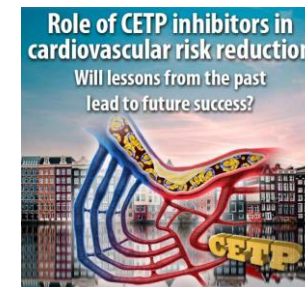


Unmet needs in lowering LDL-c: barriers to goal attainment and need for new targets

Stephen Nicholls, MD
Melbourne, Australia

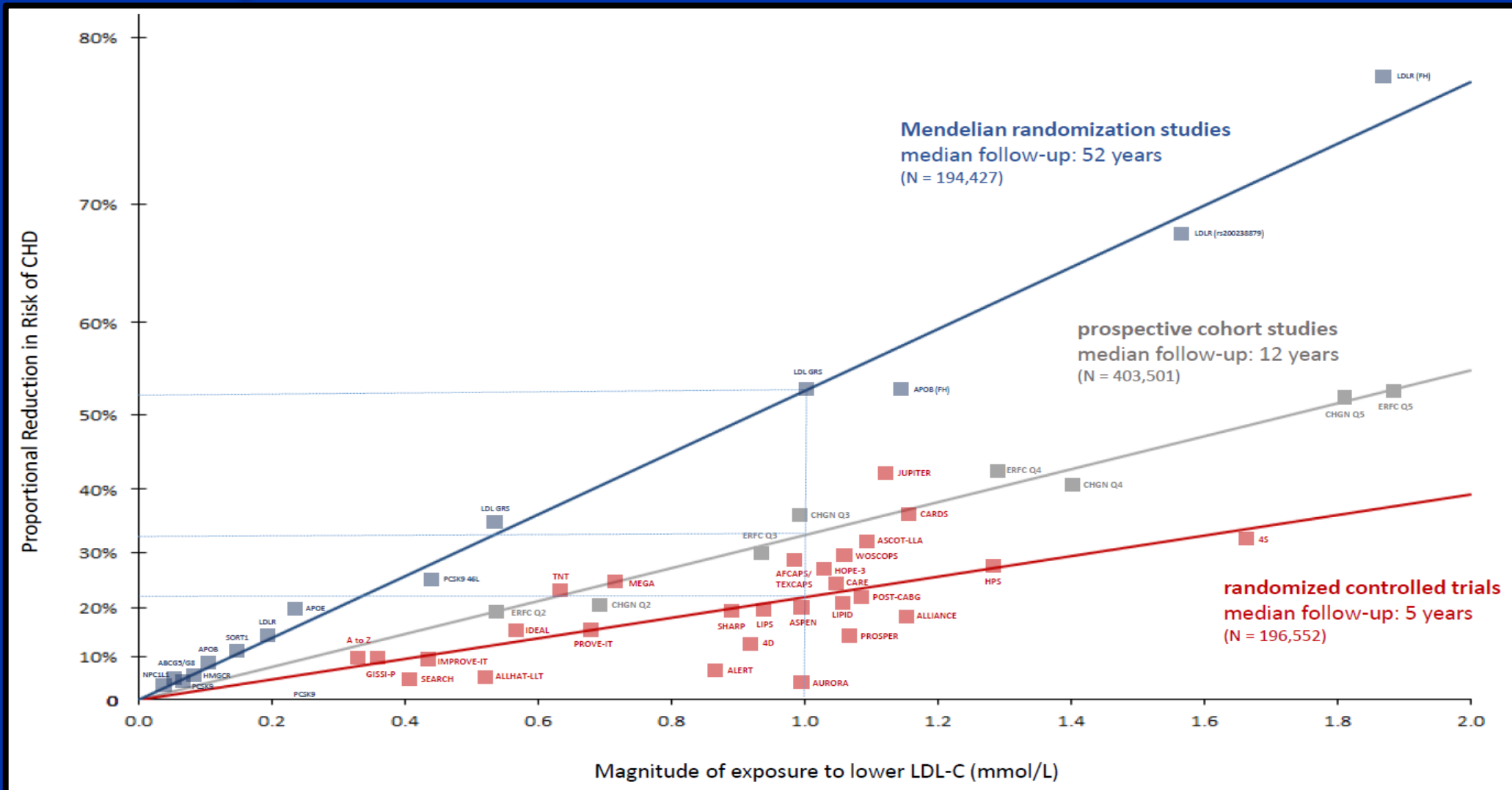
Role of CETP inhibitors in cardiovascular risk reduction - Will lessons from the past lead to future success?



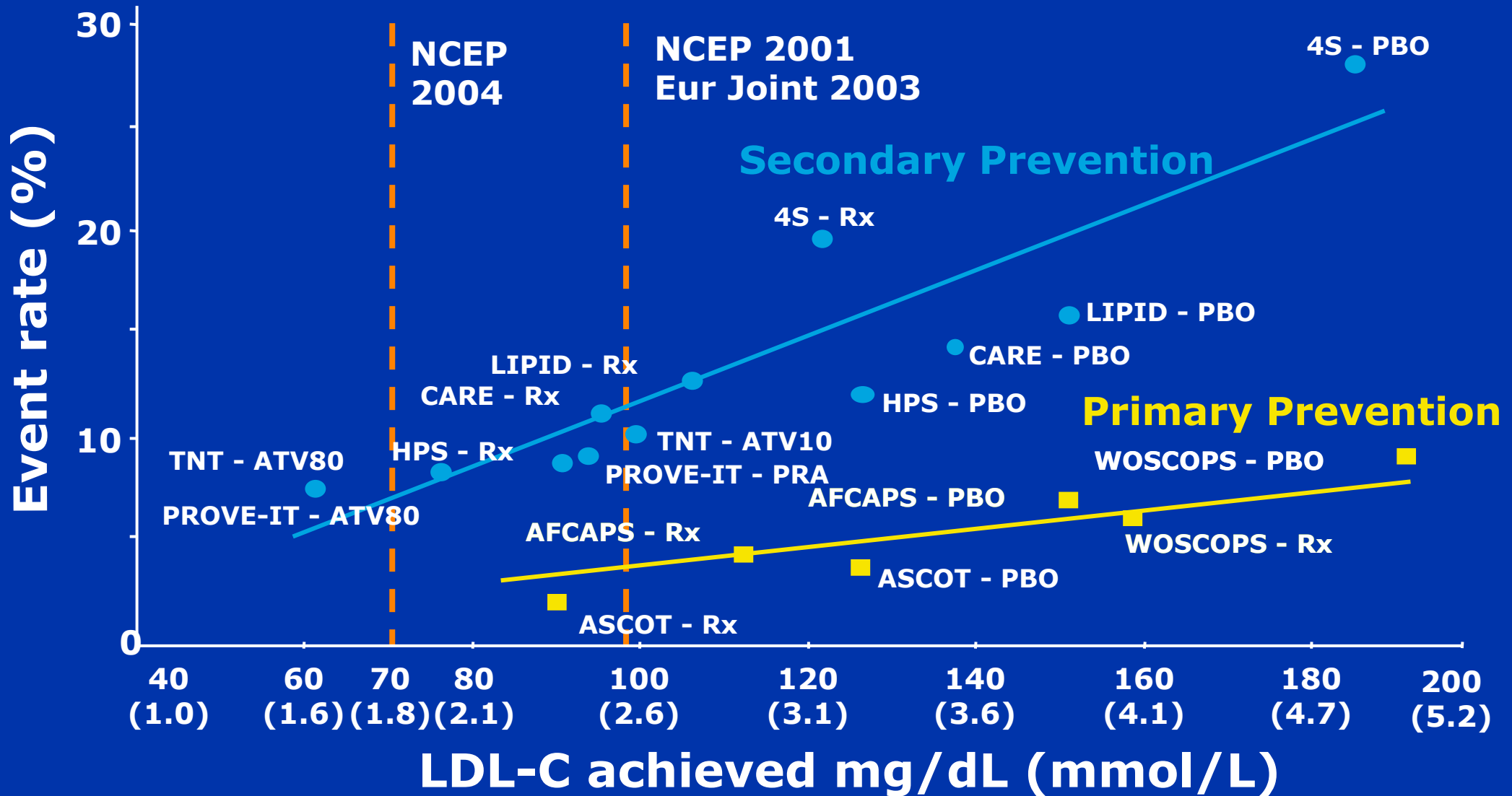
Disclosures

- Research support: AstraZeneca, Amgen, Anthera, Eli Lilly, Esperion, Novartis, Cerenis, The Medicines Company, Resverlogix, InfraReDx, Roche, Sanofi-Regeneron and LipoScience
- Consulting and honoraria: AstraZeneca, Akcea, Eli Lilly, Anthera, Omthera, Merck, Takeda, Resverlogix, Sanofi-Regeneron, CSL Behring, Esperion, Boehringer Ingelheim

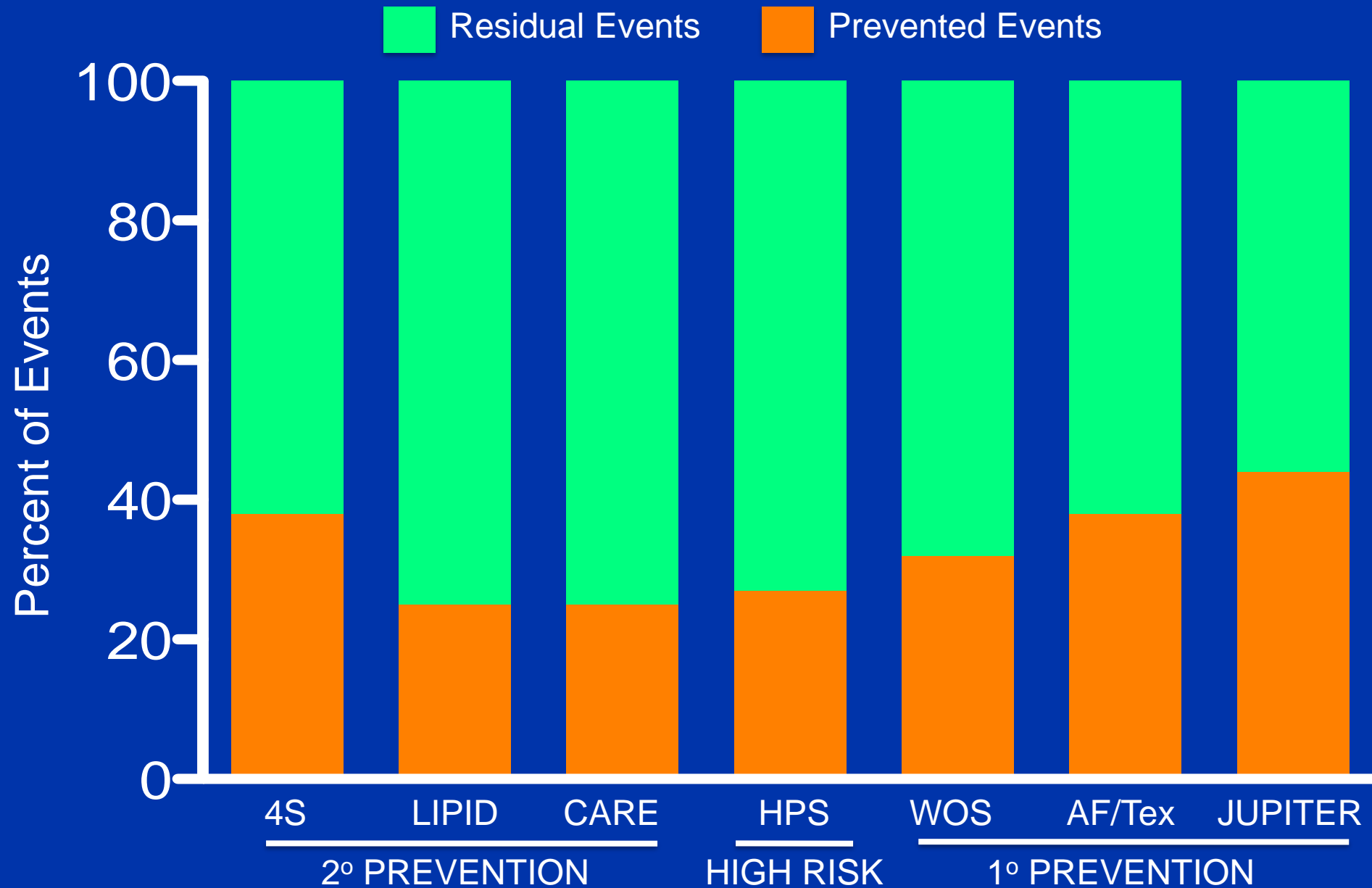
Genetic Benefits of Early Exposure to Lower LDL-C Levels



LDL-C Lowering and Benefit of Statins



Residual Clinical Risk in Statin Trials



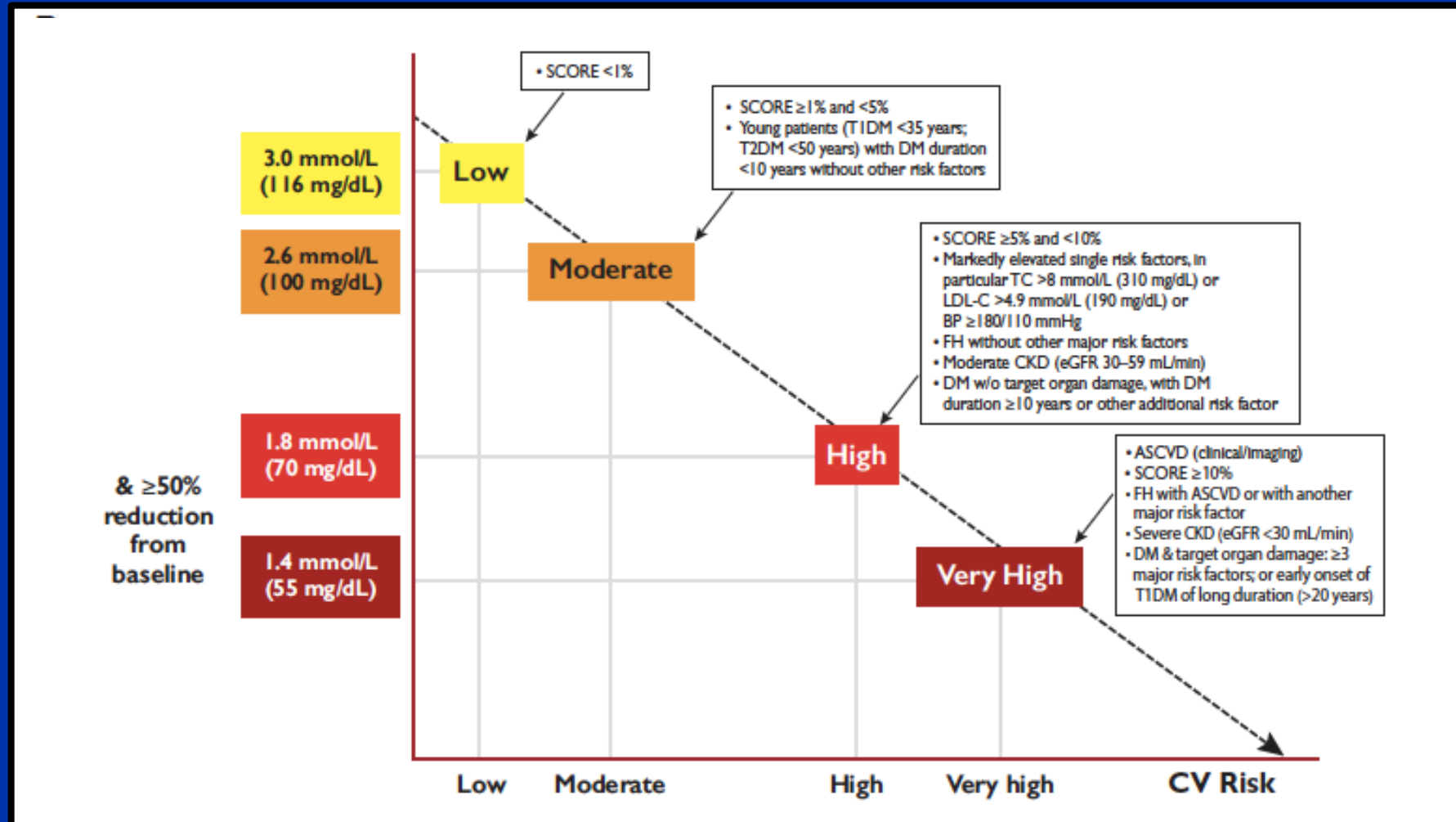
Outcomes: Non-Statin LDL-C Lowering Therapies

	3-Component MACE	Nonfatal MI
IMPROVE-IT Ezetimibe	0.90	0.87
FOURIER Evolocumab	0.80	0.73 [†]
ODYSSEY Outcomes Alirocumab	0.86 [*]	0.86
CLEAR Outcomes Bempedoic Acid	0.85	0.73

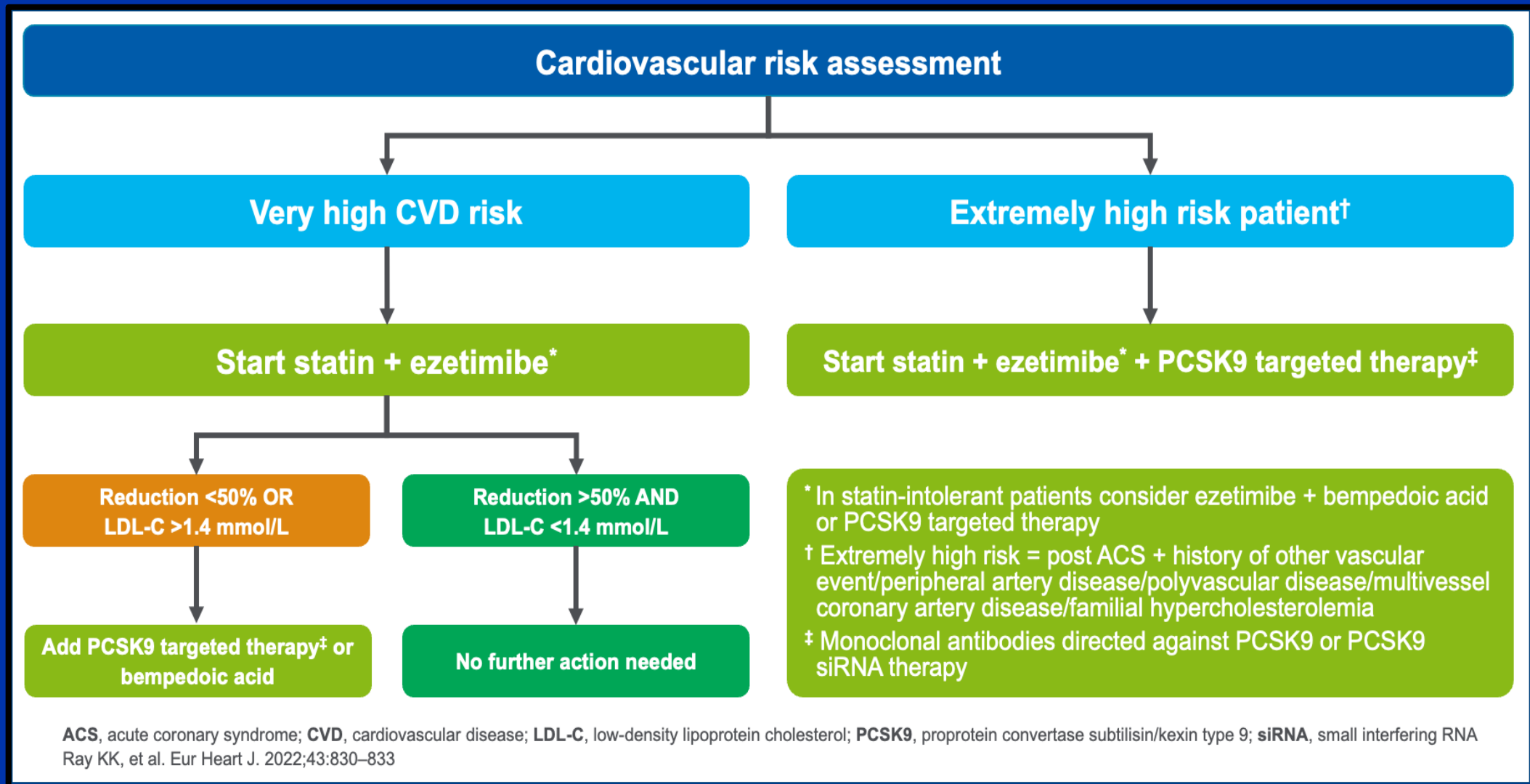
^{*}Trial used all-cause mortality rather than CV death

[†]Fatal and nonfatal MI

High Risk Patients Need Very Low LDL-C Levels



Integration of Combination of Lipid Lowering in Treatment Guidelines

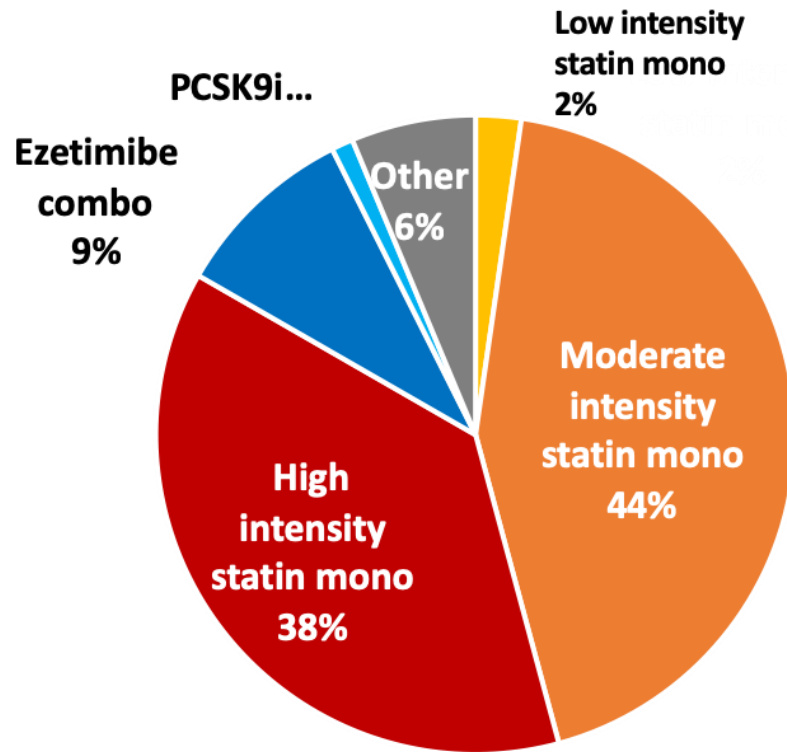


Intensity of Lipid Lowering Treatment

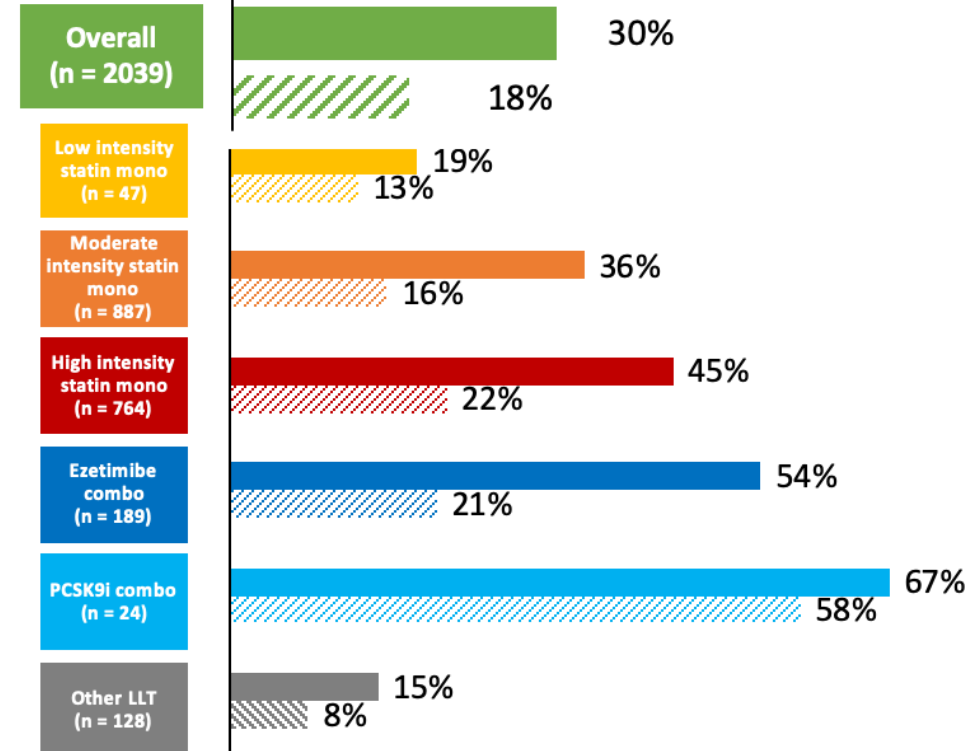
Treatment	LDL-C Reduction
Moderate intensity statin	~30%
Ezetimibe + bempedoic acid	~45%
High intensity statin	~50%
High intensity statin + ezetimibe	~65%
Moderate statin + ezetimibe + bempedoic acid	~65%
PCSK9 inhibitor	~60%
PCSK9 inhibitor + high intensity statin	~75%
PCSK9 inhibitor + high intensity statin + ezetimibe	~85%

Lipid Lowering Therapy and LDL-C Goal Attainment in Patients with ASCVD

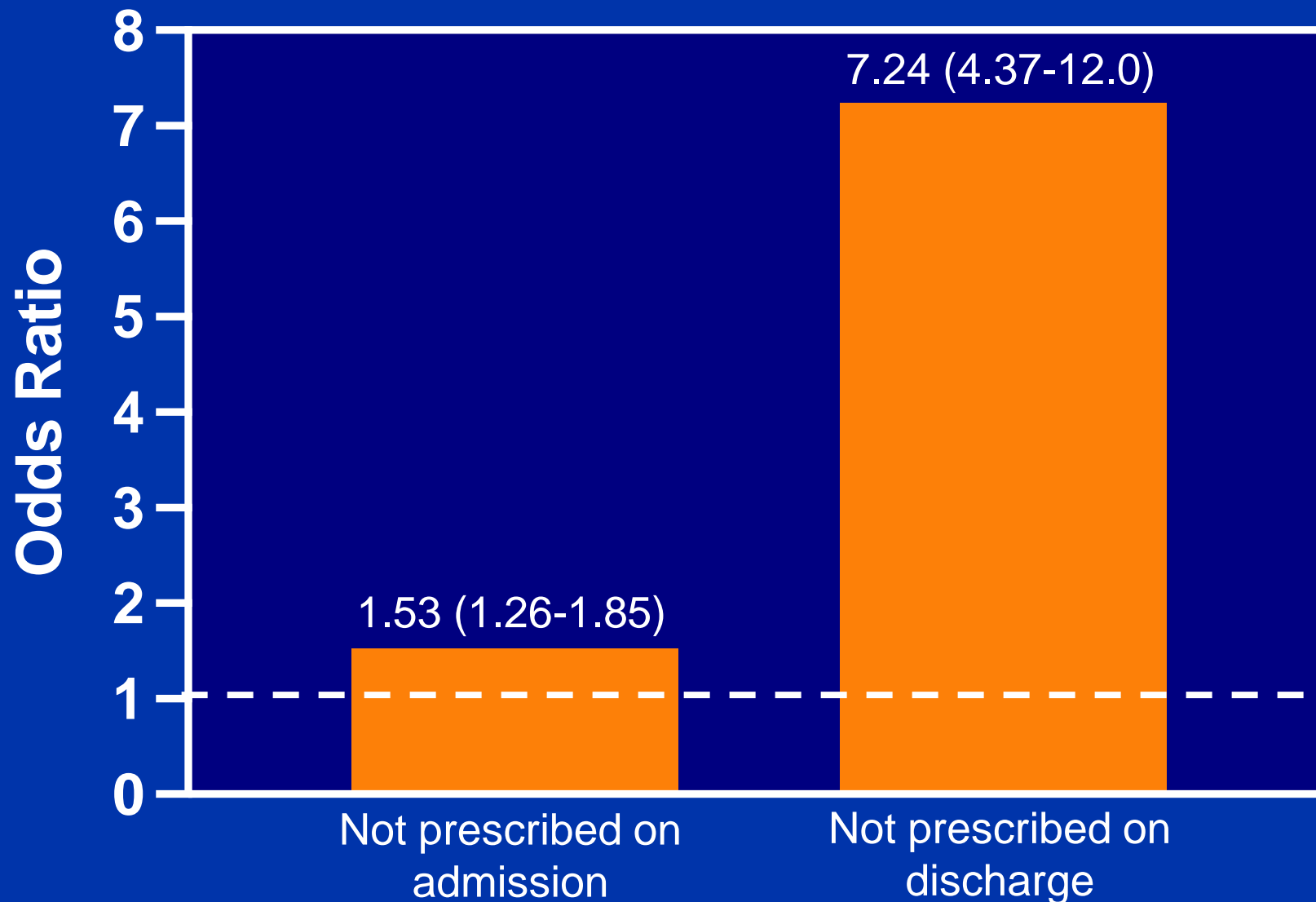
LLT use among patients with established ASCVD



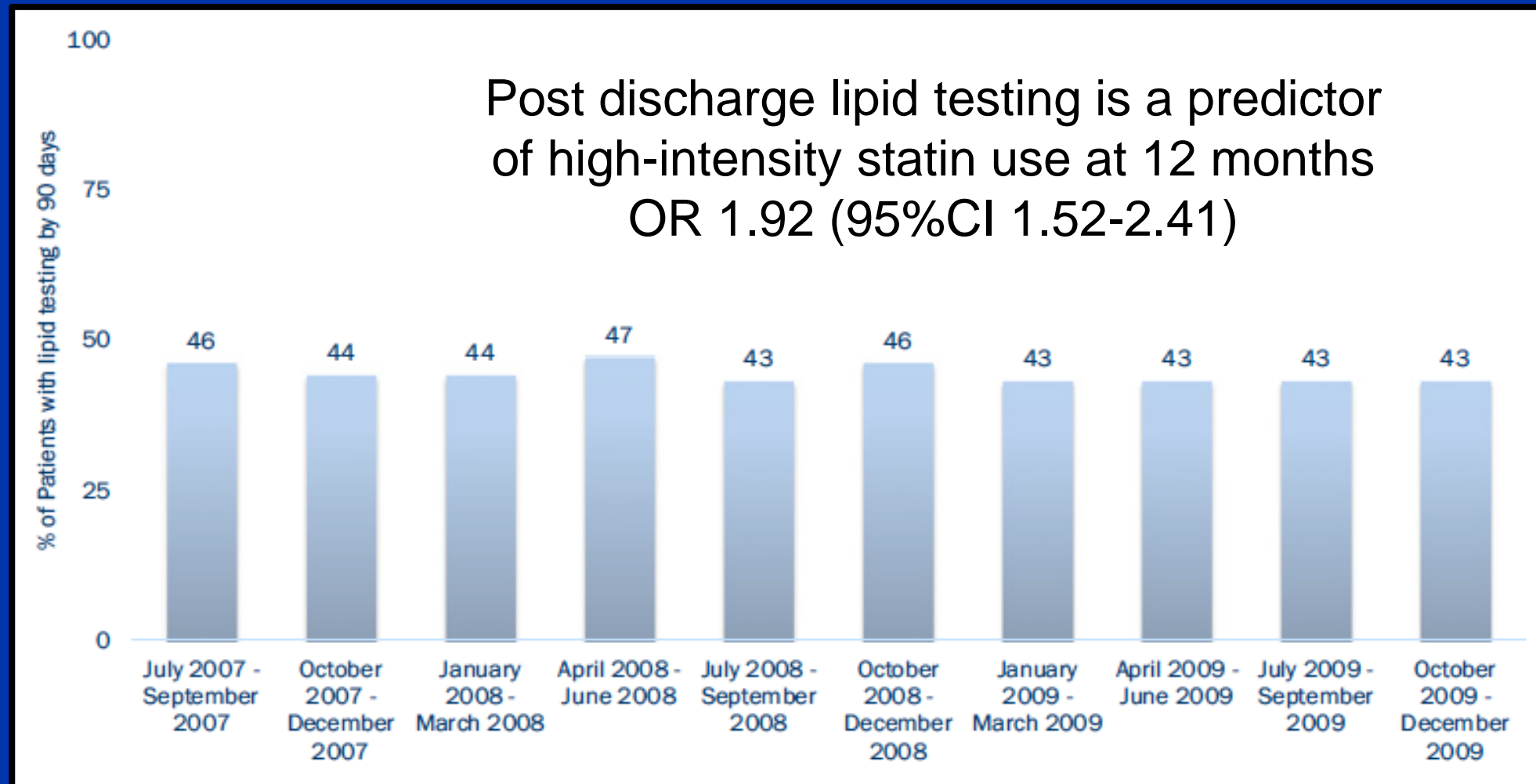
2016/2019 goal attainment in patients with established ASCVD



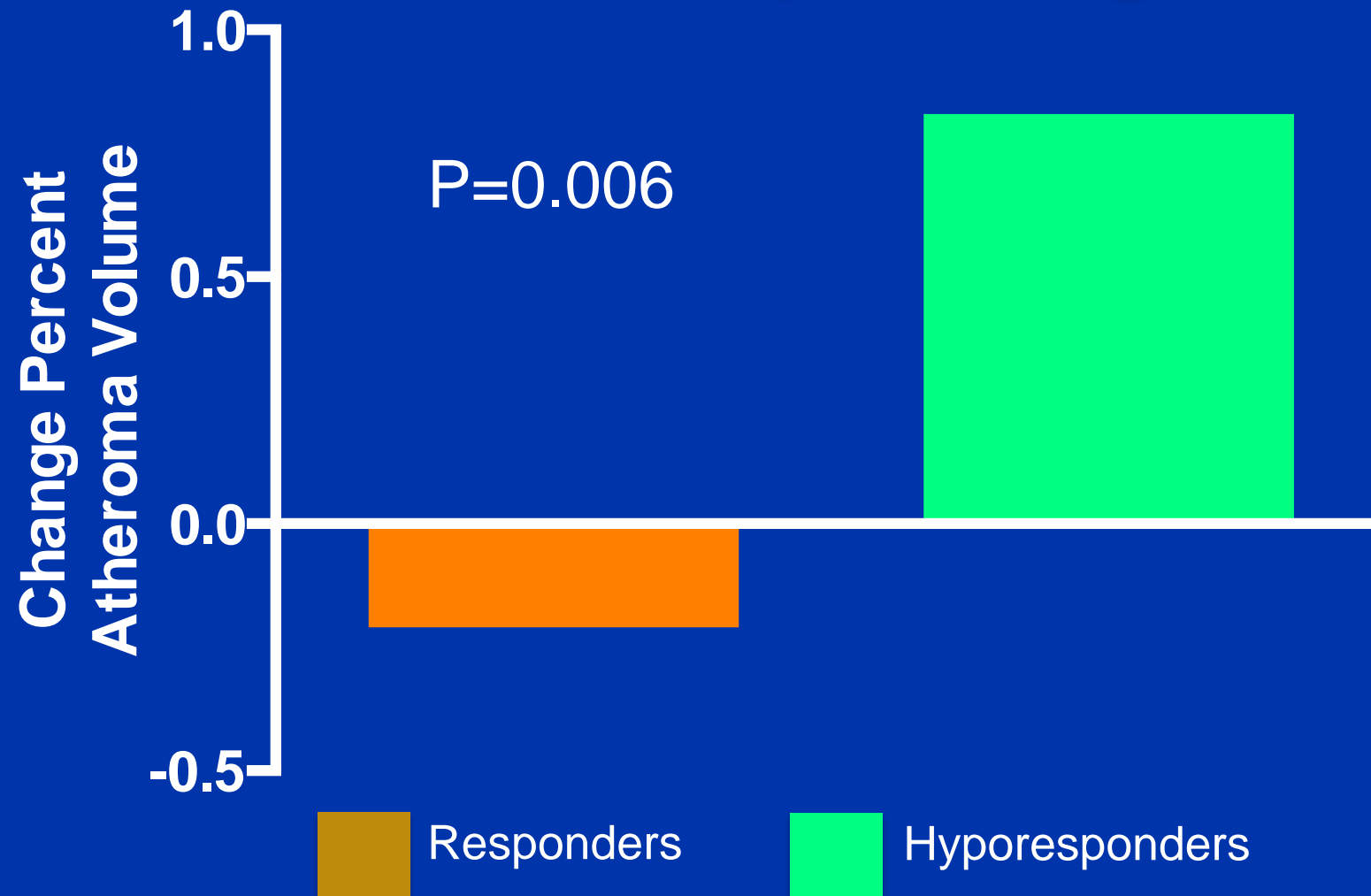
Predictors of Intensive Lipid Lowering Use 12 Months Post ACS



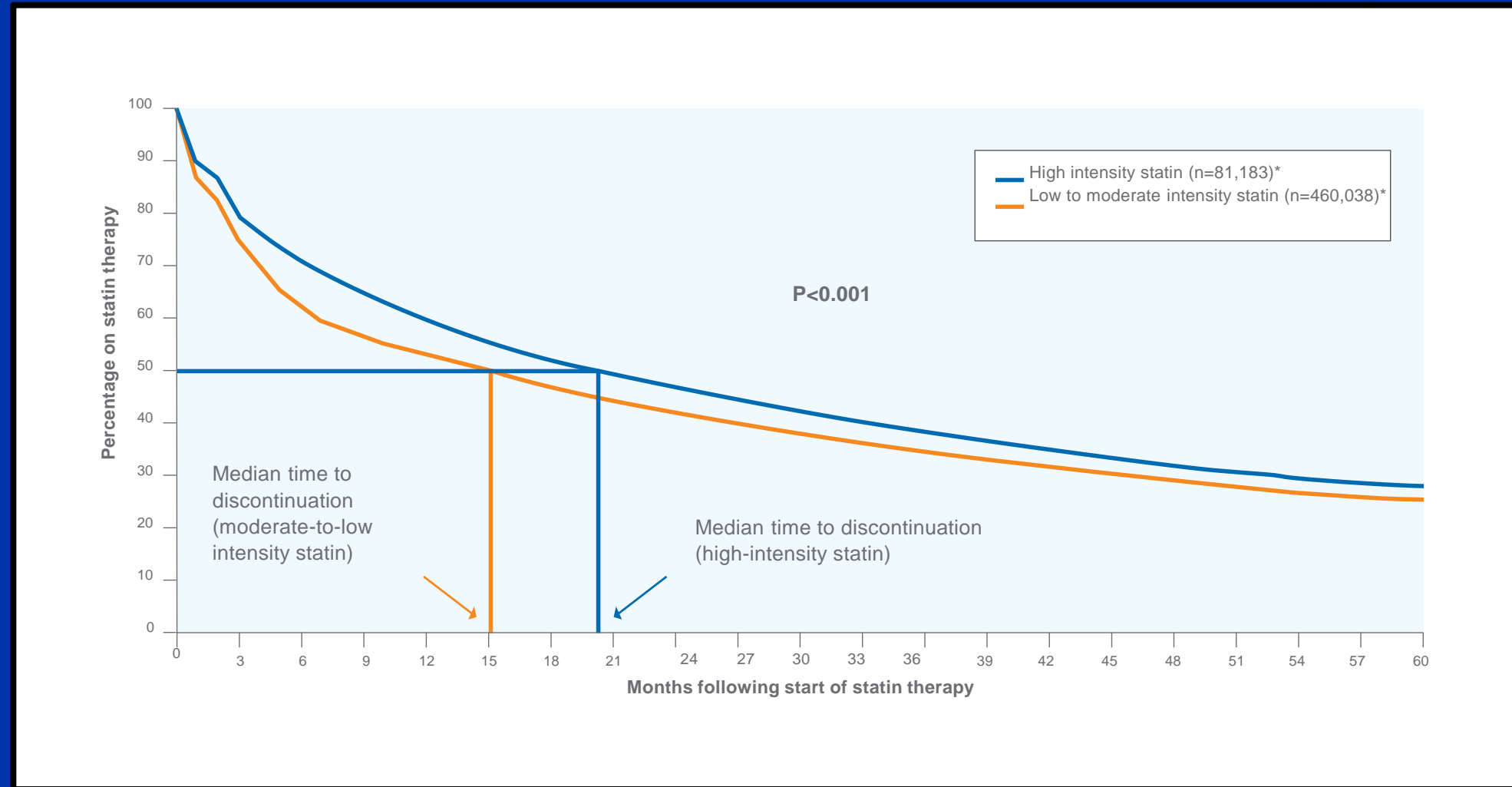
We Don't Follow up with Lipid Tests



Suboptimal LDL Response to Statins Associate with Plaque Progression



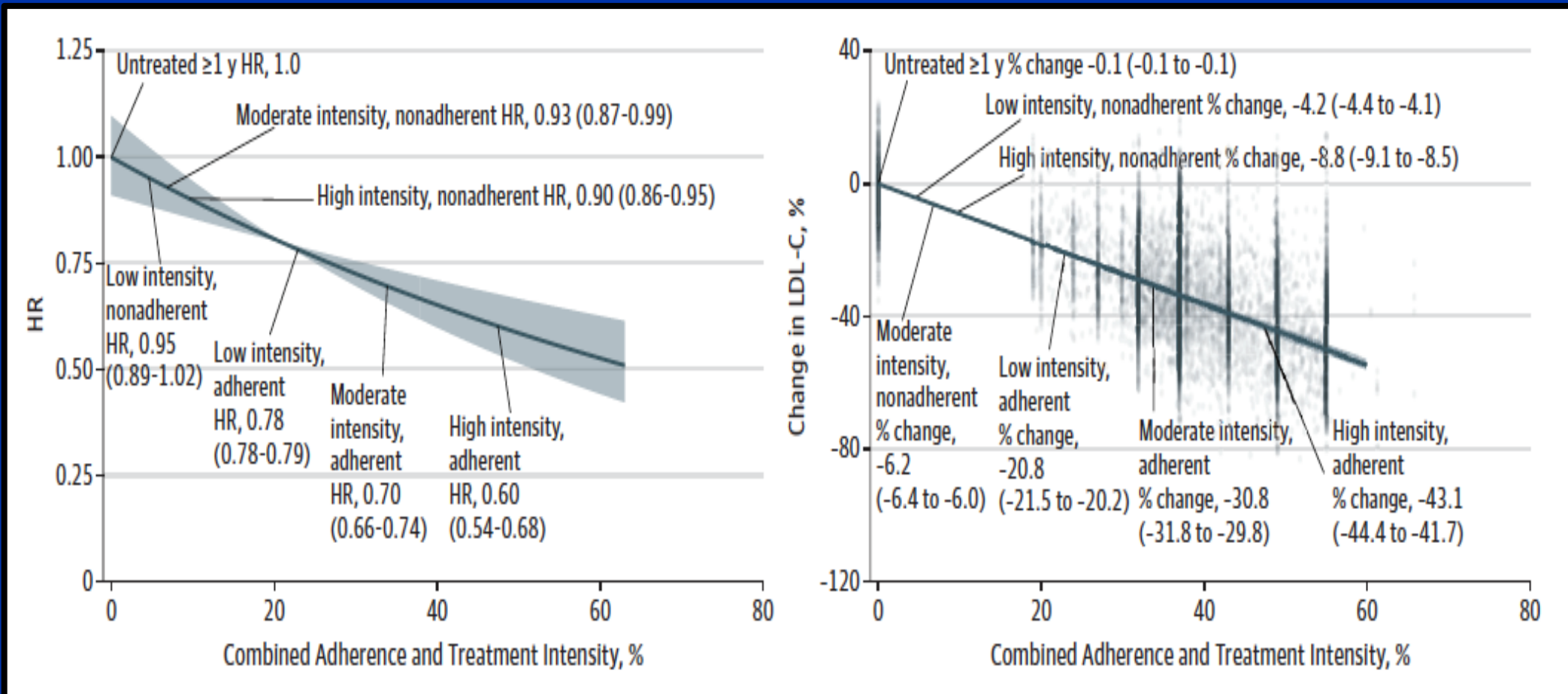
Suboptimal Adherence and Persistence with Statin Therapy



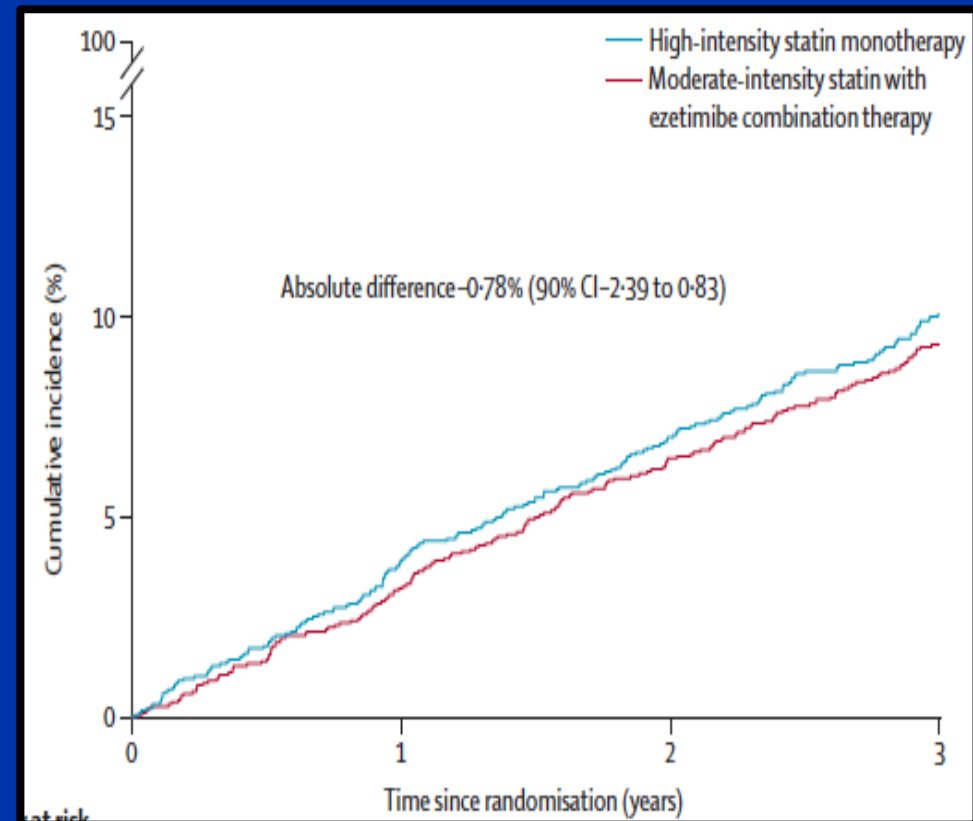
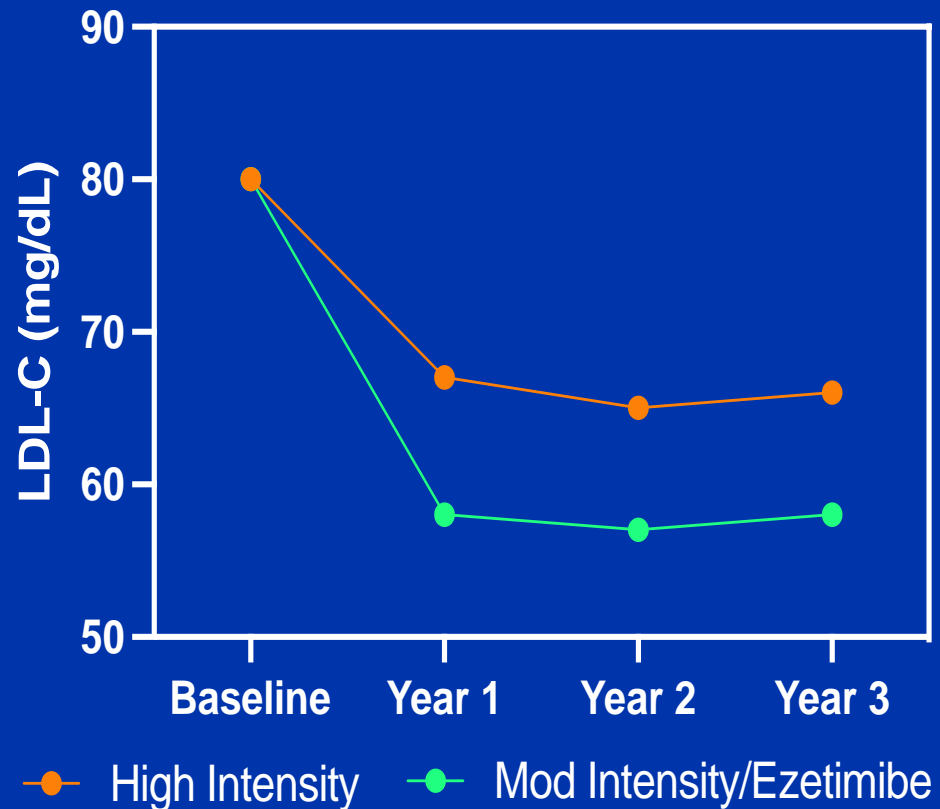
Adherence and Treatment Intensity Influence Outcomes

Cardiovascular Risk

Change in LDL-C



How About Combination Therapy with Lower Intensity Statins?



Summary

- LDL cholesterol plays a causal role in atherosclerotic cardiovascular disease
- Intensive lipid lowering produces greater reductions in cardiovascular risk in clinical trials
- Guidelines emphasize the role of combination lipid lowering therapy in high-risk patients
- Barriers limit prescription and adherence to lipid lowering therapy in cardiovascular prevention