

HIV Management
Hepatitis Management

THE NEW YORK COURSE

Beyond MI: Cardiovascular Disease in the ART-Treated Patient

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Objectives

- 1. Describe the clinical impact of myocardial infarction (MI), stroke, heart failure, and sudden cardiac death in the current ART treatment era**
- 2. Identify special considerations for evaluating and managing the spectrum of cardiovascular disease in patients with HIV**
- 3. Summarize important unanswered questions regarding cardiovascular disease and HIV infection**



- 50 years old
- AIDS in 2002; on ART since
- Nadir/current CD4+: 20/600
- BP 140/70 on amlodipine 10 mg daily
- LDL 100 mg/dl on atorvastatin 40 mg daily

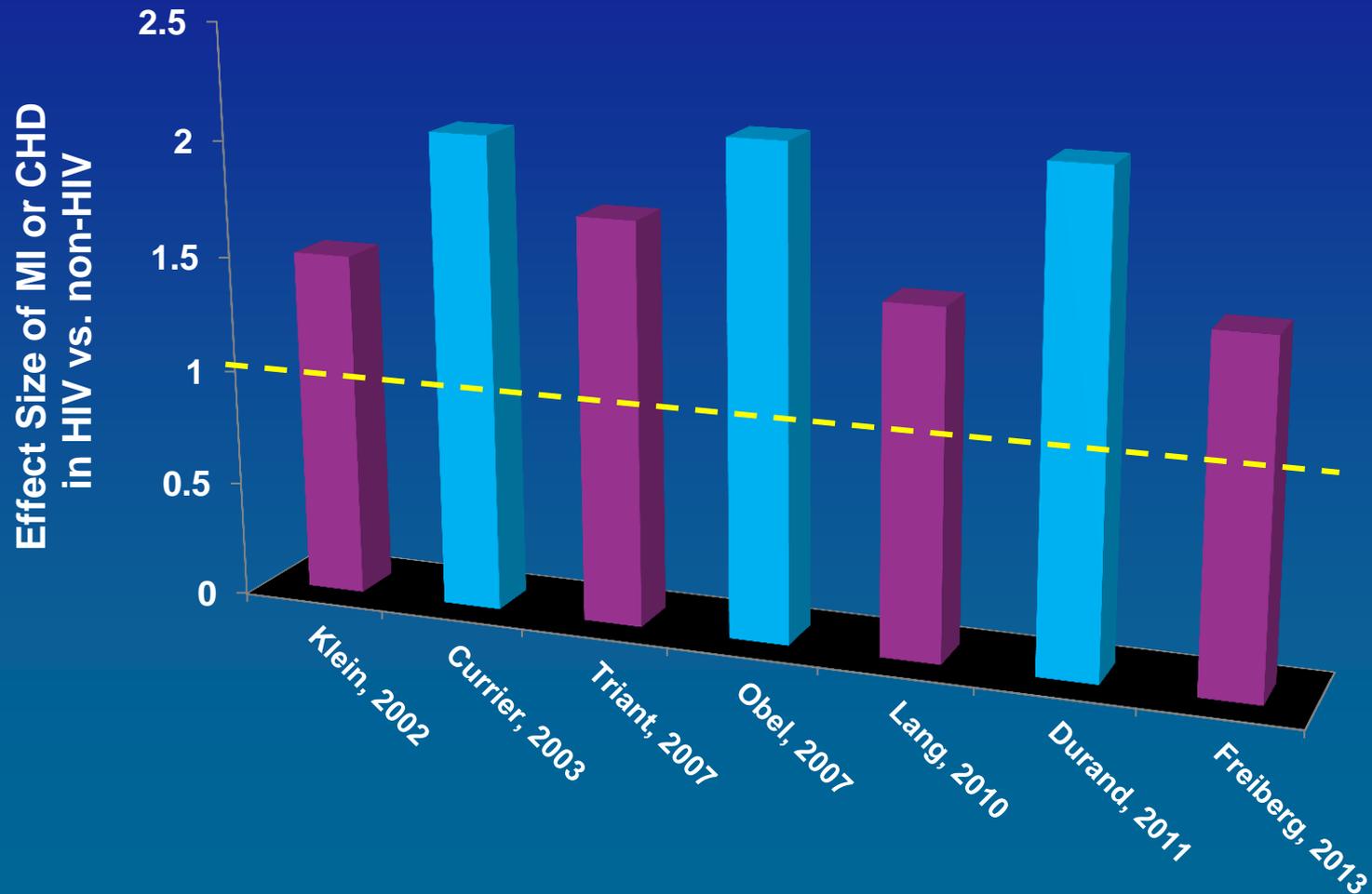


- 50 years old
- HIV-negative
- BP 150/90
- LDL 160 mg/dl



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

HIV is associated with higher risk of myocardial infarction



MI

Stroke

1.5-2x

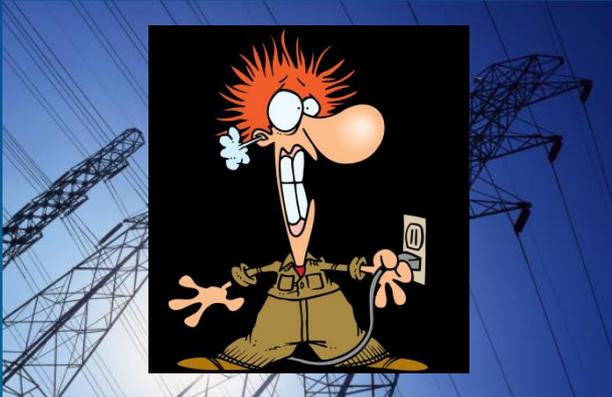
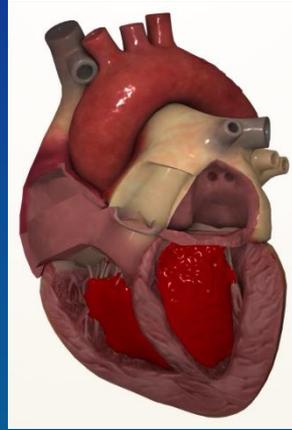
Higher Risk

**Heart
Failure**

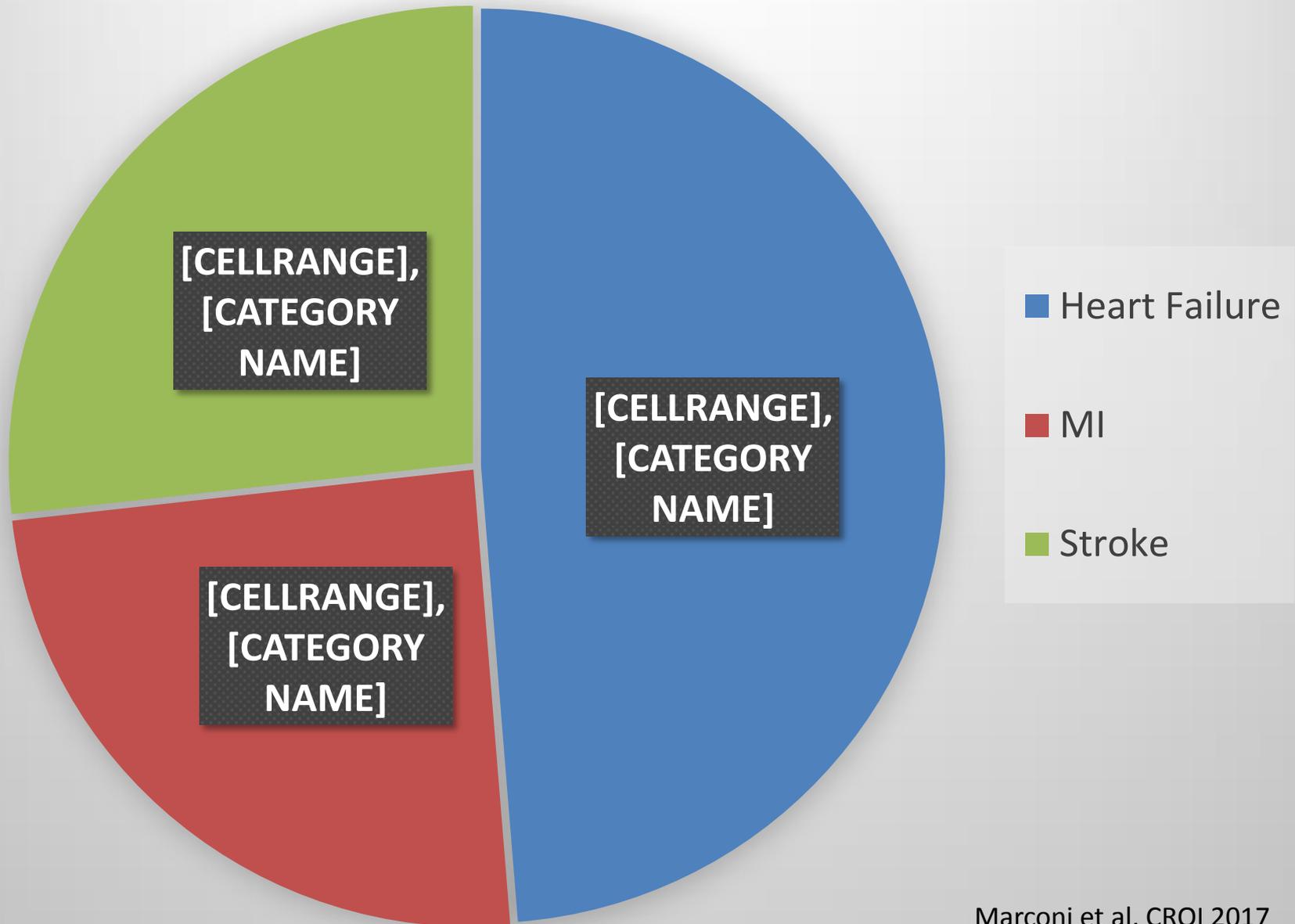
**Atrial
Fibrillation**

Freiberg et al, JAMA Intern Med 2013 (MI)
Freiberg et al, Circ Cardiovasc Qual Outcomes 2011 (CAD)
Chow et al, JAIDS 2012 (stroke)

Butt et al, Arch Intern Med 2011 (HF)
Freiberg et al, CROI 2013 (HFpEF)
Hsu et al, JACC 2013 (Afib)



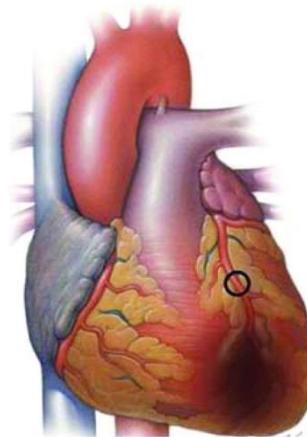
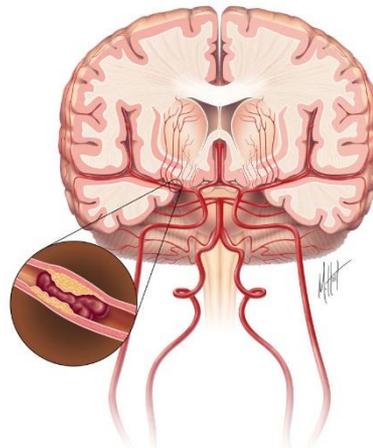
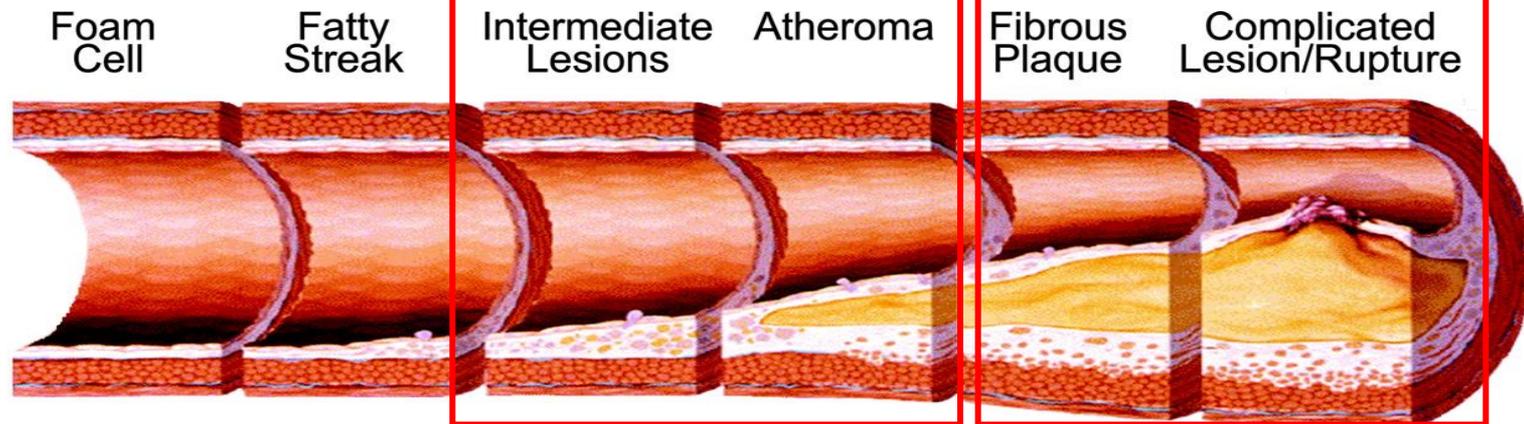
Cardiovascular Events in VACS 2003-2012



Atherosclerotic CVD

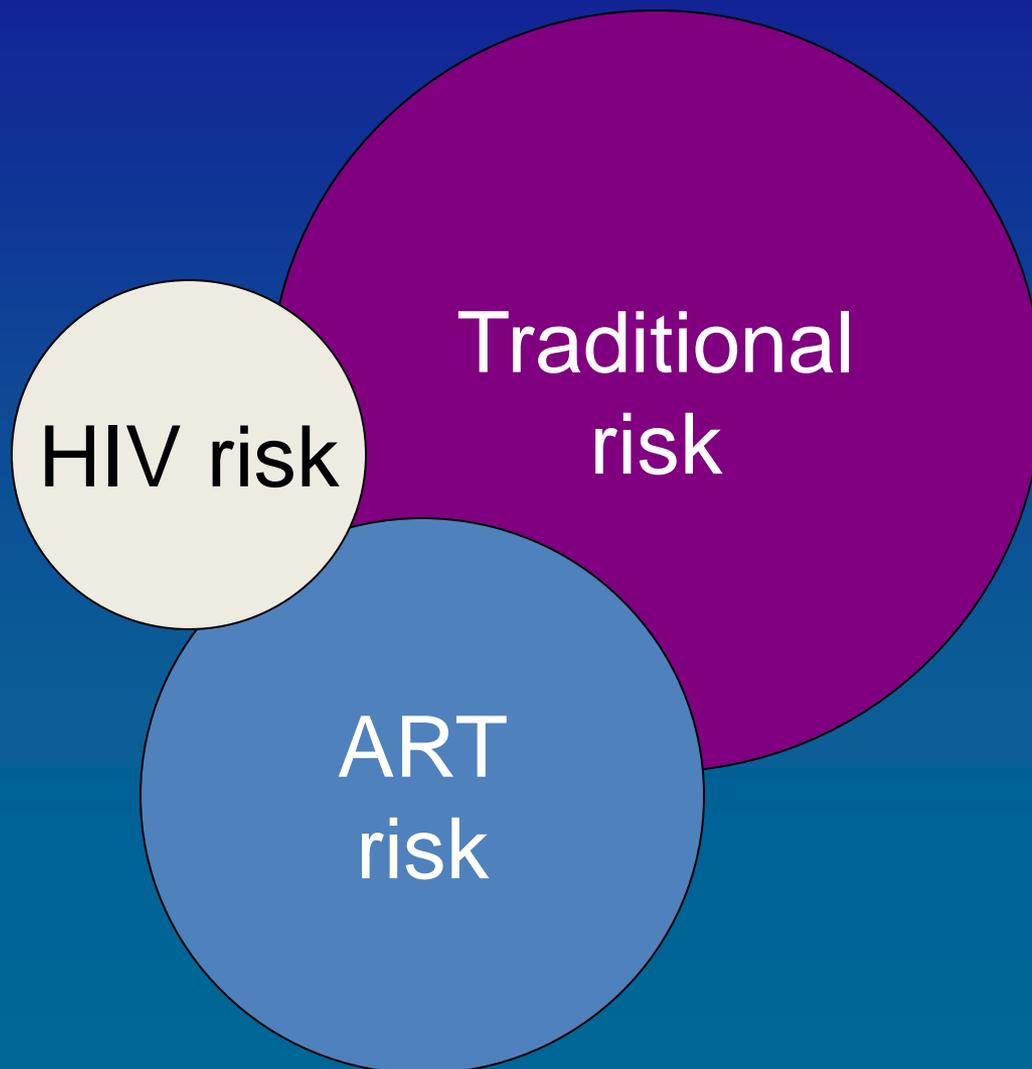
A known entity

Atherosclerotic CVD



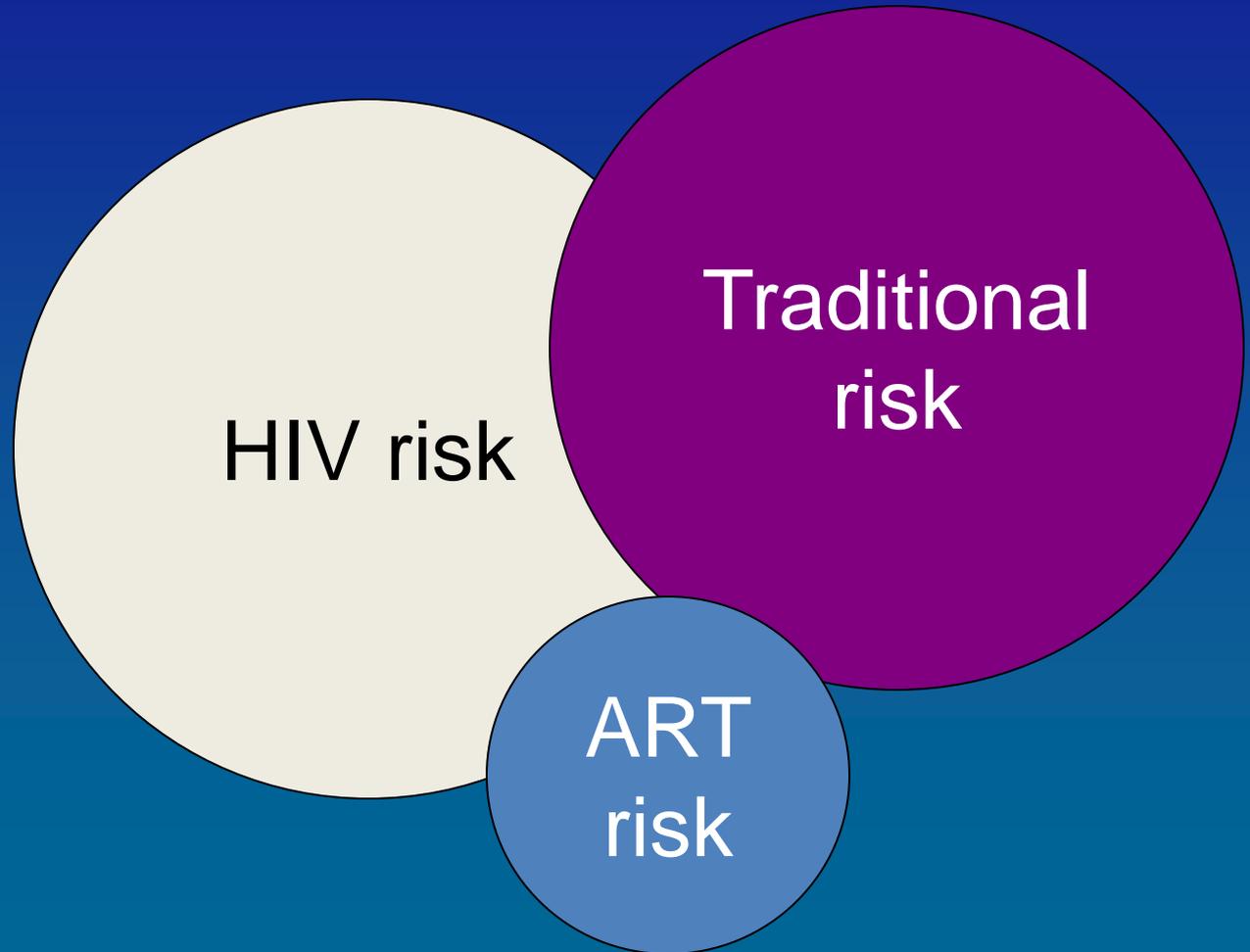
What accounts for the 1.5-2x higher risk seen in HIV?

2003



What accounts for the 1.5-2x higher risk seen in HIV?

2017



HIV risk

Traditional
risk

ART
risk

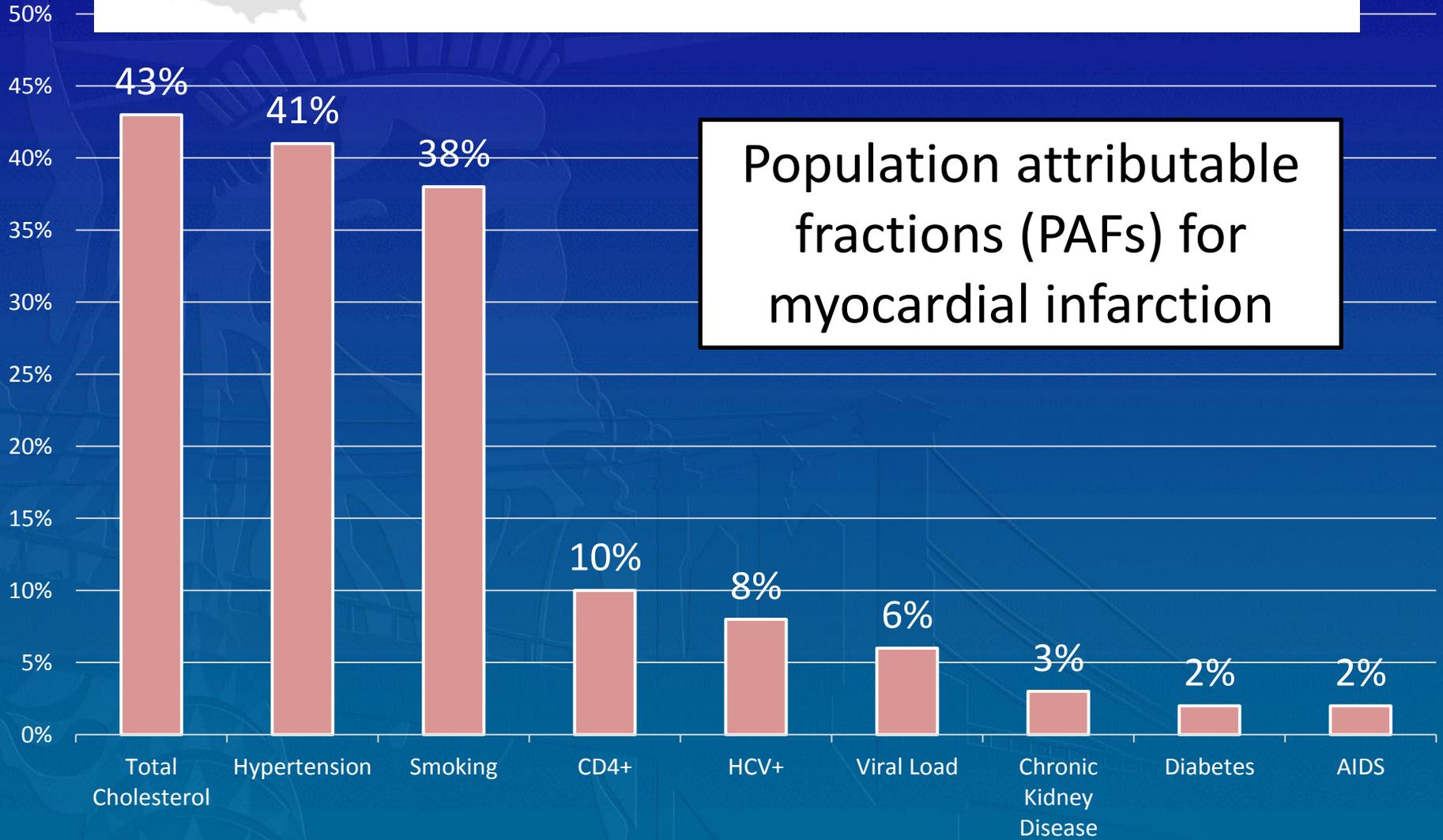
Population Attributable Risk



Proportional reduction in risk that would occur if that risk factor were absent or reduced to “normal”



North American AIDS Cohort Collaboration on Research and Design

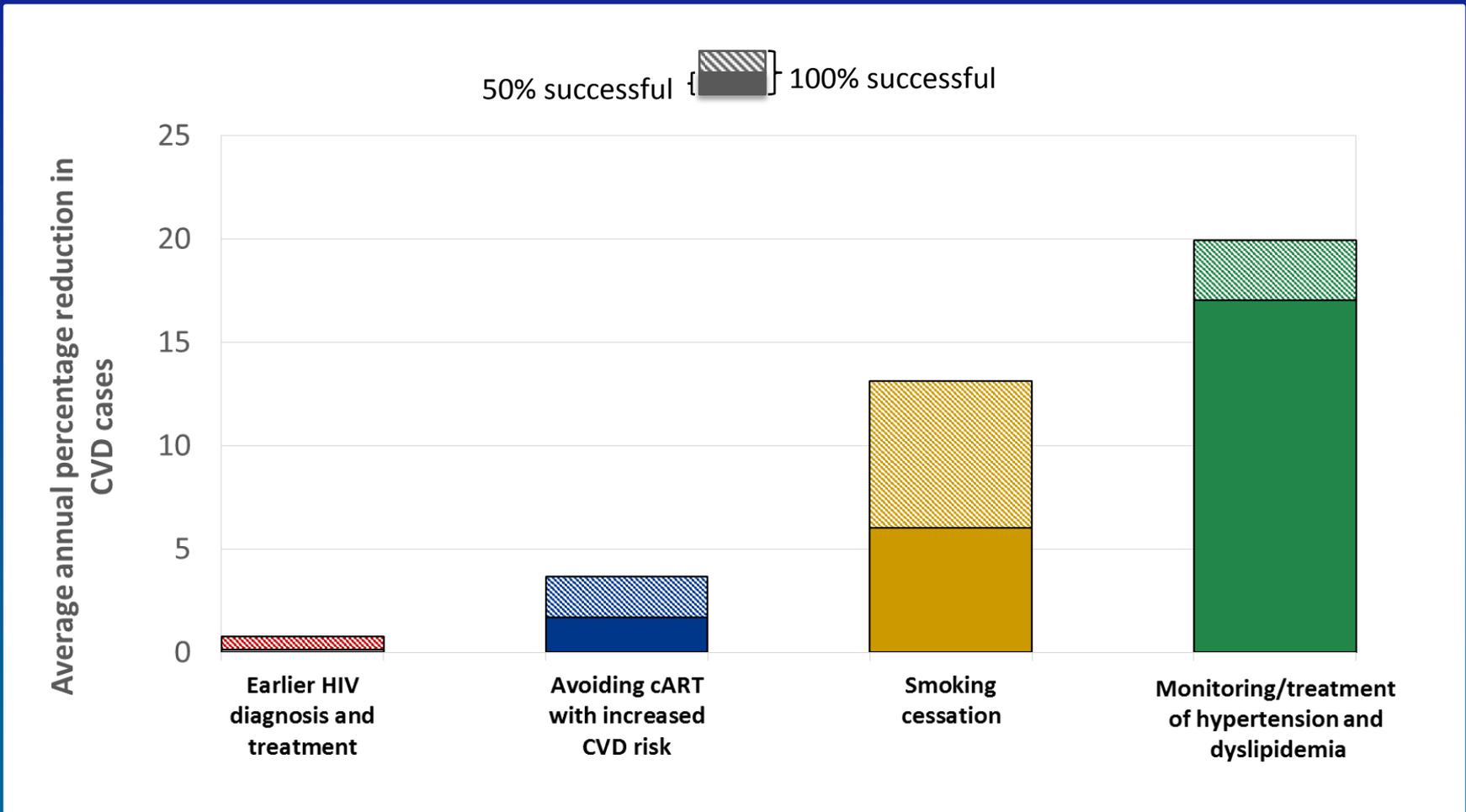


Comparison with other non-AIDS comorbidities

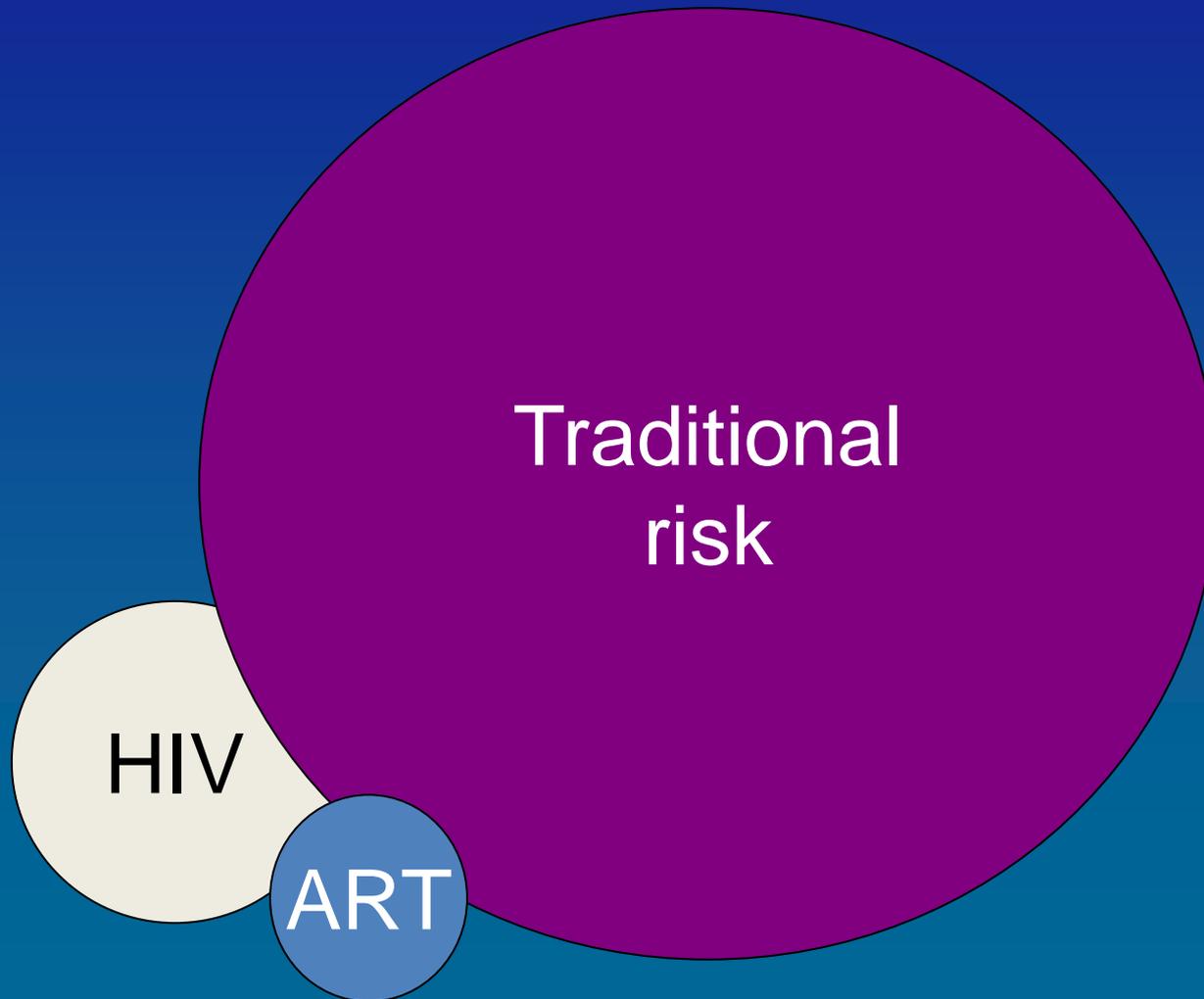
Outcome	Traditional risk factor PAF	HIV-related risk factor PAF
Cancer (CROI 2015)	1. Smoking: 35% <ul style="list-style-type: none"> • 26% after excluding lung cancer 	2. Clinical AIDS diagnosis: 10% 3. Low CD4+ count: 4%
ESRD (unpublished)	1. Elevated total cholesterol: 22%	2. Detectable HIV RNA: 20% 3. Low CD4+ count: 17%
ESLD (CROI 2016)	1. At-risk alcohol use: 33% 2. HCV infection: 31%	3. Low CD4+ count: 25%
MI (CROI 2017)	1. Elevated total cholesterol: 43% 2. Hypertension: 41% 3. Smoking: 38%	

ESRD=end-stage renal disease. ESLD=end-stage liver disease. MI=myocardial infarction.

Predicted Reduction in ASCVD Risk from 2017–2030, with 50% or 100% Success in Reducing Risk Factors: A Dutch Modeling Study



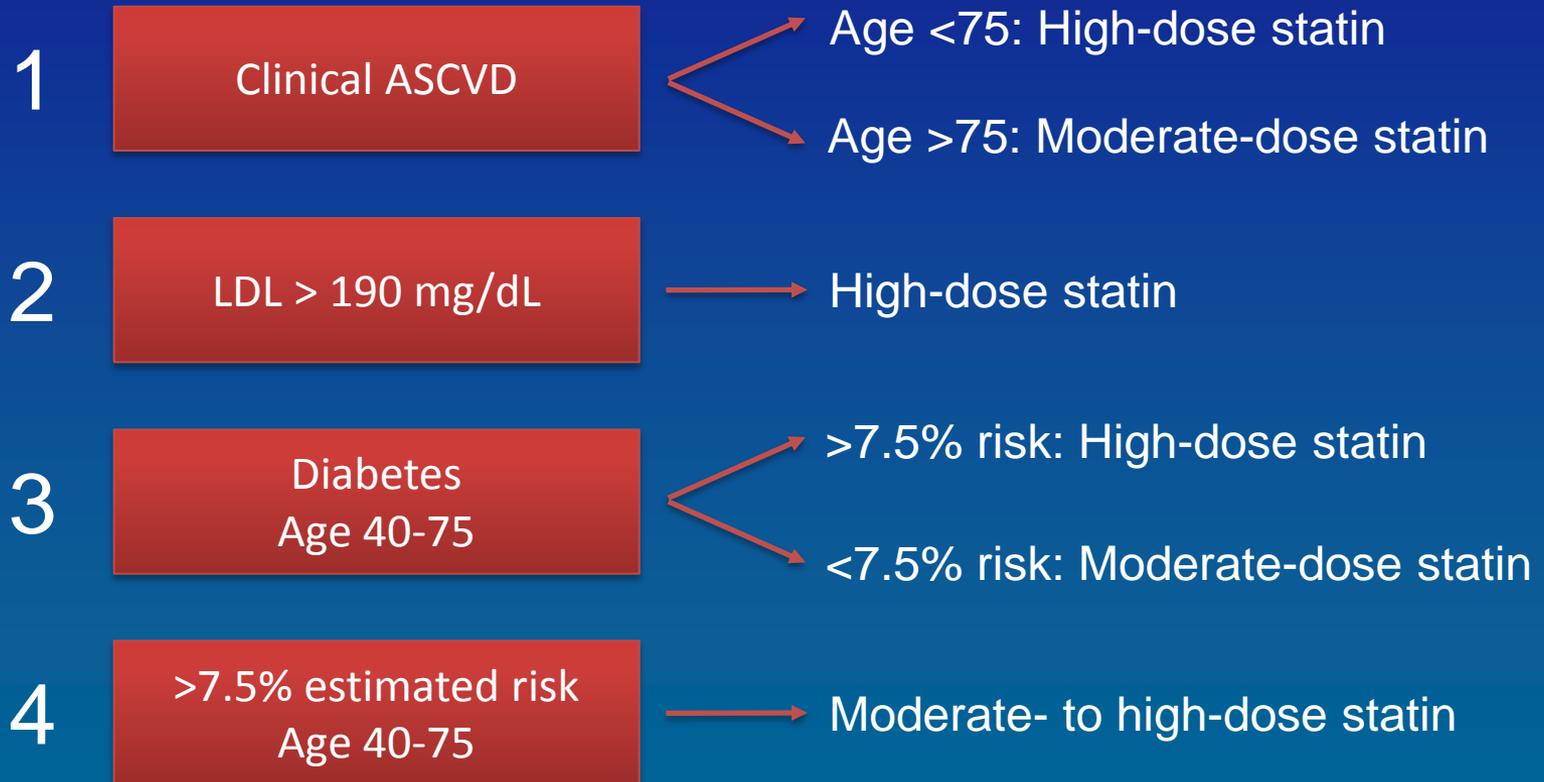
What accounts for the total risk of ASCVD events in HIV?



Primary prevention of ASCVD

- ▶ Diet and exercise
- ▶ Smoking cessation
- ▶ Statin
- ▶ Aspirin
- ▶ Appropriate management of comorbidities (blood pressure, diabetes, CKD, etc...)

2013 ACC/AHA Guidelines: Statin benefit groups



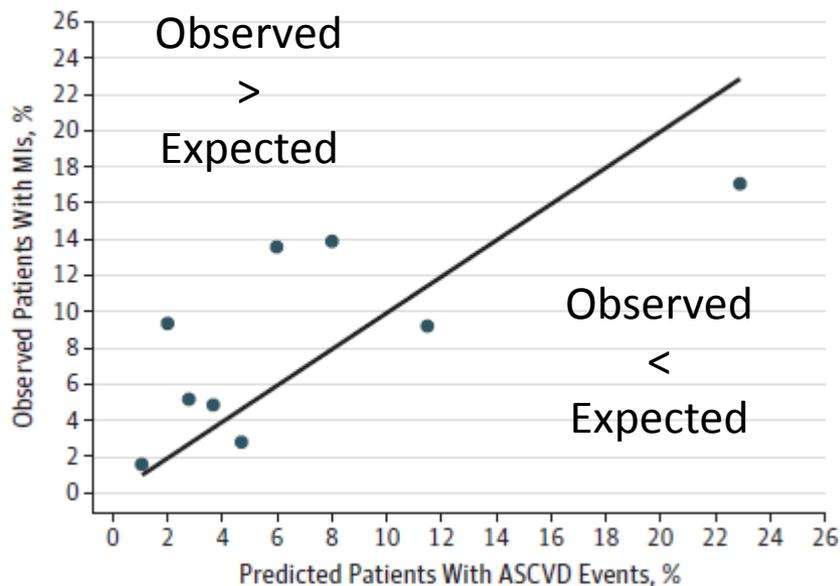
Pooled Cohort Equations Calculator

Estimator	Clinicians	Patients	About
ASCVD Risk Estimator*			
10-Year ASCVD Risk		Lifetime ASCVD Risk	
7.5% <small>calculated risk</small>		69% <small>calculated risk</small>	
3.7% <small>risk with optimal risk factors**</small>		5% <small>risk with optimal risk factors</small>	
Recommendation Based On Calculation			
Gender	Age	Race	
<input checked="" type="radio"/> Male <input type="radio"/> Female	<input type="text" value="49"/>	<input type="radio"/> White	
		<input checked="" type="radio"/> African American	
		<input type="radio"/> Other	
HDL - Cholesterol (mg/dL)	Total Cholesterol (mg/dL)	Systolic Blood Pressure	
<input type="text" value="56"/>	<input type="text" value="320"/>	<input type="text" value="114"/>	
Diabetes	Treatment for Hypertension	Smoker	
<input type="radio"/> Yes <input checked="" type="radio"/> No	<input checked="" type="radio"/> Yes <input type="radio"/> No	<input type="radio"/> Yes <input checked="" type="radio"/> No	
<small>*Intended for use if there is not ASCVD and the LDL-cholesterol is <190 mg/dL</small>			
<small>**Optimal risk factors include: Total cholesterol of 170 mg/dL, HDL-cholesterol of 50 mg/dL, Systolic BP of 110 mm Hg, Not taking medications for hypertension, Not a diabetic, Not a smoker</small>			

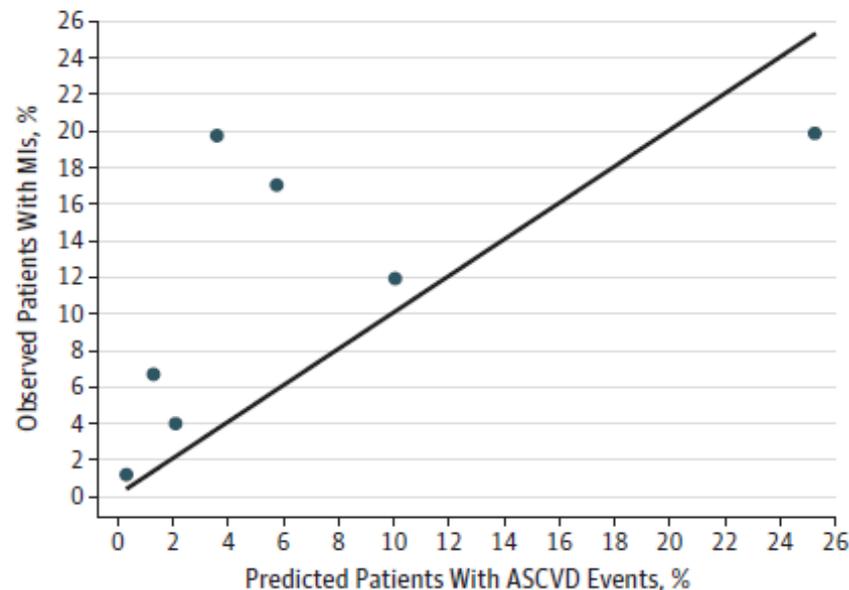
The ACC/AHA calculator may underestimate risk in HIV

Data from the CFAR Network (CNICS)

Black men



Black women



Statins in HIV: Beware of drug interactions

Efavirenz
INDUCES CYP3A4

- ▶ Many protease inhibitors (PIs), especially those boosted with ritonavir or cobicistat will *increase* statin levels in the blood (**through CYP3A4**)

CONTRAINDICATED

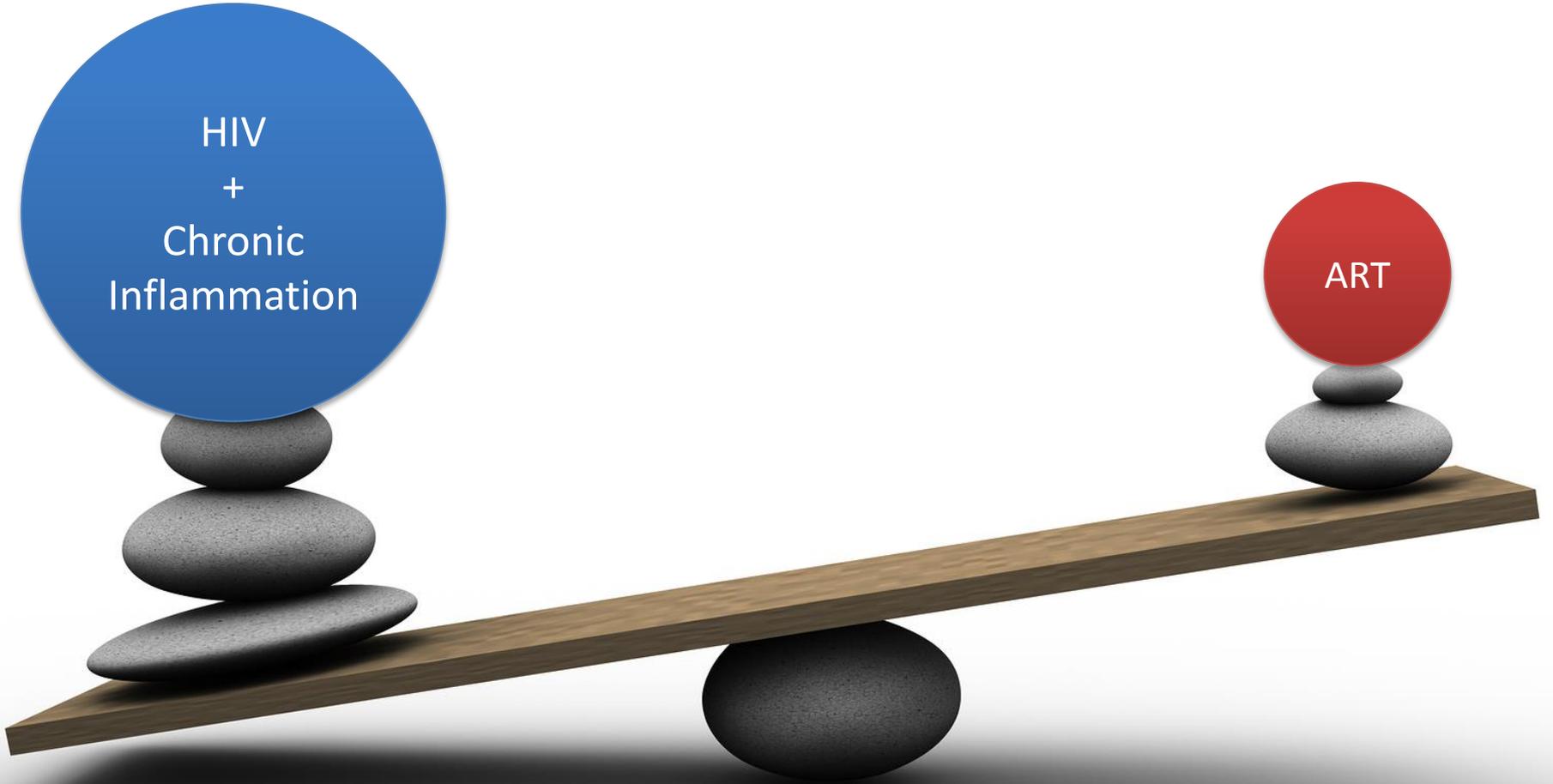
Lovastatin (Mevacor)
Simvastatin (Zocor)

CAUTION

Atorvastatin (Lipitor)
Rosuvastatin (Crestor)

NO INTERACTION

Pravastatin (Pravachol)
Pitavastatin (Livalo)



HIV
+
Chronic
Inflammation

ART

Contemporary ART and blood lipids



TDF **RAL** **RPV** **ABC** **EFV** **ATV/RTV or ATV/Cobi**
DTG **ETV** **DRV/RTV or DRV/Cobi**
EVG/COBI

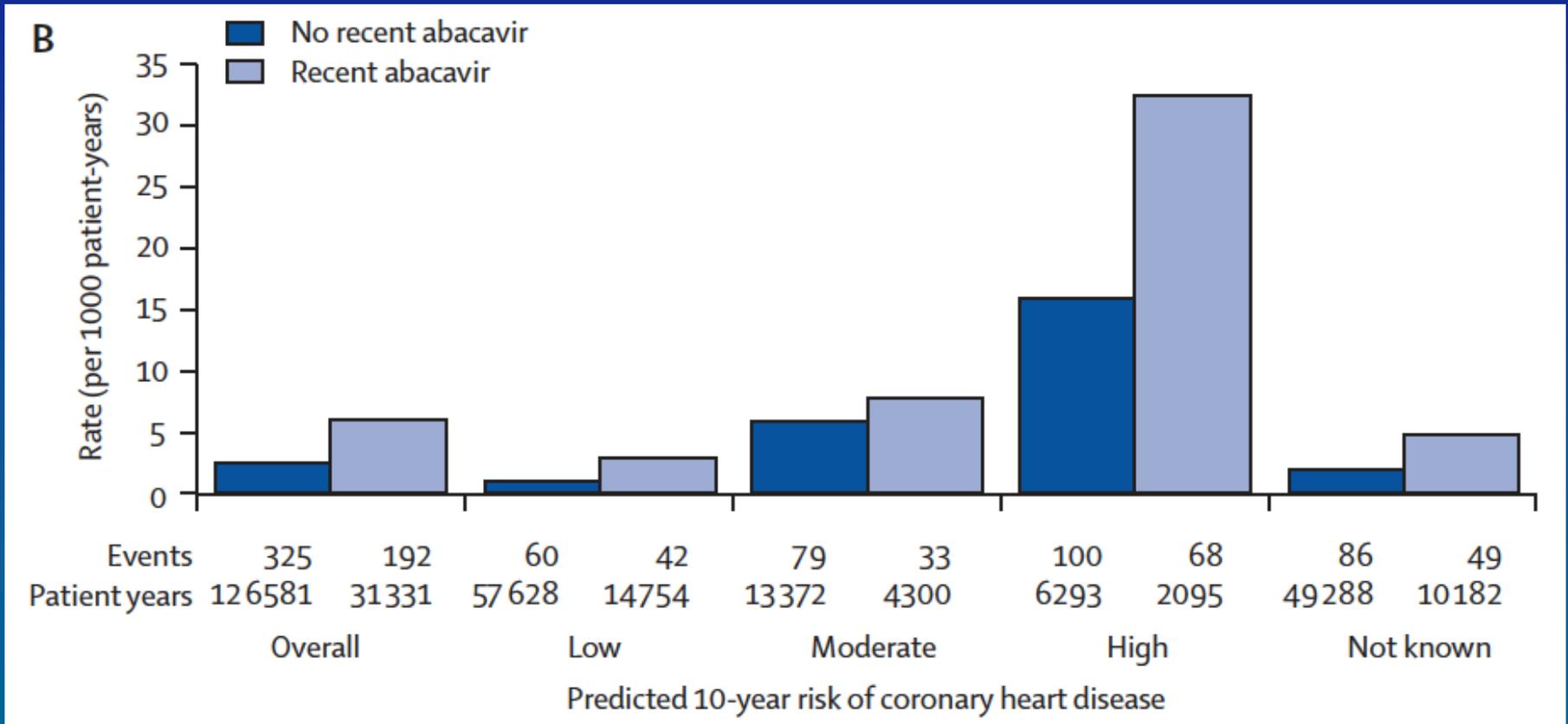
TDF = Tenofovir
RAL = Raltegravir
DTG = Dolutegravir

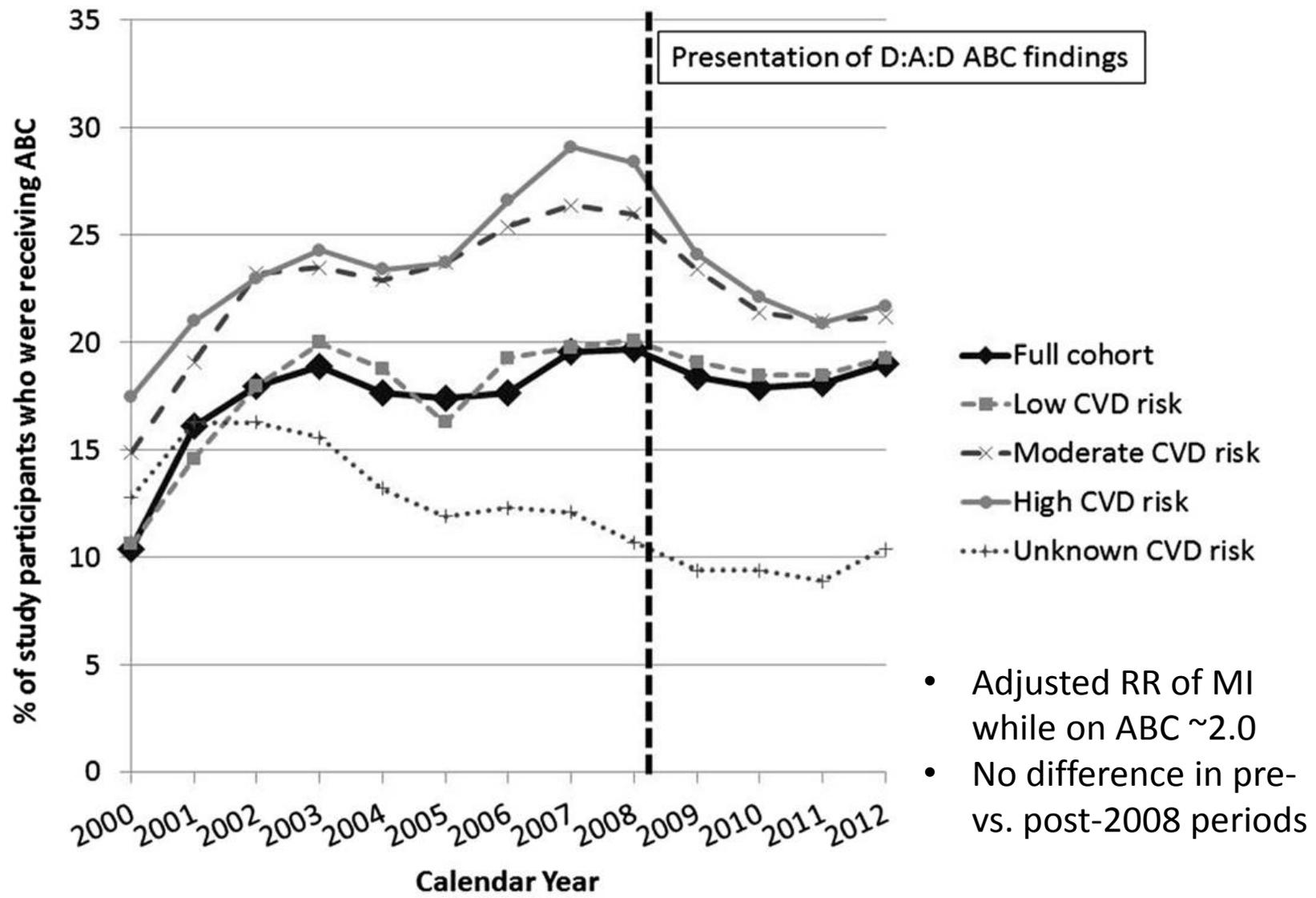
RPV = Rilpivirine
ETV = Etravirine
ABC = Abacavir

EFV = Efavirenz
ATV = Atazanavir
DRV = Darunavir

RTV = Ritonavir
EVG = Elvitegravir
COBI = Cobicistat

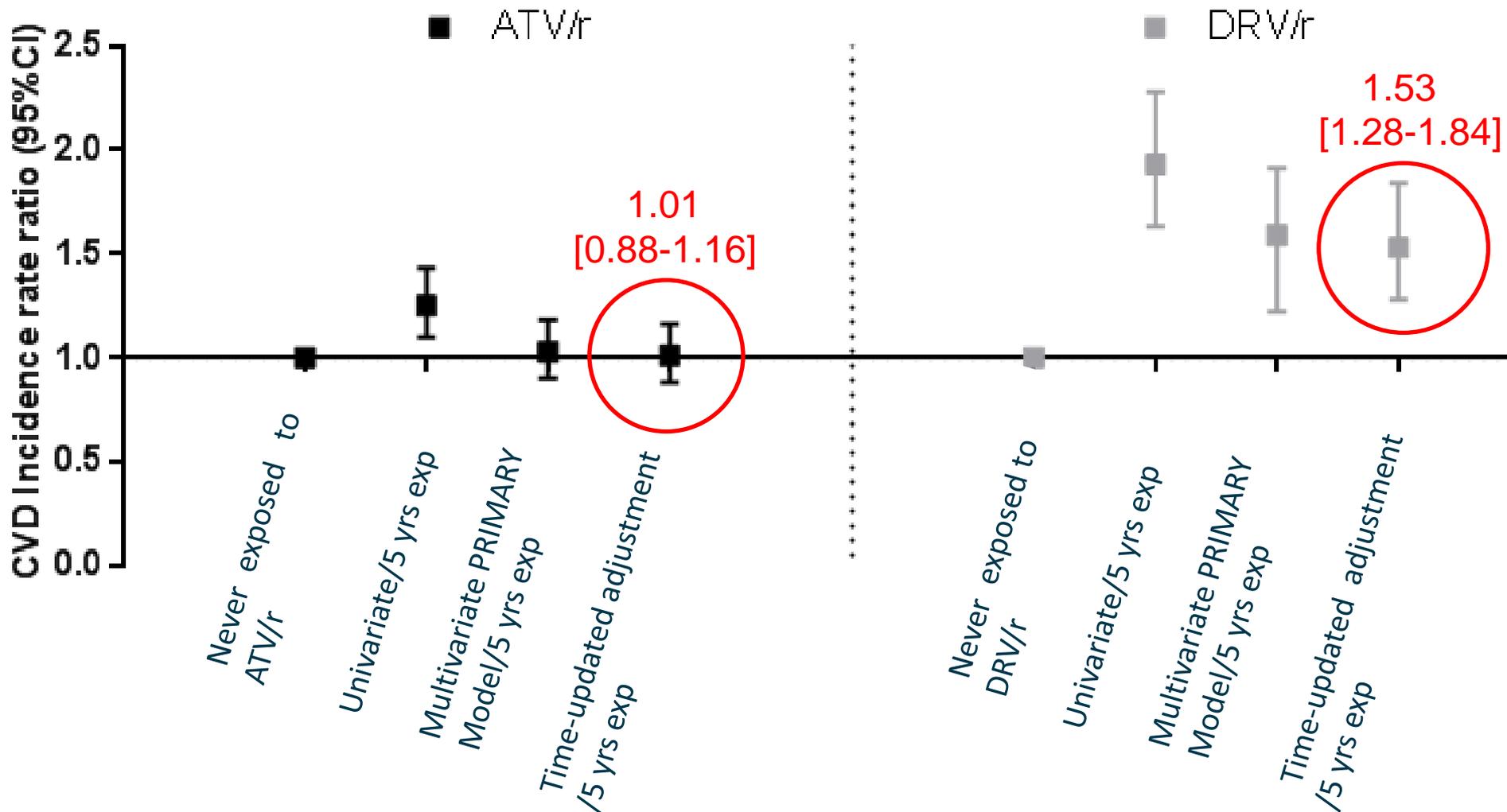
Abacavir and MI Risk: The D:A:D Study





- Adjusted RR of MI while on ABC ~2.0
- No difference in pre- vs. post-2008 periods

Association Between CVD & Cumulative ATV/r and DRV/r Use; Additional Time-updated Adjustment for Factors Potentially on the Causal Pathway between PI/r use and CVD CD4, BMI, CKD, Dyslipidaemia, Diabetes



Ryom et al. CROI, 2017
 Data from the D:A:D Study

Is risk of MI declining over time? The Kaiser Permanente story

Calendar Year	Incidence Rate/100 000 py		Rate Ratio ^a (95% CI)	
	HIV-positive	HIV-negative	Unadjusted	Adjusted
1996–2011	268	165	1.6 (1.5–1.8)	1.4 (1.2–1.6)
1996–1999	276	136	2.0 (1.5, 2.8)	1.8 (1.3, 2.6)
2000–2003	324	162	2.0 (1.6, 2.5)	1.7 (1.4, 2.1)
2004–2007	270	178	1.5 (1.2, 1.9)	1.3 (1.0, 1.6)
2008–2009	245	167	1.5 (1.1, 2.0)	1.3 (.9, 1.7)
2010–2011	195	165	1.2 (.9, 1.6)	1.0 (.7, 1.4)

ASCVD– Clinical Pearls

▶ MI and Stroke Prevention:

- Focus on traditional risk factors
- Risk calculators may underestimate risk
- ART does more good than harm, but consider avoiding certain drugs in high-risk individuals

▶ Statins:

- Beware drug interactions
- Despite interactions, don't be scared to use a potent statin with proper dosing and monitoring
- Will statins prevent ASCVD events in low-risk individuals?

ASCVD– When prevention fails

▶ Revascularization:

- After a stent, restenosis rates are similar but recurrent acute events higher in HIV+
- Stents are great, but HIV+ can safely undergo surgery as well

• Beware drug interactions:

- **Clopidogrel:** efavirenz and etravirine decrease effectiveness
- **Ticagrelor:** PI/cobicistat increase risk of bleeding
- **Prasugrel:** ritonavir/cobicistat decrease effectiveness

Heart Failure

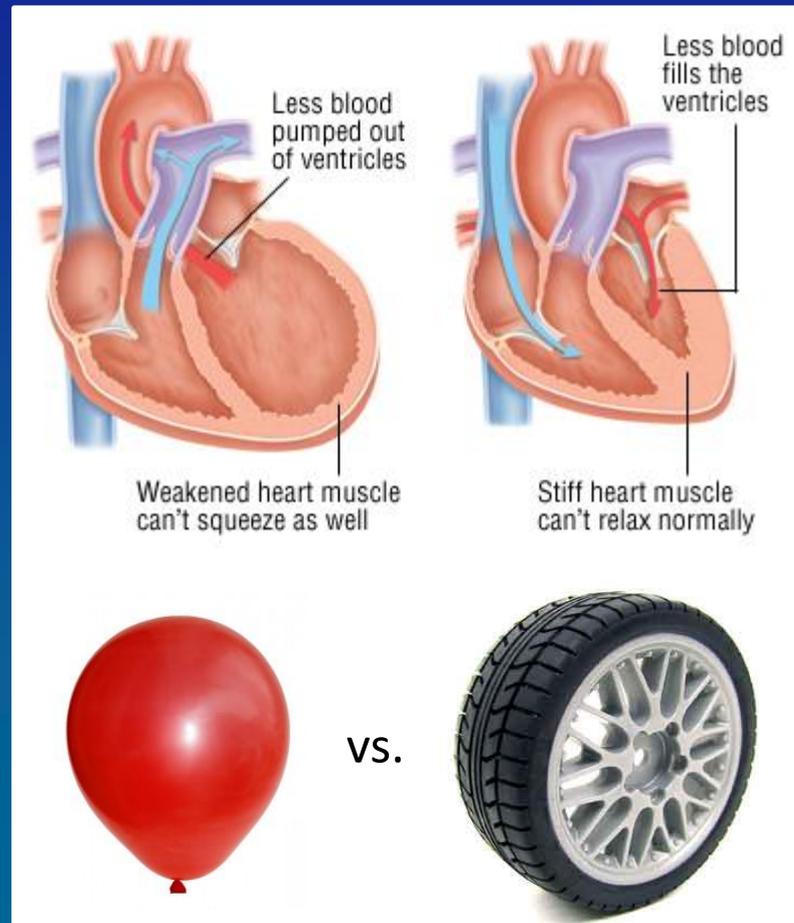
The coming epidemic

Two Kinds of Heart Failure

Systolic

↓ Ejection Fraction
(HFrEF)

- MI/Ischemic Heart Disease
- Hypertension
- Alcohol
- Diabetes
- AIDS

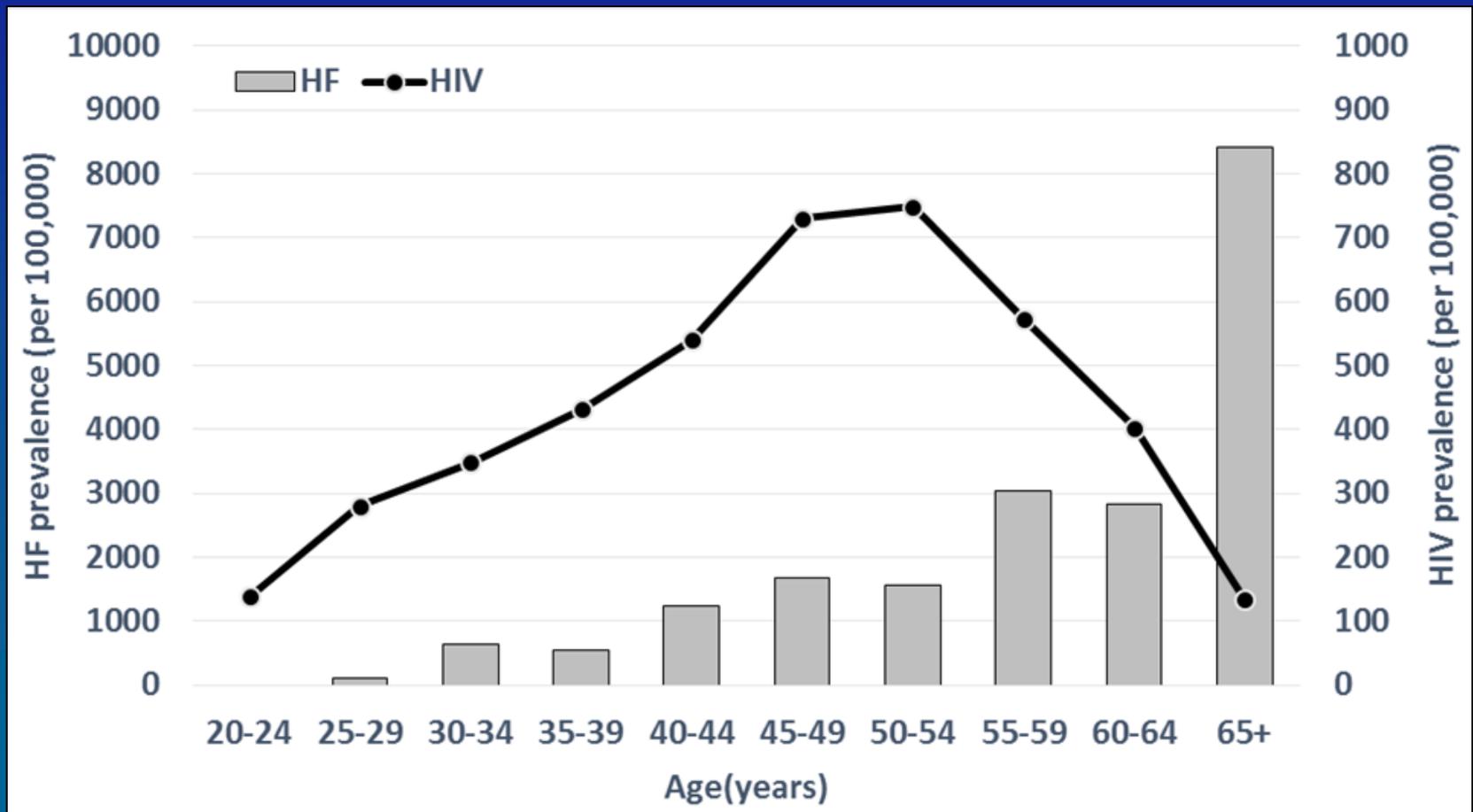


Diastolic

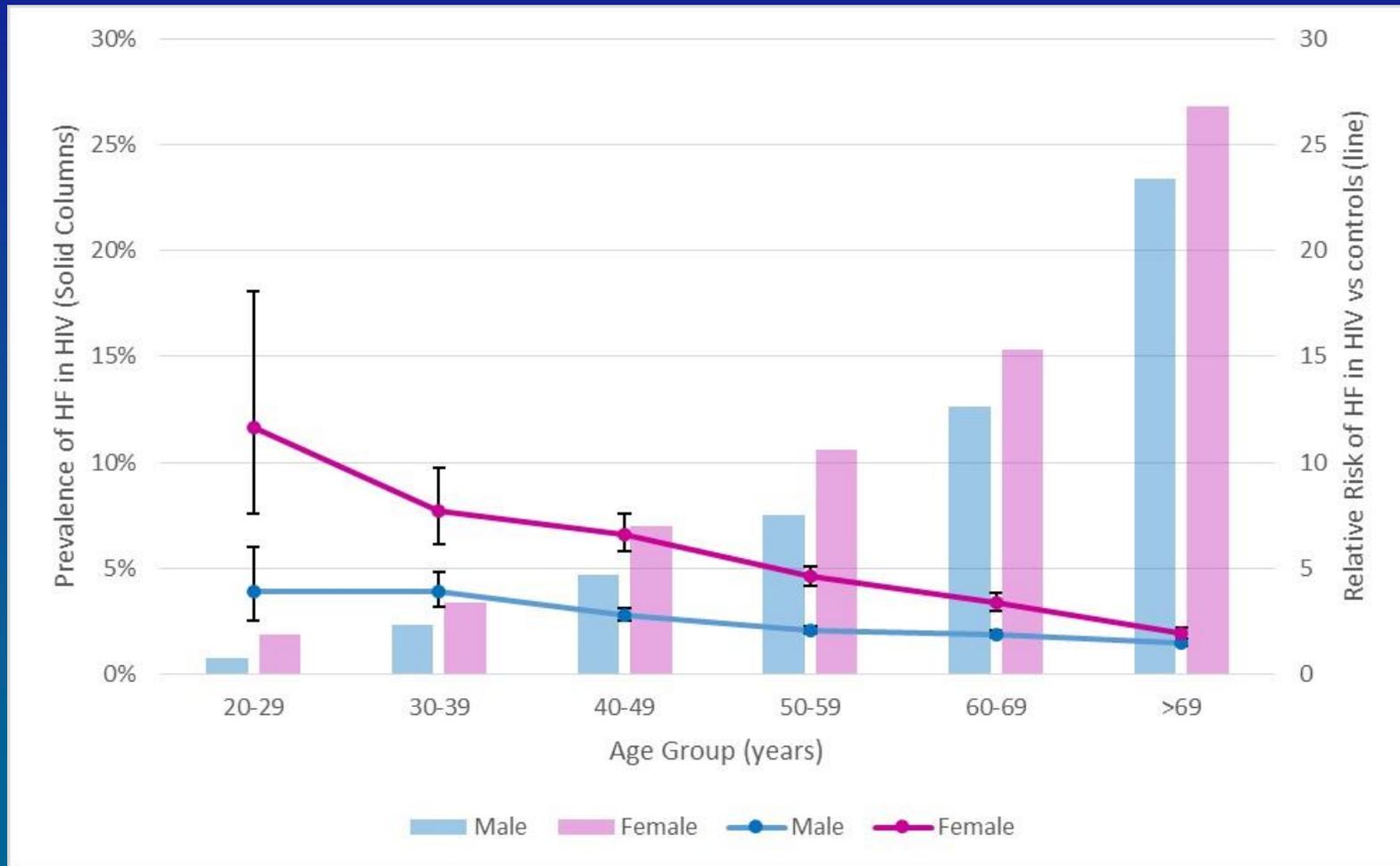
Normal EF
(HFpEF)

- Hypertension
- Kidney Disease
- Aging
- Chronic HIV

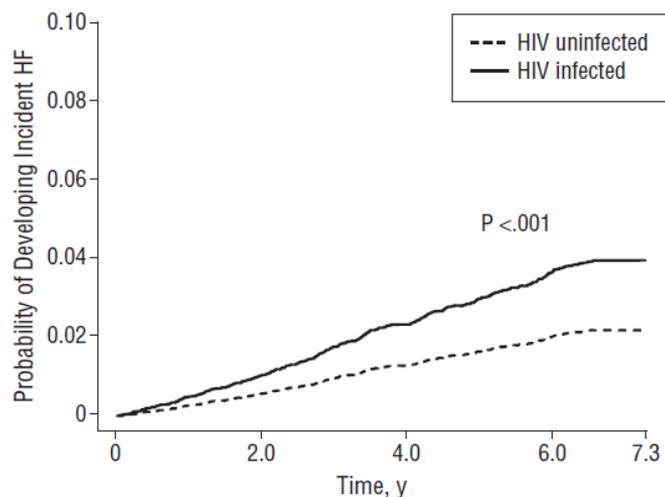
Heart failure is a disease of old age... and the HIV+ population is aging



Heart failure is prevalent in HIV+

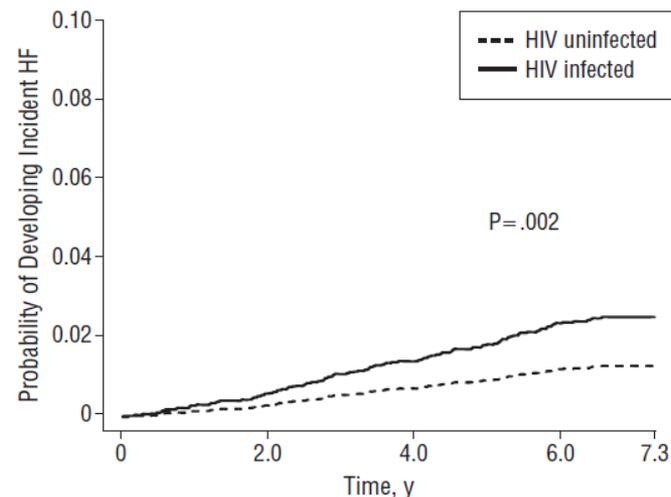


HIV is associated with higher incidence of HF



No. at Risk		0	2.0	4.0	6.0	7.3
HIV uninfected		6095	5832	5464	4909	3247
HIV infected		2391	2148	1912	1658	1268

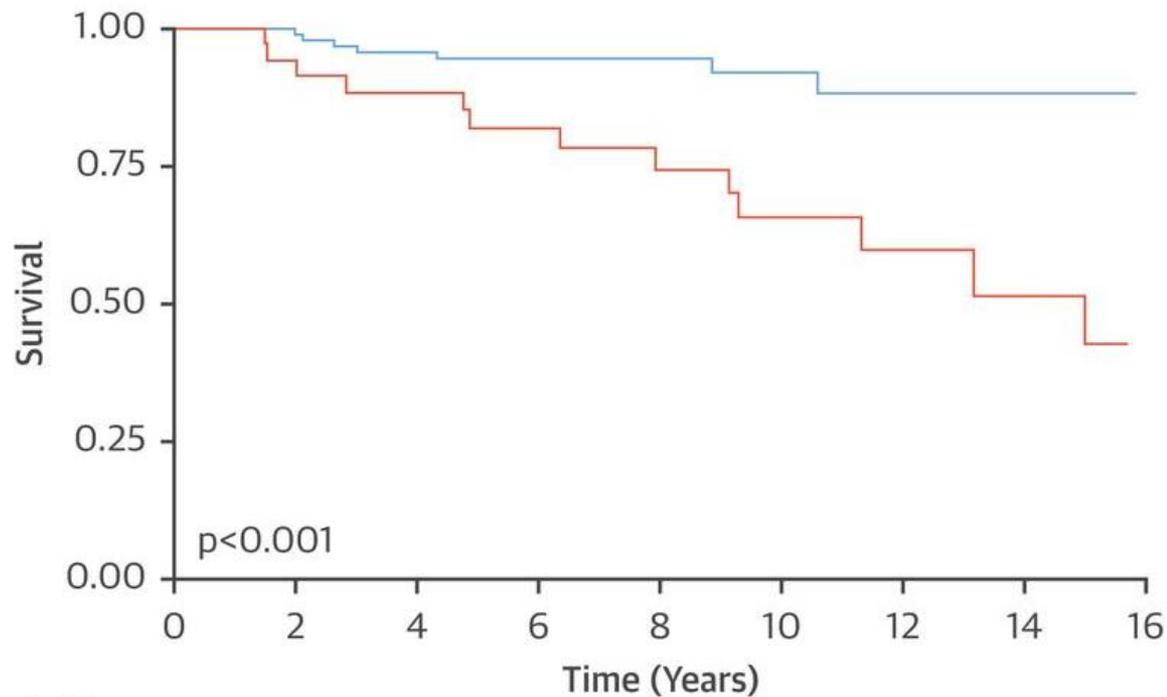
Overall



No. at Risk		0	2.0	4.0	6.0	7.3
HIV uninfected		4076	3909	3701	3364	2171
HIV infected		1562	1418	1277	1115	863

**Coronary artery disease
and alcohol excluded**

Survival may be worse for women with HIV and HF

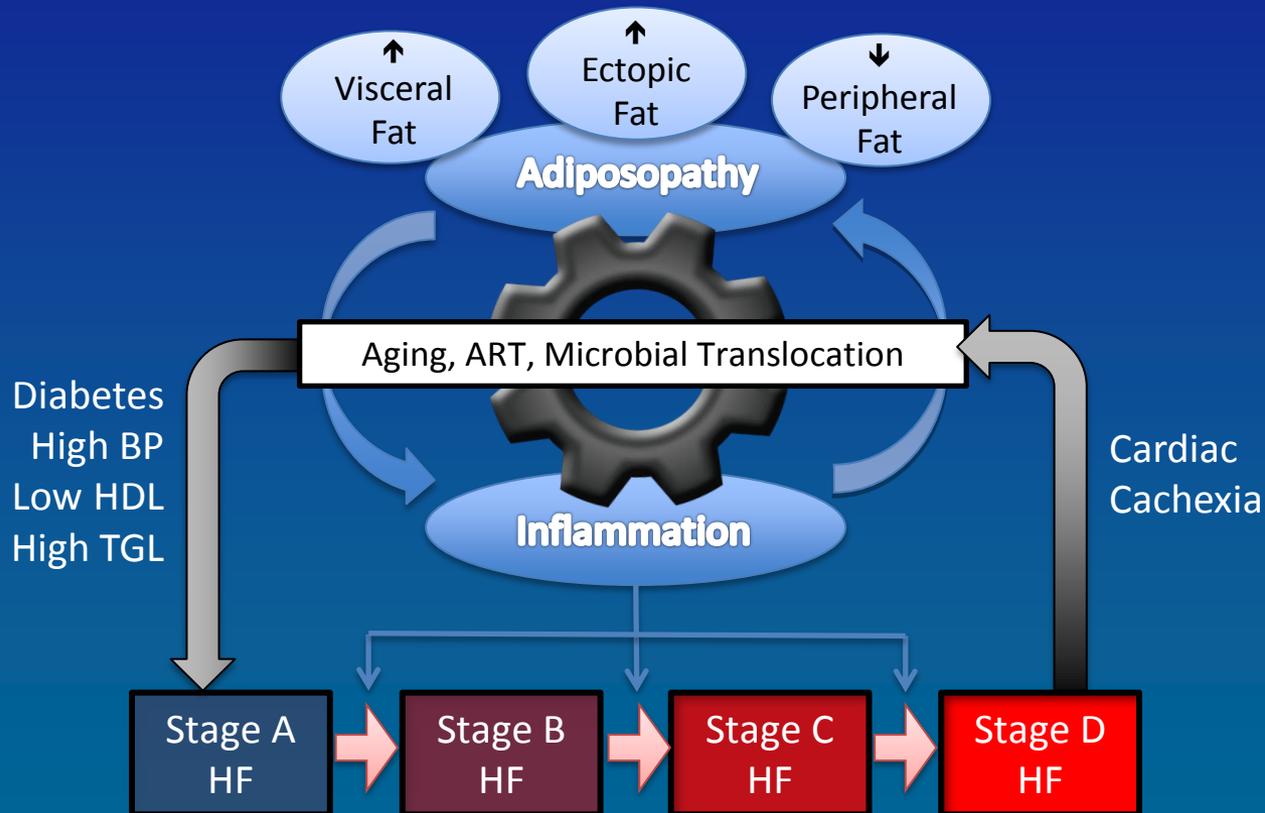


Number at risk

HIV uninfected	102	72	30	8
HIV infected	34	25	13	6

— HIV uninfected — HIV infected

Metabolic disease and inflammation may affect HF progression in HIV



Class I Recommendations for HF Management

Pharmacologic Therapy		
Diuretics		...ve symptoms
ACE Inhibitor/ARB		...ve symptoms and ...ity
ARB + Neprilysin Inhibitor (ARNI)		...ve symptoms and ...ity
Beta Blocker		...ve symptoms and ...ity
Mineralocorticoid receptor antagonists (MRA)		...ve symptoms and ...ity.
Hydralazine/isosorbide dinitrate	Receiving ACE/BB	...ve symptoms and ...ortality

0
Studies
in HIV

Class I Recommendations for HF Management

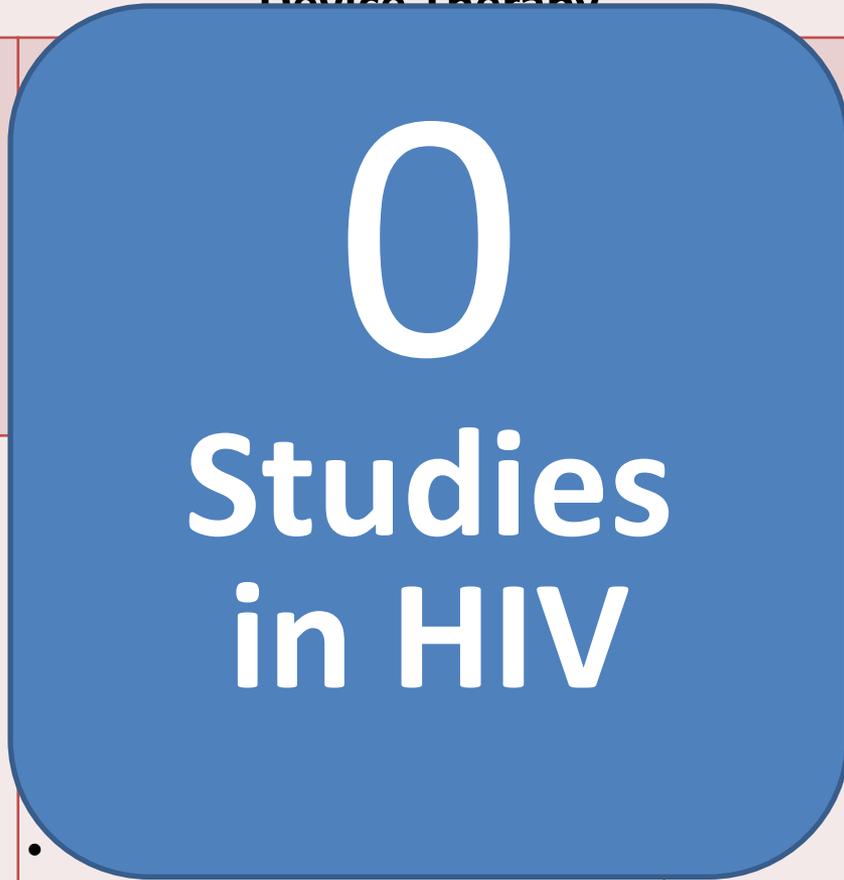
Device Therapy

**Implantable
Cardioverter
Defibrillator (ICD)**

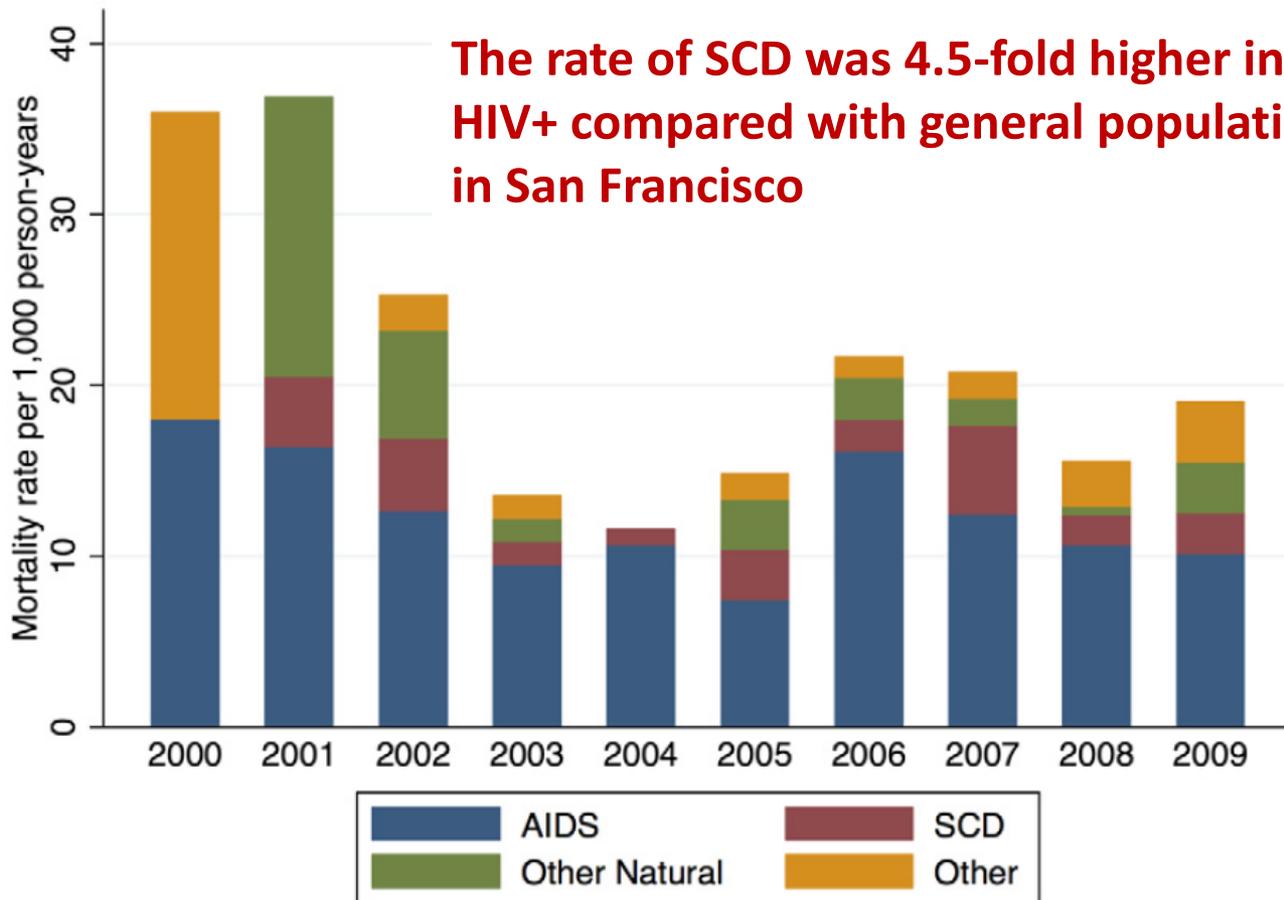
ry prevention of
n cardiac death
e mortality

**Cardiac
Resynchronization
Therapy with or
without defibrillator
(CRT or CRT-D)**

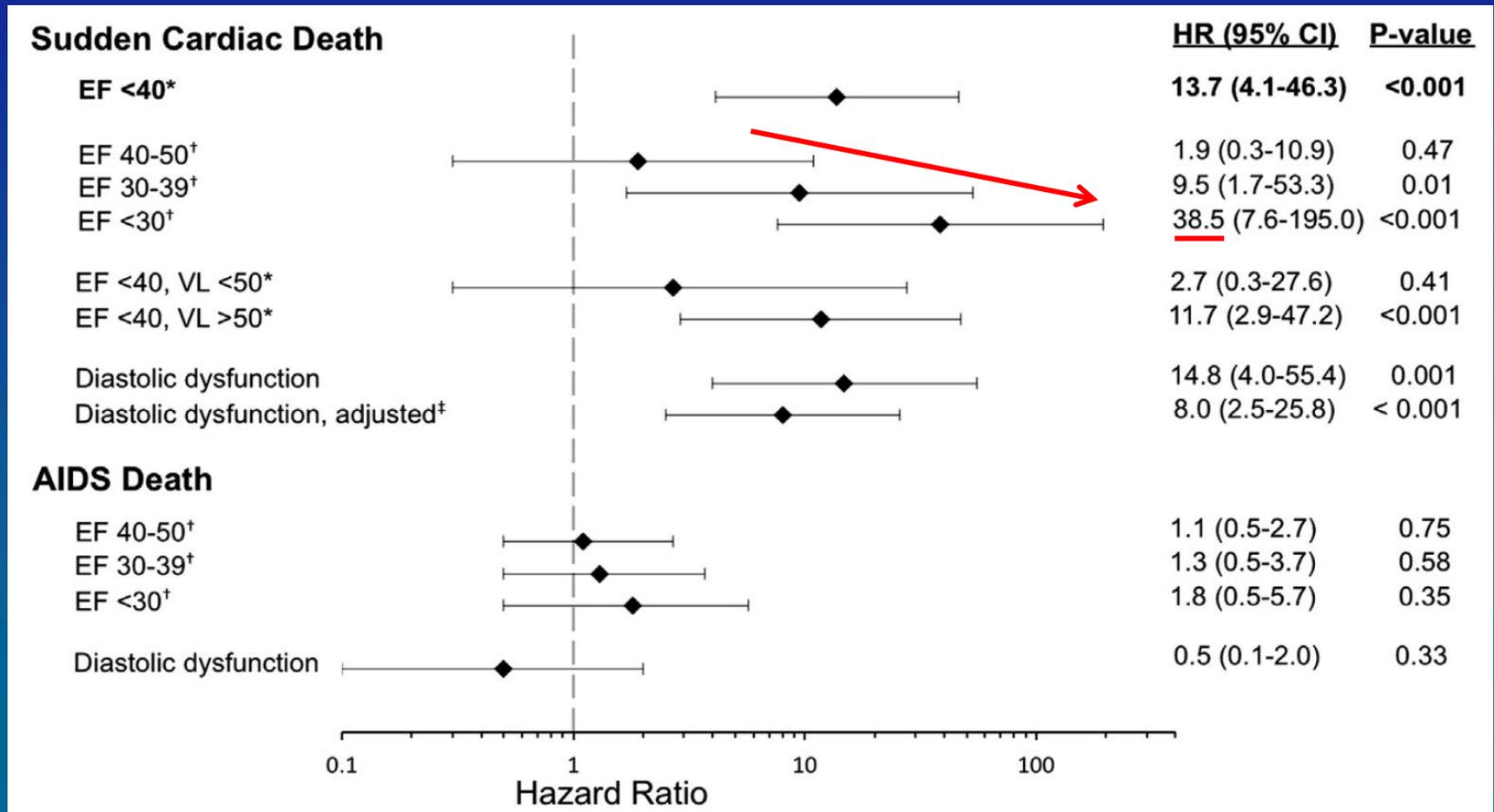
ve symptoms
e mortality



Sudden cardiac death is common in the modern ART treatment era



Ejection fraction is powerful predictor of sudden cardiac death in HIV



Advanced therapies in HIV

- ▶ In 2012, 60% of US institutions still considered HIV infection a contraindication for transplant
 - 20% for left-ventricular assist devices
- ▶ Case series suggest good outcomes
- ▶ Concerns:
 - Infection
 - Progression of HIV disease
 - Pump thrombosis



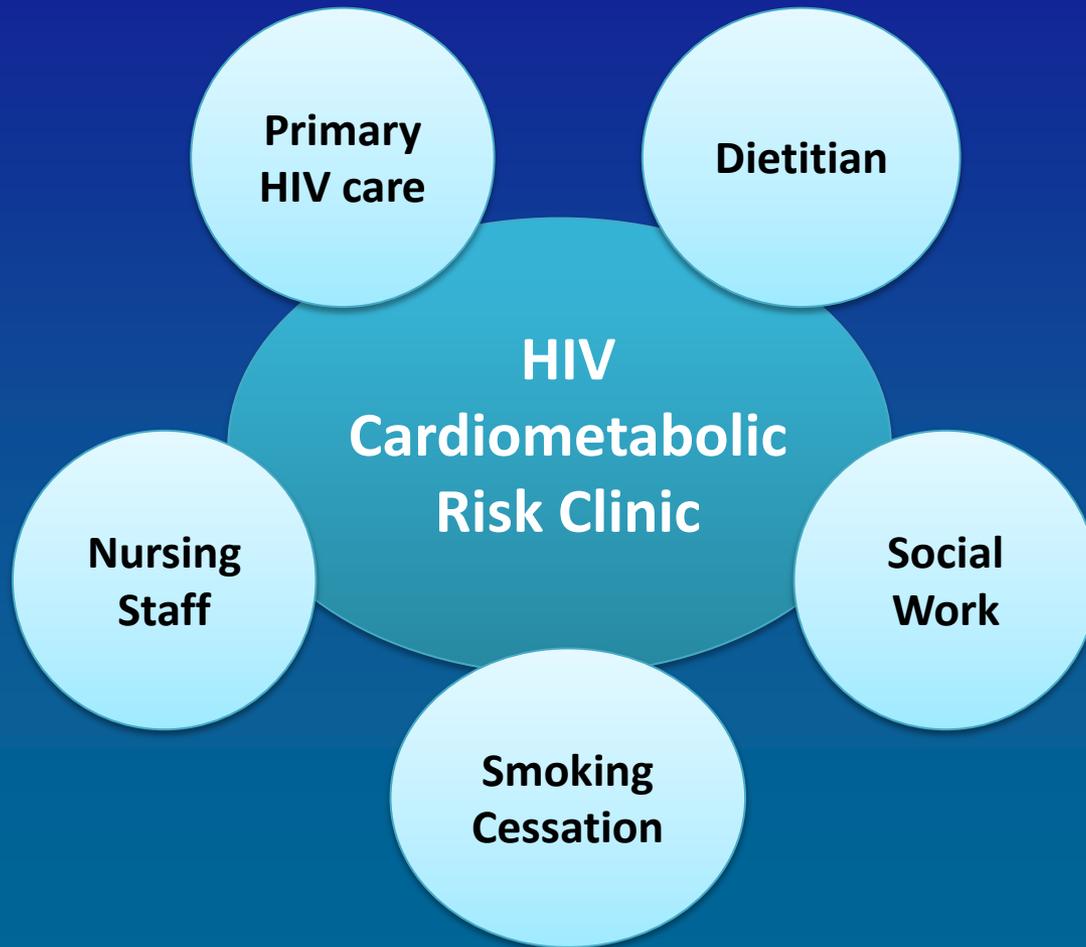
Heart Failure– Clinical Pearls

- ▶ Diastolic and systolic heart failure are both common
- ▶ Little is know about medical therapy
 - Treat as in general HIV-uninfected population
- ▶ ART does more good than harm
 - Avoid drugs with high mitochondrial toxicity (ZDV, didanosine, stavudine)
- ▶ ICD implantation must be a shared decision between patient and providers
- ▶ HIV+ on ART can safely undergo advanced therapies
 - Less is known for those with low CD4+ T-cell counts or AIDS

In Conclusion

Imagine a world where HIV+ patients achieve better outcomes and longer lifespan compared with those without HIV

Team-based cardiovascular risk reduction



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Hepatitis Management

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