The Heart of the Matter: HIV Cardiology Update

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November 8, 2023

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Other support – none

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Learning Objectives

- Cite three sources of reversible risk of cardiovascular (CV) disease in people with HIV
- Review Reprieve and other studies with clinical CV endpoints
- Optimize ART to minimize additional CV risk
- Discuss heart disease, aging, and mobility with patients

This talk will include off-label and investigational uses of antiretroviral drugs.

Outline

- **Introduction**
- Epidemiology: HIV and CV risk
- Pathogenesis
- Prevention and Treatment: 2 cases
- How to talk to PWHIV about aging, mobility, and CV disease

Reprieve Study

ORIGINAL ARTICLE FREE PREVIEW

Pitavastatin to Prevent Cardiovascular Disease in HIV Infection

Steven K. Grinspoon, M.D., Kathleen V. Fitch, M.S.N., Markella V. Zanni, M.D., Carl J. Fichtenbaum, M.D., Triin Umbleja, M.S., Judith A. Aberg, M.D., Edgar T. Overton, M.D., Carlos D. Malvestutto, M.D., M.P.H., Gerald S. Bloomfield, M.D., M.P.H., Judith S. Currier, M.D., Esteban Martinez, M.D., Ph.D., Jhoanna C. Roa, M.D., et al., for the REPRIEVE Investigators*

August 24, 2023
N Engl J Med 2023; 389:687-699
DOI: 10.1056/NEJMoa2304146

Abstract

DSMB closed study of HIV+ low-mod CV risk age >50 after 5.1 years due to efficacy
-35% decrease in Major Adverse Cardiovascular Events (MACE)
-21% decrease in MACE or all-cause mortality

ARS #1

Which of the following statements best characterizes the use of statins in people living with HIV?

1. All patients with HIV should be treated with a statin
2. Some patients with HIV should be treated with a statin
3. The evidence is not conclusive that any PWHIV should be treated with a statin
4. I am not sure

ARS #1

Which of the following statements best characterizes the use of statins in people living with HIV?

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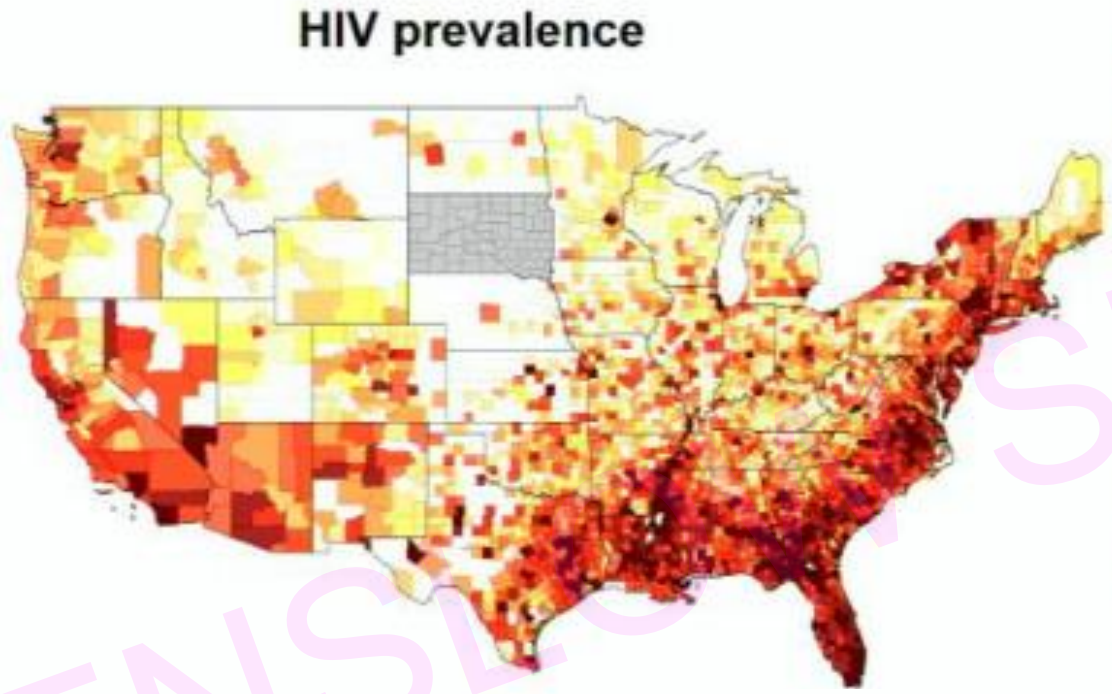
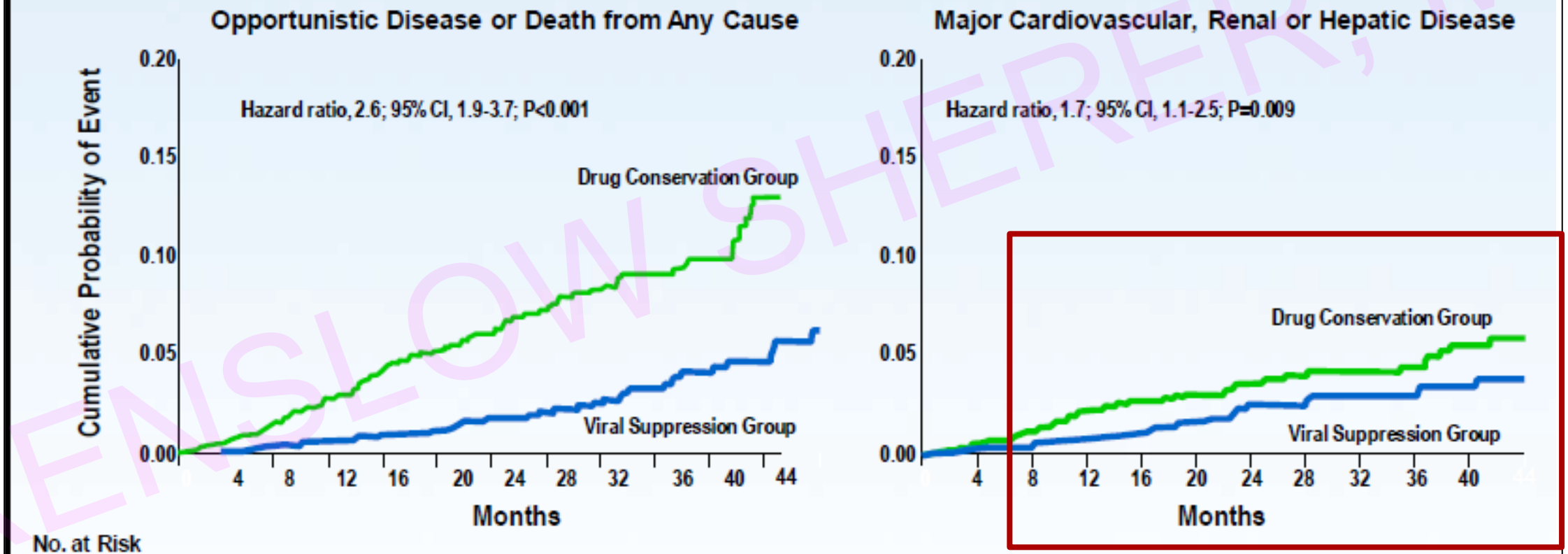
Overlapping Epidemics: HIV, Obesity, Diabetes Mellitus, and Cardiovascular Disease in the US



Koethe. CROI 2019

HIV History: SMART Study 2006

Lower incidence of CVD in pts on ART vs no ART



P Hsue: Increased ASCVD in PWHIV: Circulation 2004:13:1603

SMART Study Group NEJM 2006;355:2283-2296

Elevated D-dimer & CRP Associated w/ 3.8x increase risk of mortality in PWHIV in START, SMART, & ESPRIT Studies

Biomarkers	Event	Groups	No. With Event	No. Without Event	*P*-value	Odds Ratio[2] (with 95% CI)
CRP[1] and D-dimer	AIDS or death[3]	Both above median	32	26	.0004	3.8
		Versus otherwise	31	100		
	Death[3]	Both above median	10	8	.05	4.0
		Versus otherwise	12	36		
	IRIS[4]	Both above median	15	13	.01	5.4
		Versus otherwise	13	43		
CRP and IL-6	AIDS or death	Both above median	34	34	.0007	3.5
		Versus otherwise	29	92		
	Death	Both above median	12	11	.06	3.2
		Versus otherwise	10	33		
	IRIS	Both above median	17	17	.02	4.7
		Versus otherwise	11	39		
CRP and HA[1]	AIDS or death	Both above median	29	20	.0003	4.6
		Versus otherwise	34	106		
	Death	Both above median	10	8	.04	4.4
		Versus otherwise	12	36		
	IRIS	Both above median	19	11	.002	8.7
		Versus otherwise	9	45		
CRP, D-dimer, IL-6 and HA	AIDS or death	All above median	21	11	.0002	6.1
		Versus otherwise	42	115		
	Death	All above median	9	3	.008	9.2
		Versus otherwise	13	41		
	IRIS	All above median	12	6	.005	12.3
		Versus otherwise	16	50		

0.1 1 10 100

1. CRP = C-reactive protein; HA = hyaluronic acid

Jupiter trial shows that Rosuvastatin reduces CV Dx By 44% in people with no HIV and high CRP and chronic Inflammation
Ridker PM. NEJM 2008;359:

Boulware D et al. JID 2011;203:1637–46 DOI:10.1093/infdis/jir134

HIV History: Statin Use Associated with a 77% Lower Mortality at the Moore Clinic, JHU, 2011

Category	Subcategory	Relative Hazard (95% CI)	P-Value
Statin Use		0.33 (0.14,0.76)	0.009
Age (median years)		1.07 (1.05,1.10)	<0.0001
Race	Black	0.82 (0.47, 1.46)	0.51
	Others	1.0 (reference)	
HIV Risk Group	IDU	2.30 (1.30, 4.07)	0.004
	Heterosexual	1.50 (0.96, 2.35)	0.08
	MSM	1.0 (reference)	
CD4+ at HAART start (per 100 cell/mm^3 higher increments)		0.96 (0.84, 1.09)	0.52
HIV-1 RNA at HAART start (per log_{10} higher increments)		0.96 (0.79, 1.18)	0.16
Hemoglobin at HAART start (per g/dL higher increments)		0.80 (0.71, 0.90)	0.0003
Total Cholesterol at HAART start (per 10 mg/dL higher increments)		0.98 (0.93, 1.03	0.36
Year HAART started	<= 2004	1.20 (0.74, 2.06)	0.50
	> 2004	1.0 (reference)	
HAART Drug	NNRTI	1.23 (0.59, 1.52)	0.42
	Others	1.0 (reference)	
Prior ART		1.37 (0.82, 2.31)	0.23
Prior ADI		2.24 (1.39, 3.60)	0.001
Viral Hepatitis C Co-infection		1.07 (0.62, 1.84)	0.81

*Male vs. female sex could not be analyzed independently because of collinearity with the MSM risk group.
(Multivariate adjusted association of Statin use and each of the other variables)1 categroies are0 mg/dL increase)g/dL increase).
doi:10.1371/journal.pone.0021843.t002

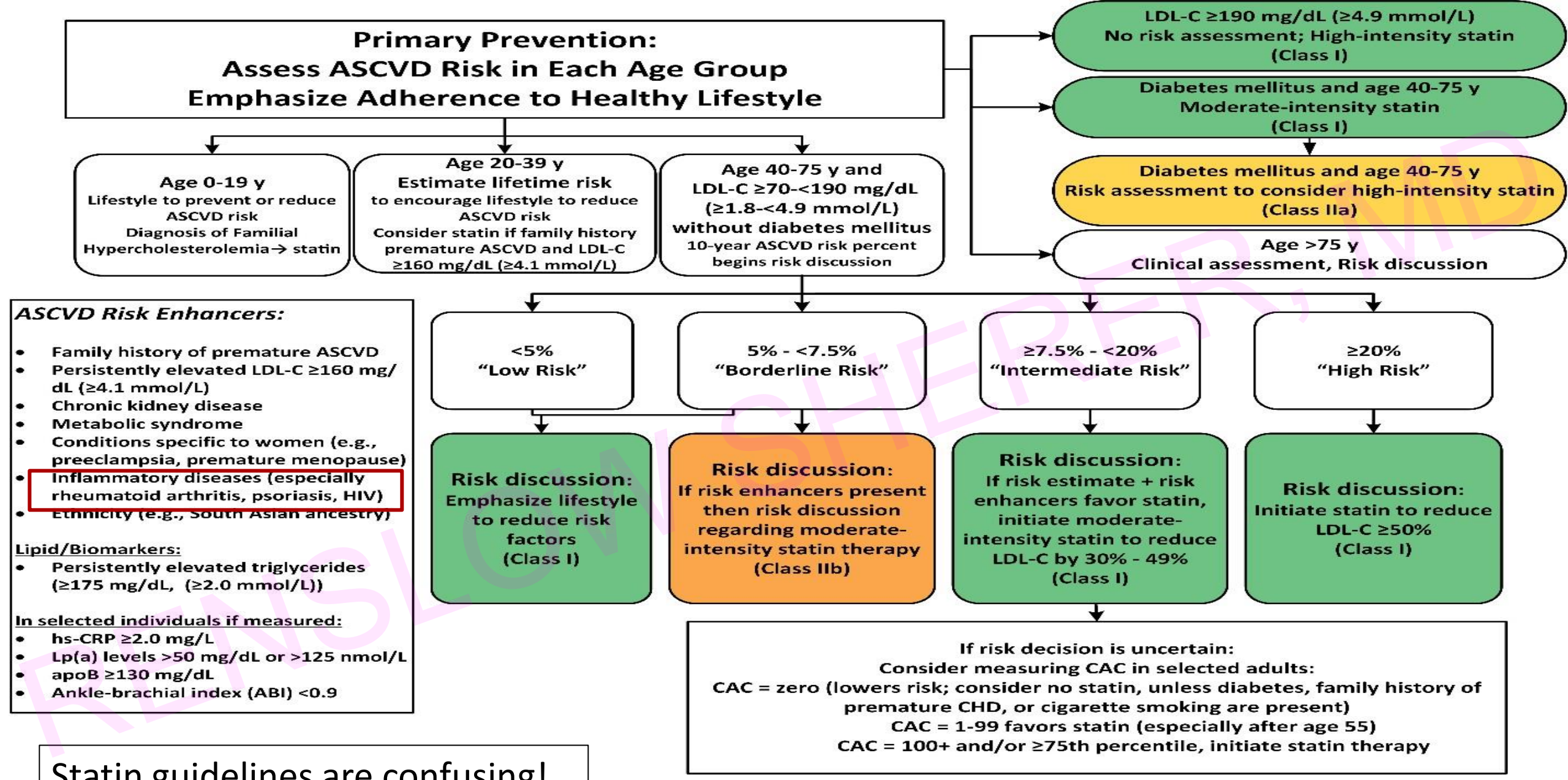
Other mortality predictors:
-low hgb
-older age
-injection drug use
-prior AIDS

CONFOUNDERS

Higher CV risk factors In statin users:
-older age
-more prior AIDS
-higher cholesterol
-2x use of BP Rx

Lower CV risk factors In statin users:
-Lower HCV
-Higher CD4

Moore, Bartlett, Gallant. Plos One July 12, 2011. https://doi.org/10.1371/journal.pone.0021843 .



Statin guidelines are confusing!
HIV is a CV Dx "RISK ENHANCER"

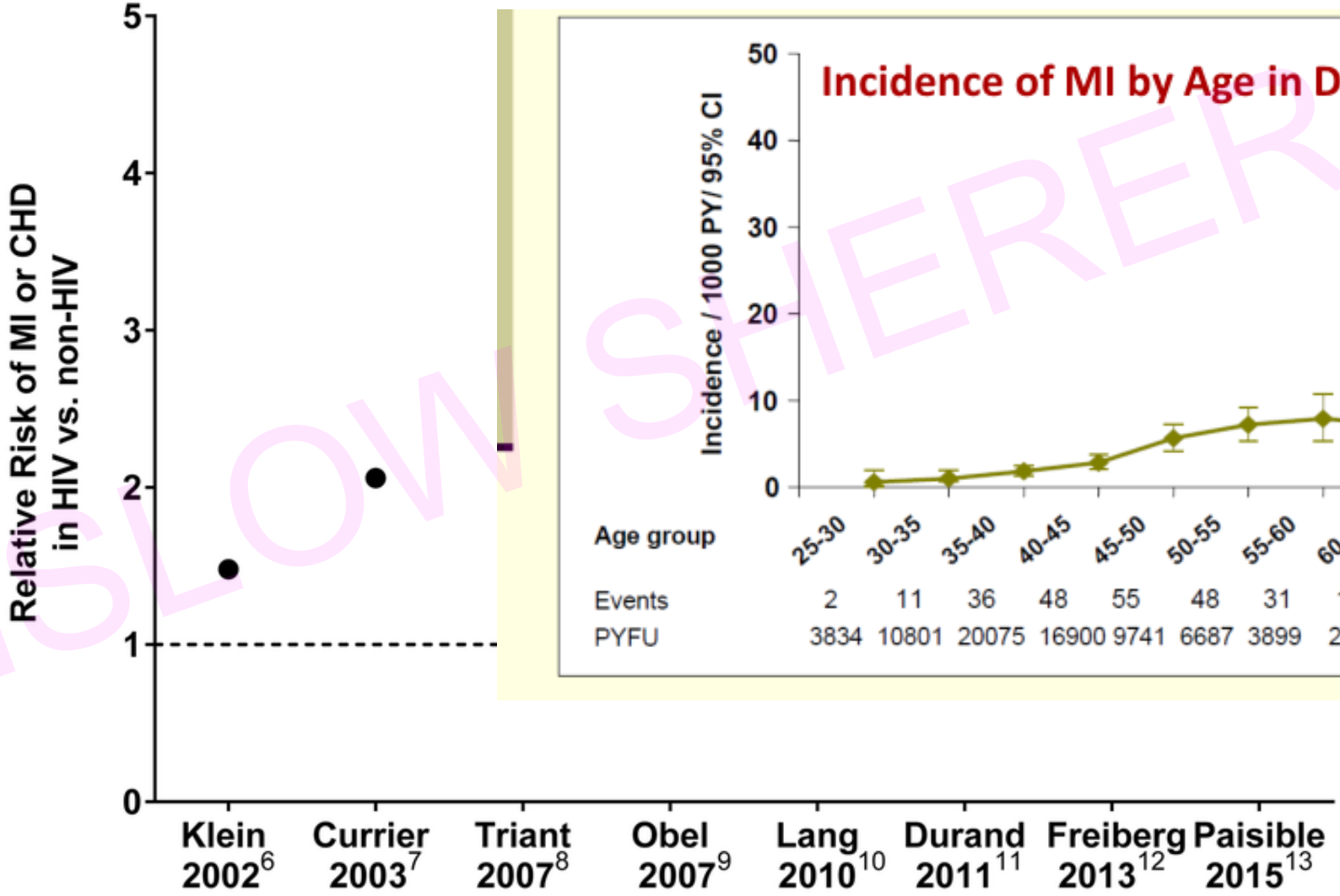
Grundy SM. Circulation. 2018;139:25. DOI: (10.1161/CIR.0000000000000625)

Introduction: HIV and Cardiovascular Disease (CVD)

How to talk to patients about aging, mobility, CV risk #1

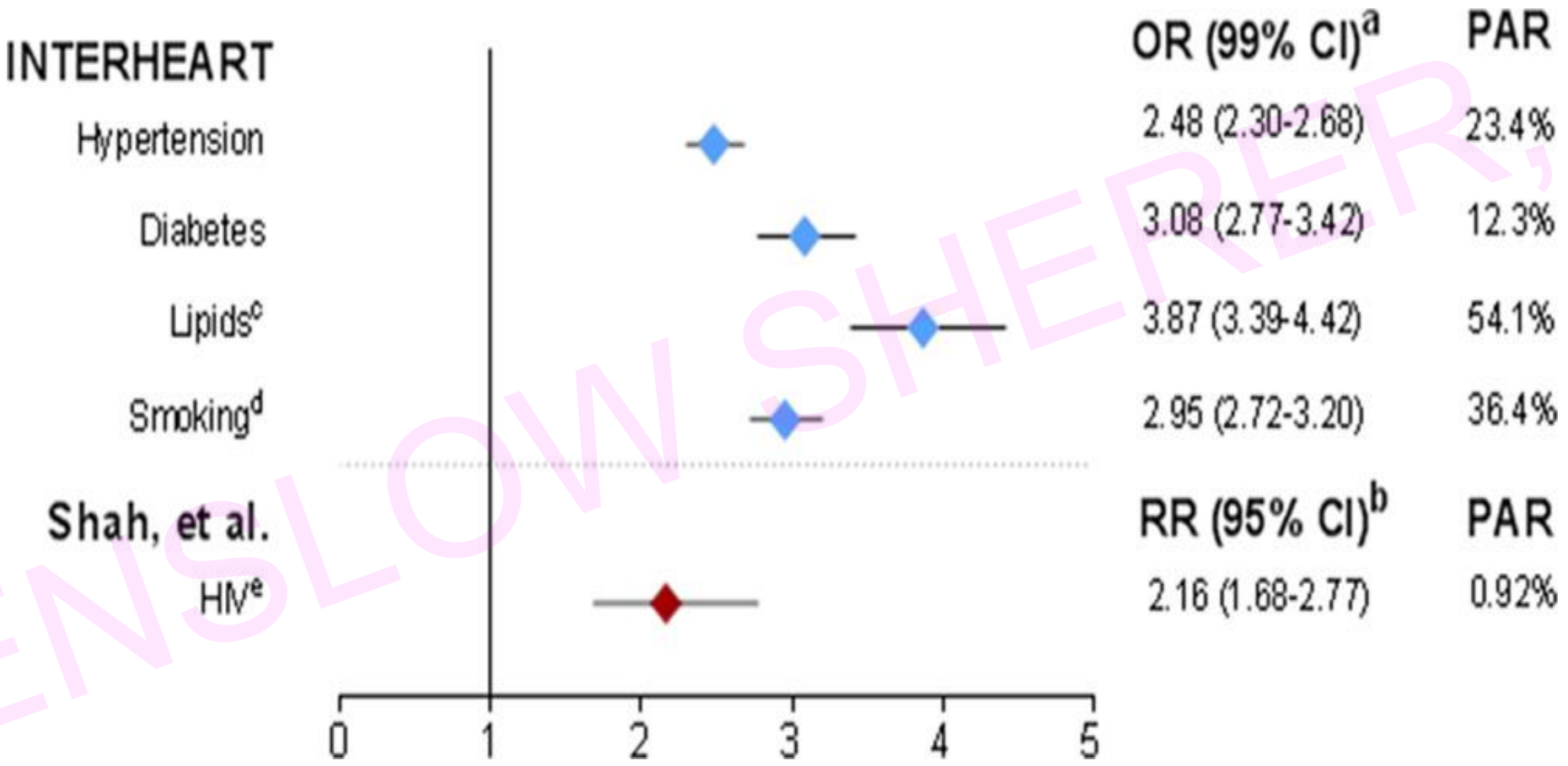
- People with HIV have **2x higher rates of CVD**
  - Includes CVA, peripheral vascular disease; effect comparable to DM
- 50% of PWHIV are age > 50 years. CVD risk increases w/ age
  - **Life-long prevention** is useful; increasing imperative in aging PWHIVs
- Older PWIHV have more comorbidities
  - DM, CV, CA, CKD, lipids, liver, coag'pathy, MH, CNS, frailty, polypharm
  - Additional rationale for **prevention, recognition and management**
  - **Mobility and exercise** are key elements of CV disease reduction

Risk of MI in PWH compared to HIV negative controls



Nou, Eric & Lo, Janet & Hadigan, Colleen & Grinspoon, Steven. (2016). Pathophysiology and management of cardiovascular disease in patients with HIV. The Lancet Diabetes & Endocrinology. 4. 10.1016/S2213-8587(15)00388-5.

Comparative Risk of MI by Risk Factor



Priscilla Y. Hsue. Circulation. Time to Recognize HIV Infection as a Major Cardiovascular Risk Factor, Volume: 138, Issue: 11, Pages: 1113-1115, DOI: (10.1161/CIRCULATIONAHA.118.036211)

Risk Factor Management for CV Disease in PWHIV

How to talk to patients about aging, mobility, & CV disease #2

- Exercise, smoking cessation, BP control, healthy lifestyle, DM control, ART selection, lipid control, and other CV risk reduction are key elements
  - Some recent evidence of improvement in management in past decade in the US*

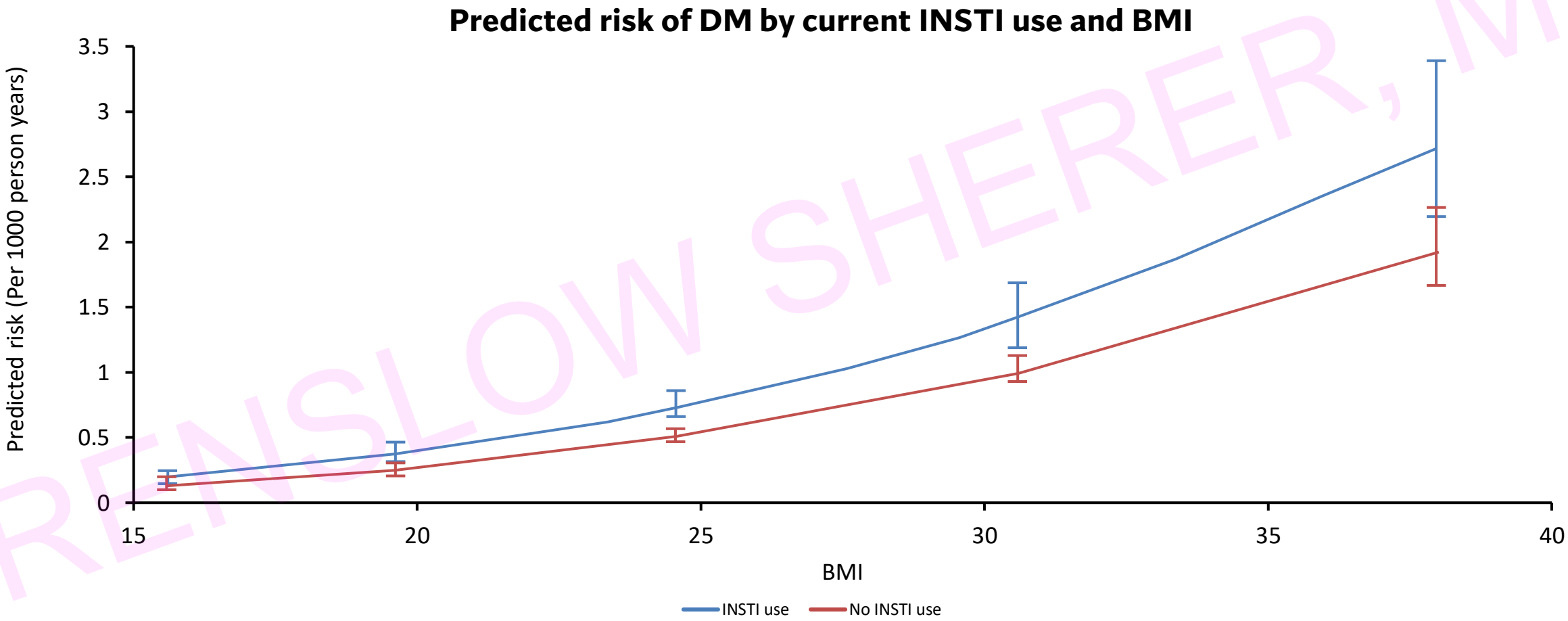
1. Klein DB, et al. Clin Infect Dis. 2015;60:1278-1280.
2. Marcus JL, et al. AIDS. 2014;28:1911-1919.
Silverberg M, et al. Virtual CROI 2021; March 6-10, 2021. Abst. 97.

Risk Factor Management for CV Disease in PWHIV

How to talk to patients about aging, mobility, & CV risk #3

- Exercise, smoking cessation, BP control, healthy lifestyle, DM control, ART selection, lipid control, and other CV risk reduction are key elements
  - Some recent evidence of improvement in management in past decade in the US
- Increasing weight gain, insulin resistance, & DM in PWHIV are contributing to increased risk of CV disease
  - No proven new strategies or ART switches to date

Respond Cohort:
New Onset DM by BMI and INSTI Use

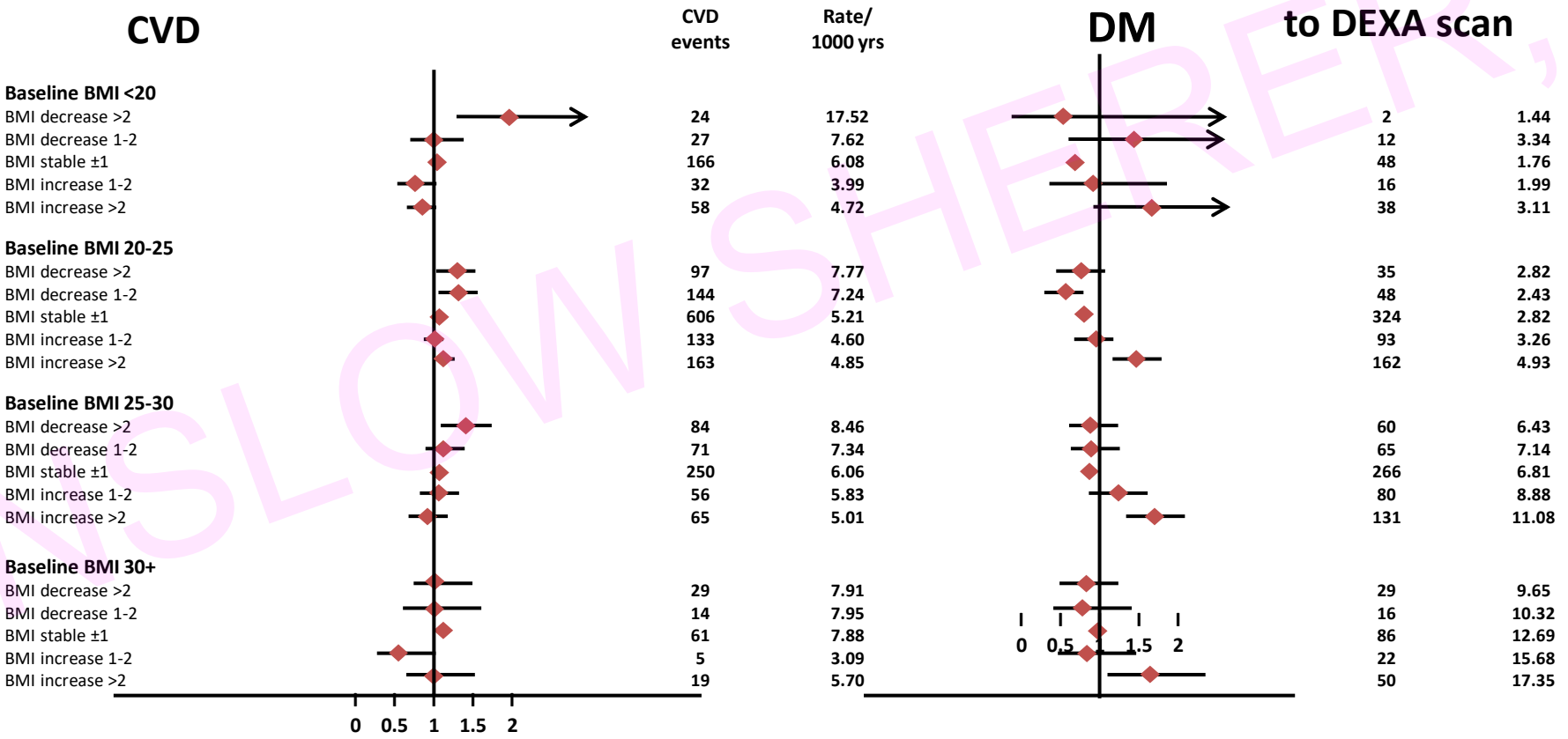


Note: Figure 1 shows the predicted risk per 1000 person years of DM for BMI (antilog of logBMI) among INSTI and non-INSTI users when adjusted for sex, natural log of Age, HIV risk group, ethnicity, CD4, current TDF/TAF use. Among INSTI users, raltegravir (RAL) 12%, dolutegravir (DTG) 60%, other INSTIs (elvitegravir (EVG), bictegravir (BIC), cabotegravir (CBG))28%.

Rupasinghe D, et al. IAS 2023; Brisbane, Australia; July 23-26, 2023. Abst. OAB0402.

D:A:D: BMI Increase is Associated With Risk of DM2, but Not Risk of CVD

Results – CVD and DM Risk



EACS Nov 2023: BMI is a superior predictor of incident DM and metabolic syndrome compared to DEXA scan

CVD: Adjusted for age, race, mode of transmission, sex, recent abacavir and other NRTI use, cumulative protease inhibitor use, CD4 count, family history of CVD, smoking status

DM: Adjusted for age, race, mode of transmission, sex, stavudine use, triglycerides, CD4 count, smoking status and HDL (high-density lipoprotein)

Petousenos K, et al. 27th CROI; Boston, MA; March 8-11, 2020. Abst. 83.

Taramasso L, et al. EACS 2023; Warsaw, Poland; October 18-21, 2023. Abst. 1004.

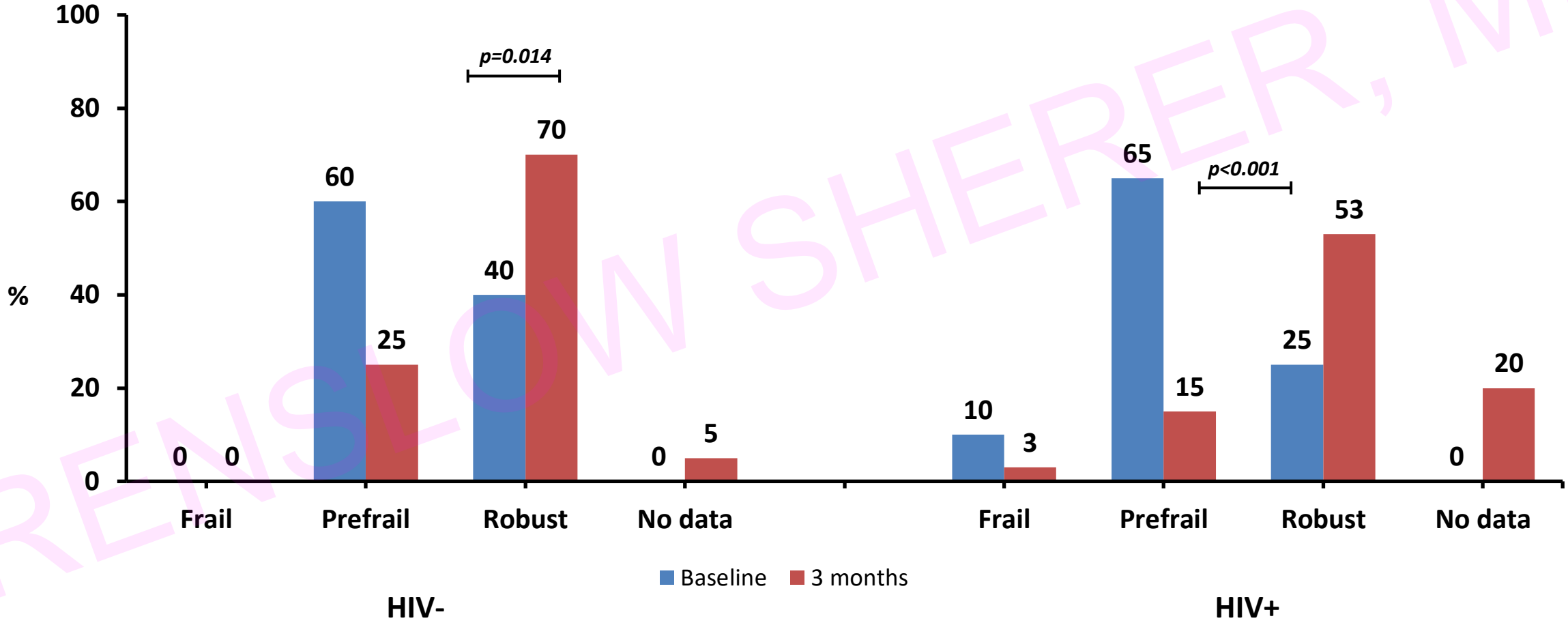
ART and Weight Gain, 2023

How to talk to patients about CV disease #4

- TDF and EFV are weight suppressive
  - Weight gain following d/c of either drug
- 20-30% of weight gain on ART is return to health in advanced HIV disease
- INSTIs do not independently cause weight increase
  - Social norms and obesogenic lifestyles are contributors
- No evidence to date that ART switch leads to weight reduction
- Metabolic risk: risk of DM and metabolic syndrome with weight gain
- Diet and exercise can mitigate weight gain associated w/ INSTIs & TAF
  - GLP-1 inhibitors are effective in PWHIV in early trials

A 12-Week Multicomponent Exercise Program Reverses Frailty in Older Adults With HIV

Frailty (Frailty Phenotype), physical function (Senior Fitness Test (SFT), hand grip strength, SPPB), mood (HADS, GDS-SF), and quality of life (WHOQOL-HIV-BREF)



Brañas F, et al. CROI 2023; Seattle, WA; February 19-22, 2023. Abst. 701.

Use of GLP-1 Agonists in HIV: Retrospective cohort

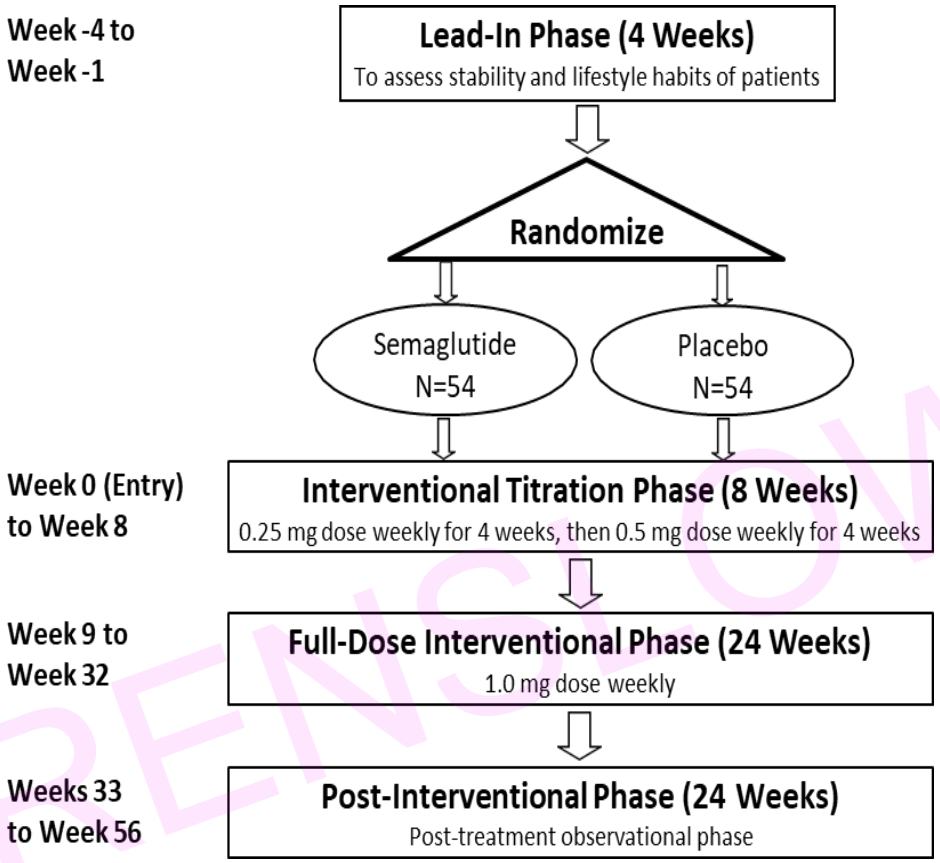
- Retrospective cohort study (2/2021 - 2/2023) at UCSD
- Inclusion criteria
  - Age ≥ 18 years old
  - Prescribed GLP-1 RA during study period
- Exclusion criteria
  - PWH with no weight data available after GLP-1 RAs initiation
- BMI 34.1kg/m2
- 49% white, 38% Hispanic, 17% female
- 52% Semaglutide, 31% dulagutide
- Only 41% reached maximal dose
- Mean 15.4 month FU

	Baseline	Follow-up on GLP-1 RA	Δ
Mean Weight, kg (± Std. dev)	103.4 (83.5 – 123.4)	98 (78.5 – 117.9)	-5.4 kg
Mean BMI, kg/m^2, (± Std. dev)	34.1 (28.5 – 39.8)	32.3 (26.6 – 38.2)	-1.8 kg/m^2
Mean Hgb A1C, (± Std. dev)	7.0 (5.0 – 8.9)	6.4 (4.9 – 8.0)	-0.6

- 53 patients (23.5%) had >5% weight loss
- 41 patients (18.2%) changed from obese to overweight
- Factors associated with >5% weight loss (multivariable analysis)
  - Higher baseline BMI [OR 1.07 (1.02-1.3)]
  - Longer duration of treatment (months) [OR 1.04 (1.01-1.07)]
- The use of dulaglutide was associated with decreased odds of achieving
- >5% weight loss [OR 0.33 (0.17-0.66)] as compared to the other GLP-1 RAs

Nguyen Q, et al. IDWeek 2023; Boston, MA; October 11-15, 2023. Abst. 1983.

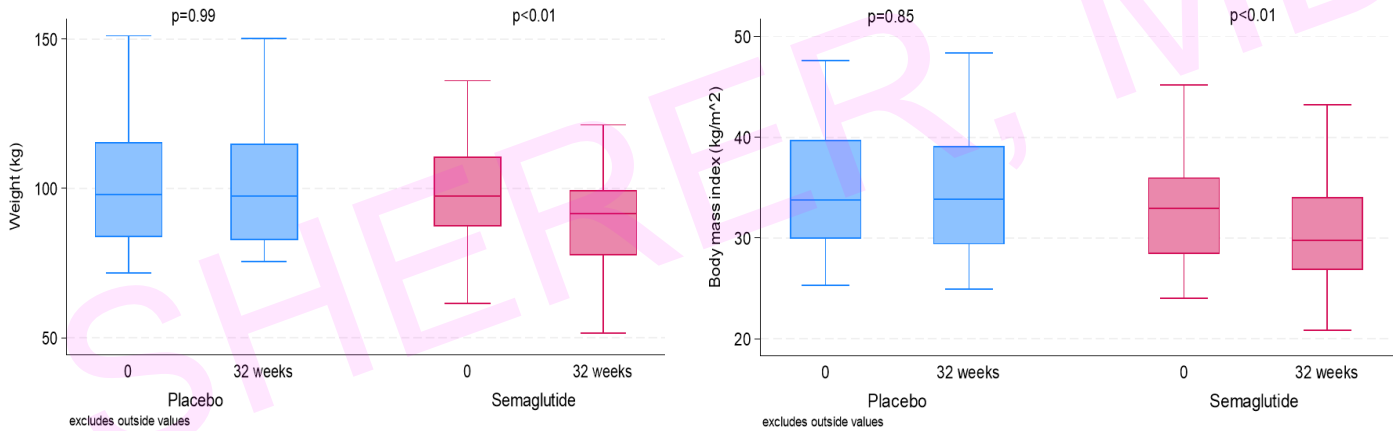
First RCT of Semaglutide in HIV+ subjects



NB: No changes in liver, pericardial fat

McComsey G, et al. IDWeek 2023; Boston, MA; October 11-15, 2023. Abst. 1984.

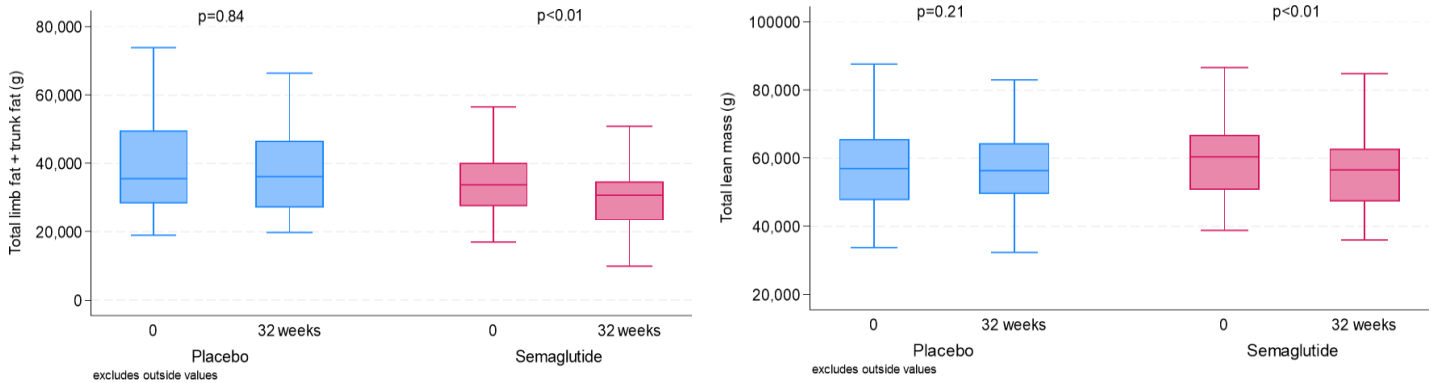
Changes in Weight and BMI



Weight ↓ 8.3% vs ↑0.2%

65% on semaglutide vs. 4% on placebo lost ≥5% weight

DXA Changes in Body Composition



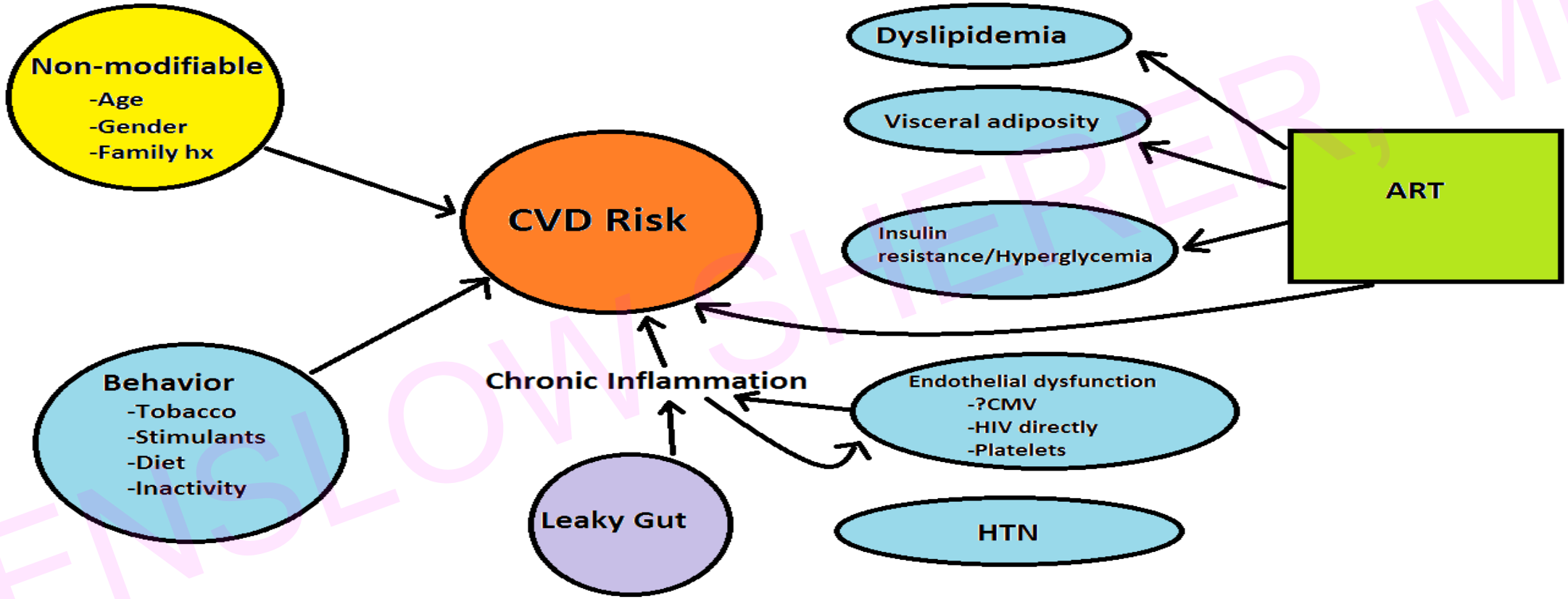
Total fat ↓ 15% vs ↑0.2%

Total lean mass ↓ 5.4% vs ↓0.6%

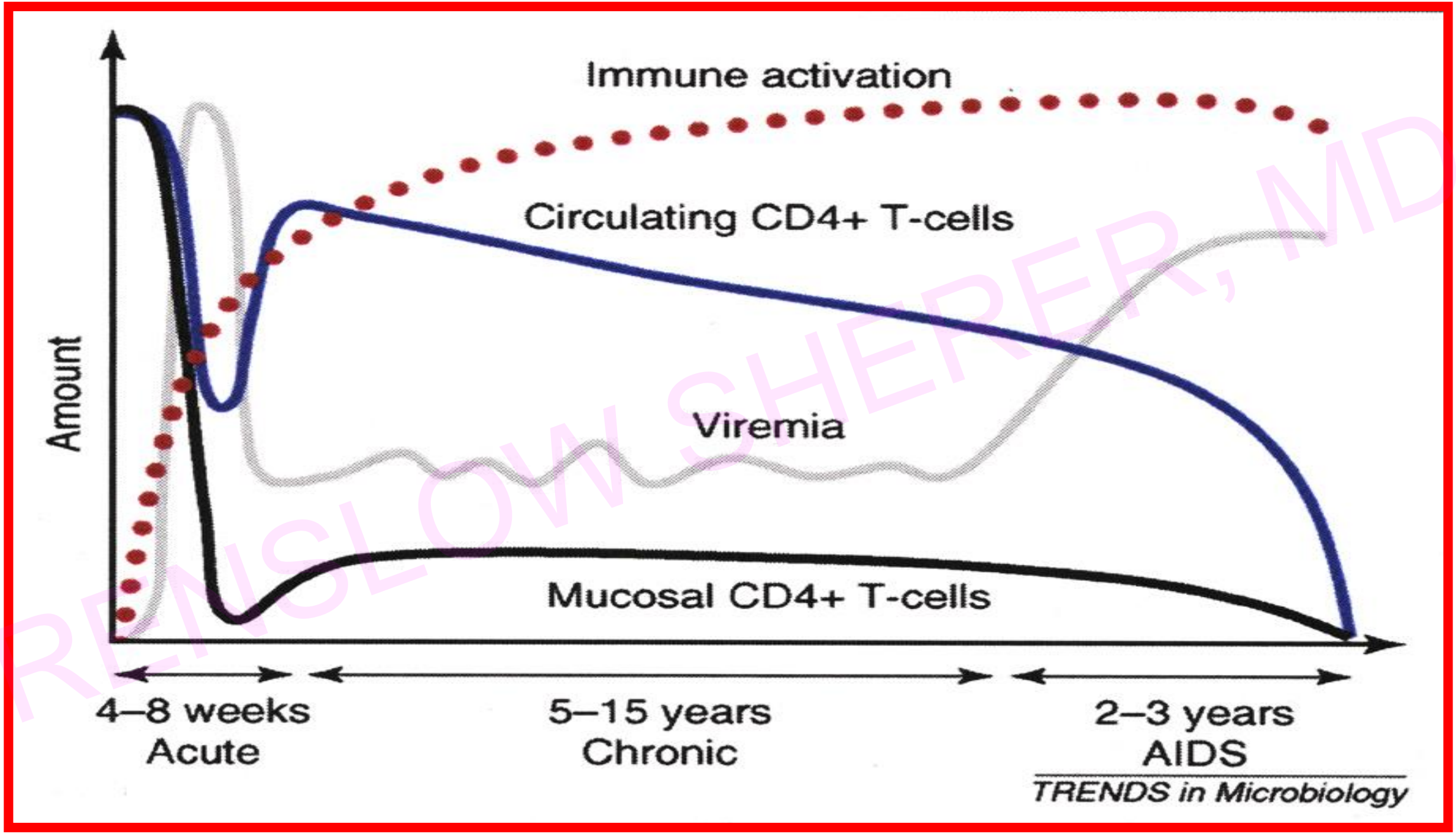
Outline

- Introduction
- Epidemiology: HIV and CV risk
- **Pathogenesis**
- Prevention and Treatment
- How to talk to PWHIV about aging, mobility, and heart disease

Multifactorial etiology of CVD in HIV



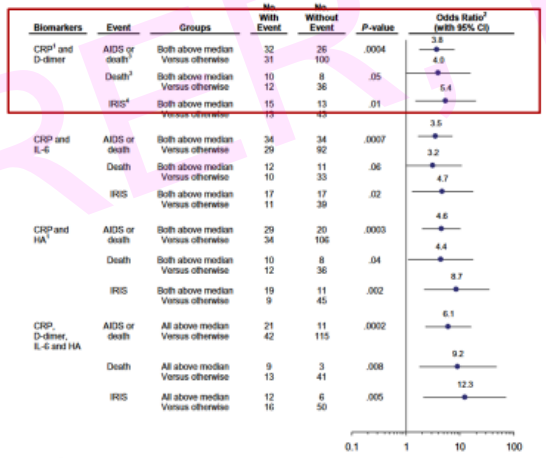
Slide from J. Aberg, ACTHIV 2019.



Impact of Chronic Immune Activation and Inflammation

- Premature aging
- Cardiovascular disease
- Chronic liver disease
- Osteopenia, osteoporosis
- Chronic kidney disease
- Non-AIDS-associated cancer
- Thrombo-embolism, DVT & PE
- Neurocognitive deficits

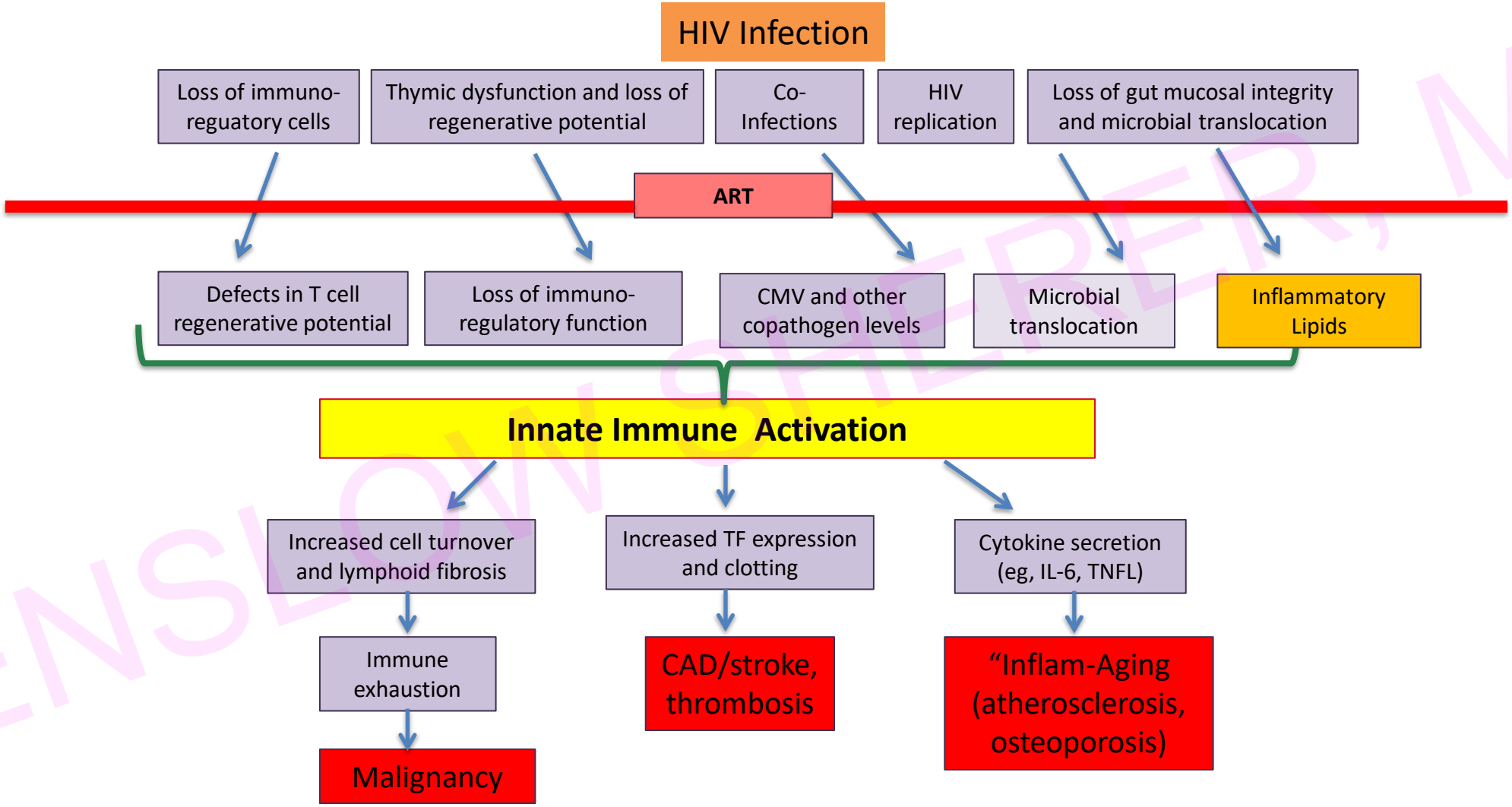
Elevated D-dimer & CRP Associated w/ 3.8x increase risk of mortality in PWHIV in START, SMART, & ESPRIT Studies



Boulware D et al. JID 2011;203:1637–46 DOI:10.1093/infdis/jir134

…..rationale for earlier ART initiation

Early ART reduces but does not eliminate excess risk of CV Dx



Deeks SG. 2001. Annu Rev Med, 62:141-55
Appay V, et al. J Pathol. 2008;214:231-241
Lederman ML, et al. Adv Immunol. 2013;119:51-83

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Prevention and Treatment of CV Disease

Reversible risks

- Smoking cessation
- Mobility & exercise
- Sensible eating
- BP control
- Insulin resistance & DM control
- ART selection
- Lipid management

Irreversible risks

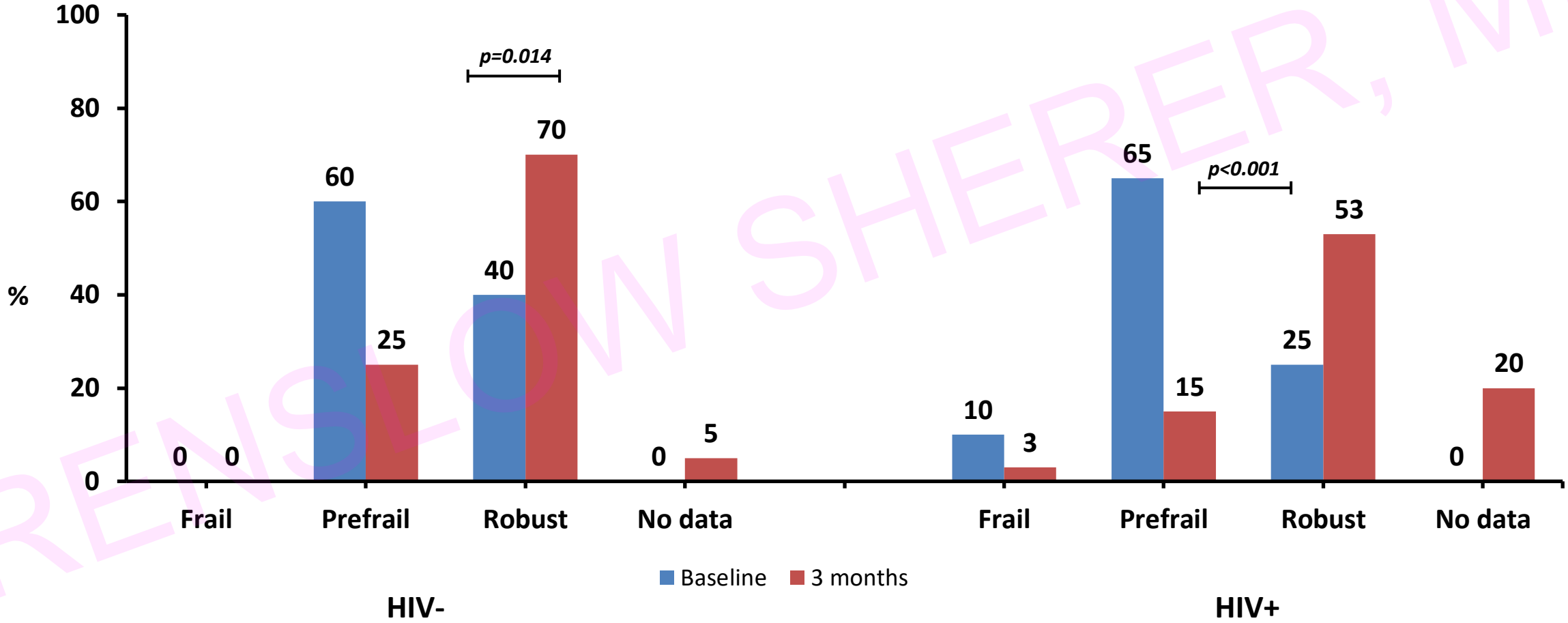
- Older age
- Gender
- Genetics

Possible reversible risks

- Dental & gingival health

A 12-Week Multicomponent Exercise Program Reverses Frailty in Older Adults With HIV

Frailty (Frailty Phenotype), physical function (Senior Fitness Test (SFT), hand grip strength, SPPB), mood (HADS, GDS-SF), and quality of life (WHOQOL-HIV-BREF)



Brañas F, et al. CROI 2023; Seattle, WA; February 19-22, 2023. Abst. 701.

ARS #2

Which of the following is known about pitavastatin relative to other statins?

1. It is the strongest statin for lowering LDL
2. It is the strongest statin for reducing inflammation
3. It is the statin with the least amount of drug-drug interactions
4. It is the statin with the lowest incidence of muscle-related symptoms
5. None of the above, it is similar to other statins

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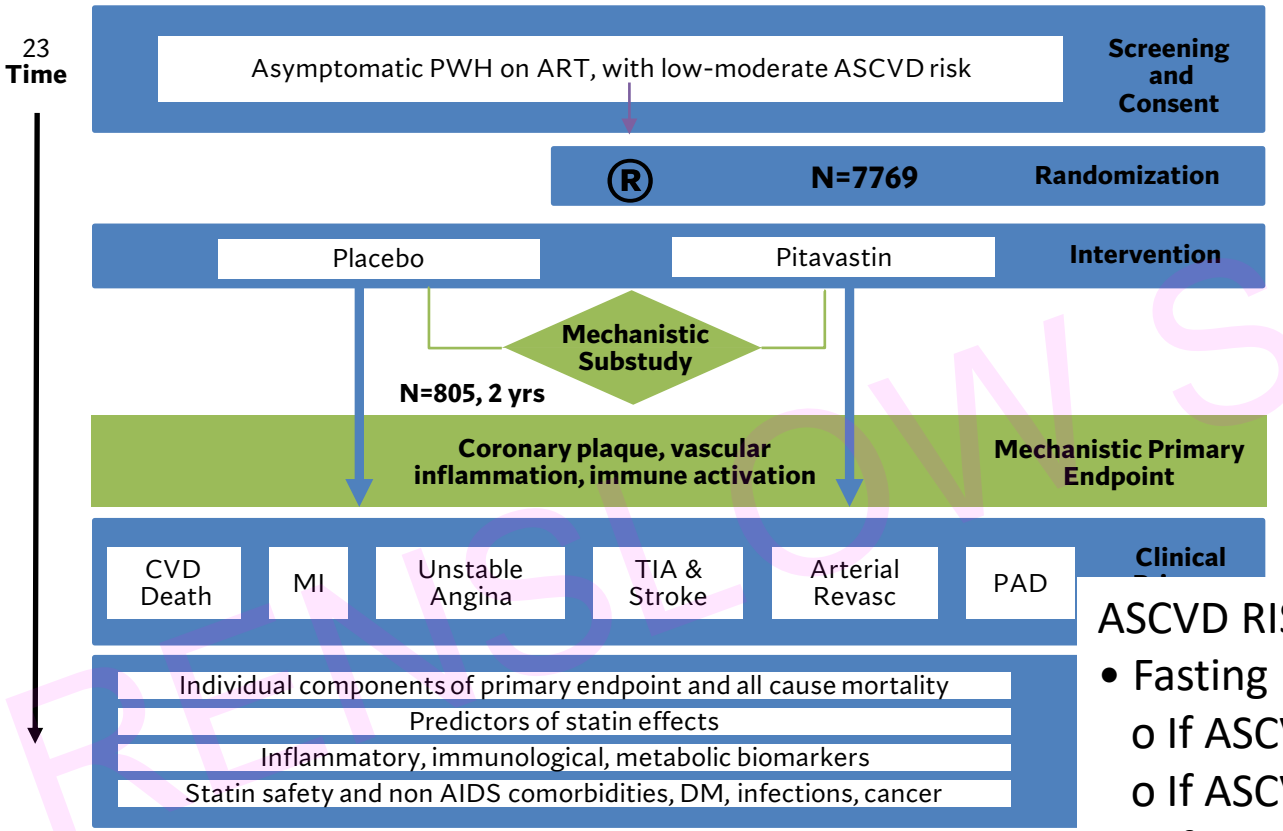
REPRIEVE: Pitavastatin Calcium 4mg vs Placebo in PLWH age > 50 yrs and Low/Moderate CV Risk: Schema and Baseline Characteristics



Baseline Characteristics		Total (N-7769)	Pitavastatin (N=3888)	Placebo (N=3881)
Age (years)	Median (Q1-Q3)	50 (45-55)	50 (45-55)	50 (45-55)
Natal Sex	Male	5350 (69%)	2677 (69%)	2673 (69%)
	Female	2419 (31%)	1211 (31%)	1208 (31%)
Gender Identity	Cisgender	7367 (95%)	3687 (95%)	3680 (95%)
	Transgender spectrum	127 (2%)	63 (2%)	64 (2%)
	Not reported	275 (4%)	138 (4%)	137 (4%)
Race	White	2704 (35%)	1634 (35%)	1340 (35%)
	Black/African American	3208 (41%)	1569 (40%)	1639 (42%)
	Asian	1138 (15%)	571 (15%)	567 (15%)
CD4 count (cells/mm³)	Median (Q1-Q3)	621 (448-827)	620 (449-832)	622 (455-824)

ASCVD RISK & LIPID ENROLLMENT CRITERIA

- Fasting LDL cholesterol as follows:
  - o If ASCVD risk score <7.5%, LDL cholesterol must be <190 mg/dL
  - o If ASCVD risk score ≥7.5% and ≤10%, LDL must be <160 mg/dL
  - o If ASCVD risk score >10% and ≤15%, LDL must be <130 mg/dL

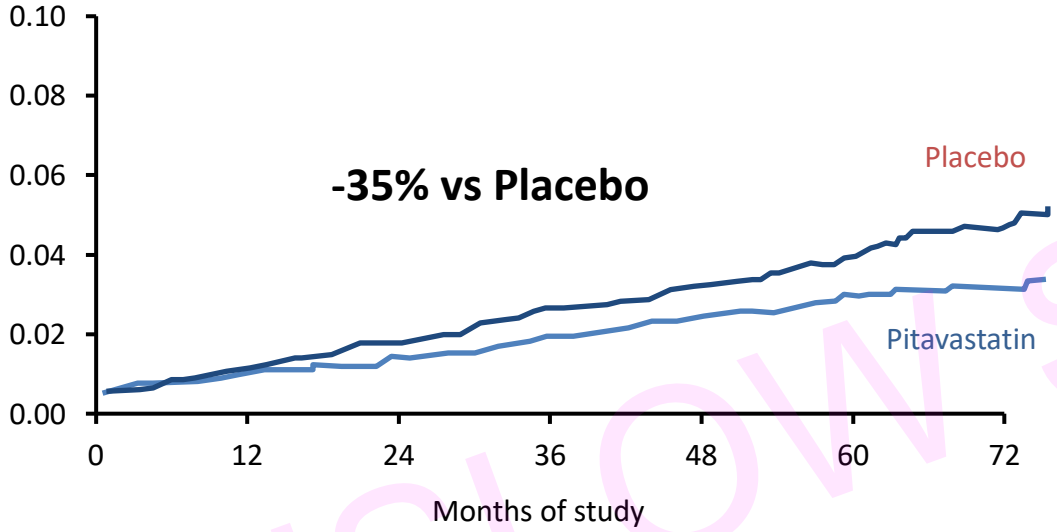
NOTE: If LDL <70 mg/dL, participant is eligible regardless of 10-year ASCVD risk score in line with the ACC/AHA 2013 Prevention Guidelines.

- Fasting triglycerides <500 mg/dL

Grinspoon S, et al. IAS 2023; Brisbane, Australia; July 23-26, 2023. Abst. SY06.

REPRIEVE Trial: Primary Endpoints

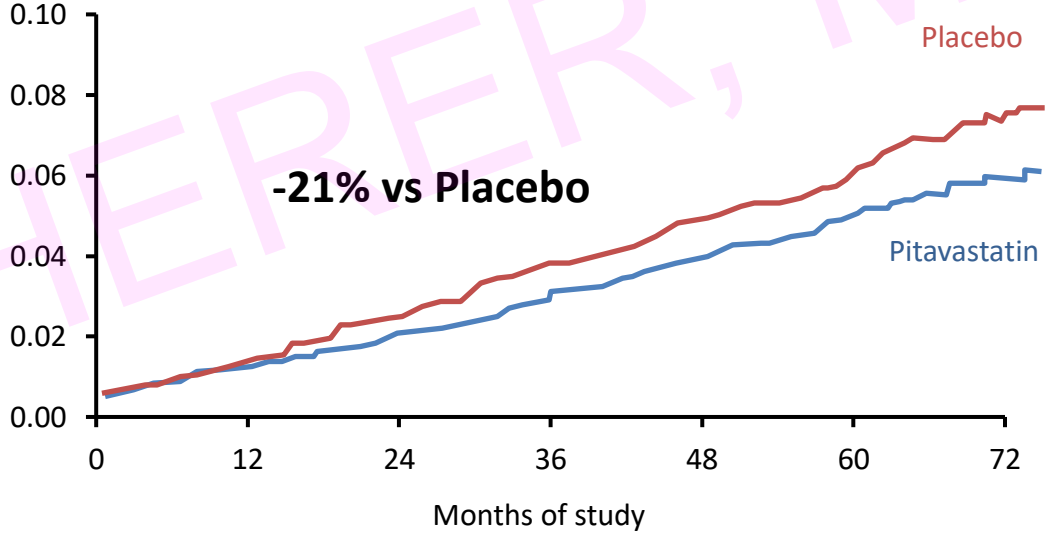
(a) First Primary MACE (Major Adverse CV Event)



Cumulative incidence of event						
0%	0.6%	1.0%	1.4%	1.9%	2.4%	2.7%
0%	0.7%	1.4%	2.1%	2.7%	3.4%	4.4%

Number at risk							
Pitavastatin	3888	3647	3475	3364	2997	1947	1052
Placebo	3881	3693	3506	3356	2997	2182	959

(b) First MACE or Death

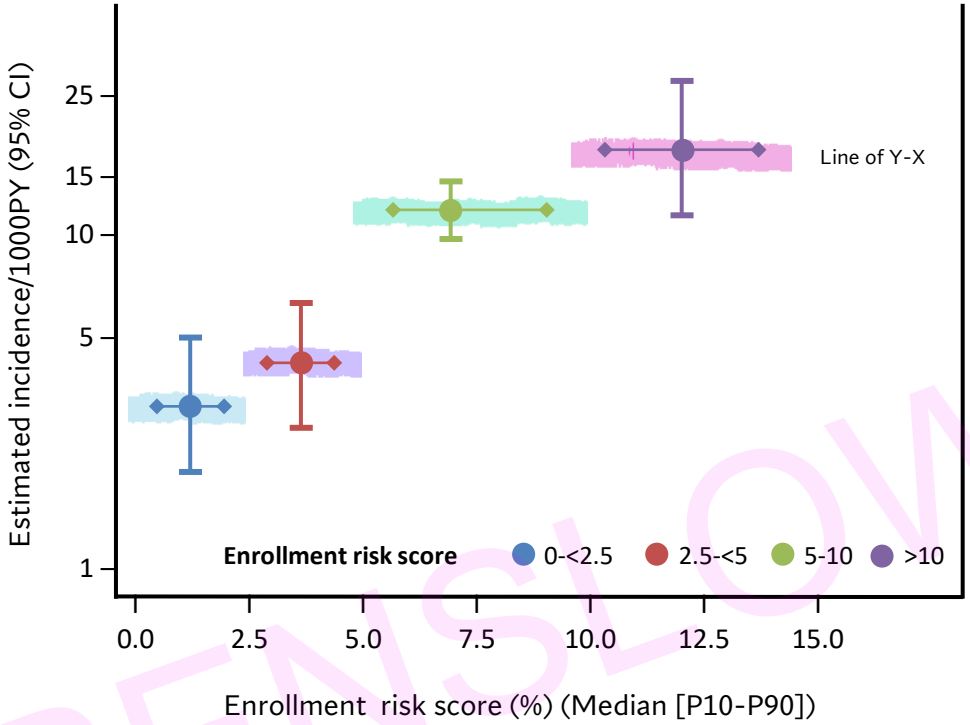


Cumulative incidence of event						
0%	0.8%	1.6%	2.4%	3.4%	4.5%	5.5%
0%	0.8%	2.0%	3.3%	4.4%	5.3%	7.1%

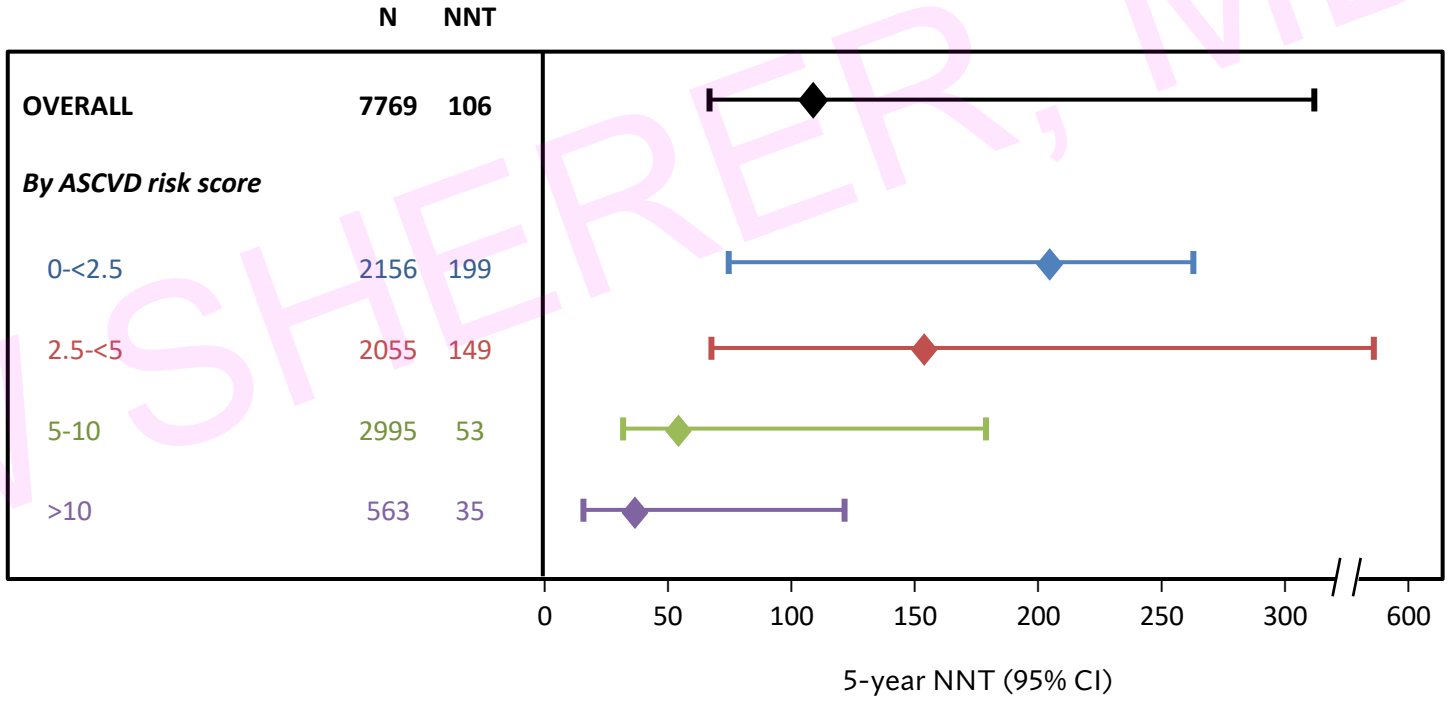
Number at risk							
Pitavastatin	3888	3647	3475	3364	2998	1948	1027
Placebo	3881	3693	3506	3356	2997	1975	919

Grinspoon S, et al. IAS 2023; Brisbane, Australia; July 23-26, 2023. Abst. SY06.

REPRIEVE Trial: Event Risk by Baseline ASCVD and Number Needed to Treat (NNT)



Increasing MACE events with increasing ASCVD risk score



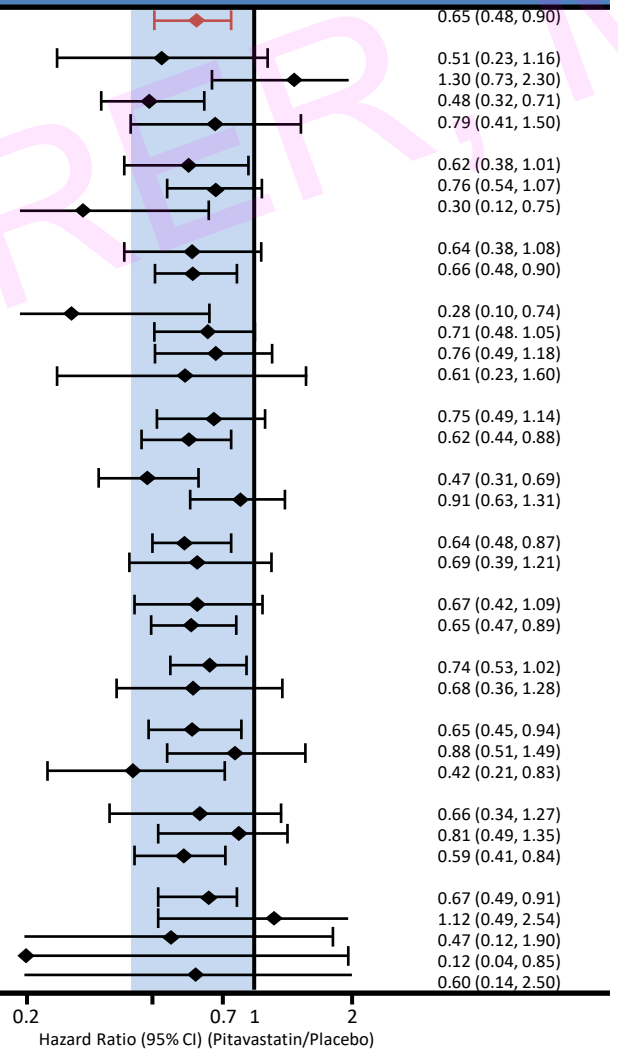
Decreasing NNT with increasing ASCVD risk score

NNT = number needed to treat MACE = majr adverse cardiovascular event

Grinspoon S, et al. IAS 2023; Brisbane, Australia; July 23-26, 2023. Abst. SY06.

REPRIEVE Trial:
Consistent Effects Across Sub-groups

	N	Pitavastatin IR/1000PY (# events)	N	Placebo IR/1000PY (# events)	HR (95% CI)
Overall	3888	4.81 (89)	3881	7.32 (136)	0.65 (0.48, 0.90)
ASCVD Risk Score					
0-<2.5	1096	1.6 (9)	1060	3.1 (17)	0.51 (0.23, 1.16)
2.5-<5	1030	5.3 (27)	1025	4.1 (21)	1.30 (0.73, 2.30)
5-10	1474	5.5 (36)	1521	11.5 (78)	0.48 (0.32, 0.71)
>10	288	113.9 (17)	275	17.5 (20)	0.79 (0.41, 1.50)
Age (years)					
40-49	1842	2.9 (26)	1888	4.7 (43)	0.62 (0.38, 1.01)
50-59	1712	7.1 (57)	1849	9.4 (73)	0.76 (0.54, 1.07)
≥60	334	3.9 (6)	344	13.0 (20)	0.30 (0.12, 0.75)
Natal Sex					
Female	1211	3.8 (23)	1208	5.9 (36)	0.64 (0.38, 1.08)
Male	2677	5.3 (66)	2673	8.0 (100)	0.66 (0.48, 0.90)
Race					
Asian	571	1.7 (5)	567	6.2 (18)	0.28 (0.10, 0.74)
Black. African American	1569	5.7 (42)	1639	8.1 (63)	0.71 (0.48. 1.05)
White	1364	5.5 (35)	1340	7.2 (45)	0.76 (0.49, 1.18)
Other	384	3.8 (7)	335	6.3 (10)	0.61 (0.23, 1.60)
Smoking Status					
Current Smoker	920	9.0 (36)	1014	12.0 (54)	0.75 (0.49, 1.14)
Former/Never	2965	3.7 (53)	2862	5.8 (82)	0.62 (0.44, 0.88)
Hypertension					
No	2496	3.0 (36)	2499	6.4 (77)	0.47 (0.31, 0.69)
Yes	1392	8.3 (53)	1382	9.1 (59)	0.91 (0.63, 1.31)
LDL-C (mg/dL)					
<130	2973	4.8 (68)	3044	7.4 (107)	0.64 (0.48, 0.87)
≥130	915	4.9 (21)	837	7.2 (29)	0.69 (0.39, 1.21)
CD4 count (cells/mm³)					
≤500	1257	4.7 (28)	1253	6.9 (41)	0.67 (0.42, 1.09)
>500	2631	4.9 (61)	2628	7.5 (95)	0.65 (0.47, 0.89)
HIV-1 RNA (copies/mL)					
<LLQ	2641	5.0 (64)	2609	6.8 (86)	0.74 (0.53, 1.02)
≥LLQ	368	9.4 (16)	379	13.7 (24)	0.68 (0.36, 1.28)
NadirCD4 count (cells/mm³)					
<200	1890	5.1 (47)	1911	7.8 (73)	0.65 (0.45, 0.94)
200-349	1019	5.1 (25)	1022	5.9 (29)	0.88 (0.51, 1.49)
≥350	840	3.0 (12)	825	7.2 (28)	0.42 (0.21, 0.83)
ART Duration (years)					
<5	847	3.7 (15)	857	5.6 (23)	0.66 (0.34, 1.27)
5-10	1190	5.0 (28)	1118	6.2 (33)	0.81 (0.49, 1.35)
≥10	1851	5.2 (46)	1904	8.8 (80)	0.59 (0.41, 0.84)
GBD Super Region					
High Income	2044	7.2 (69)	2051	10.7 (103)	0.67 (0.49, 0.91)
Latin Am. & Caribbean	709	3.6 (12)	714	3.2 (11)	1.12 (0.49, 2.54)
S. East/ East Asia	304	1.8 (3)	286	3.7 (6)	0.47 (0.12, 1.90)
South Asia	246	1.8 (2)	258	9.5 (11)	0.12 (0.04, 0.85)
Sub-Saharan African	585	1.1 (3)	572	1.8 (5)	0.60 (0.14, 2.50)

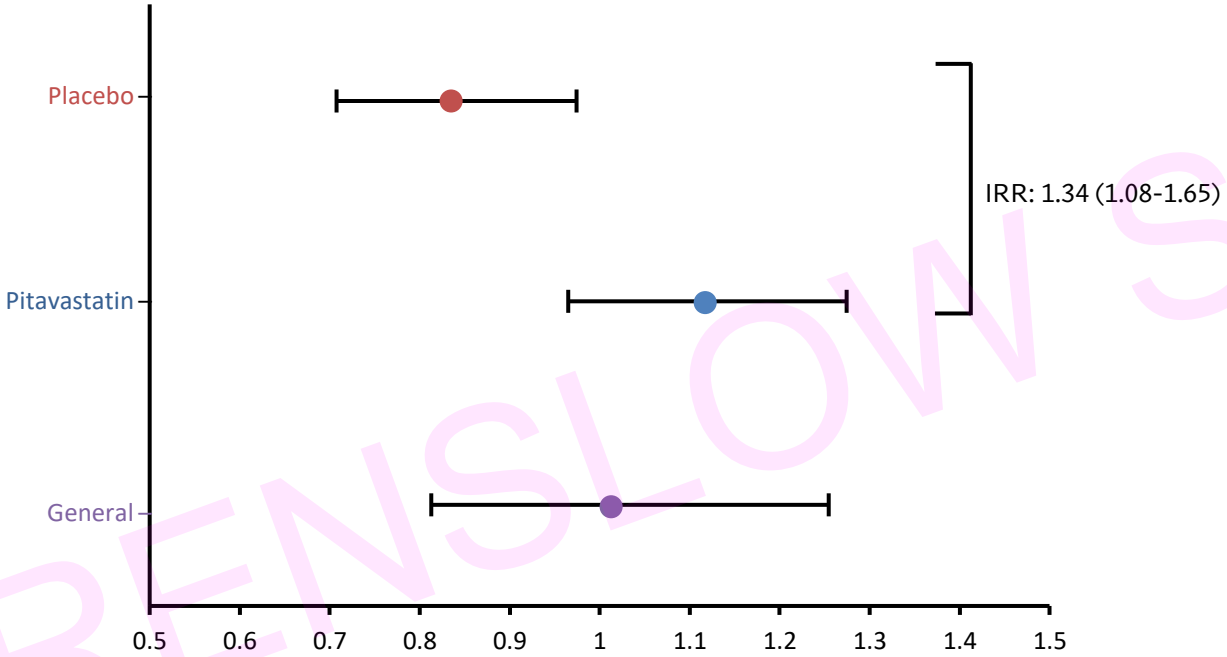


Grinspoon S, et al. IAS 2023; Brisbane, Australia; July 23-26, 2023. Abst. SY06.

REPRIEVE Trial: Safety Outcomes:

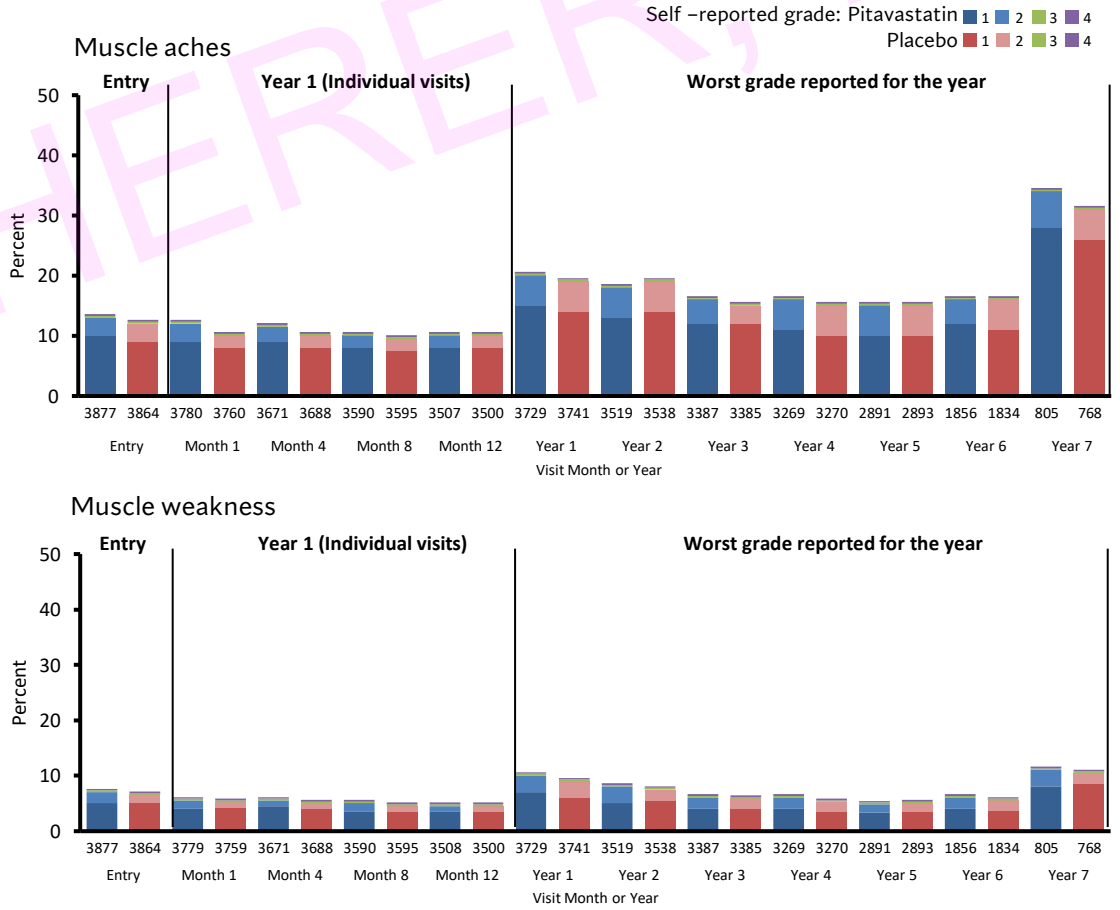
Small increase in DM incidence, mild myalgias

Diabetes Rates in REPRIEVE vs. General Population Aged 45-64 per US Centers for Disease Control



IRR: Incidence rate ratio

Effects on Muscle Aches and Myalgias



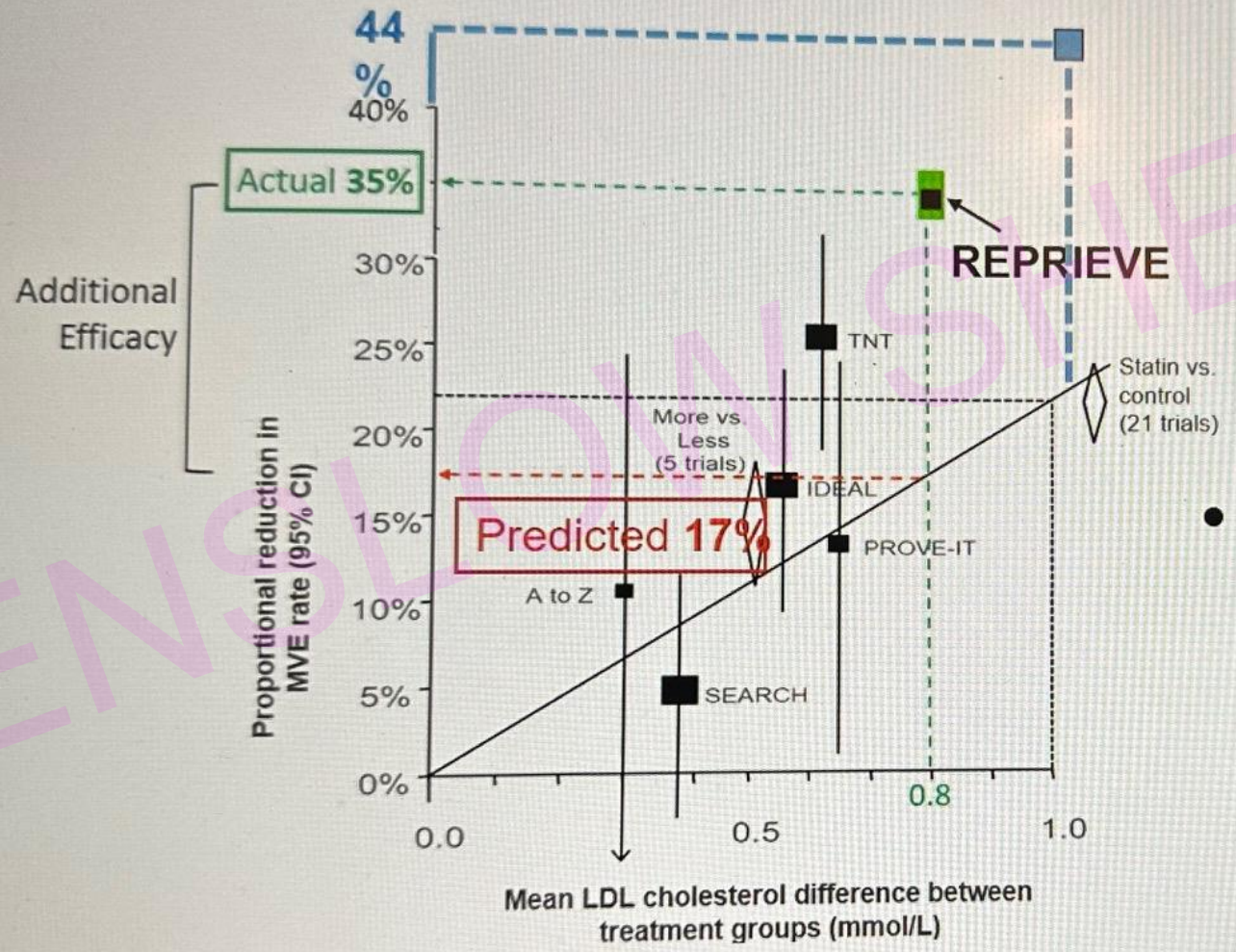
Grinspoon S, et al. IAS 2023; Brisbane, Australia; July 23-26, 2023. Abst. SY06. Centers for Disease Control and Prevention. Incidence of Newly Diagnosed Diabetes. https://www.cdc.gov/diabetes/data.statistics-report/newly-diagnosed-diabetes.html#print

Key Points: REPRIEVE Trial

- Pitavastatin calcium 4mg reduces MACE risk 35% vs placebo over 5.1yrs in low/moderate CVD risk pLWH of age > 40 yrs
- Treatment effect is similar across sex, race and baseline ASCVD baseline risk
  - Lipid lowering observed but does not explain degree of reduced risk alone due to lower LDL
- NNT 106 overall, 35 in this with ASCVD risk >10% at baseline
- Low risk of safety issues, small increase in DM2 incidence
- Suggests statins would be widely offered to PLWH age 40-55 years with low/moderate CVD risk
  - Pitavastatin, atorvastatin, rosuvastatin, pravastatin are reasonable options

IAS 2023

Effect Larger than Anticipated Based on Lowering of LDL



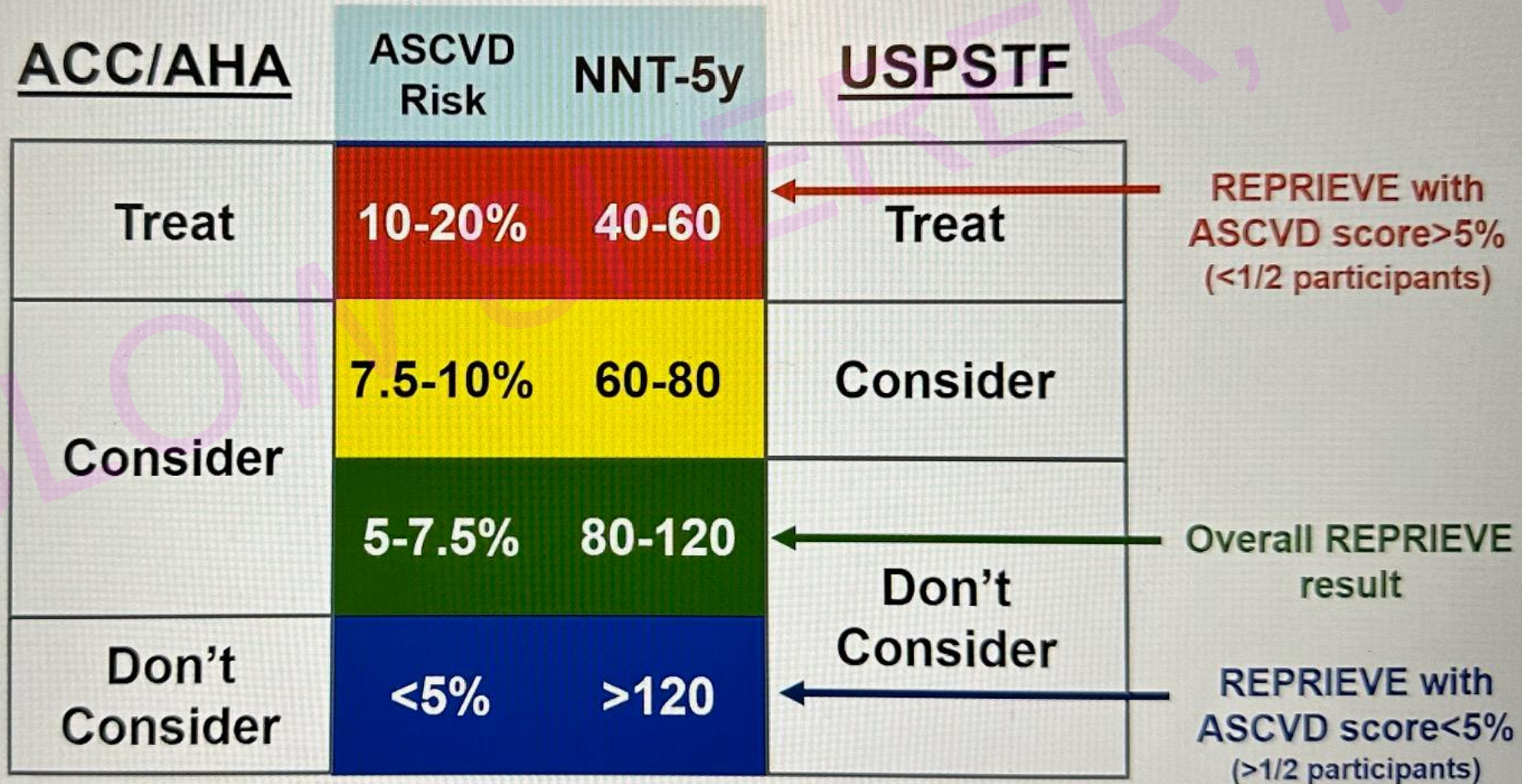
Relative reduction in JUPITER was -44%, predicted ~23%

- **LDL lowering matters but statin effect is beyond wh is expected for LDL lower alone**

Slide credit: Peter Hunt, UCSF, 11.6.23

How Does REPRIEVE Result Compare to Existing Treatment Thresholds?

(https://tools.acc.org/ascvd-risk-estimator-plus/#!/calculate/estimate/)

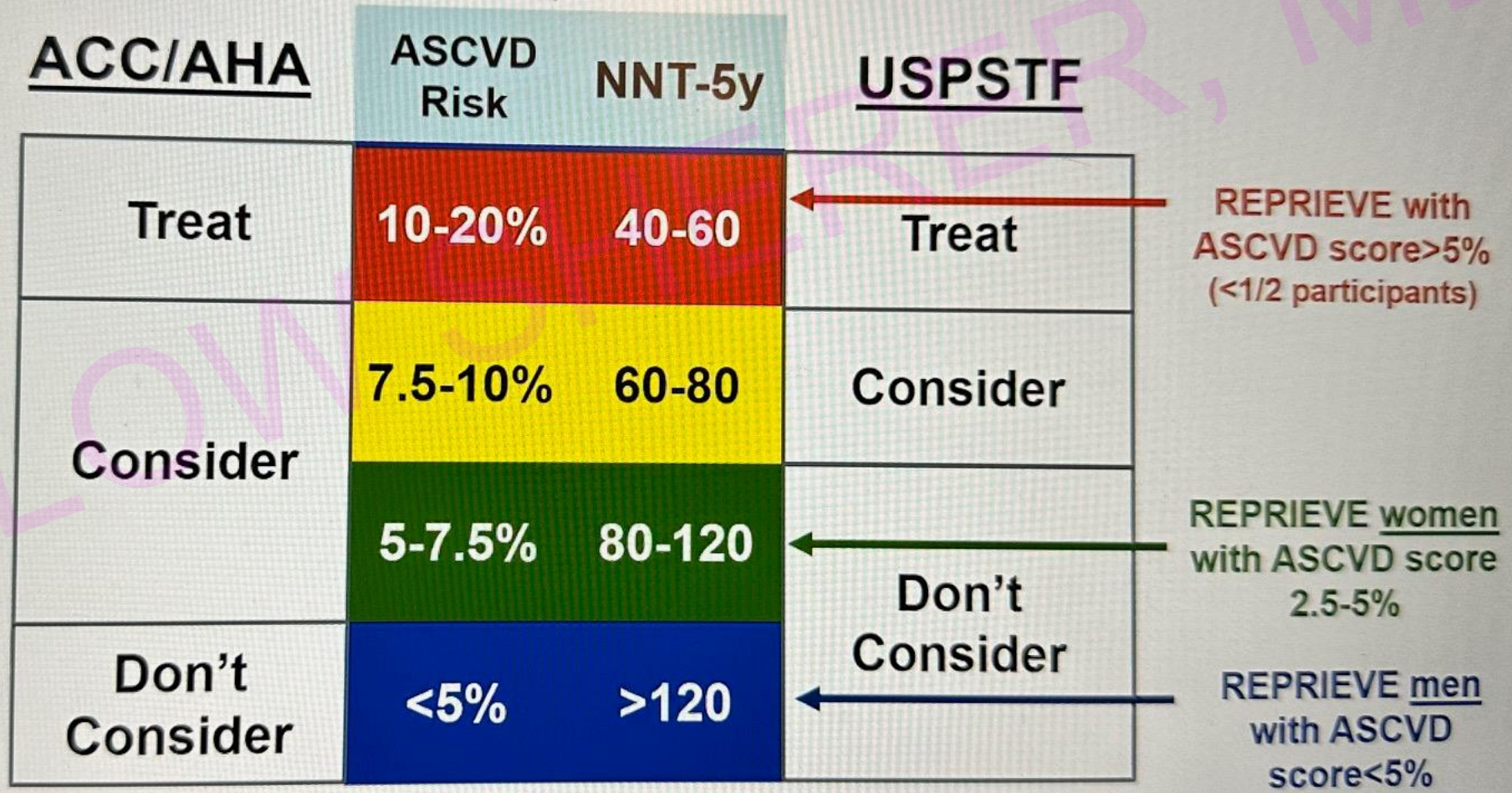


AHA/ACC Guidelines, Circulation, 2018; USPSTF, JAMA, 2022

Slide credit: Peter Hunt, UCSF, 11.6.23

In PWH with Low ASCVD Risk (2.5-5%), More Women than Men Should be Considered for Statins

(https://tools.acc.org/ascvd-risk-estimator-plus/#!/calculate/estimate/)



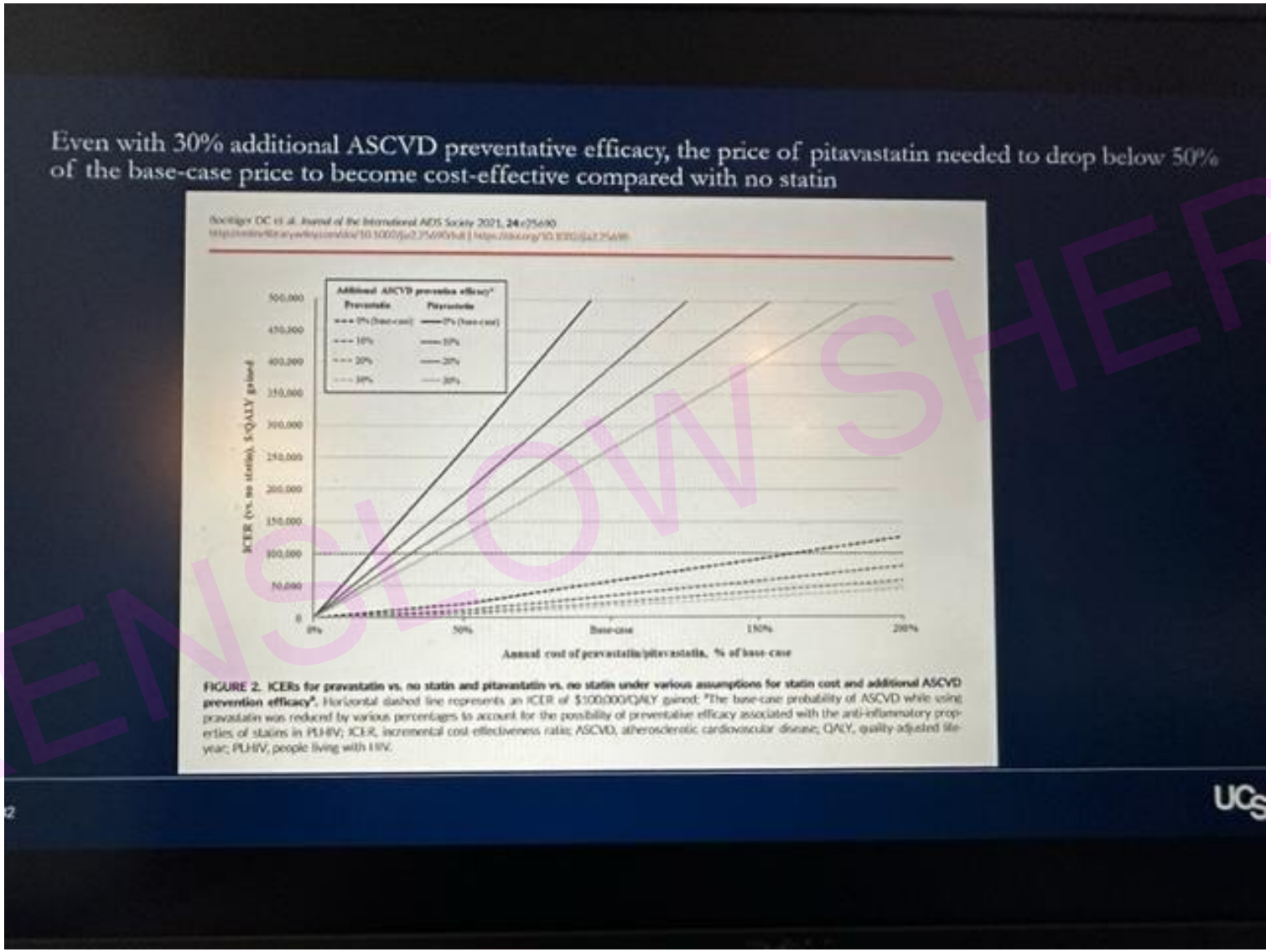
AHA/ACC Guidelines, Circulation, 2018; USPSTF, JAMA, 2022

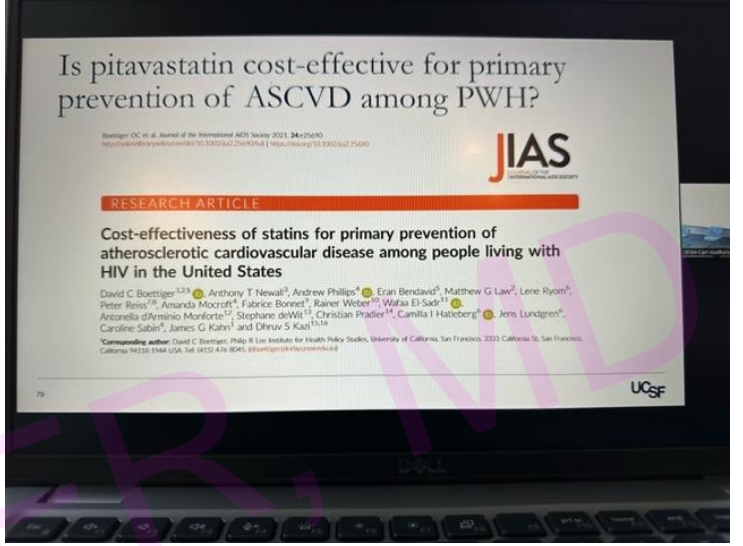
Slide credit: Peter Hunt, UCSF, 11.6.23

Remaining Questions

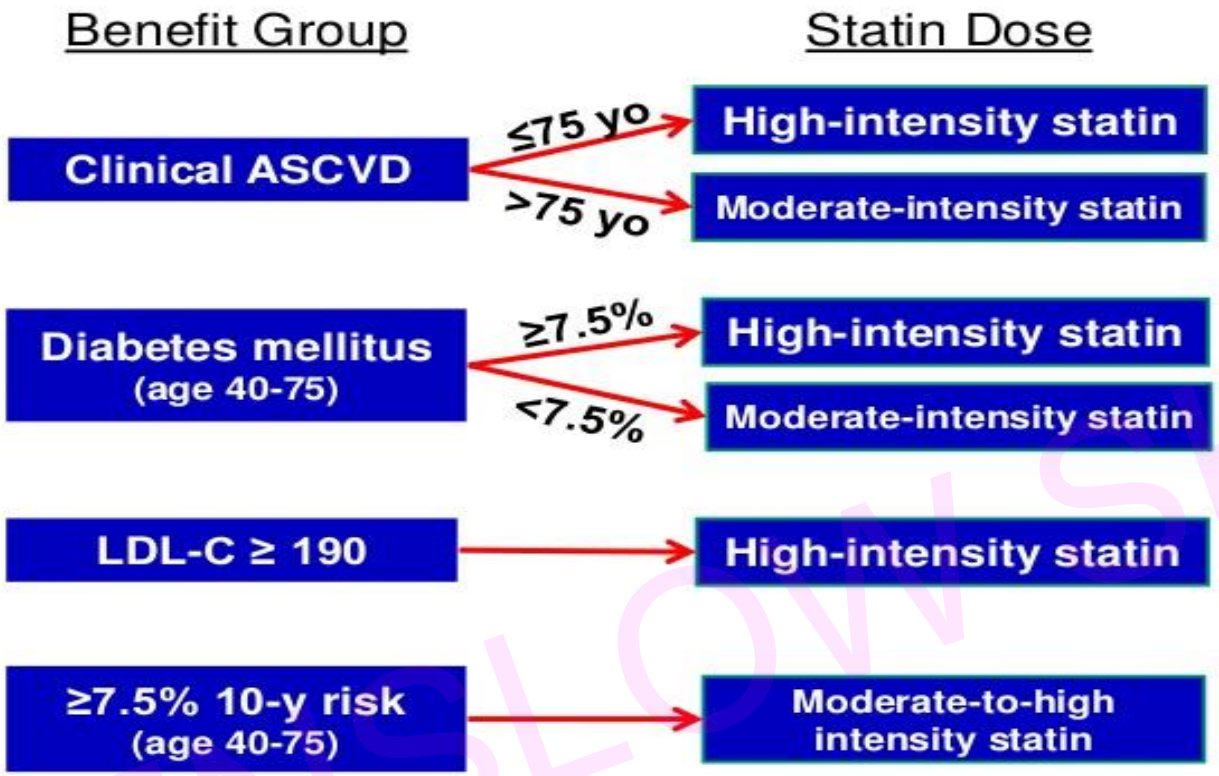
- Mechanisms of disease and effect by CoA reductase inhibitors
- Further analysis of race, gender effects, alternate statins
- Mechanisms of reduced CV/vasc disease
  - LDL lowering vs other anti-inflammatory actions of statins
- Non-CV effects of statins
- Impact on cancer incidence
- Effects on age < 40 years with higher degrees of CV risk
- How should guidelines change?
  - HIV+, age > 40 with low-moderate CV risk
  - HIV+, age < 40 with high CV risk? With mow-moderate CV risk? Any HIV+?

Cost Effectiveness of Pitavastatin





Lipids: Four Statin Benefit Groups; ART DDIs



Statin	Level with PI/c, PI/r	Use
Pitavastatin	--	
Pravastatin	--	
Atorvastatin	↑	
Rosuvastatin	↑	
Simvastatin	↑↑↑	
Lovastatin	↑↑↑	

Safe (Prava caution with DRV/r)

Use with caution/low dose

Contraindicated

Screen w/ fasting lipids: At HIV diagnosis

- Start of ART
- Change of ART
- Every 6-12 months

Aberg J. ACTHIV 2019.

Sosman J. MATEC Annual Update 2019

DHHS Guidelines: Excess CV Risk with Certain ART Agents

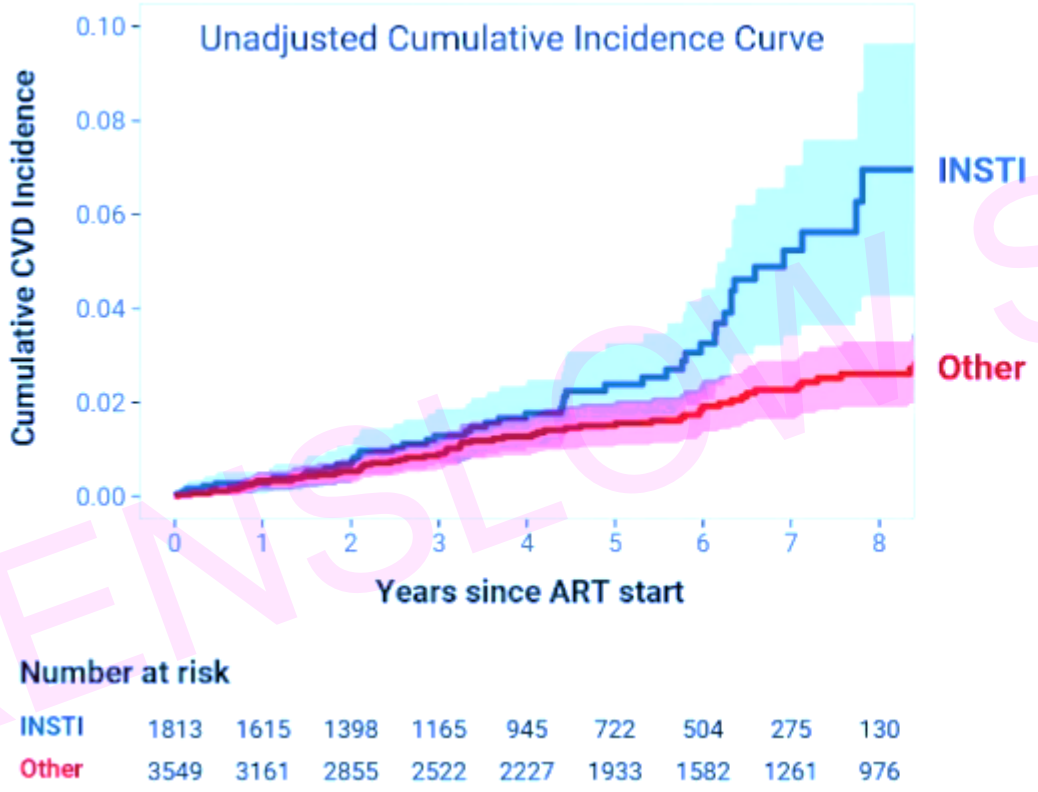
- Abacavir
  - "Increase in CV events is associated with abacavir use in some cohort studies."
- Darunavir
  - "Increased CV risk reported in one observational cohort study."

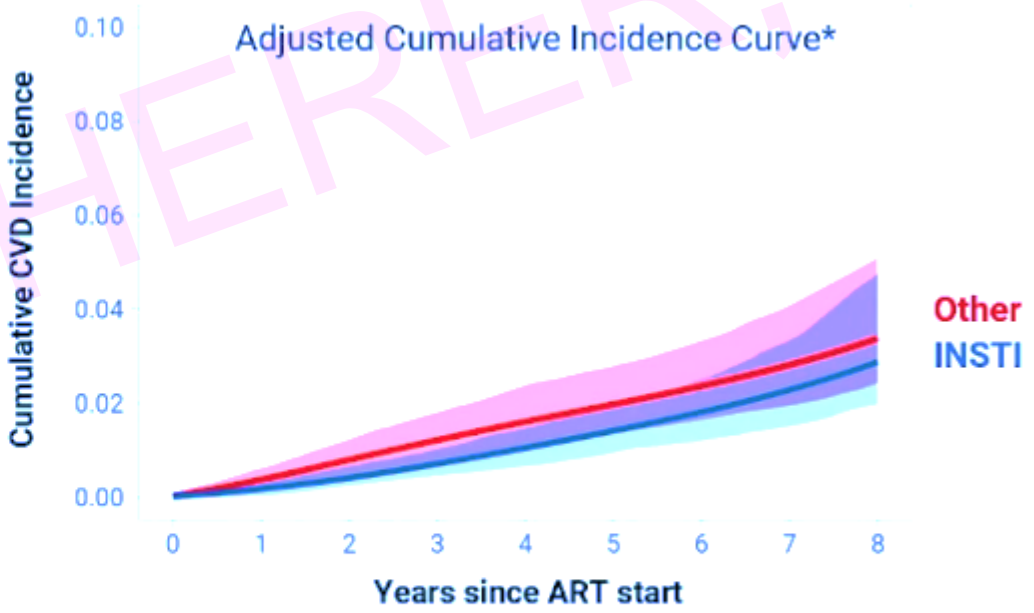
High Cardiac Risk	**Avoid abacavir and LPV/r** - If a PI/r is needed, ATV/r may have advantages See lipid guideines below for more favorable lipid profiles, tho evidence that this leads to improved CVD outcomes is lacking	Increased risk of CV events w/ ABC in some studies **Increased risk of CV events w/ PI/rs (LPV, DRV, IDV, FPV) in observational studies, not seen with ATV**
Hyperlipidemia	**The following ARVs associated with dyslipidemia:** **PI/r, PI/c, EVG/c, EFV** **More favorable lipid profiles w/** **BIC, DOR, RAL, DTG, RPV** **TDF lowers lipids; therefore, switch from TDF->TAF is associated w/ lipid elevations**	TDF has been associated with lower lipid levels than TAF or ABC

Ref: DHHS Guidelines. Accessed 10.26.23

SWISS Cohort: No Increase Risk of MI With INSTI in Naive Subjects

116 CVC events within 4.9 years (IQR 2.4 – 7.4)





Number at risk

INSTI	1813	1615	1398	1165	945	722	504	275	130
Other	3549	3161	2855	2522	2227	1933	1582	1261	976

Surial B, et al. CROI 2023; Seattle, WA; February 19-22, 2023. Abst. 149.

Smoking in PWHIV vs US population, 2009

Table 3. Adjusted Prevalence and Adjusted Prevalence Difference of Current Cigarette Smoking Among Adults With HIV Who Received Medical Care (MMP) and the General Adult Population (NHIS) in the United States in 2009

Characteristic	Adjusted Current Smoking	Adjusted Prevalence Difference	*P* Value
		NHIS *e points*†	
Total			<0.001
Age			
18-29 y			<0.001
30-39 y			<0.001
40-49 y			<0.001
≥50 y			<0.001
Sex			
Male			<0.001
Female			<0.001
Race/ethnicity			
Non-Hispanic wh			<0.001
Non-Hispanic bl			<0.001
Hispanic/Latino			<0.001
Highest educatio			
Less than high sc			<0.001
High school			<0.001
More than high s			<0.001
Income			
At or above the			<0.001
Below the pover			<0.001

MMP = Medical M
* Prevalence of cur amples included 4207 persons in the MMP and 27
† Adjusted prevale who received medical care in 2009) minus that in the NHIS (U.S. general adult population in 2009) adjusted for age, sex, race/ethnicity, education level, and poverty level. Differences may not be exact due to rounding.

Interventions:

Talk about it at every visit!

Buproprion (Wellbutrin)

Varenicline

Nicotine patch, gum

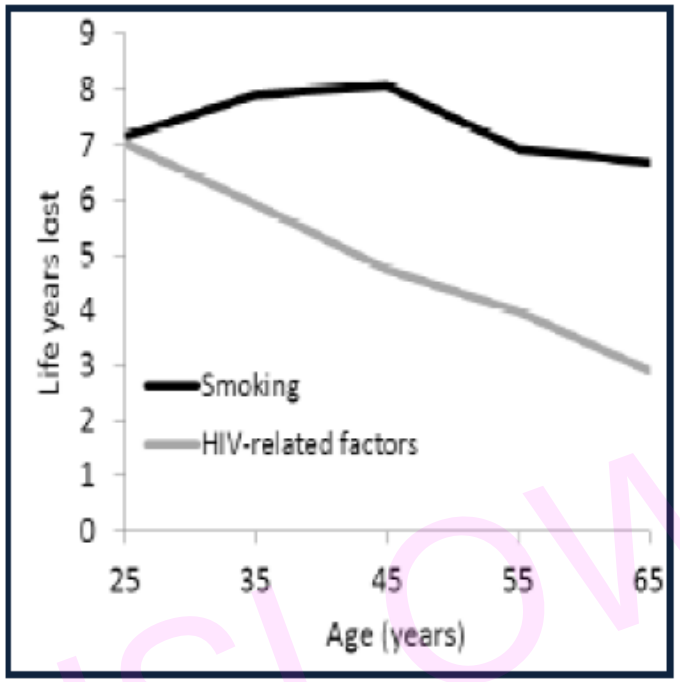
Cognitive behavioral therapy

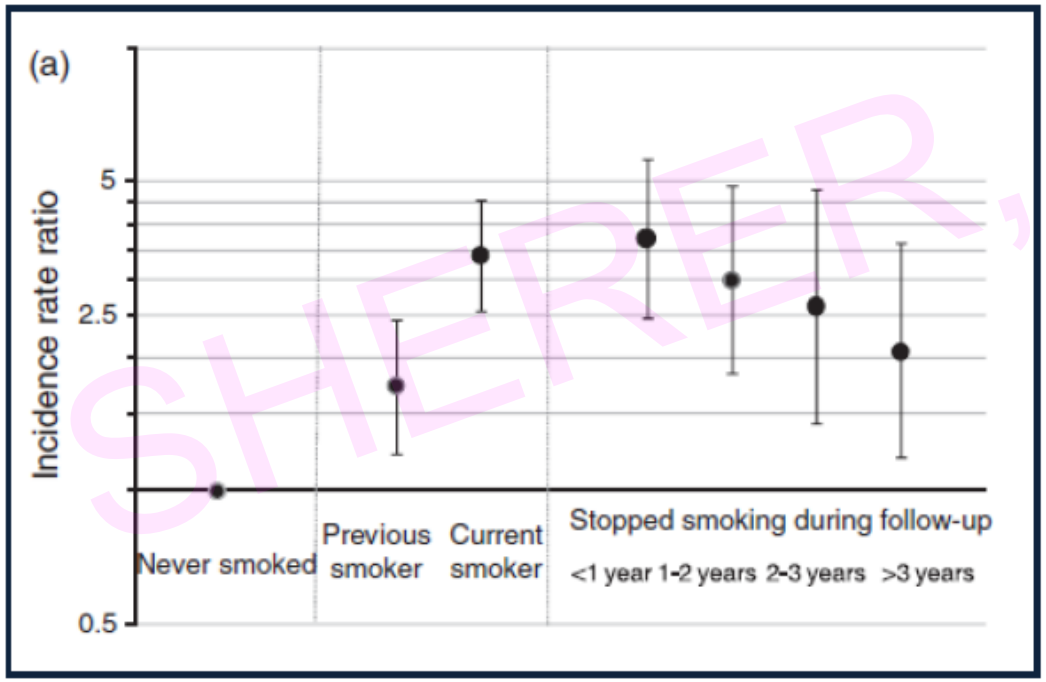
Provider recommendation

Team support and reinforcement

Other non-pharmacologic Rx

Impact of Smoking & Cessation on AMI in PWHIV





- 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

Helleberg, CROI 2014. Abstract 1011; Petoumenos HIV Med 2011.

Aspirin Effective for Secondary Prevention of MI, CVA
Not Recommended for Primary CVD Prevention (except in DM)

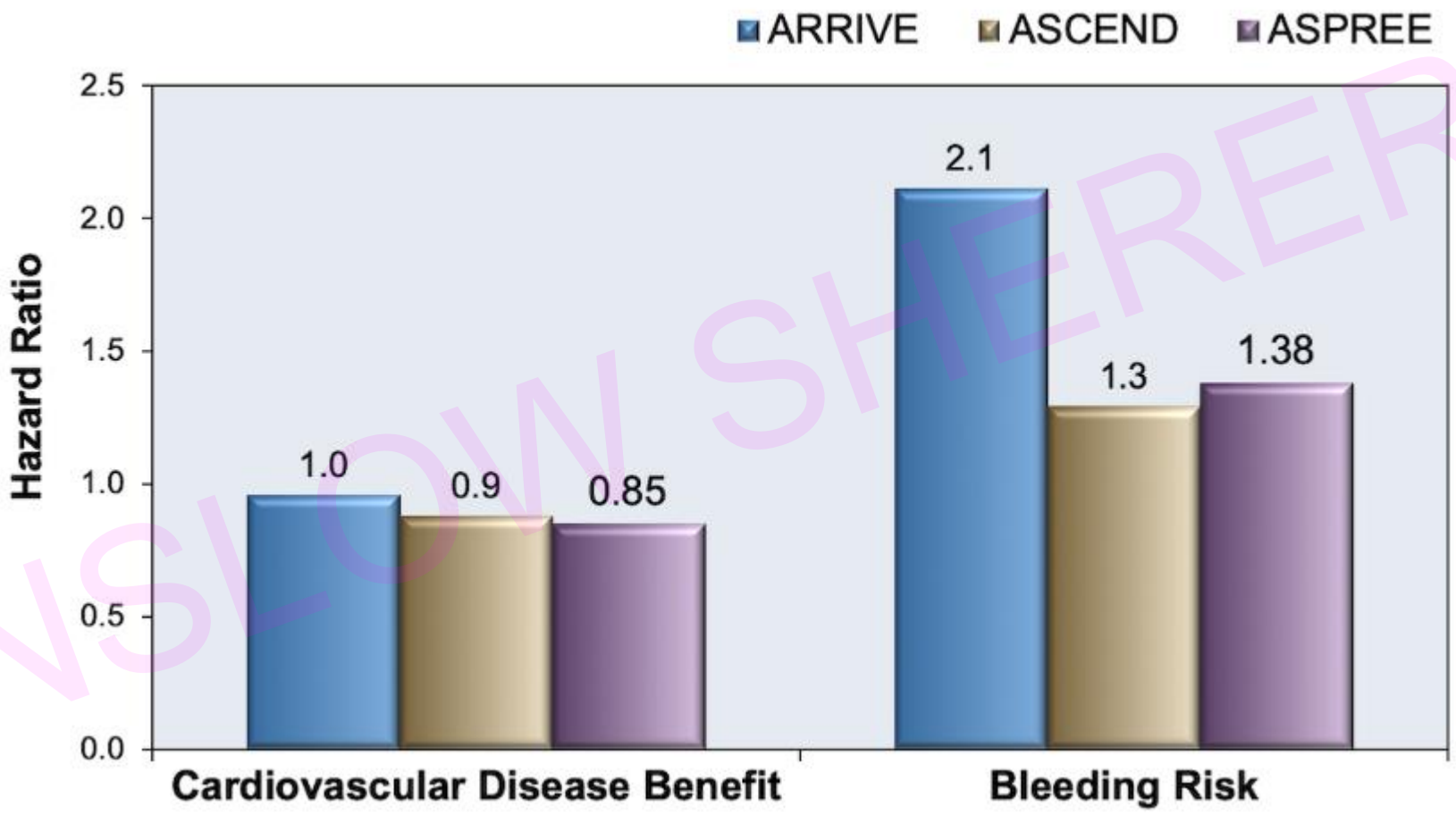


Figure 1 - Summary of Three Aspirin Trials for Primary Prevention of Cardiovascular Disease

Source: Knickelbine T, Miedema MD. Aspirin for primary prevention of cardiovascular disease: is it time to move on? Curr Opin Cardiol. 2019;34:510-13

Case 1

- CJ is a 23 yo MSM with new HIV w/ CD4 660, VL 18,000
  - Was on PrEP for 1 year, but moved and lost insurance
- Non-smoker, no significant PMHx other than STIs x 2
  - No HTN, DM, non-smoker
  - Works as a waiter, grad student
- Unremarkable labs

Does CJ have an increased risk of CV disease?

What ART choices and other steps are appropriate for his care?

Case 1

- CJ is a 23 yo MSM with new HIV w/ CD4 660, VL 18,000
  - Was on PrEP for 1 year, but moved and lost insurance
- Non-smoker, no significant PMHx other than STIs x 2
  - No HTN, DM, non-smoker
  - Works as a waiter, grad student in economics
- Unremarkable labs

- Does CJ have an increased risk of CV disease?
  - **YES vs HIV-, but still very low risk overall, << 7.5%**
- What ART choices and other steps are appropriate for his care?
  - **Any recommended option (w/o ABC, PI/r). Healthy food, exercise, lifestyle from start.**
  - **Discussion of weight gain w/ INSTIs, monitoring**

Case 2

- GT is a 53-year-old man with stable HIV
- Diagnosed in 2011 on routine screening; MSM risk factor; baseline CD4 440, HIV RNA 12,000; no viral hepatitis or co-infections
  - No history of HIV-related complications
- Started ART and rapidly achieved viral suppression
- Currently asymptomatic, receiving BIC/FTC/TAF with no side effects
  - Taking no other medications
  - Lipids: Total cholesterol 197; HDL 43; LDL 141
- ASCVD 2013 Risk Calculator from AHA/ACC: 4.6% risk of cardiovascular event (coronary or stroke death or non-fatal MI or stroke) in next 10 years

Acknowledgement: Paul Sax

Case 2

- You cite for him a study study showing that statin therapy reduces risk of major CV in PWH
- He is strongly opposed to taking more medications – “I’m a therapeutic nihilist.”
- How would you counsel him? Does his ART regimen contribute to excess CV risk?

Case 2

- You explain to him that the ASCVD risk score might be underestimating his CV risk since he has HIV
- Atorvastatin 20 mg recommended
  - Would start of 10 mg reduce chance of side effects?
- He says he'll consider it, but declines for now – but will work to improve his diet and increase exercise in the meantime

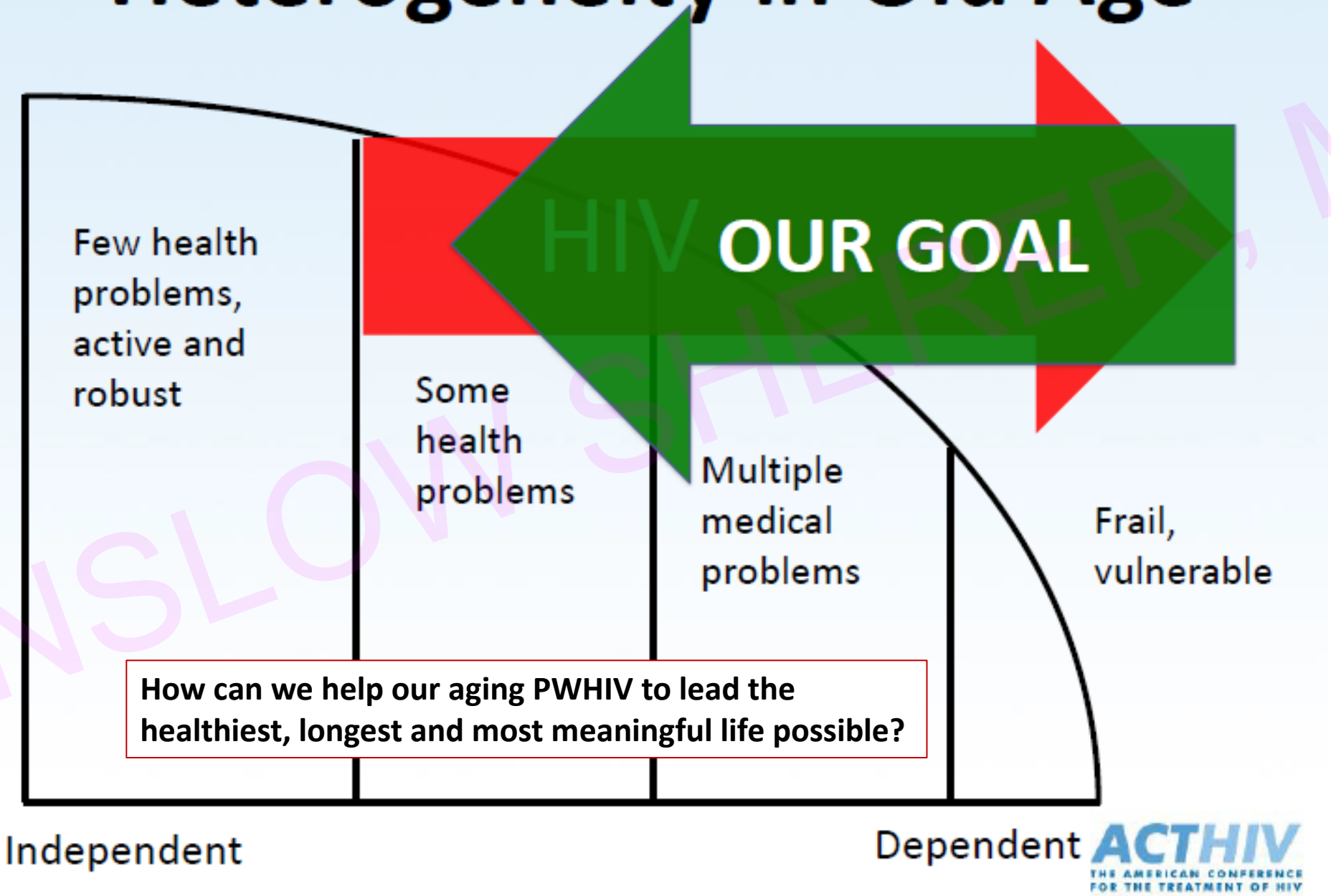
Key Points

- Numerous studies have shown an increased risk of cardiovascular disease in PWH compared to population without HIV
- Some argue that HIV be listed a major CV risk factor
- Immune activation and inflammation, and traditional CV risk factors, contribute to excess risk
  - risk only partially reversed by ART
- Current data do not support excess CV risk from the INSTI class – contrasts with PIs (atazanavir excepted)
- Pitavastatin lowers risk in PWH at low-moderate risk of cardiovascular disease

HIV and CVD: Summary I

- 2x increased risk of CVD in PWHIV; 50% of PWHIV are age > 50
- Early, life long CVD prevention based on modifiable risk factors
- Stop smoking; BP, lipid, & glucose control; exercise, healthy food
- Many ART options w/ favorable CVD profile
  - Avoid PIs (or use ATV/r), avoid abacavir
  - Statins effective for lipid control, consider DDIs
  - Any diabetic w/ LDL >70 should be on a statin and aspirin (often overlooked population in HIV clinical practice)

Heterogeneity in Old Age



ACTHIV
THE AMERICAN CONFERENCE FOR THE TREATMENT OF HIV

CLINICAL REVIEW

BMJ, 2009, 338:a3172

HIV infection, antiretroviral treatment, ageing, and non-AIDS related morbidity

Steven G Deeks,[1] Andrew N Phillips[2]

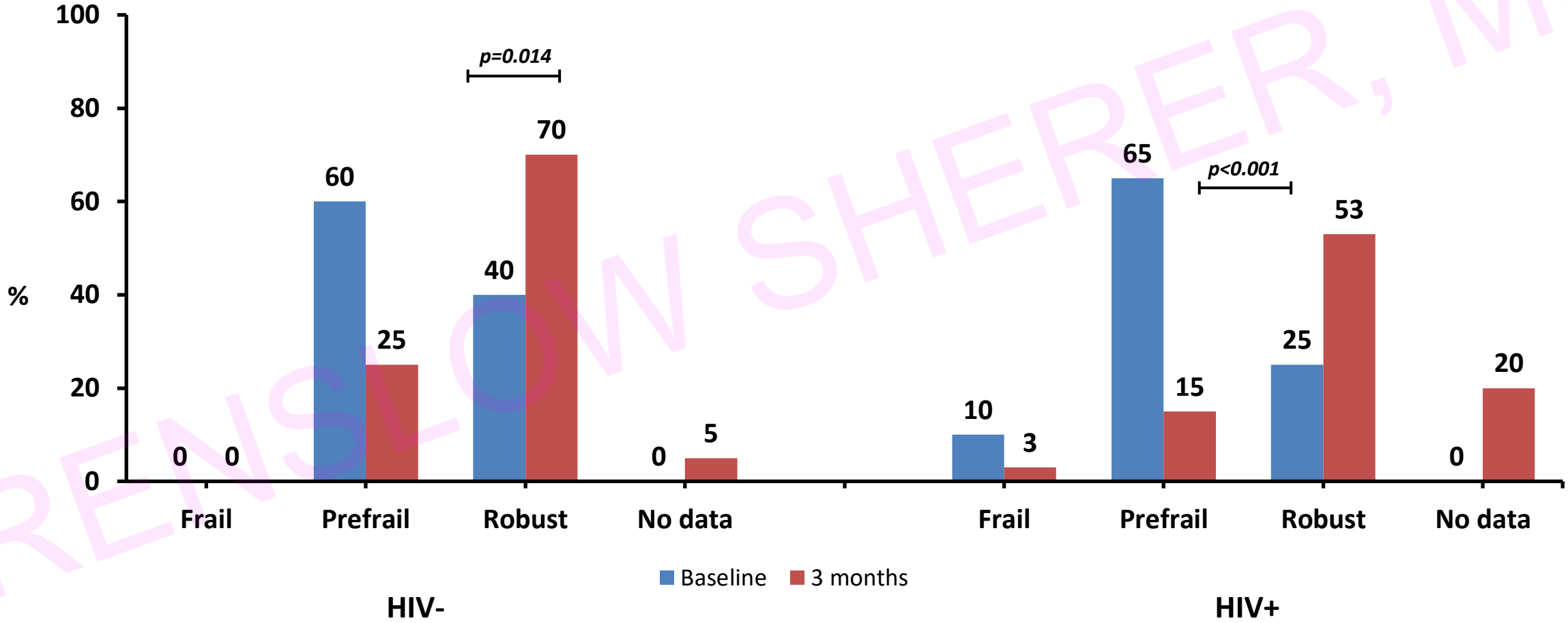
EXERCISE Is Effective Prevention & Treatment

Box 2 Non-AIDS related complications that may be more common in patients with HIV

- √ Hypertension
- √ Diabetes mellitus and insulin resistance
- √ Cardiovascular disease
- √ Pulmonary hypertension
- Cancer
- √ Osteopenia and osteoporosis
- Liver failure
- Kidney failure
- √ Peripheral neuropathy
- √ Frailty
- √ Cognitive decline and dementia

A 12-Week Multicomponent Exercise Program Reverses Frailty in Older Adults With HIV

Frailty (Frailty Phenotype), physical function (Senior Fitness Test (SFT), hand grip strength, SPPB), mood (HADS, GDS-SF), and quality of life (WHOQOL-HIV-BREF)



Brañas F, et al. CROI 2023; Seattle, WA; February 19-22, 2023. Abst. 701.

HIV and CVDx: Summary II

- Weight gain on INSTIs increase metabolic syndrome
  - CV effects unclear, no strong association with CVD to date
- 50% of PWHIV age > 50 years
  - Rising co-morbidities and polypharmacy in older PWHIV
  - Aging and frailty are increasingly common; plan for fall prevention
- Critical role for HIV primary caregiver
  - Set early goals of mobility and independence, monitor progress
  - Coordination with geriatrician useful for age > 65 years

Useful References

Primary Care Guidance for Persons With Human Immunodeficiency Virus: 2020 Update by the HIV Medicine Association of the Infectious Diseases Society of America

← View all Guidelines

Get the Guidelines App!

GET IT ON Google Play Download on the App Store

Correction (12/8/2021)

Abstract

Methods

Full Recommendations for the Primary Care of Persons with HIV

Notes

References

Primary Care Guidance for Persons With Human Immunodeficiency Virus: 2020 Update by the HIV Medicine Association of the Infectious Diseases Society of America

Published CID, 12/8/2021

Clinical Infectious Diseases, Volume 73, Issue 11, 1 December 2021, Pages e3572–e3605, https://doi.org/10.1093/cid/ciaa1391

Published: 6 November 2020; Correction Issued 8 December 2021

Melanie A. Thompson, Michael A. Horberg, Allison L. Agwu, Jonathan A. Colasanti, Mamta K. Jain, William R. Short, Tulika Singh, and Judith A. Aberg

https://www.idsociety.org/practice-guideline/primary-care-management-of-people-with-hiv/#FullRecommendationsforthePrimaryCareofPersonswithHIV

Illinois Tobacco Quitline: quityes.org

American Heart Association guidelines: professional.heart.org

MATEC Resources

- National Clinician Consultation Center
  http://nccc.ucsf.edu/
  - HIV Management
  - Perinatal HIV
  - HIV PrEP
  - HIV PEP line
  - HCV Management
  - Substance Use Management
- AETC National HIV Curriculum
  https://aidsetc.org/nhc
- AETC National HIV-HCV Curriculum
  https://aidsetc.org/hivhcv
- Hepatitis C Online
  https://www.hepatitisc.uw.edu
- AETC National Coordinating Resource Center
  https://aidsetc.org/
- Additional Trainings https://matec.info

AETC AIDS Education & Training Center Program Midwest

ACTHIV 2013: A State-of-the-Science Conference for Frontline Health Professionals

Atlanta, May 2-4, 2024

www.acthiv.org

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- David Pitrak
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- Collette Dejong
- Melanie Thompson
- Cathy Creticos
- Jose Arribas
- Jim Sosman
- Paul Sax
- Ian Frank
- Graeme Moyle
- Juergen Rockstroh
- Judy Currier
- Judy Aberg

Thank you

Please complete the post evaluation survey.
The link is in the chatbox.