AETC AIDS Education & Training Center Program Mountain West

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

Chris Longenecker, MD
Director, HIV-Cardiology Clinic
Harborview Medical Center
Associate Professor of Medicine
University of Washington

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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

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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?

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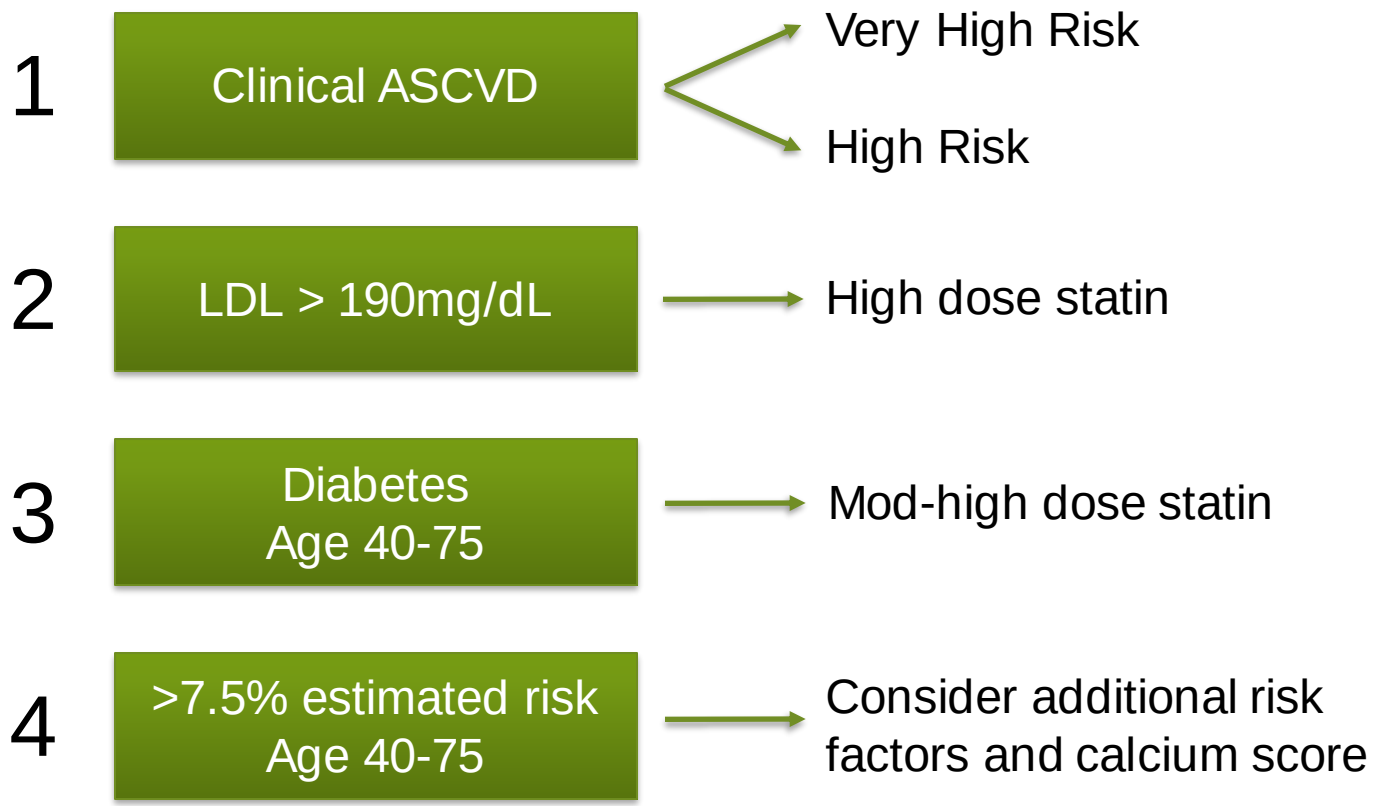
2018 ACC/AHA Cholesterol Guidelines



Grundy et al, Circulation 2018

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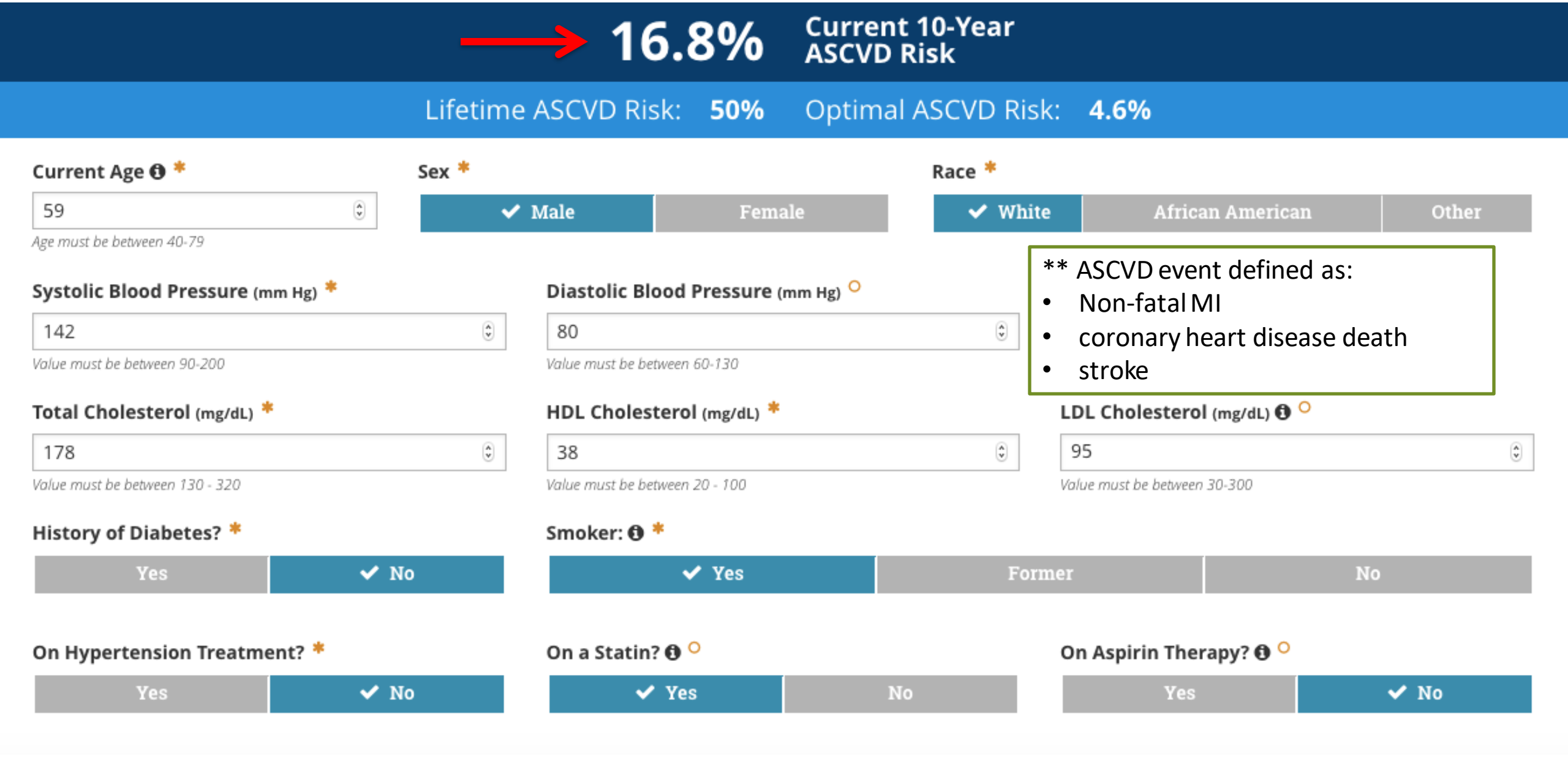

http://tools.acc.org/ascvd-risk-estimator-plus

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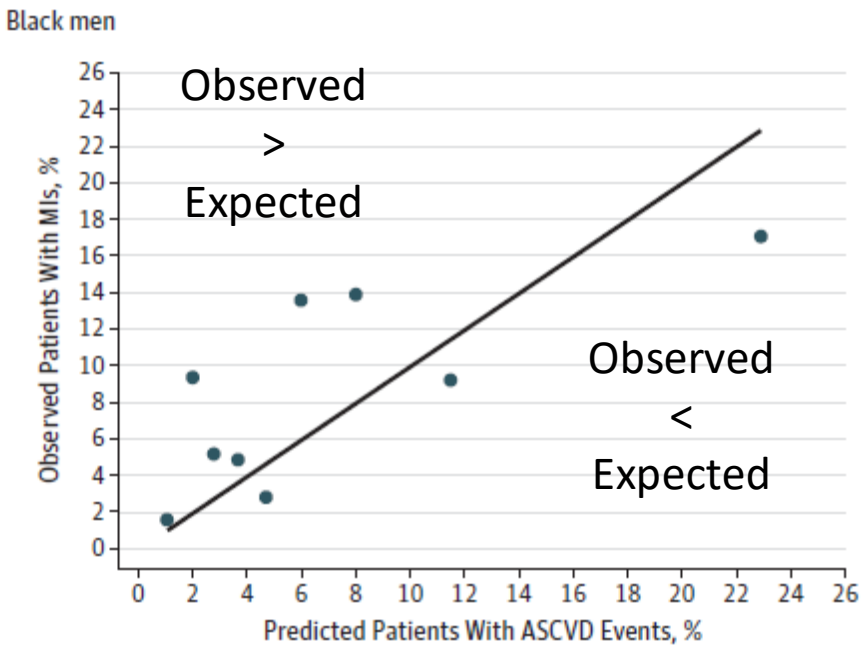
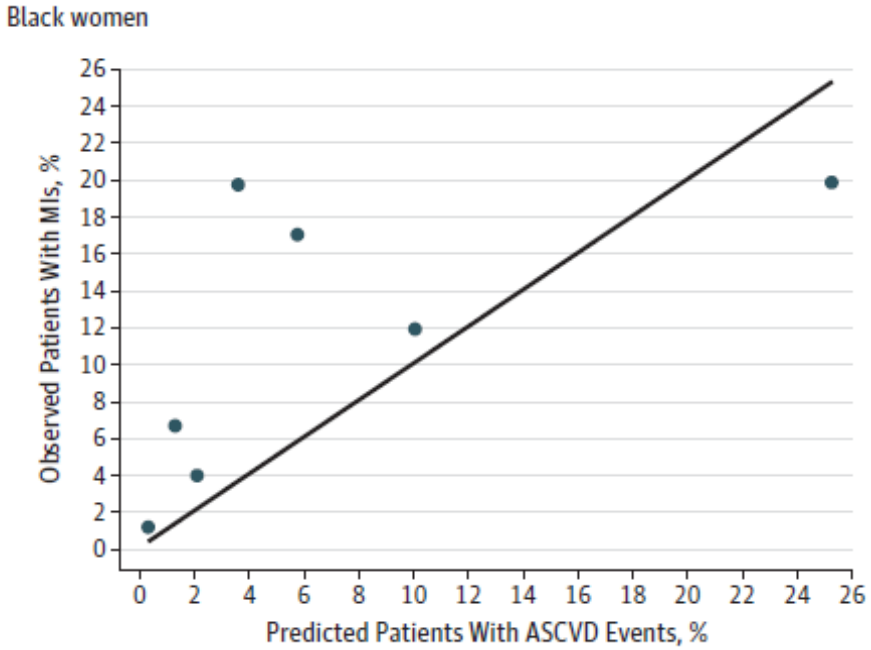
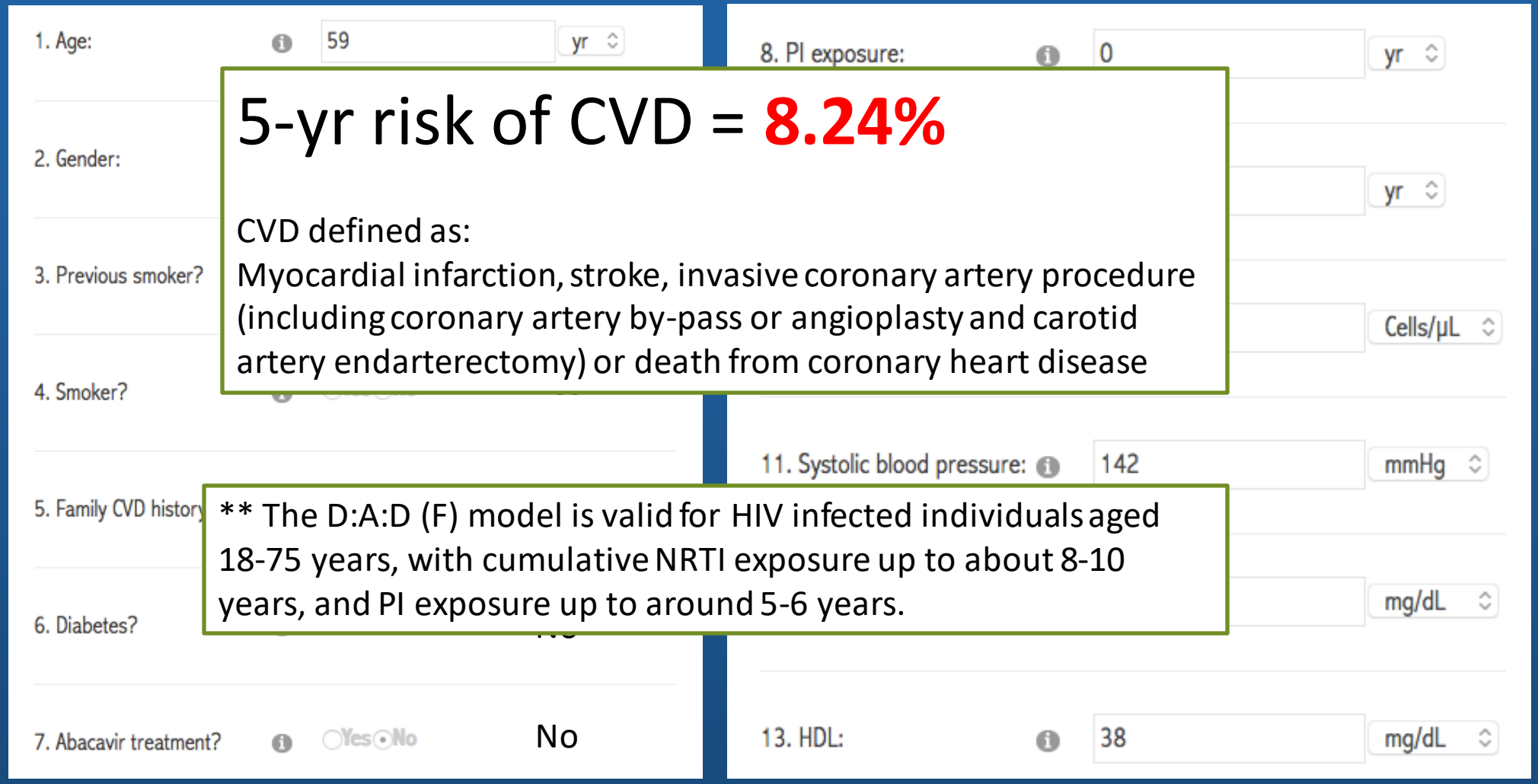
The ACC/AHA calculator may underestimate risk in Blacks despite including a race/ethnicity term





Feinstein et al, JAMA Cardiology 2016

D:A:D Risk Score (ART version)



www.chip.dk/Tools-Standards/Clinical-risk-scores

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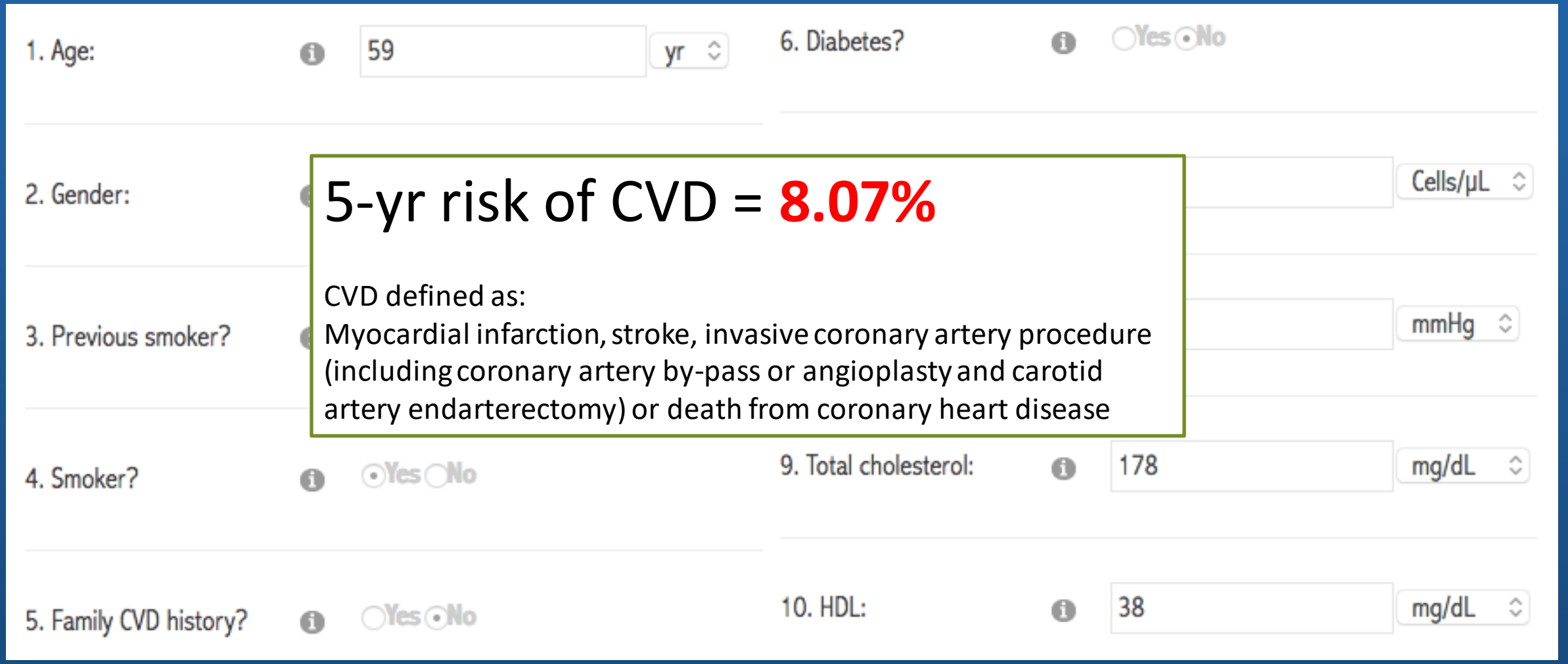
D:A:D Risk Score (No ART)



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

www.chip.dk/Tools-Standards/Clinical-risk-scores

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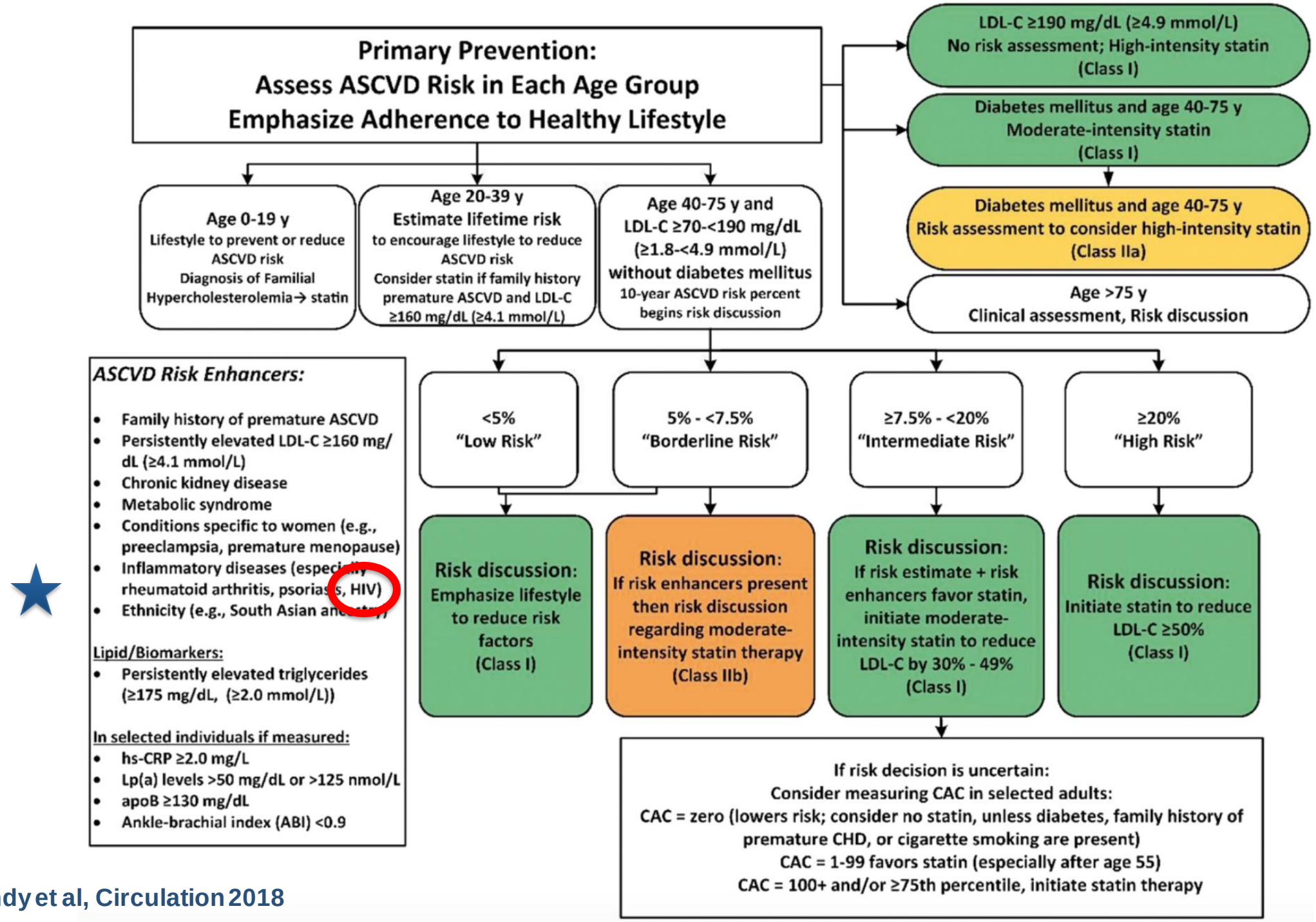
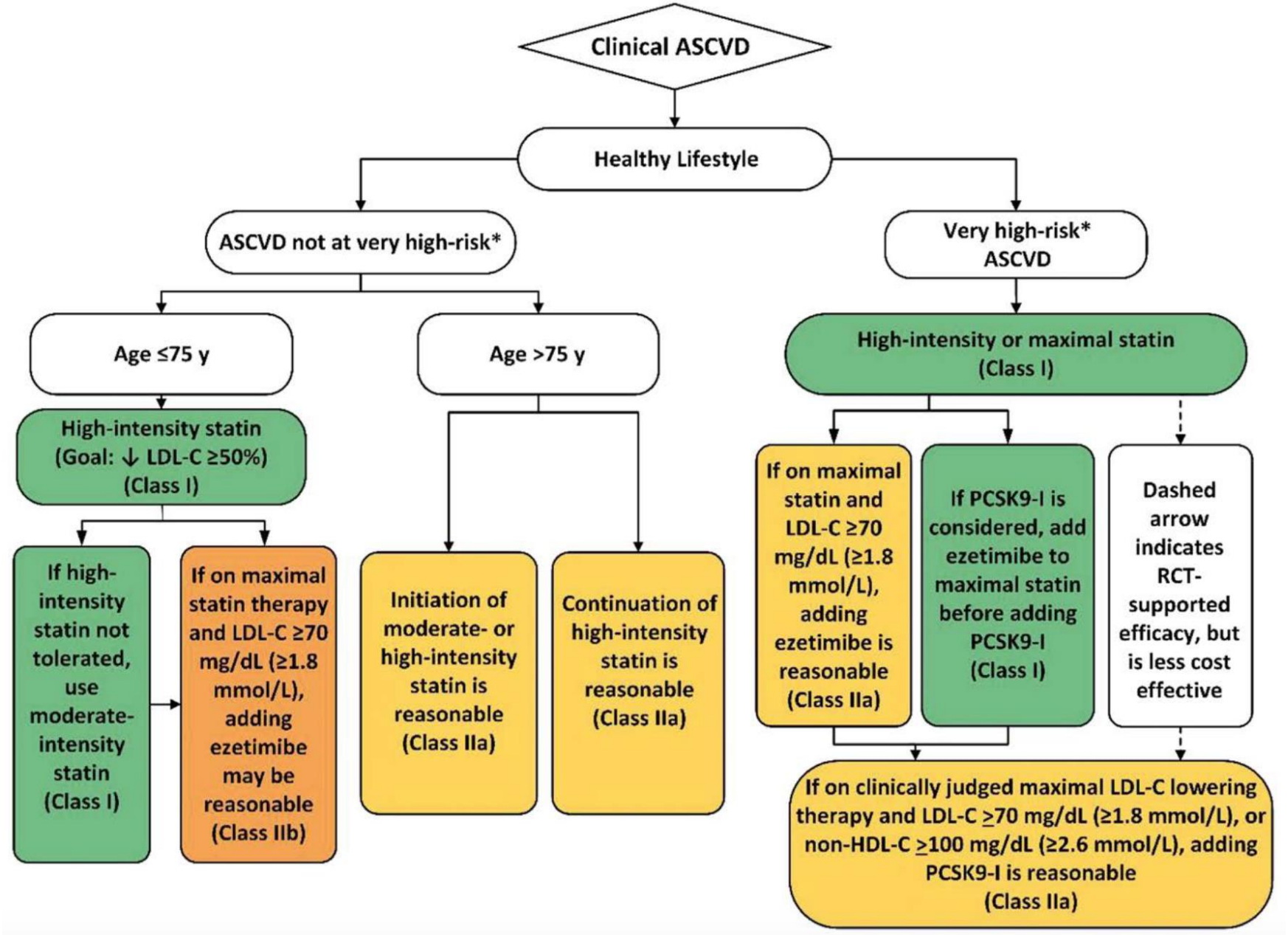


Grundy et al, Circulation 2018

Recommendations for Adults With Chronic Inflammatory Disorders and HIV Referenced studies that support recommendations are summarized in Online Data Supplement 39.		
COR	**LOE**	**Recommendations**
IIa	B-NR	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).
IIa	B-NR	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).
IIa	B-NR	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).



* 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

Major ASCVD Events
Recent ACS (within the past 12 mo)
History of MI (other than recent ACS event listed above)
History of ischemic stroke
Symptomatic peripheral arterial disease (history of claudication with ABI <0.85, or previous revascularization or amputation (S4.1-39))
High-Risk Conditions
Age ≥65 y
Heterozygous familial hypercholesterolemia
History of prior coronary artery bypass surgery or percutaneous coronary intervention outside of the major ASCVD event(s)
Diabetes mellitus
Hypertension
CKD (eGFR 15-59 mL/min/1.73 m^2) (S4.1-15, S4.1-17)
Current smoking
Persistently elevated LDL-C (LDL-C ≥100 mg/dL [≥2.6 mmol/L]) despite maximally tolerated statin therapy and ezetimibe
History of congestive HF

*Very high-risk includes a history of multiple major ASCVD events or one major ASCVD event and multiple high-risk conditions.

Grundy et al, Circulation 2018

National Lipid Association– Lipid Goals

Risk Category	**Criteria**	**Consider drug therapy** **Non-HDL-C** **LDL-C**
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.		

Jacobson et al, J Clin Lipidol 2015

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National Lipid Association– Lipid Goals

Risk Category	Criteria	Consider drug therapy Non-HDL-C LDL-C
Low		
Moderate		
High		
Very High		

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.

Jacobson et al, J Clin Lipidol 2015

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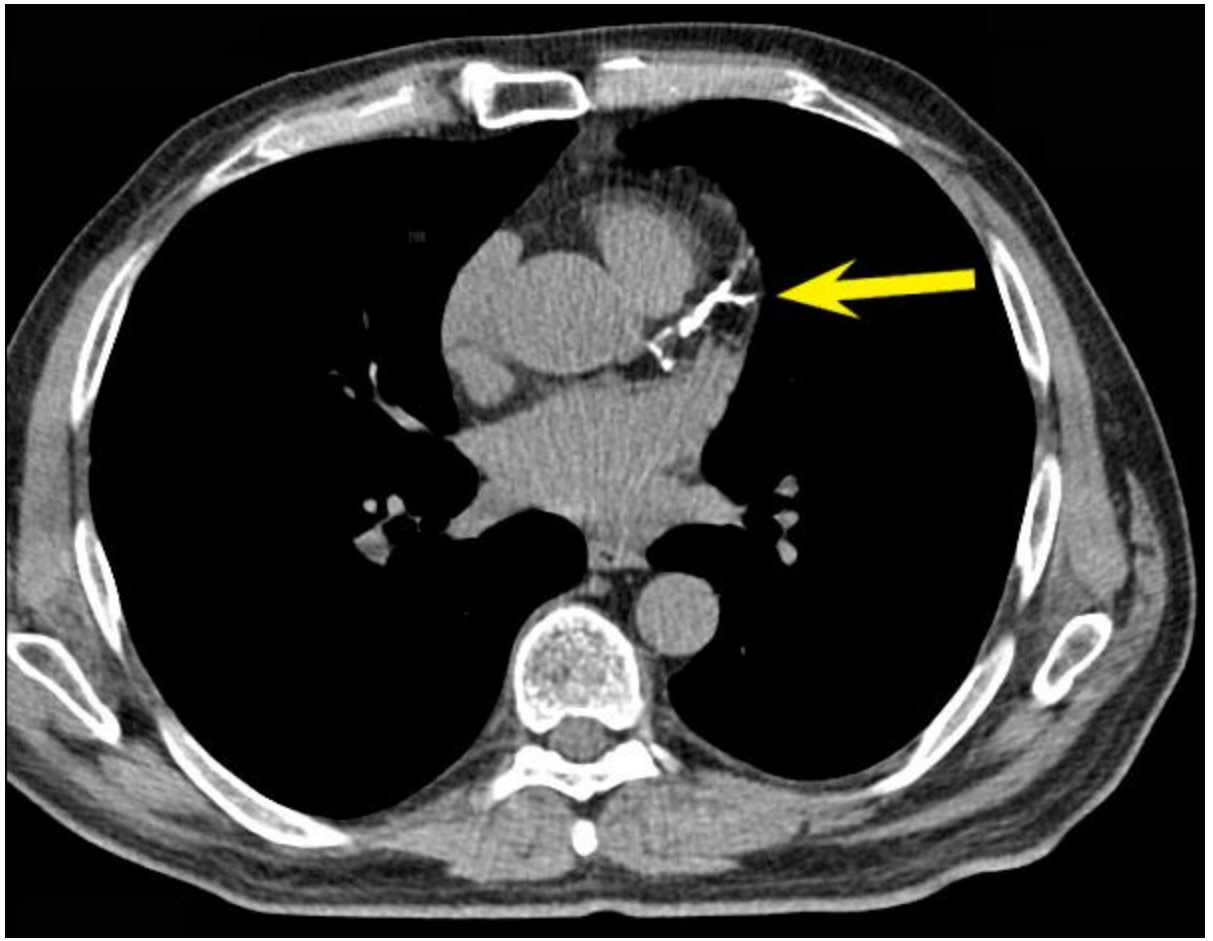
Coronary Artery Calcium (CAC) Scoring

- 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

Calcium score	10-year risk for CVD event	Risk interpretation
0	<1%	Very low
1-99	4%	Low
100-399	13%	Moderate
400 or greater	24%	High

www.uhhospitals.org. Data from MESA cohort study.

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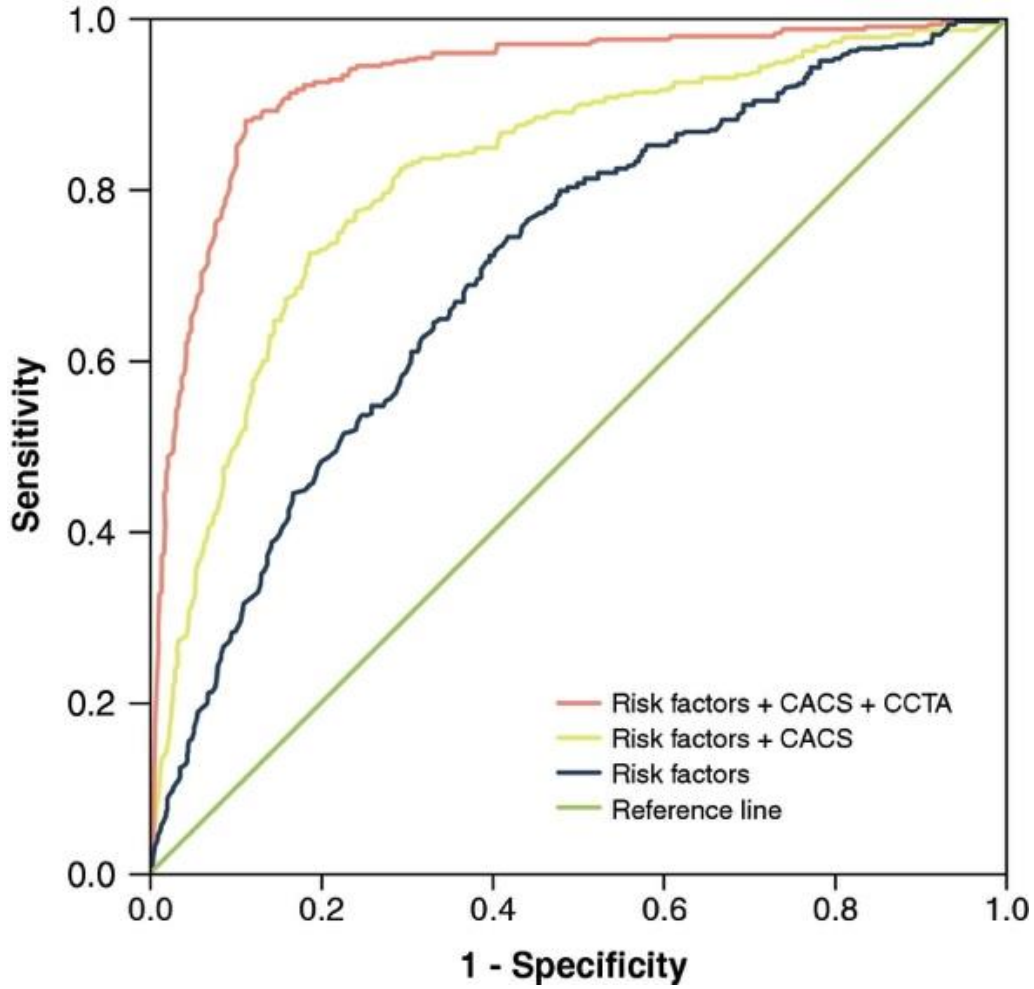
CAC and CTA provide additional prognostic information beyond traditional risk factors

- **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



Hou et al, JACC CV Img 2012

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?

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Importance of shared decision making

- ASCVD risk assessment to inform the discussion of primary prevention strategies
  - http://tools.acc.org/ASCVD-Risk-Estimator-Plus
  - 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

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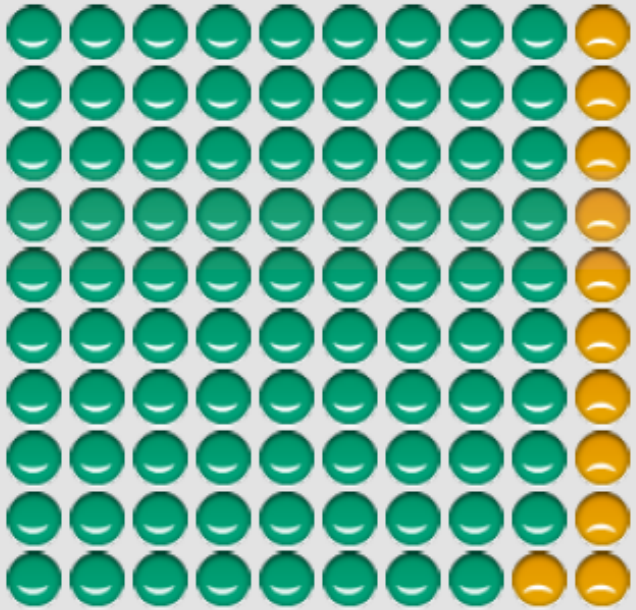
Your decision was: to take high dose statins

Current Risk
of having a heart attack

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

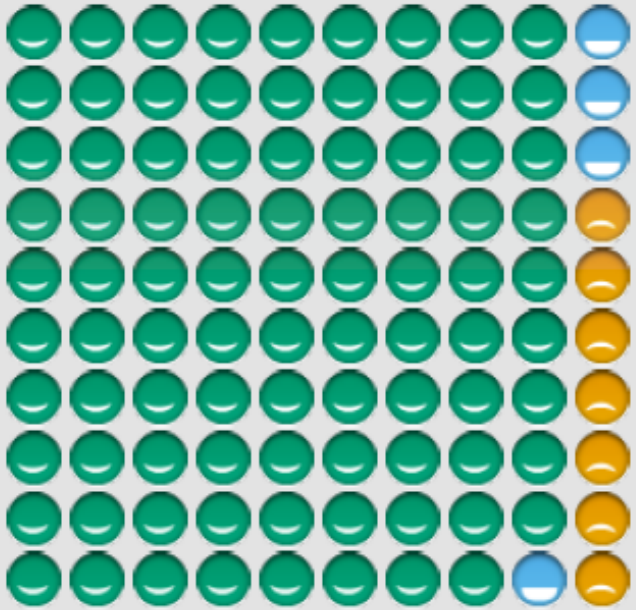


In your current situation you have 89 in 100 chances of no heart attack happening to you in the next 10 years.

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/

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Statin intensity

	High Intensity	Moderate Intensity	Low Intensity
LDL-C lowering†	≥50%	30%–49%	<30%
Statins	**Atorvastatin (40 mg‡) 80 mg** **Rosuvastatin 20 mg (*40 mg***	**Atorvastatin 10 mg** (20 mg) **Rosuvastatin** (5 mg) **10 mg** **Simvastatin 20–40 mg§**	Simvastatin 10 mg
	…	**Pravastatin 40 mg** (80 mg) **Lovastatin 40 mg** (80 mg) Fluvastatin XL 80 mg **Fluvastatin 40 mg BID** Pitavastatin 1–4 mg	**Pravastatin 10–20 mg** **Lovastatin 20 mg** Fluvastatin 20–40 mg

Grundy et al, Circulation 2018

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Cobicistat/PI interaction

- Start low and go slow
  - Start atorvastatin at 10mg and titrate to max dose of 40mg daily
  - Start rosuvastatin 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 rosuvastatin, then consider pitavastatin (if insurance will cover) or pravastatin (cheap, generic alternative)

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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