 mg/dL (≥4.1 mmol/L)

Age 40-75 y
LDL-C ≥190 mg/dL (≥4.9 mmol/L)
No risk assessment; High-intensity statin (Class I)

Diabetes mellitus and age 40-75 y
Moderate-intensity statin (Class I)

Age >75 y
Clinical assessment, Risk discussion

Diabetes mellitus and age 40-75 y
Risk assessment to consider high-intensity statin (Class IIa)

ASCVD Risk Enhancers:
- Family history of premature ASCVD
- Persistently elevated LDL-C ≥160 mg/dL (≥4.1 mmol/L)
- Chronic kidney disease
- Metabolic syndrome
- Conditions specific to women (e.g., preeclampsia, premature menopause)
- Inflammatory diseases (e.g., rheumatoid arthritis, psoriasis, HIV)
- Ethnicity (e.g., South Asian ancestry)

Lipid/Biomarkers:
- Persistently elevated triglycerides (≥175 mg/dL, ≥2.0 mmol/L)

In selected individuals if measured:
- hs-CRP ≥2.0 mg/L
- Lp(a) levels >50 mg/dL or >125 nmol/L
- apoB ≥130 mg/dL
- Ankle-brachial index (ABI) <0.9

Risk discussion:
- <5% “Low Risk”
- 5% - <7.5% “Borderline Risk”
- ≥7.5% - <20% “Intermediate Risk”
- ≥20% “High Risk”

Risk discussion:
If risk enhancers present then risk discussion regarding moderate-intensity statin therapy (Class IIb)

Risk discussion:
If risk estimate + risk enhancers favor statin, initiate moderate-intensity statin to reduce LDL-C by 30% - 49% (Class I)

Risk discussion:
Initiate statin to reduce LDL-C ≥50% (Class I)

If risk decision is uncertain:
Consider measuring CAC in selected adults:
CAC = zero (lowers risk; consider no statin, unless diabetes, family history of premature CHD, or cigarette smoking are present)
CAC = 1-99 favors statin (especially after age 55)
CAC = 100+ and/or ≥75th percentile, initiate statin therapy

Grundy et al, Circulation 2018
### Recommendations for Adults With Chronic Inflammatory Disorders and HIV

Referenced studies that support recommendations are summarized in [Online Data Supplement 39](#).

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ila</td>
<td>B-NR</td>
<td>1. In adults 40 to 75 years of age with LDL-C 70 to 189 mg/dL (1.7 to 4.8 mmol/L) who have a 10-year ASCVD risk of 7.5% or higher, chronic inflammatory disorders and HIV are risk-enhancing factors and in risk discussion favor moderate-intensity statin therapy or high-intensity statin therapy (S4.5.5-1–S4.5.5-12).</td>
</tr>
<tr>
<td>Ila</td>
<td>B-NR</td>
<td>2. In patients with chronic inflammatory disorders or HIV, a fasting lipid profile and assessment of ASCVD risk factors can be useful as a) a guide to benefit of statin therapy and b) for monitoring or adjusting lipid-lowering drug therapy before and 4 to 12 weeks after starting inflammatory disease-modifying therapy or antiretroviral therapy (S4.5.5-12–S4.5.5-20).</td>
</tr>
<tr>
<td>Ila</td>
<td>B-NR</td>
<td>3. In adults with RA who undergo ASCVD risk assessment with measurement of a lipid profile, it can be useful to recheck lipid values and other major ASCVD risk factors 2 to 4 months after the patient’s inflammatory disease has been controlled (S4.5.5-21–S4.5.5-23).</td>
</tr>
</tbody>
</table>
* Very high-risk includes a history of multiple major ASCVD events or 1 major ASCVD event and multiple high-risk conditions

Grundy et al, Circulation 2018
<table>
<thead>
<tr>
<th>Major ASCVD Events</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recent ACS (within the past 12 mo)</td>
</tr>
<tr>
<td>History of MI (other than recent ACS event listed above)</td>
</tr>
<tr>
<td>History of ischemic stroke</td>
</tr>
<tr>
<td>Symptomatic peripheral arterial disease (history of claudication with ABI &lt;0.85, or previous revascularization or amputation (S4.1-39))</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>High-Risk Conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ≥65 y</td>
</tr>
<tr>
<td>Heterozygous familial hypercholesterolemia</td>
</tr>
<tr>
<td>History of prior coronary artery bypass surgery or percutaneous coronary intervention outside of the major ASCVD event(s)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
</tr>
<tr>
<td>Hypertension</td>
</tr>
<tr>
<td>CKD (eGFR 15-59 mL/min/1.73 m²) (S4.1-15, S4.1-17)</td>
</tr>
<tr>
<td>Current smoking</td>
</tr>
<tr>
<td>Persistently elevated LDL-C (LDL-C ≥100 mg/dL [≥2.6 mmol/L]) despite maximally tolerated statin therapy and ezetimibe</td>
</tr>
<tr>
<td>History of congestive HF</td>
</tr>
</tbody>
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*Very high-risk includes a history of multiple major ASCVD events or one major ASCVD event and multiple high-risk conditions.
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<tr>
<th>Risk Category</th>
<th>Criteria</th>
<th>Consider drug therapy Non-HDL-C LDL-C</th>
</tr>
</thead>
</table>
| Low           | 0-1 major risk factor                  | <190 mg/dl  
<160 mg/dl |
| Moderate      | 2 major risk factors (i.e. HIV + high BP only) | <160 mg/dl  
<130 mg/dl |
| High          | ≥ 3 major risk factors                | <130 mg/dl  
<100 mg/dl |
| Very High     | Known ASCVD OR Diabetes + ≥2 major risk factors | <100 mg/dl  
<70 mg/dl |

Major risk factors include: HIV, Age >45 men or >55 women, family history of early CAD, smoking, hypertension, low HDL-C. **HIV added as major risk factor by NLA Expert Panel in 2015.**
### National Lipid Association–Lipid Goals

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<tr>
<th>Risk Category</th>
<th>Criteria</th>
<th>Consider drug therapy Non-HDL-C LDL-C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>0–1 major risk factor, &lt;190 mg/dl</td>
<td>≥190 mg/dl</td>
</tr>
<tr>
<td>Moderate</td>
<td>2 major risk factors (i.e. HIV + high BP only), &lt;160 mg/dl</td>
<td>≥160 mg/dl</td>
</tr>
<tr>
<td>High</td>
<td>≥3 major risk factors, &lt;130 mg/dl</td>
<td>≥130 mg/dl</td>
</tr>
<tr>
<td>Very High</td>
<td>Known ASCVD OR Diabetes + ≥2 major risk factors, &lt;100 mg/dl</td>
<td>≥100 mg/dl</td>
</tr>
</tbody>
</table>

Non-HDL = Total – HDL

178 – 38 = **140**

Major risk factors include: HIV, Age >45 men or >55 women, family history of early CAD, smoking, hypertension, low HDL-C. **HIV added as major risk factor by NLA Expert Panel in 2015.**
Coronary Artery Calcium (CAC) Scoring

- Non-contrast, **ECG-gated** CT scan of the chest
- Different than CT angiography which requires IV contrast
- Result typically expressed as whole heart Agatston score
CAC scoring can improve assessment of absolute risk

<table>
<thead>
<tr>
<th>Calcium score</th>
<th>10-year risk for CVD event</th>
<th>Risk interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>&lt;1%</td>
<td>Very low</td>
</tr>
<tr>
<td>1-99</td>
<td>4%</td>
<td>Low</td>
</tr>
<tr>
<td>100-399</td>
<td>13%</td>
<td>Moderate</td>
</tr>
<tr>
<td>400 or greater</td>
<td>24%</td>
<td>High</td>
</tr>
</tbody>
</table>

www.uhhospitals.org. Data from MESA cohort study.
CAC and CTA provide additional prognostic information beyond traditional risk factors

- **Discrimination**—the ability to sort high vs. low risk—is significantly improved with cardiac CT data

- **C statistic (AUROC)**
  - RF alone 0.71
  - RF + CAC 0.82
  - RF + CAC + CTA 0.93
Case 1 – Additional work-up

• CAC score:
  - LAD 1004
  - LCx 41
  - RCA 445
  - Total 1490 (VERY High)

• Invasive coronary angiography
  - Proximal LAD 60%
  - Mid LAD 80%
  - Proximal-Mid RCA 80% + 90%
Initial Management

• Optimal medical management
  - ASA 81 (*We also added plavix after discussion of risk/benefit)
  - Statin: atorva 80
  - Beta blocker: metoprol 25 bid
  - ACE inhibitor: lisinopril 5mg
  - Calcium channel blocker: amlodipine 5mg

• Revascularization if symptoms poorly controlled
  - PCI vs. CABG?
Importance of shared decision making

• ASCVD risk assessment to inform the discussion of primary prevention strategies
  - Consider a decision support tool to aid comprehension: https://statindecisionaid.mayoclinic.org/

• Reinforce the importance of lifestyle factors

• Include patient costs of therapy in the discussion

• Make sure that the patient feels heard, has a chance to ask questions, and owns decisions that are made
Your decision was: to take high dose statins

**Current Risk of having a heart attack**

Risk for 100 people like you who do not medicate for heart problems

In your current situation you have 89 in 100 chances of no heart attack happening to you in the next 10 years.

Using ACC/AHA ASCVD Risk Calculator

**Future Risk of having a heart attack**

Risk for 100 people like you who do take high dose statins

By going forward with your decision you now have 93 in 100 chances of no heart attack happening to you in the next 10 years.

- no heart attack
- heart attack
- heart attack prevented by selected intervention

https://statindecisionaid.mayoclinic.org/
<table>
<thead>
<tr>
<th>Statin intensity</th>
<th>High Intensity</th>
<th>Moderate Intensity</th>
<th>Low Intensity</th>
</tr>
</thead>
<tbody>
<tr>
<td>LDL-C lowering†</td>
<td>≥50%</td>
<td>30%–49%</td>
<td>&lt;30%</td>
</tr>
<tr>
<td>Statins</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Atorvastatin (40 mg‡) 80 mg</td>
<td>Atorvastatin 10 mg (20 mg)</td>
<td>Simvastatin 10 mg</td>
</tr>
<tr>
<td></td>
<td>Rosuvastatin 20 mg (40 mg)</td>
<td>Rosuvastatin (5 mg) 10 mg</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Simvastatin 20–40 mg§</td>
<td></td>
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<tr>
<td></td>
<td>...</td>
<td>Pravastatin 40 mg (80 mg)</td>
<td>Pravastatin 10–20 mg</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Lovastatin 40 mg (80 mg)</td>
<td>Lovastatin 20 mg</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fluvastatin XL 80 mg</td>
<td>Fluvastatin 20 mg</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fluvastatin 40 mg BID</td>
<td>Fluvastatin 20–40 mg</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pitavastatin 1–4 mg</td>
<td></td>
</tr>
</tbody>
</table>
Cobicistat/PI interaction

• Start low and go slow
  - Start atorvastatin at 10mg and titrate to max dose of 40mg daily
  - Start rosvastatin at 10mg and titrate to max 20mg daily

• If compelling indication for high dose statin without worrying about drug interactions, consider ART switch

• If ART cannot be switched and not willing to use atorvastatin or rosvastatin, then consider pitavastatin (if insurance will cover) or pravastatin (cheap, generic alternative)
Clinical Pearls

• Initial risk-stratification for PLHIV is to use a risk calculator (e.g. ACC/AHA pooled cohorts estimator) to estimate 10-year risk of CVD event
  - Why? Because magnitude of absolute risk reduction depends on baseline absolute risk
  - I favor the ACC/AHA estimator in US populations

• Cardiac CT is emerging as the gold standard for imaging subclinical disease when further risk stratification is needed
  - CAC scoring provides good information, is typically cheaper, and does not require IV contrast
  - CT angiography is better able to define the anatomy