
Extending the Evidence: What did the FOURIER trial teach us on managing high risk patients?

*PCSK9i, Changing Practice in Cardiology:
The Emerging Story*

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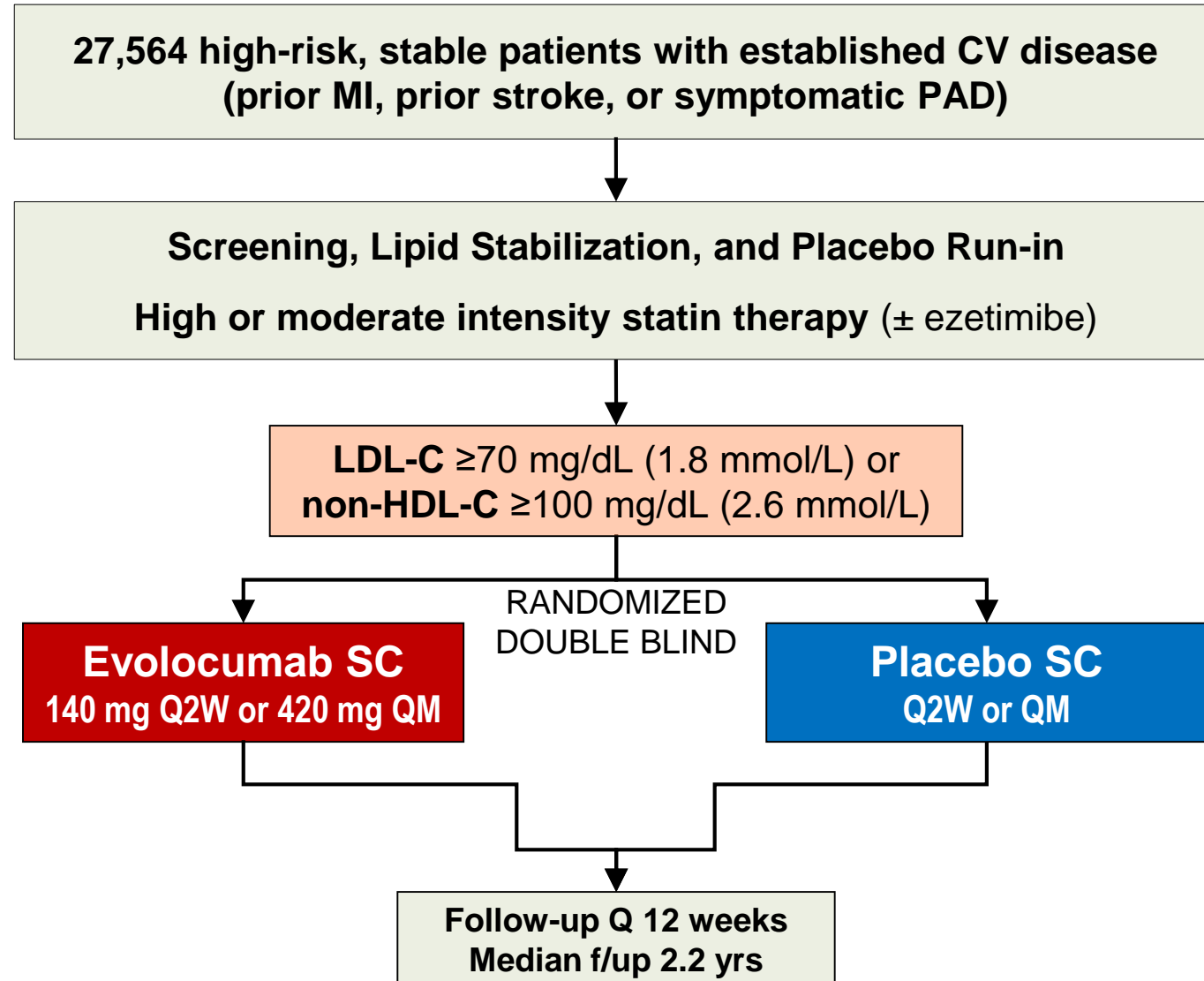
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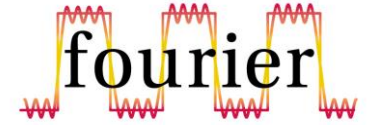


Trial Design

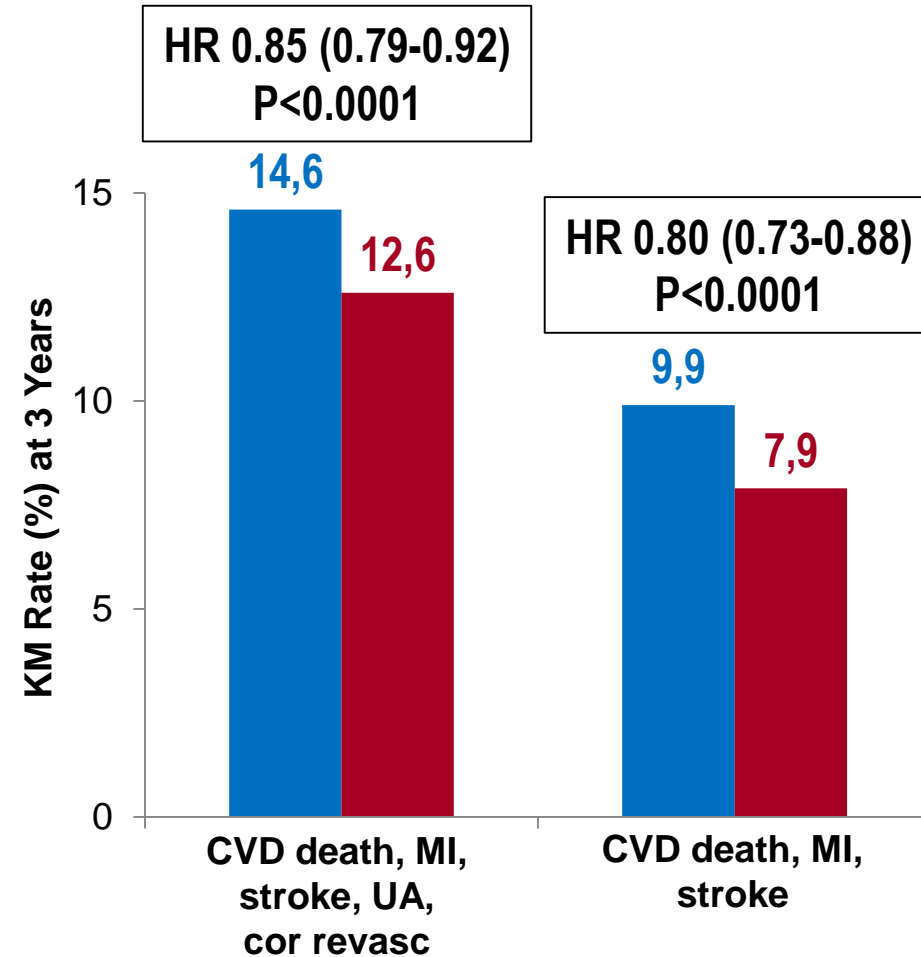
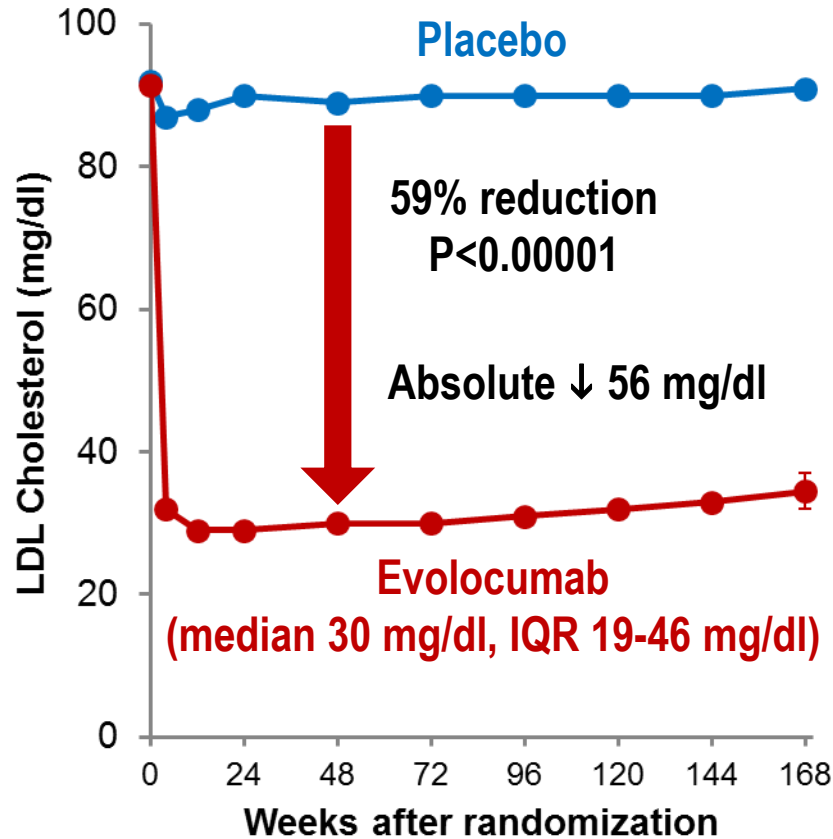




Summary of Effects of PCSK9i Evolocumab

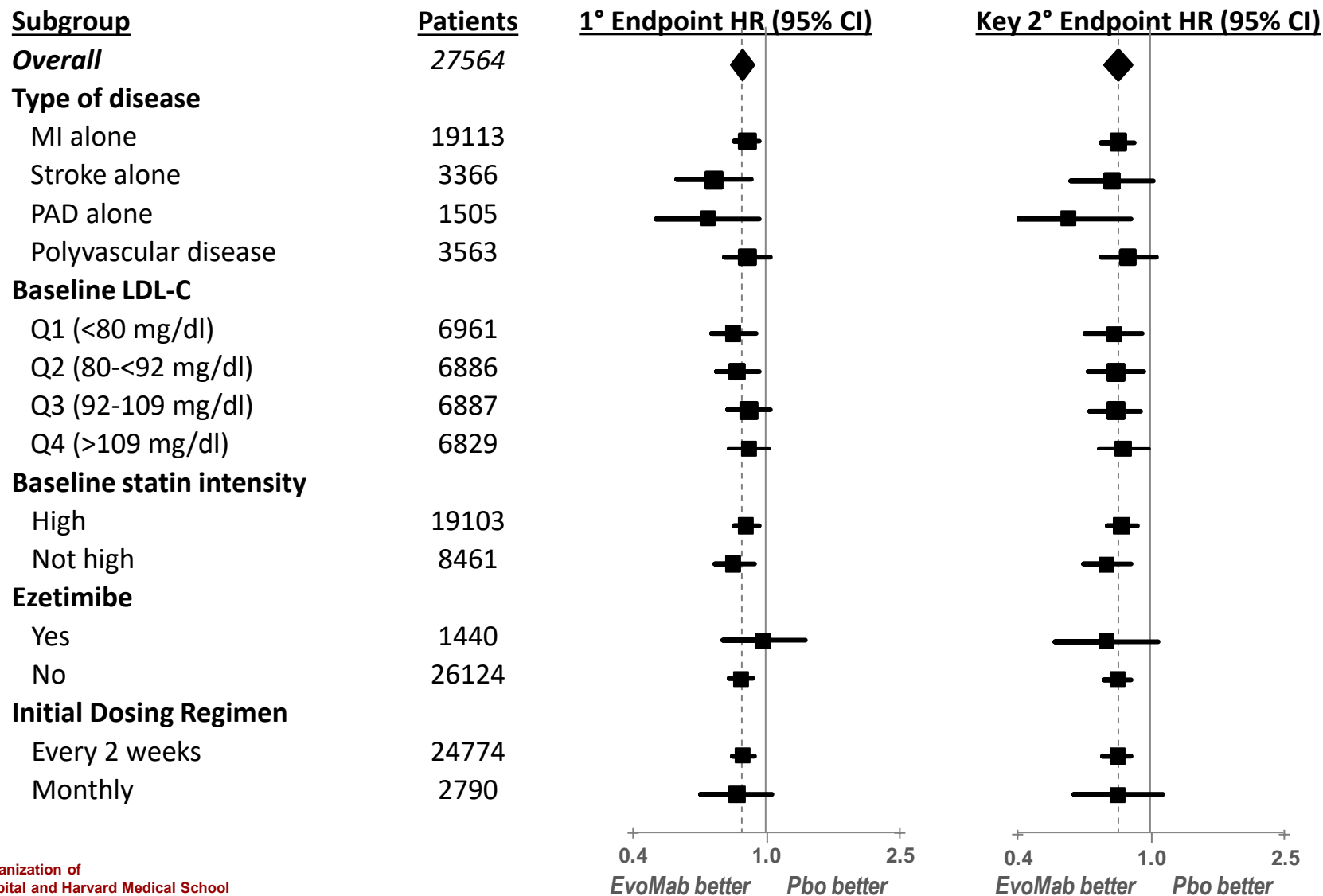
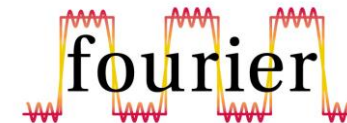


- ↓ LDL-C by 59% down to a median of 30 mg/dl
- ↓ CV outcomes in patients on statin
- Safe and well-tolerated





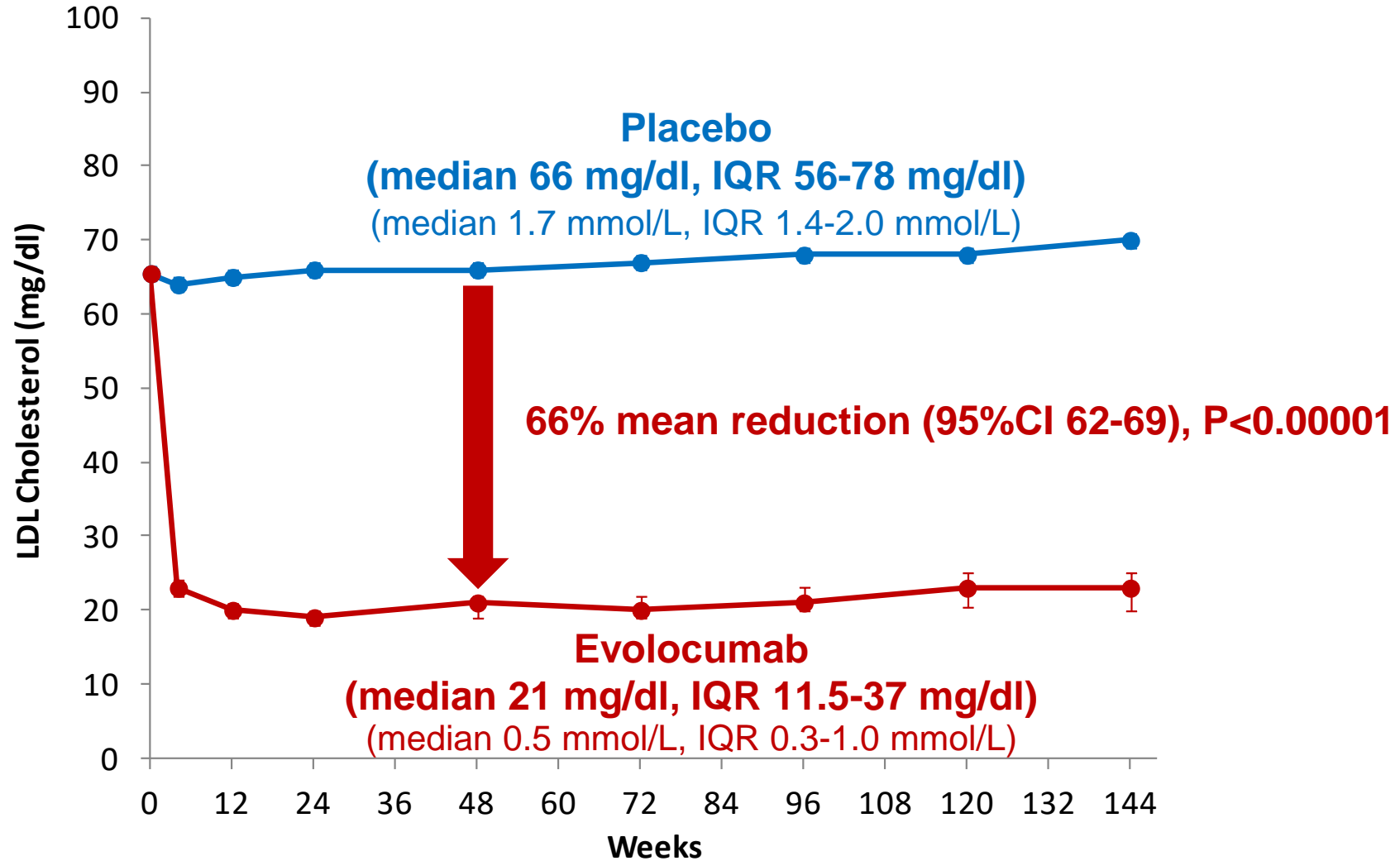
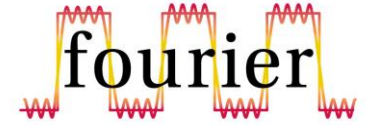
Key Subgroups





LDL Cholesterol

2034 patients w/ baseline LDL-C < 70 mg/dL





Clinical Outcomes by Baseline LDL-C



CVD, MI, stroke, UA, or cor revasc

HR (95% CI)

$P_{\text{interaction}}$

All Patients

0.85 (0.79-0.92)

Baseline LDL-C <70 mg/dL



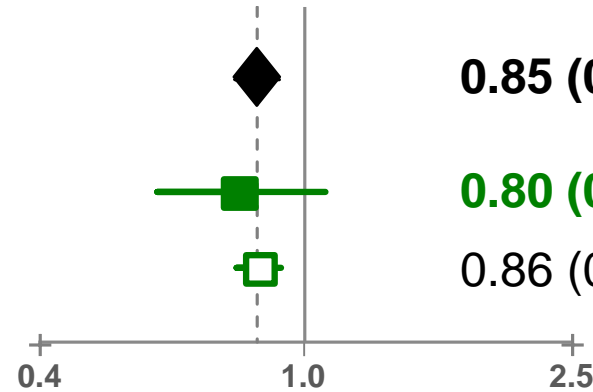
0.80 (0.60-1.07)

Baseline LDL-C ≥70 mg/dL



0.86 (0.79-0.92)

0.65



CVD, MI, or stroke

All Patients

0.80 (0.73-0.88)

Baseline LDL-C <70 mg/dL



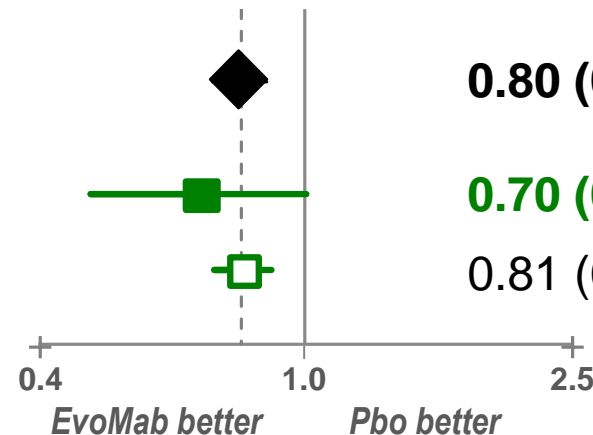
0.70 (0.48-1.01)

Baseline LDL-C ≥70 mg/dL



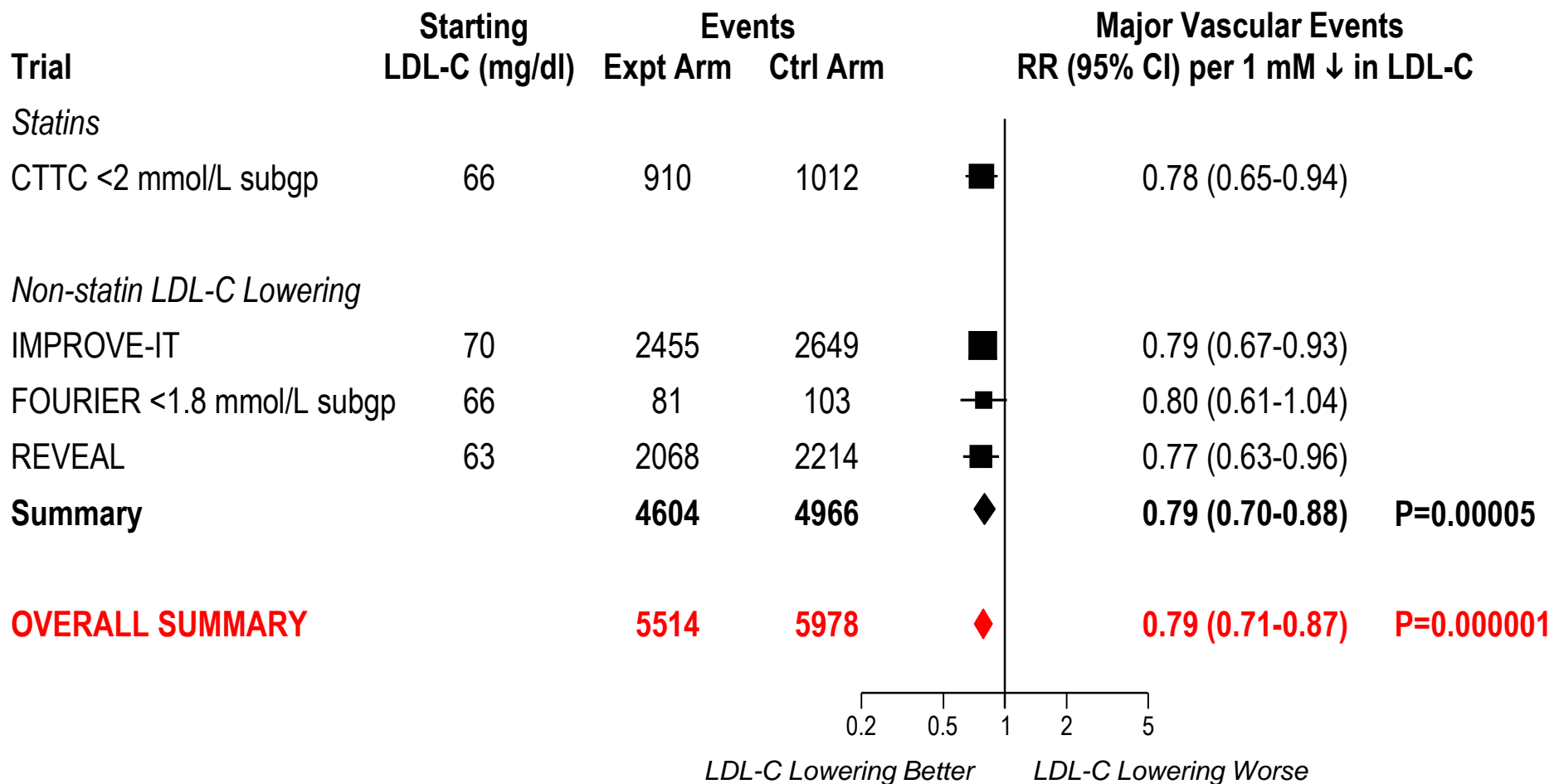
0.81 (0.73-0.89)

0.44



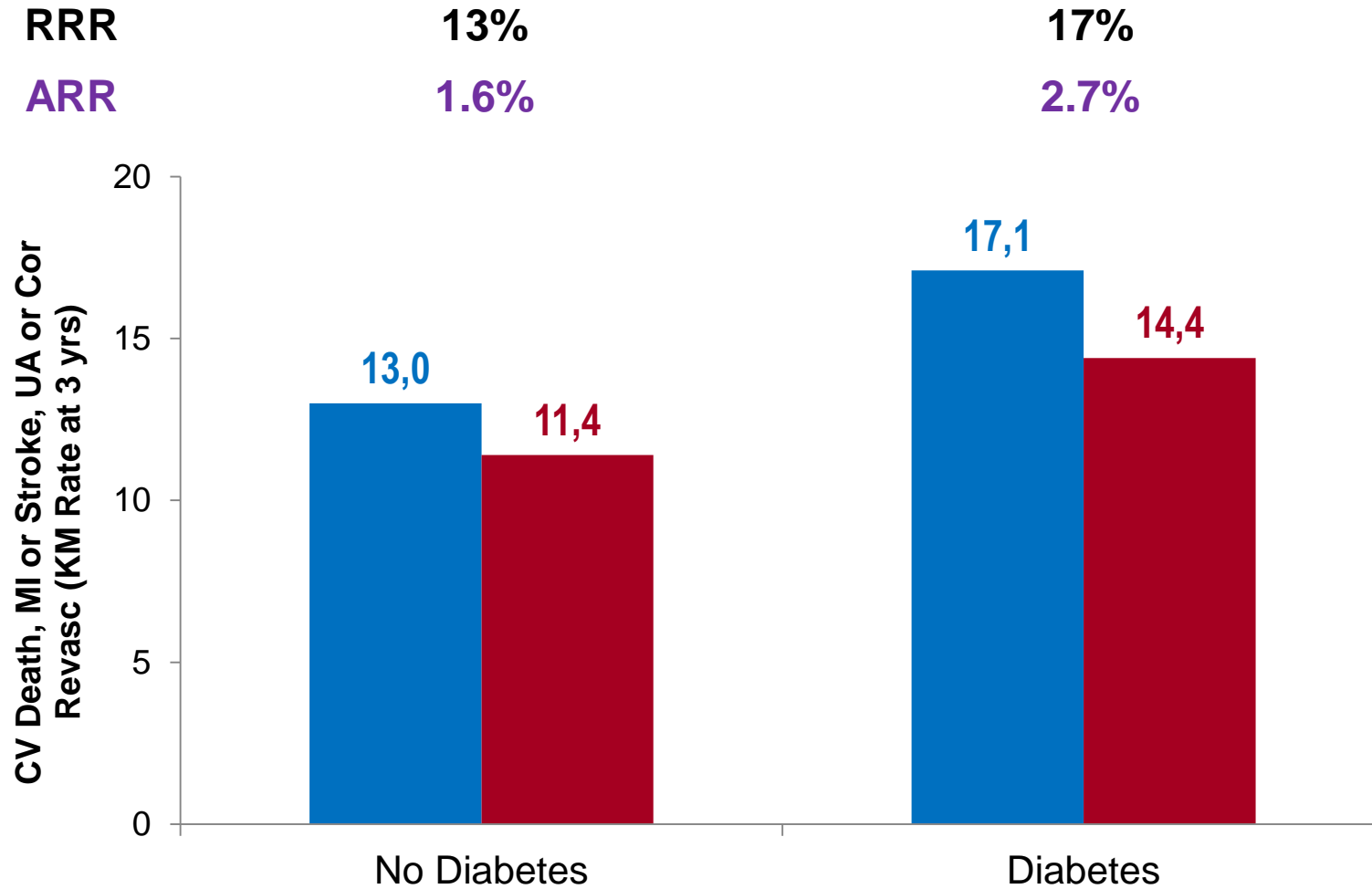
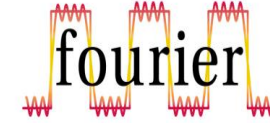


Efficacy of LDL-C Lowering Even When LDL-C ≤ 70 mg/dL (1.8 mM)



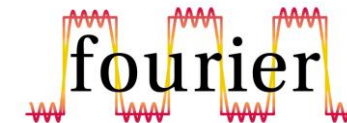


Efficacy by Diabetes Status

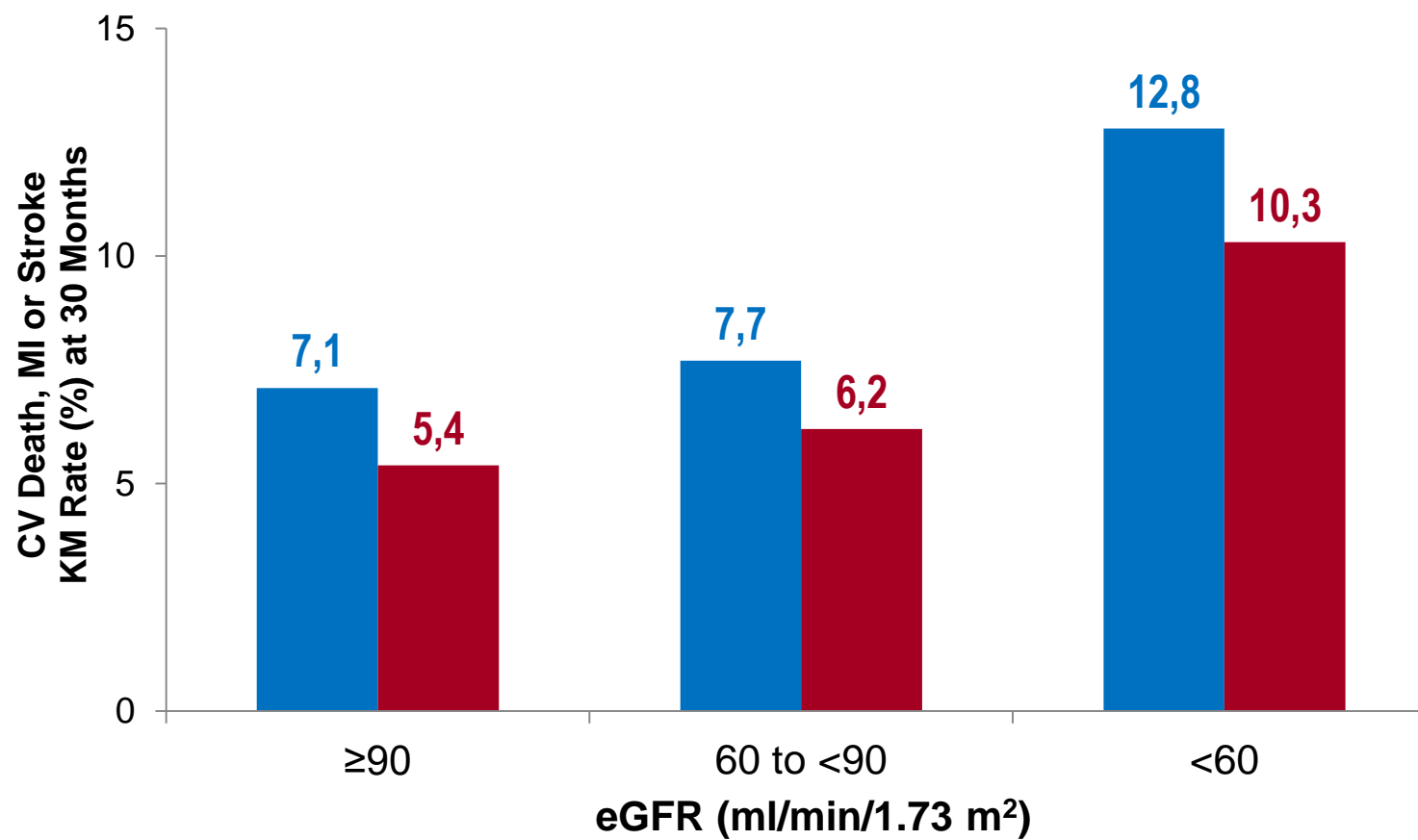




Efficacy by Baseline CKD Stage

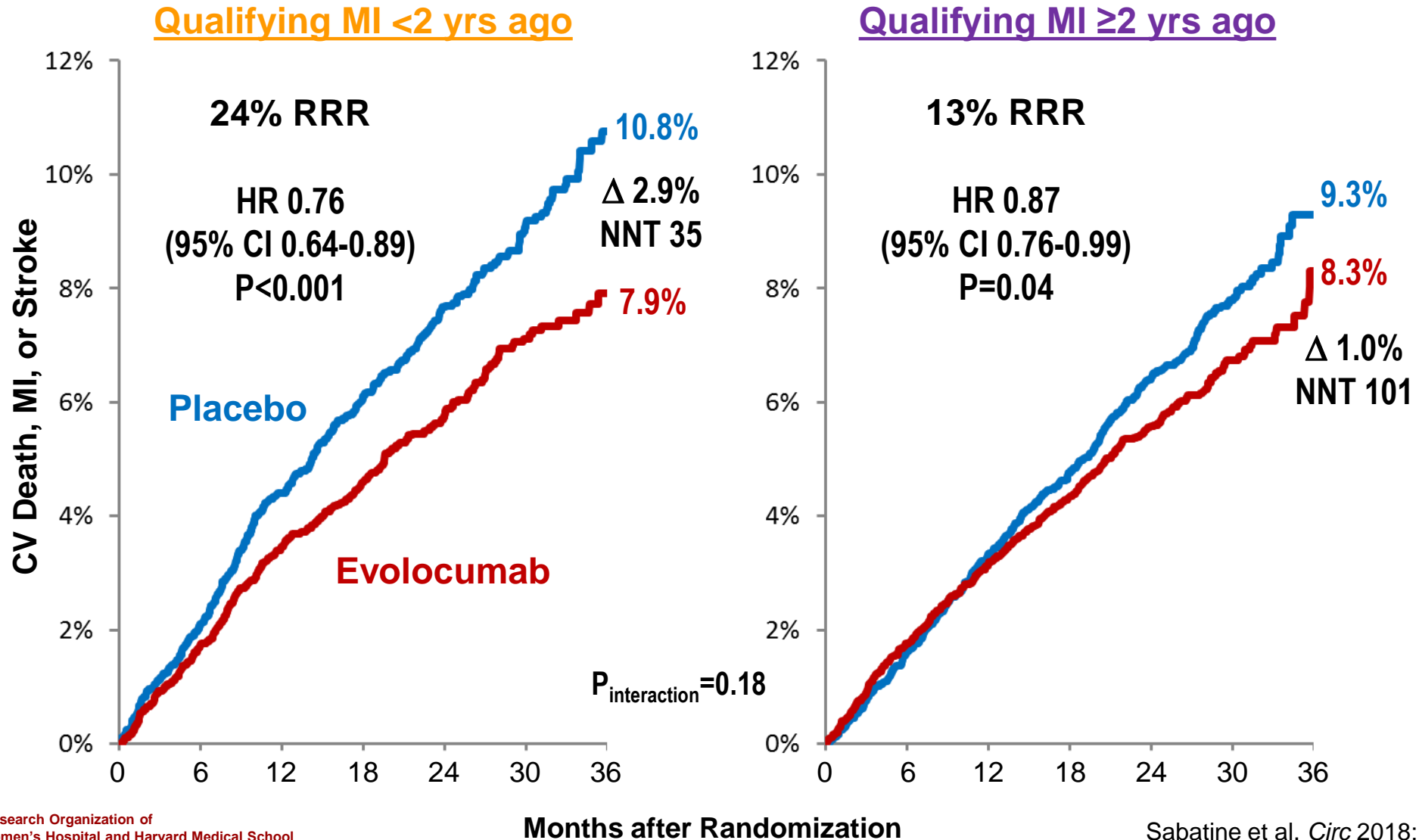


RRR	25%	18%	21%
ARR	1.7%	1.5%	2.5%



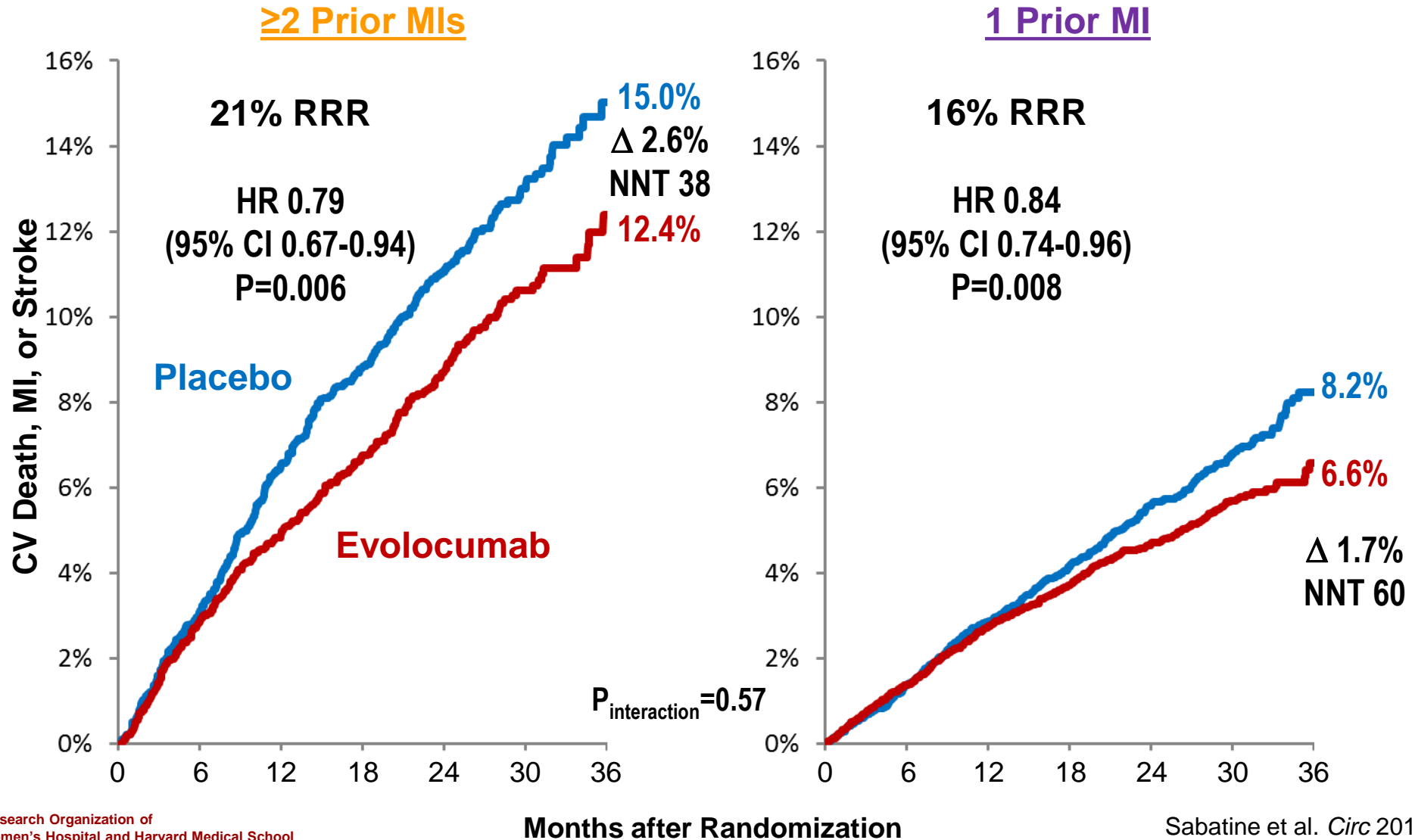


Benefit of EvoMab Based on Time from Qualifying MI



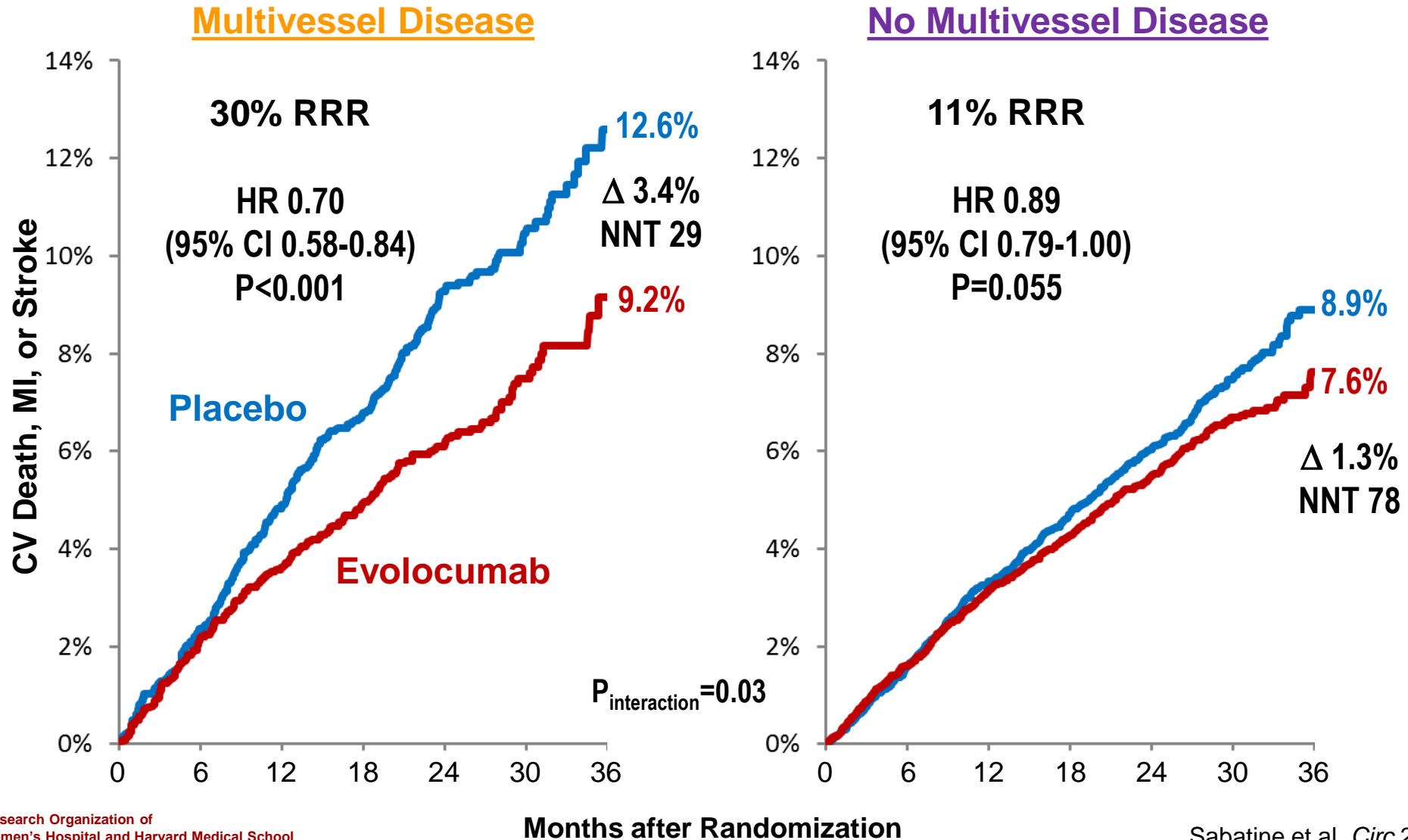


Benefit of EvoMab Based on # of Prior MIs



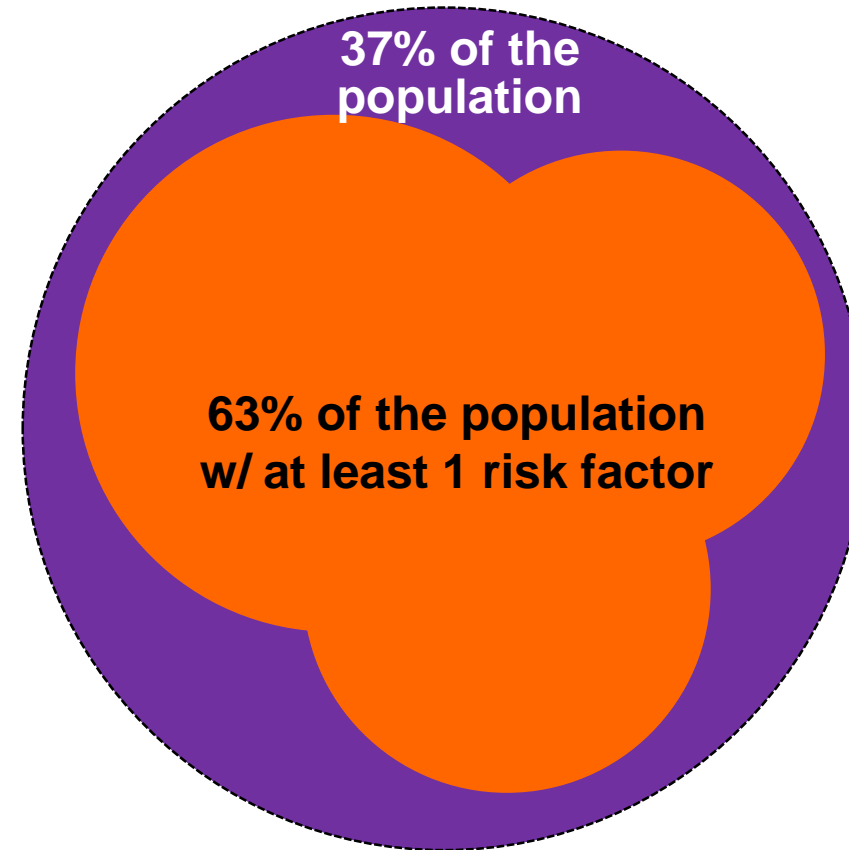
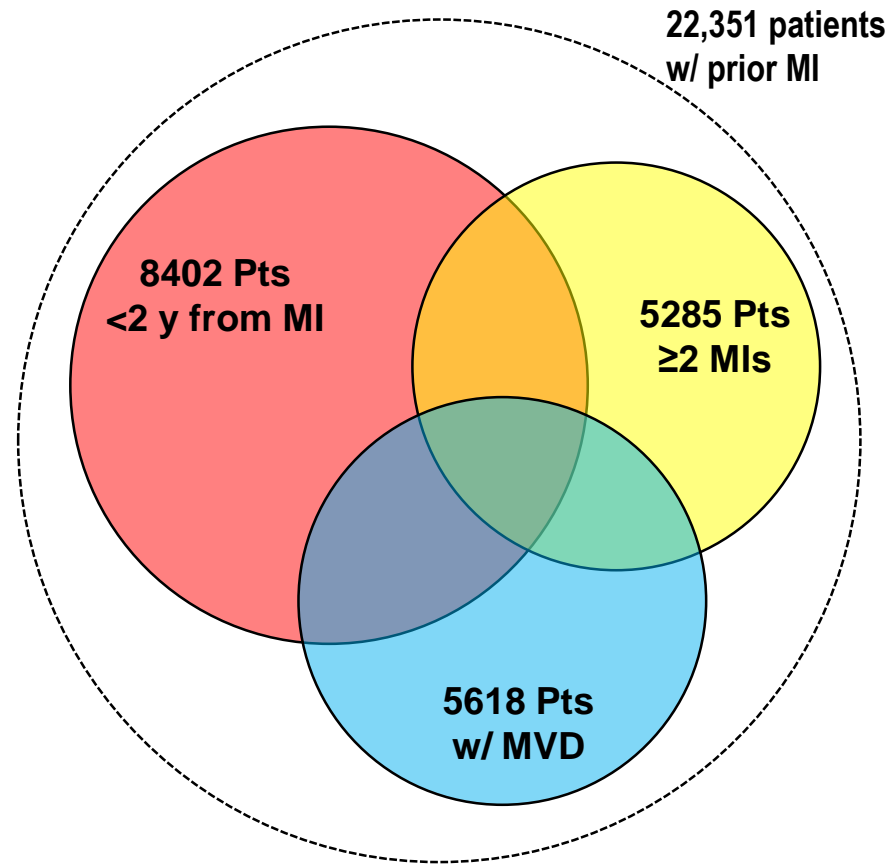
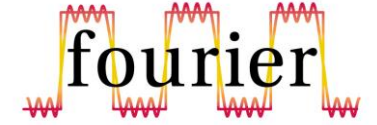


Benefit of EvoMab Based on Multivessel Disease



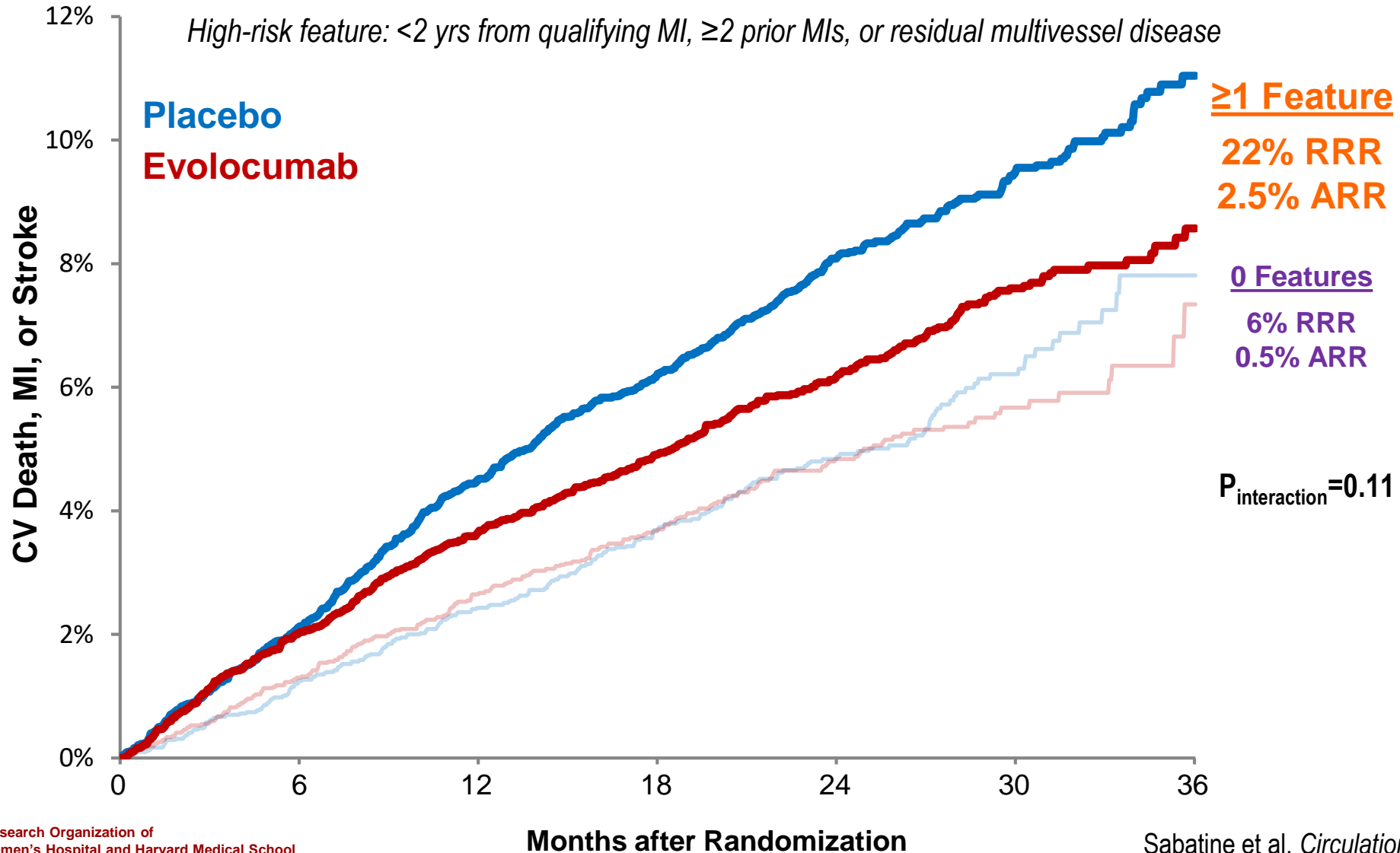


Overlap Between Factors



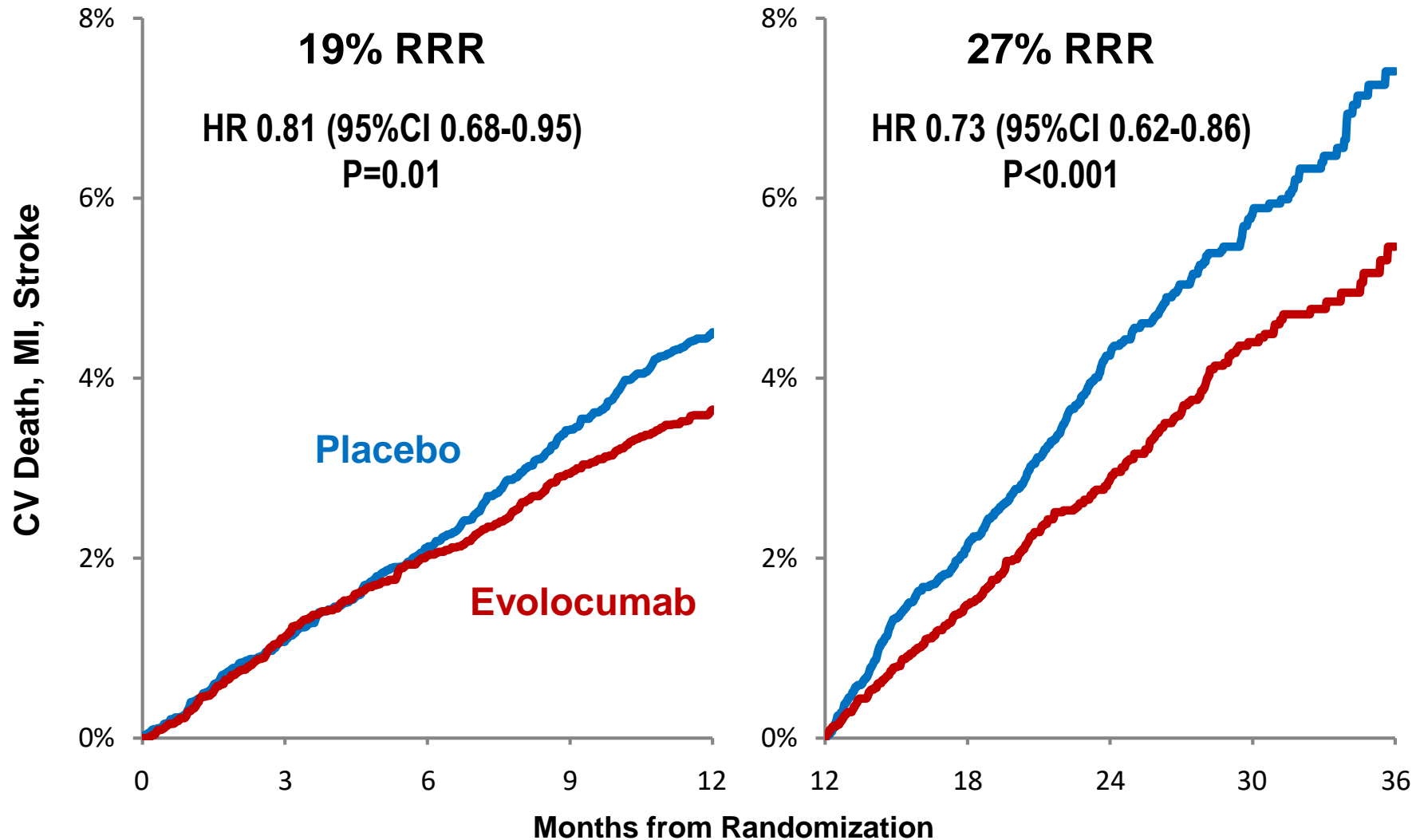
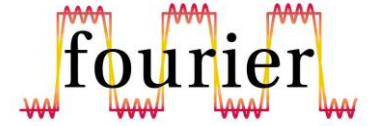


Benefit of EvoMab Based on # of High-Risk MI Features



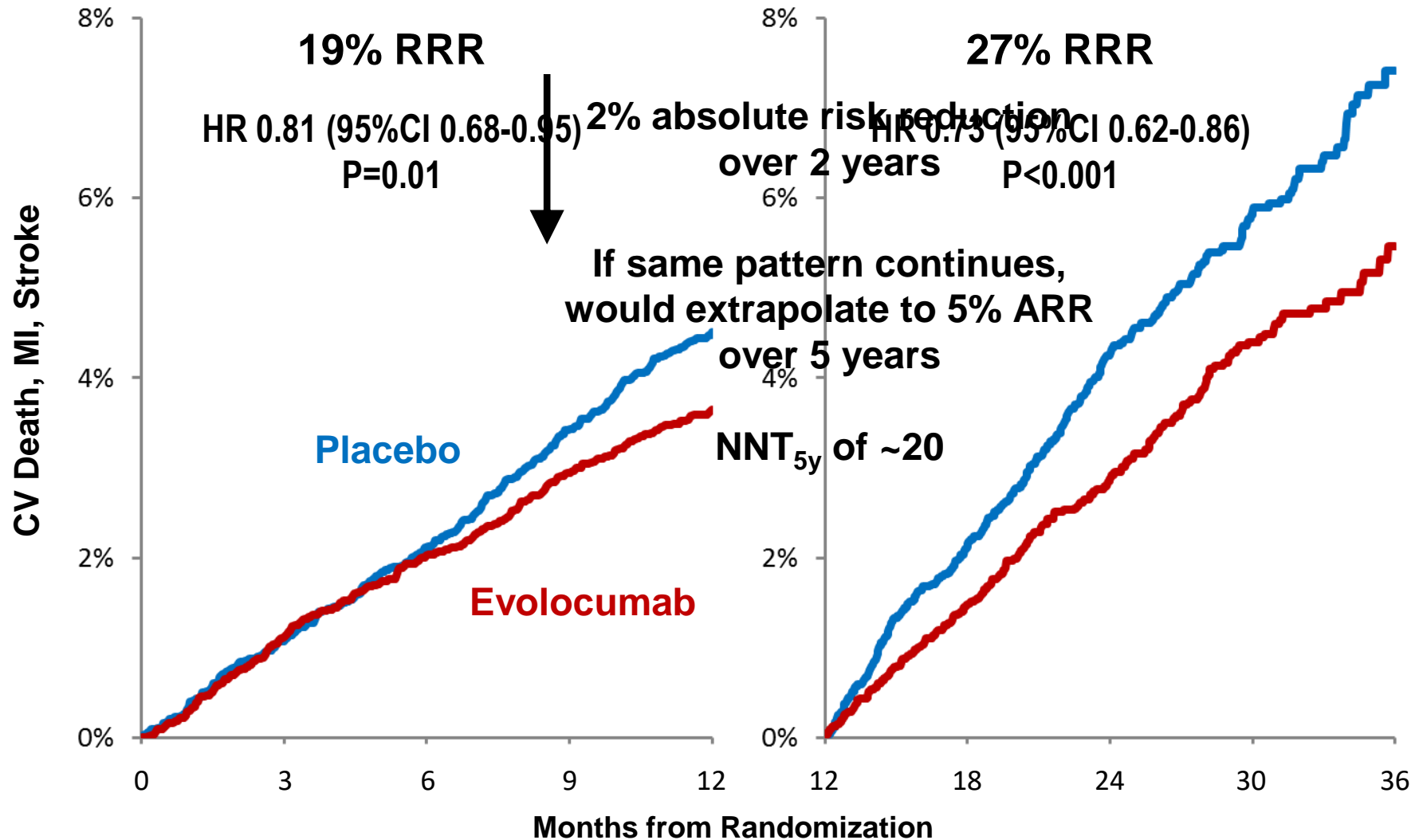


Landmark Analyses in Pts w/ a High-Risk MI Feature



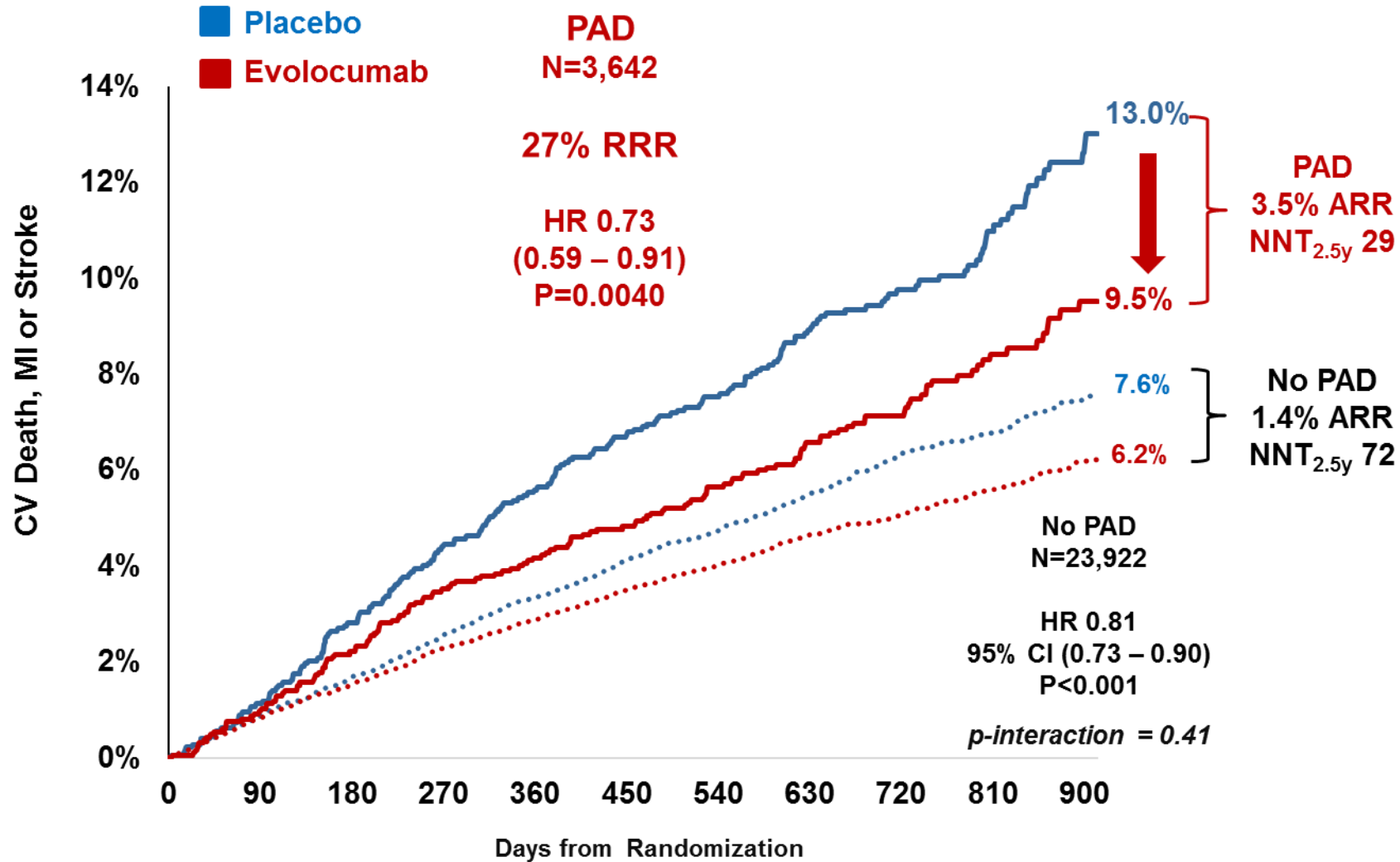


Landmark Analyses in Pts w/ a High-Risk MI Feature



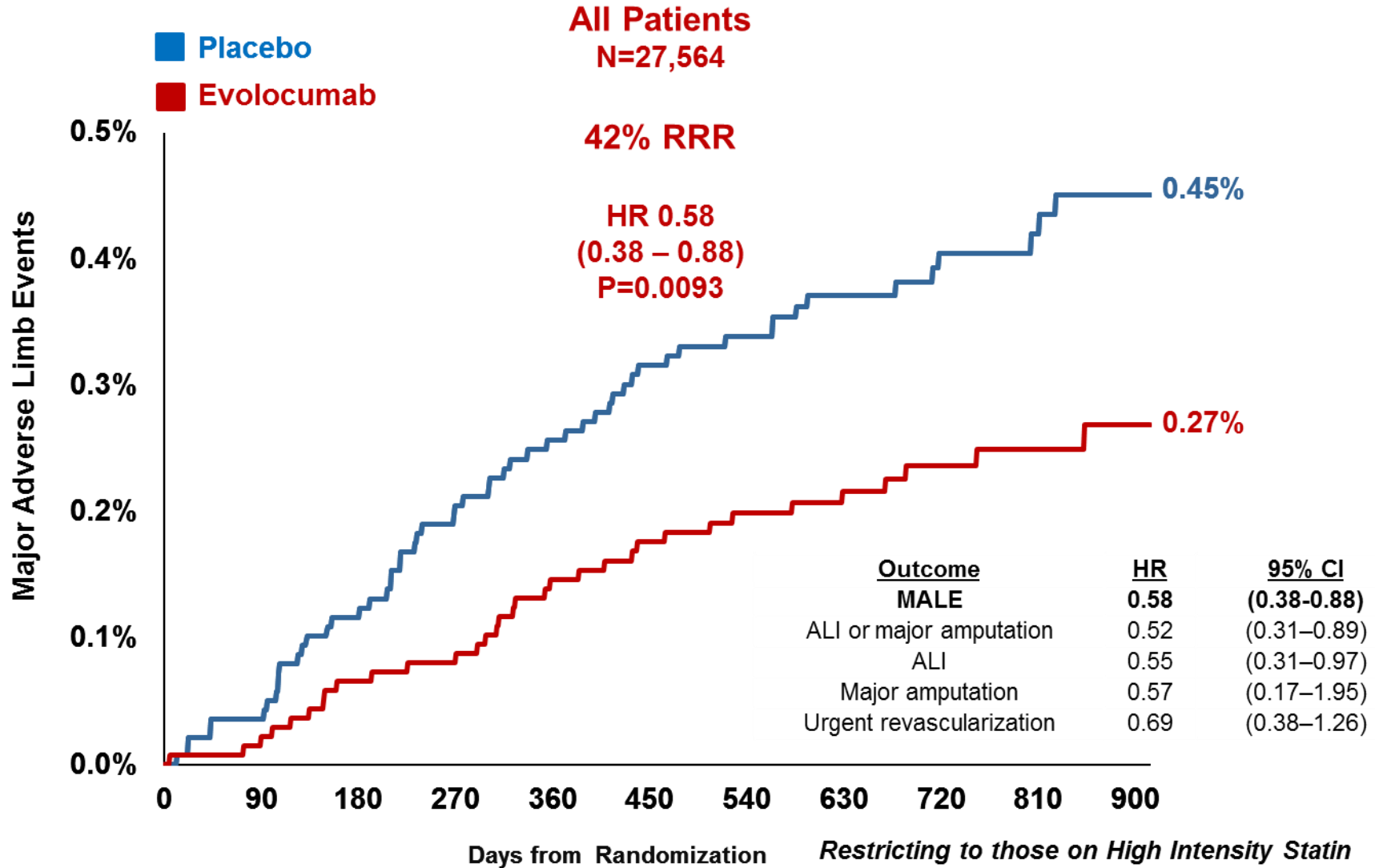
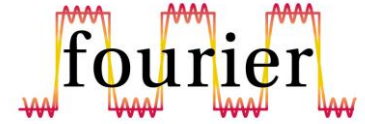


CV Death, MI or Stroke in Patients w/ & w/o Peripheral Artery Disease





Major Adverse Limb Events





Conclusions

- 1. Evolocumab reliably reduces LDL-C by ~60%**
- 2. Reduces risk of major vascular events in Pts w/ ASCVD already on statin**
 - Confirms benefit from lowering LDL-C to <1 mM
 - Benefit grows over time
- 3. Largest absolute risk reductions in Pts w/ highest baseline risk & largest amount of athero**
 - Diabetes, CKD
 - Closer to MI, multiple prior MIs, multivessel CAD
 - PAD