

The REPRIEVE Trial: Practice Changing or Practice Affirming?

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Disclosures

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Disclaimer

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Data Considerations

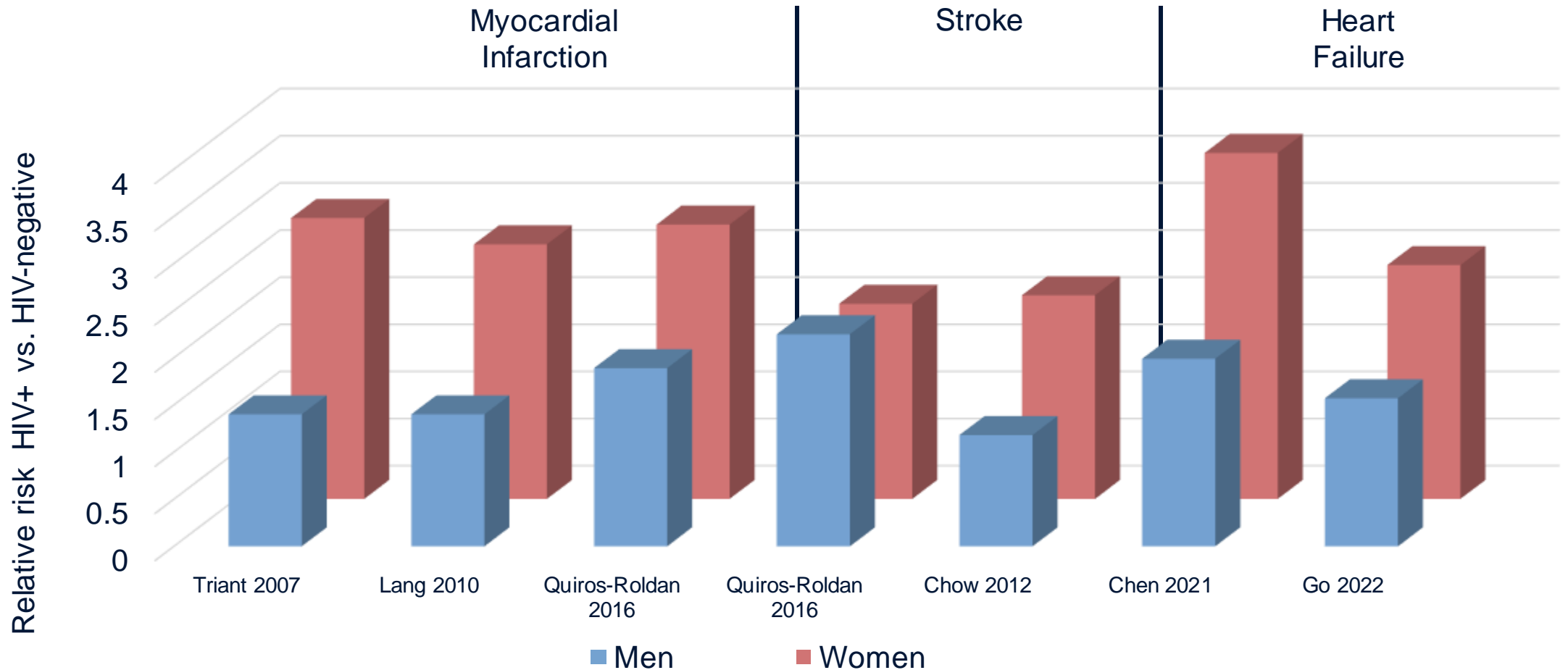
Data in this presentation offer a limited perspective of how systemic, social, and economic factors impact health. We recognize that racism, not race, creates and perpetuates health disparities.

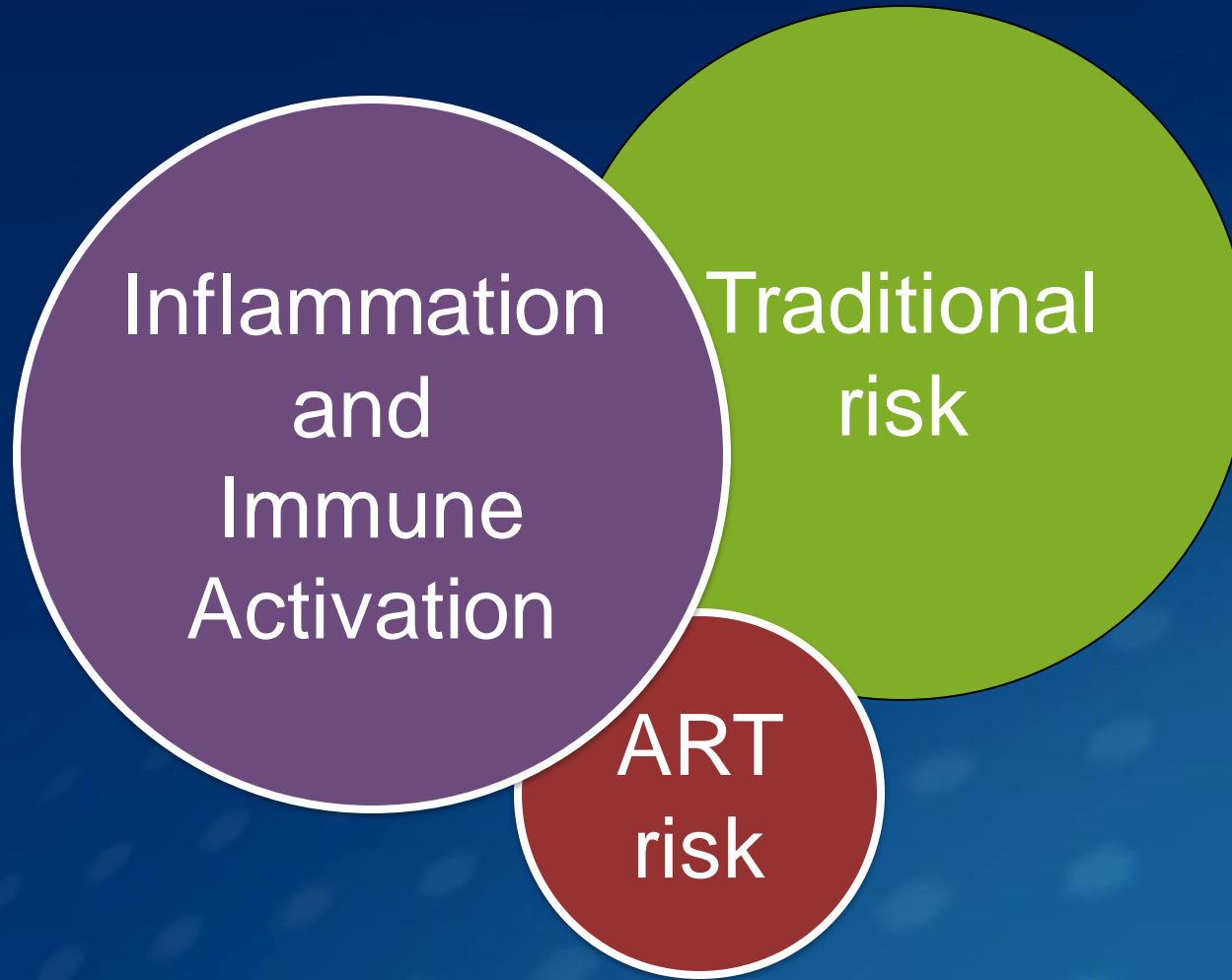


To Learn More:

<https://www.cdc.gov/minorityhealth/racism-disparities>

People with HIV have a higher risk of cardiovascular disease





Statins and Inflammation: The JUPITER Study

The NEW ENGLAND
JOURNAL *of* MEDICINE

ESTABLISHED IN 1812

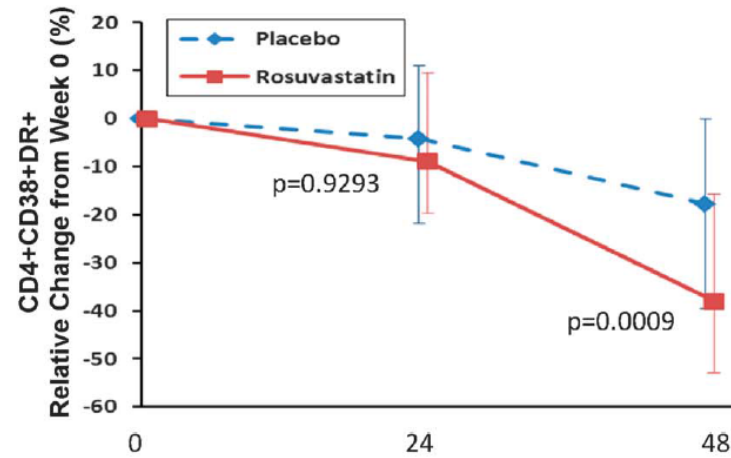
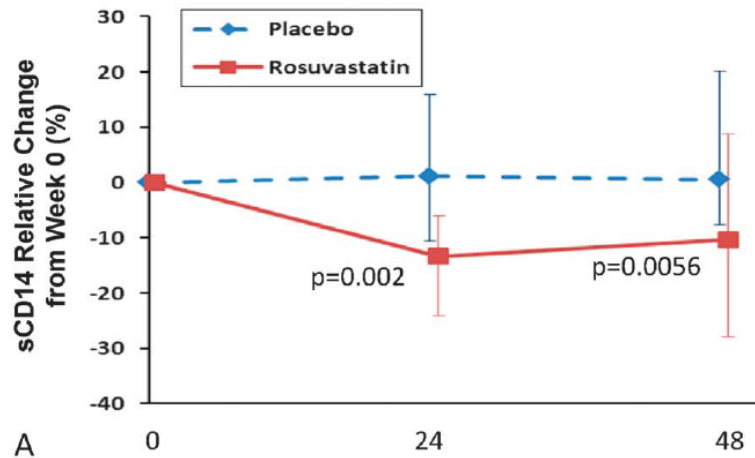
NOVEMBER 20, 2008

VOL. 359 NO. 21

Rosuvastatin to Prevent Vascular Events in Men and Women
with Elevated C-Reactive Protein



Statins may reduce inflammation in PWH

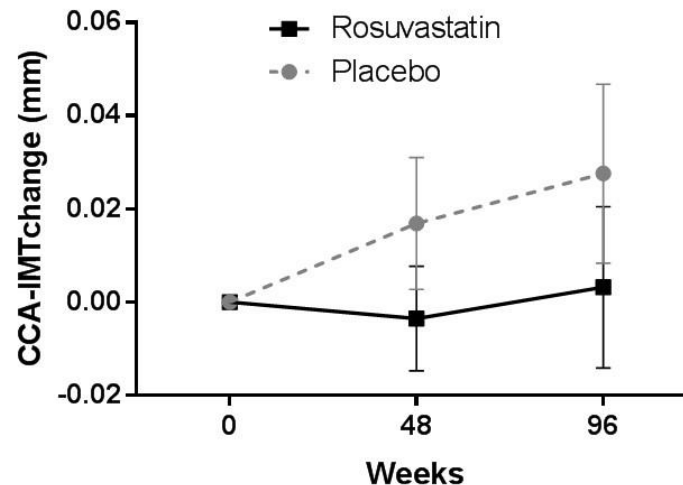
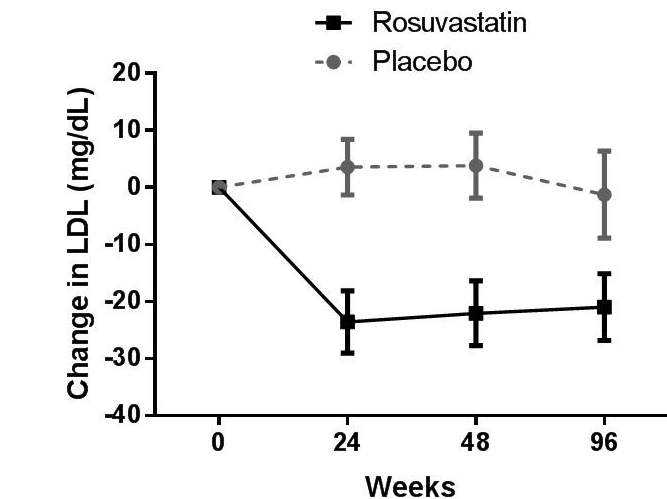


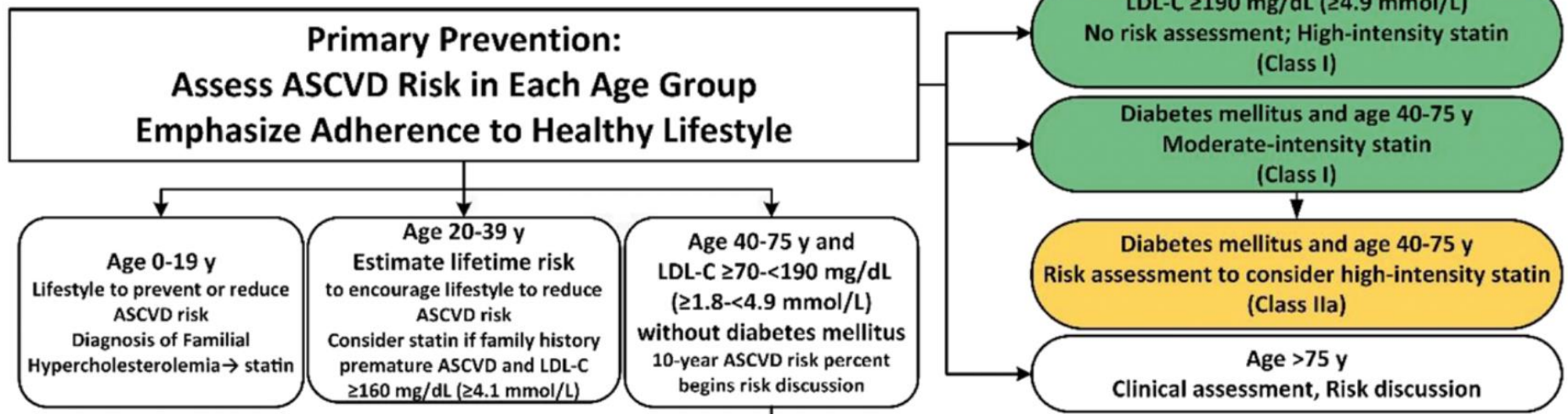
PWH ≥18 years

On ART >6mo & HIV-1 RNA ≤1000 cps/ml

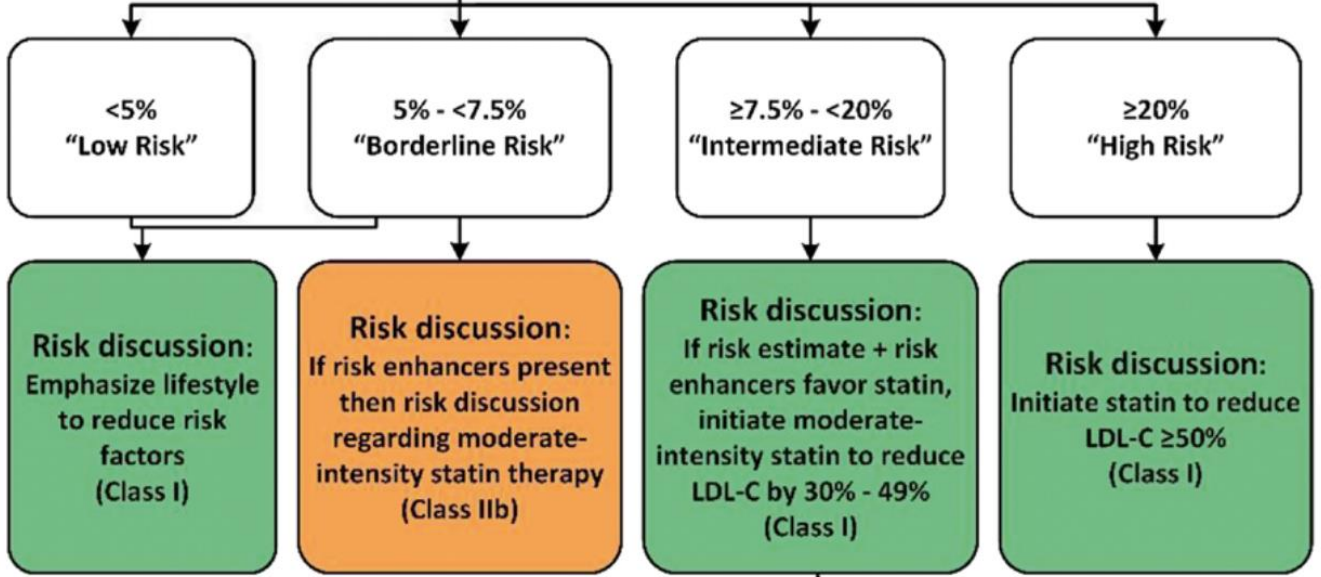
Fasting LDL-C ≤130mg/dl

Heightened immune activation (CD8+CD38+DR+ ≥19% or hsCRP ≥2μg/ml)





- 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 (especially 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



**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 ≥ 75 th percentile, initiate statin therapy



The REPRIEVE Trial

ORIGINAL ARTICLE

Pitavastatin to Prevent Cardiovascular Disease in HIV Infection

Subgroup	Pitavastatin		Placebo		Hazard Ratio (95% CI)
	no. of participants	no. of events	no. of participants	no. of events	
Overall	3888	4.81 (89)	3881	7.32 (136)	0.65 (0.48–0.90)
ASCVD risk score					
0 to <2.5%	1096	1.6 (9)	1060	3.1 (17)	0.51 (0.23–1.16)
2.5 to <5%	1030	5.3 (27)	1025	4.1 (21)	1.30 (0.73–2.30)
5 to 10%	1474	5.5 (36)	1521	11.5 (78)	0.48 (0.32–0.71)
>10%	288	13.9 (17)	275	17.5 (20)	0.79 (0.41–1.50)

Inclusion/Exclusion Criteria

- Age 40-75
- 10-year ASCVD Risk Score $\leq 15\%$
- Fasting LDL cholesterol:
 - If ASCVD risk score $< 7.5\%$, LDL < 190 mg/dL
 - If ASCVD risk score $\geq 7.5\%$ and $\leq 10\%$, LDL < 160 mg/dL
 - If ASCVD risk score $> 10\%$ and $\leq 15\%$, LDL < 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.”
- Clinical ASCVD, diabetes (if LDL > 70) excluded

Enrollment
2015 - 2019

Stopped early by
DSMB
March 30, 2023

Median follow-up
5.1 (4.3-5.9) years

Table 1

Characteristic	Pitavastatin (N = 3888)	Placebo (N = 3881)	Total (N = 7769)
Region of global burden of disease — no. (%)			
High income	2044 (52.6)	2051 (52.8)	4095 (52.7)
Latin America or Caribbean	709 (18.2)	714 (18.4)	1423 (18.3)
Southeast or East Asia	304 (7.8)	286 (7.4)	590 (7.6)
South Asia	246 (6.3)	258 (6.6)	504 (6.5)
Sub-Saharan Africa	585 (15.0)	572 (14.7)	1157 (14.9)
Age			
Median (IQR) — yr	50 (45–55)	50 (45–55)	50 (45–55)
Range — yr	40 to 72	40 to 74	40 to 74
Distribution — no. (%)			
40–49 yr	1842 (47.4)	1888 (48.6)	3730 (48.0)
50–59 yr	1712 (44.0)	1649 (42.5)	3361 (43.3)
≥60 yr	334 (8.6)	344 (8.9)	678 (8.7)
Sex — no. (%)†			
Male	2677 (68.9)	2673 (68.9)	5350 (68.9)
Female	1211 (31.1)	1208 (31.1)	2419 (31.1)

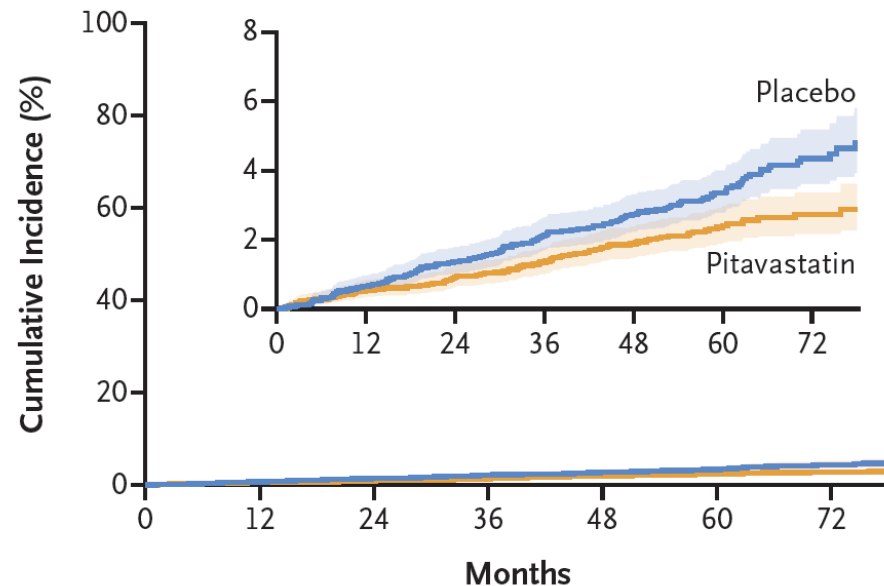
Table 1

Atherosclerotic Cardiovascular Disease risk score — %¶

Median (IQR)	4.5 (2.1–7.0)	4.5 (2.2–7.0)	4.5 (2.1–7.0)
Distribution — no. (%)			
0 to <2.5	1096 (28.2)	1060 (27.3)	2156 (27.8)
2.5 to <5	1030 (26.5)	1025 (26.4)	2055 (26.5)
5 to <7.5	934 (24.0)	960 (24.7)	1894 (24.4)
7.5 to 10	540 (13.9)	561 (14.5)	1101 (14.2)
>10	288 (7.4)	275 (7.1)	563 (7.2)

Primary Outcome

B First MACE



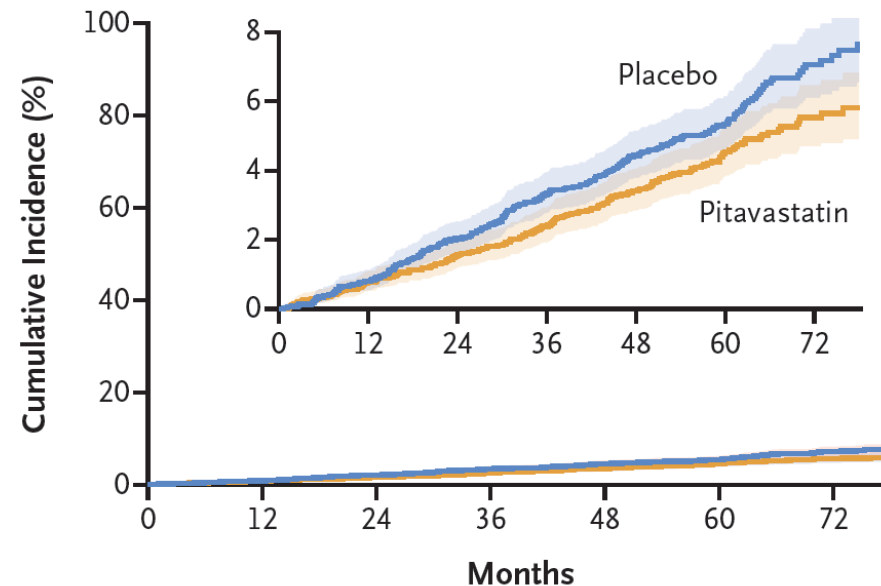
Cumulative Incidence of Event (%)

Placebo	0.00	0.66	1.38	2.14	2.74	3.36	4.36
Pitavastatin	0.00	0.56	0.95	1.35	1.89	2.41	2.73

No. at Risk

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

C First MACE or Death



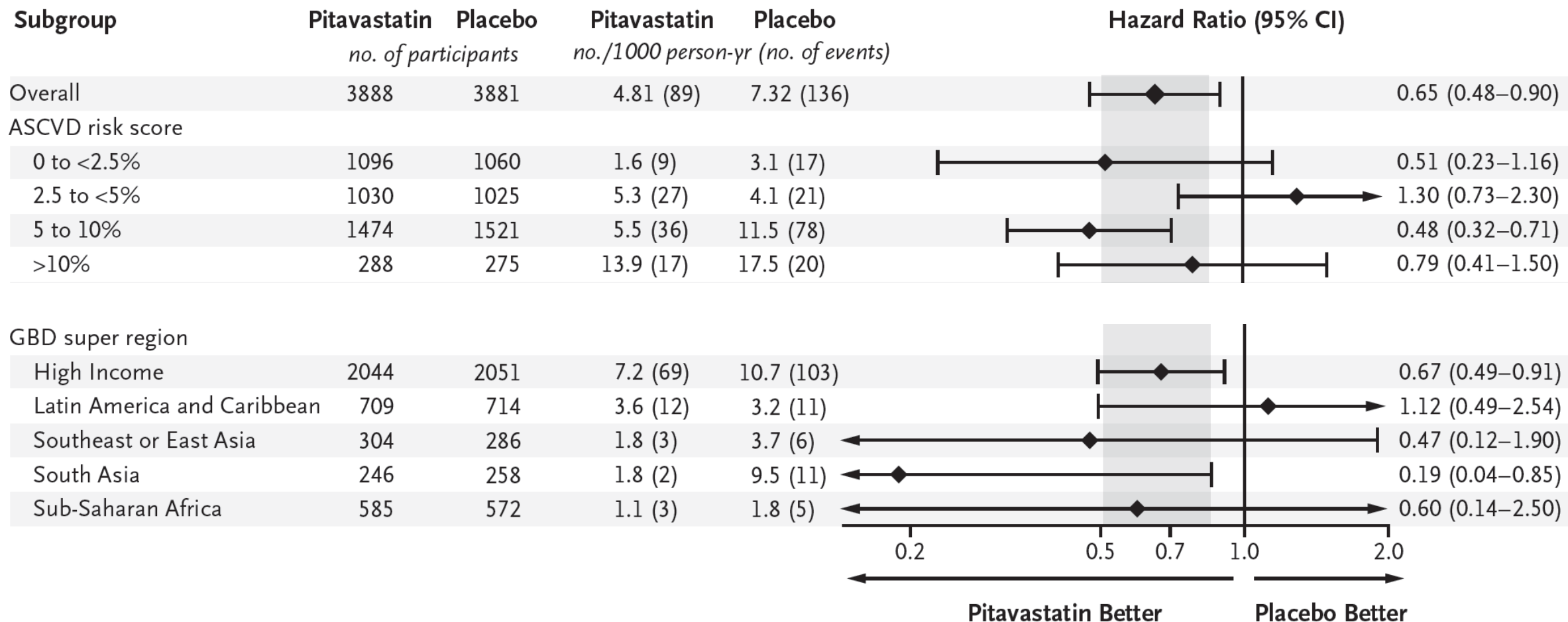
Cumulative Incidence of Event (%)

Placebo	0.00	0.80	2.03	3.34	4.44	5.35	7.06
Pitavastatin	0.00	0.77	1.58	2.39	3.40	4.54	5.54

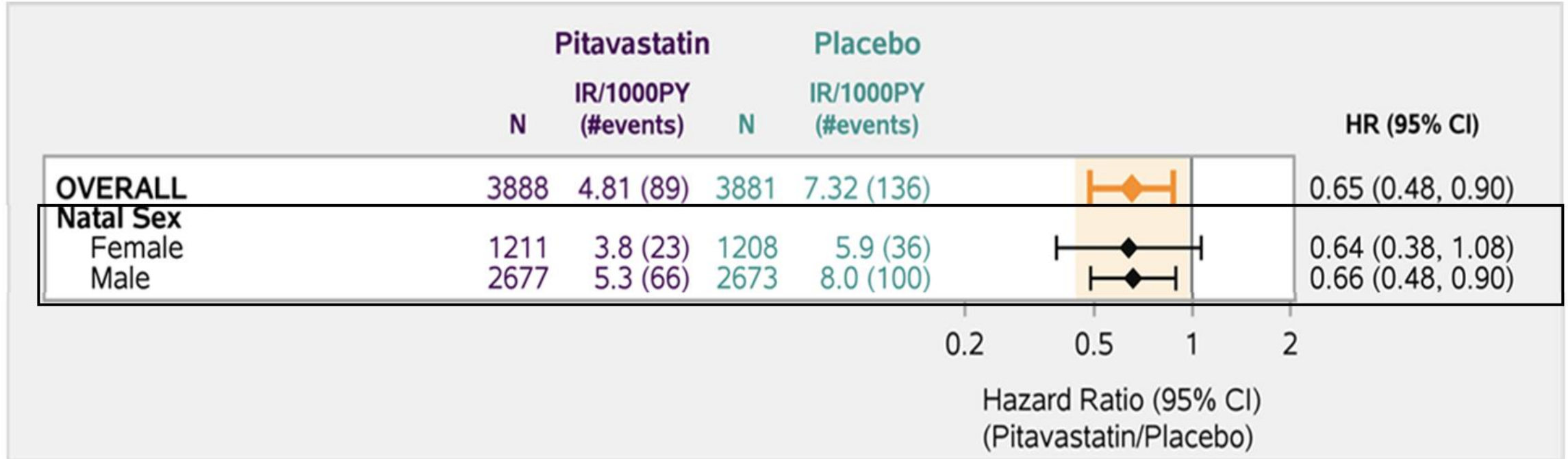
No. at Risk

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

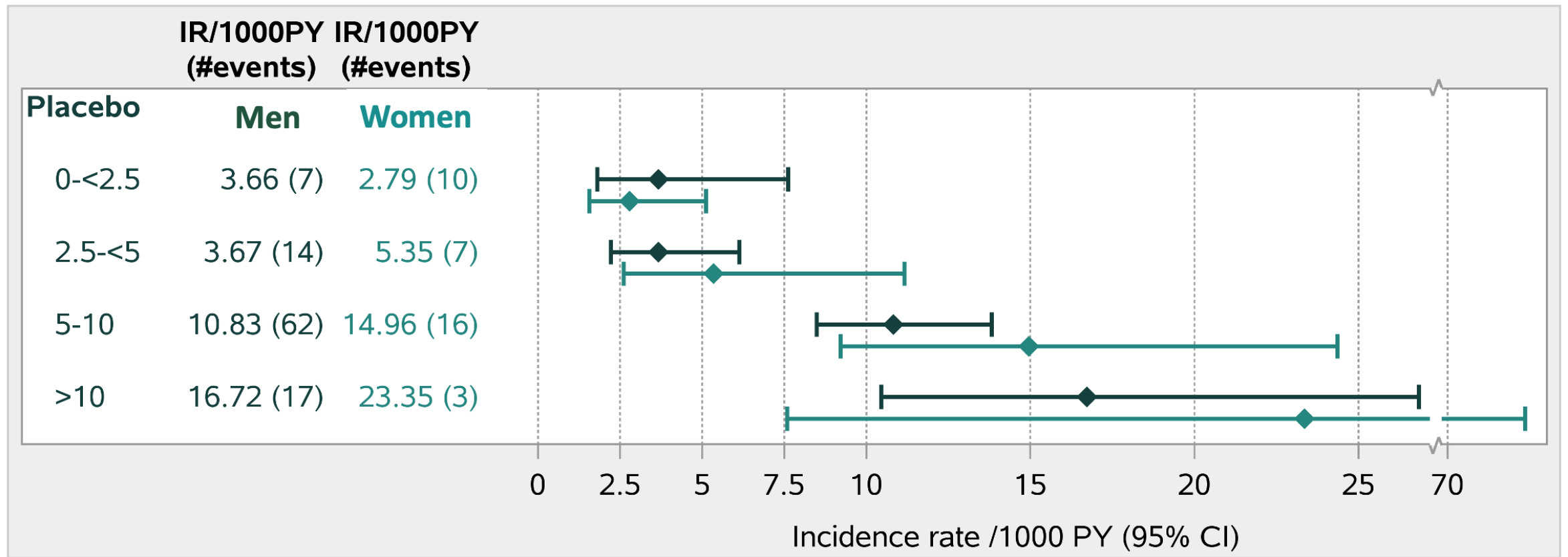
Subgroup Analyses



Statin effect size is similar by sex



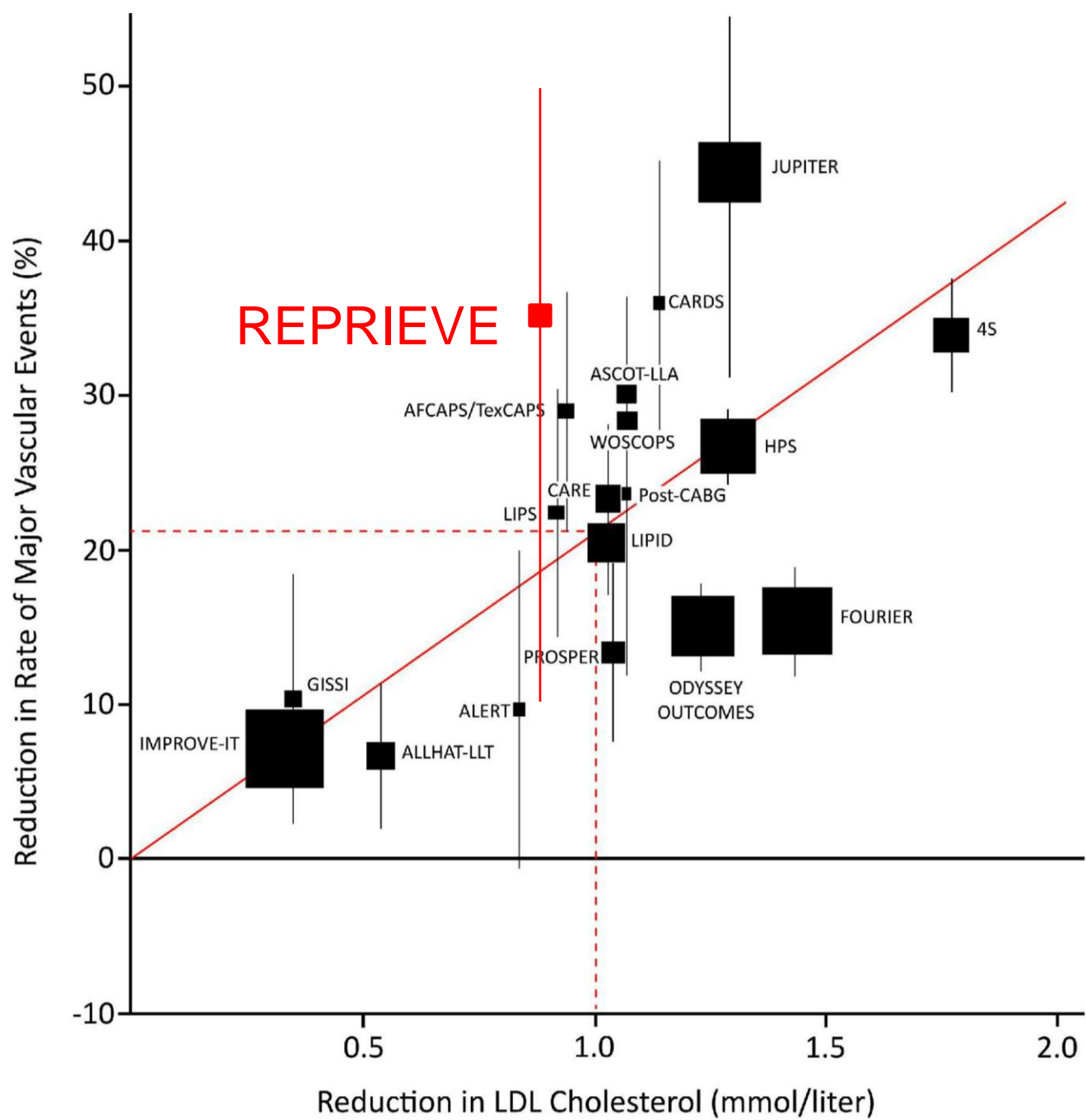
But ASCVD risk score underpredicts risk in women



Safety

Table 2. Adverse Events.

Event	Pitavastatin (N = 3888)		Placebo (N = 3881)		Incidence Rate Ratio (95% CI)*
	No. with Event	Incidence Rate (95% CI) <i>no./100 person-yr</i>	No. with Event	Incidence Rate (95% CI) <i>no./100 person-yr</i>	
Nonfatal serious adverse event	695	4.16 (3.86–4.48)	694	4.13 (3.84–4.45)	1.01 (0.91–1.12)
Diabetes mellitus†	206	1.13 (0.99–1.30)	155	0.84 (0.72–0.99)	1.35 (1.09–1.66)
Myalgia, muscle weakness, or myopathy of grade ≥3 or treatment-limiting‡	91	0.49 (0.40–0.61)	53	0.28 (0.22–0.37)	1.74 (1.24–2.45)
Rhabdomyolysis of grade ≥3 or treat- ment-limiting	3	0.02 (0.01–0.05)	4	0.02 (0.01–0.06)	0.75 (0.17–3.37)§
Alanine aminotransferase elevation of grade ≥3	11	0.06 (0.03–0.11)	8	0.04 (0.02–0.08)	1.38 (0.56–3.43)§
Any adverse event¶	1304	8.88 (8.41–9.38)	1256	8.37 (7.92–8.84)	1.06 (0.98–1.15)



Take Home Points

- For me, REPRIEVE is practice affirming NOT practice changing
- Statins are safe, with similar AEs as general population
- Efforts to revise clinical practice guidelines are underway
 - Guidelines are unlikely to routinely recommend statins for people with 10-year ASCVD risk <5% (**personal opinion**)
- For populations with lower overall ASCVD risk (e.g. sub-Saharan Africa) implementation is a lower priority compared to other drivers of risk (i.e. hypertension control)
 - Implementation may be a **higher priority for higher ASCVD risk populations** (e.g., South Asians)

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