

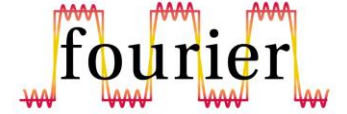
Association Between Achieved LDL-Cholesterol and Long-term Cardiovascular and Safety Outcomes: An Analysis of the FOURIER and FOURIER-OLE Studies

Prakriti Gaba MD, Michelle L. O'Donoghue MD MPH, Jeong-Gun Park, PhD, Stephen D. Wiviott MD, Dan Atar MD, Anthony Keech MBBS, Julia F. Kuder MA, KyungAh Im PhD, Sabina A. Murphy MPH, Jose H. Flores-Arredondo MD, J. Antonio G. López MD, Mary Elliott-Davey MSc, Bei Wang PhD, Maria Laura Monsalvo MD, Siddique Abbasi MD, Robert P. Giugliano, MD SM, Marc S. Sabatine, MD MPH





Disclosures

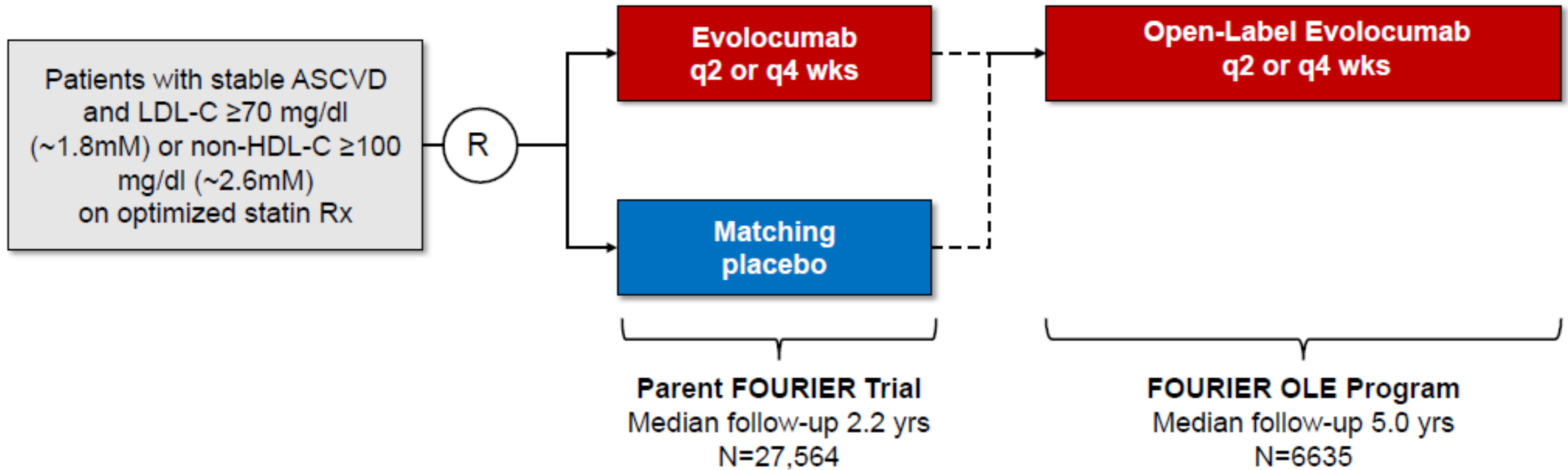
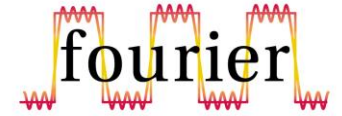


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- This study was funded by Amgen Inc.



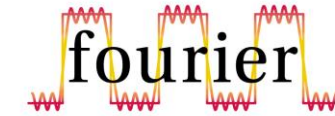


Study Schema: FOURIER and FOURIER-OLE

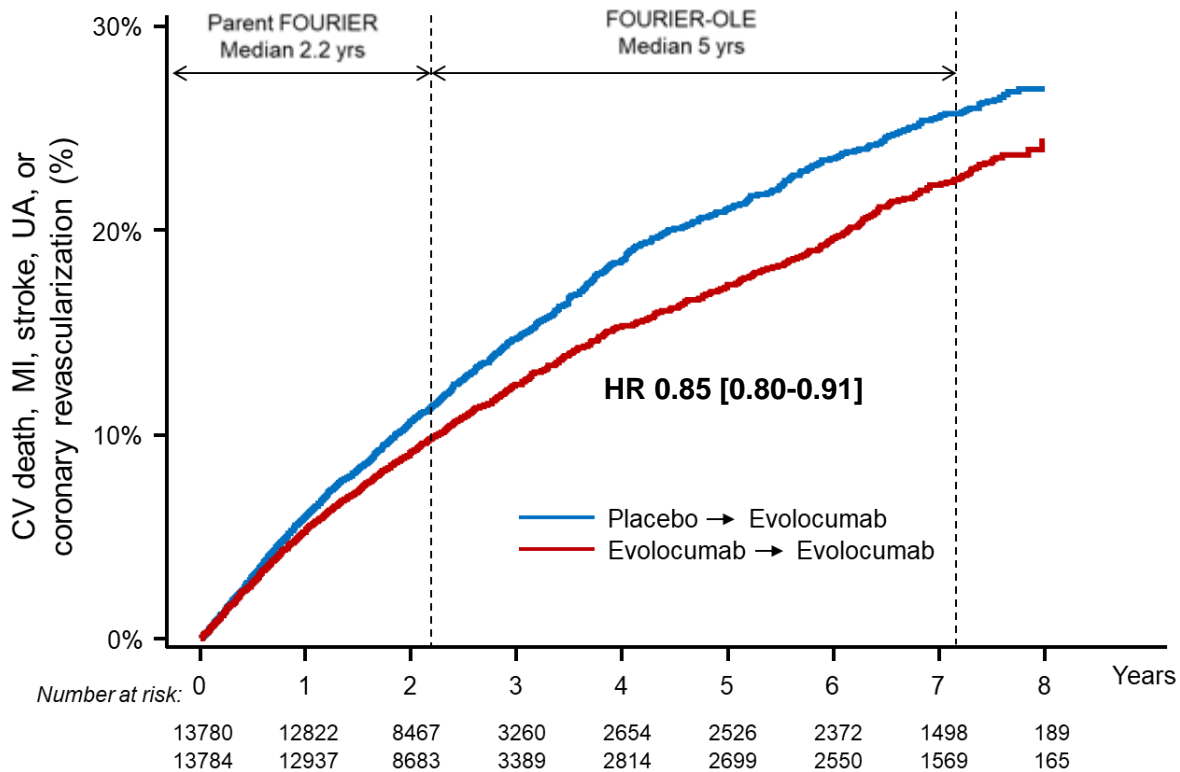




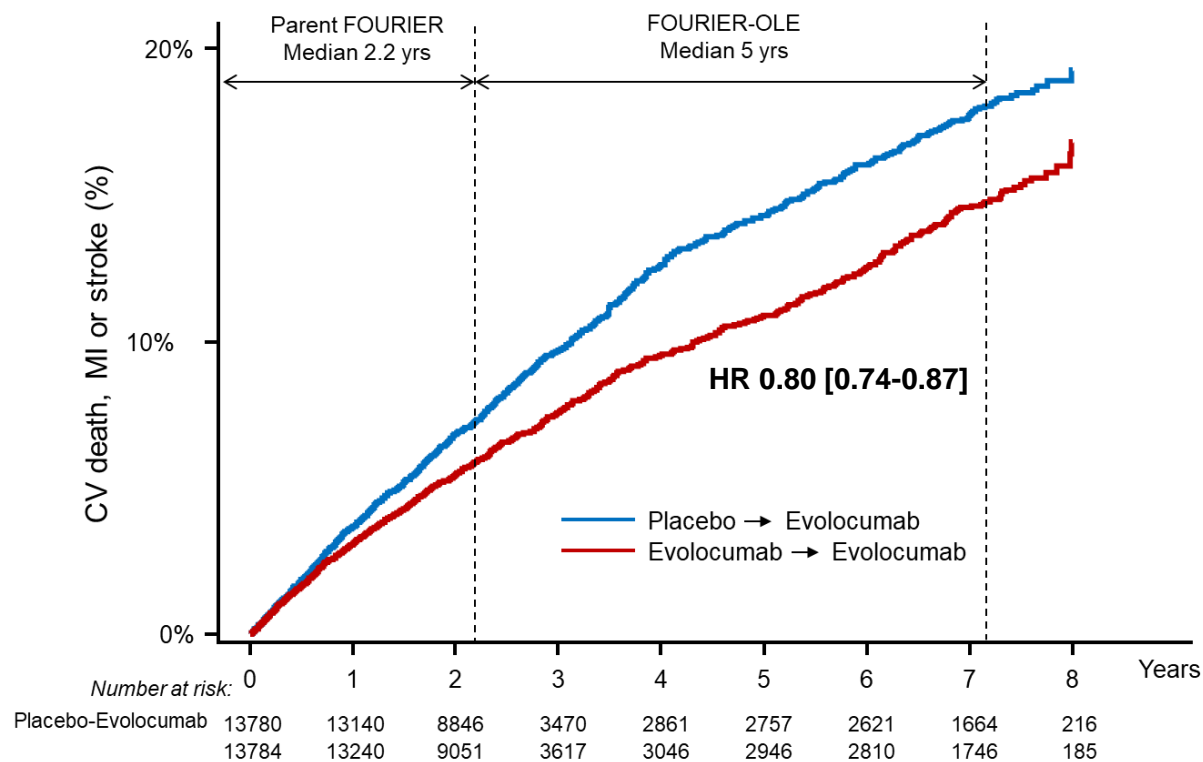
Results of FOURIER and FOURIER-OLE – CV Outcomes



Primary Efficacy Endpoint

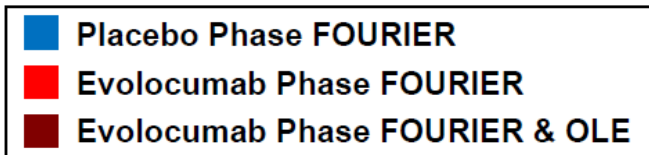
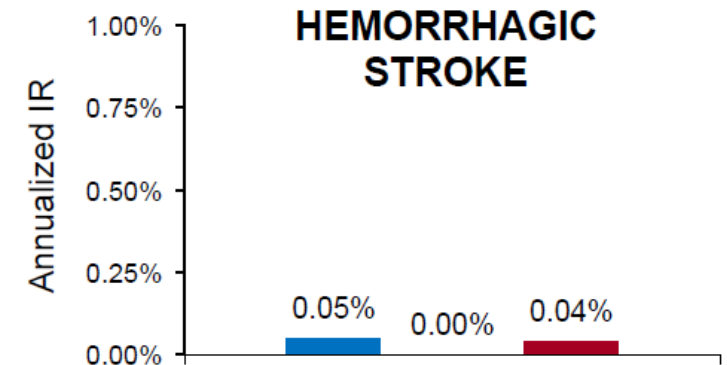
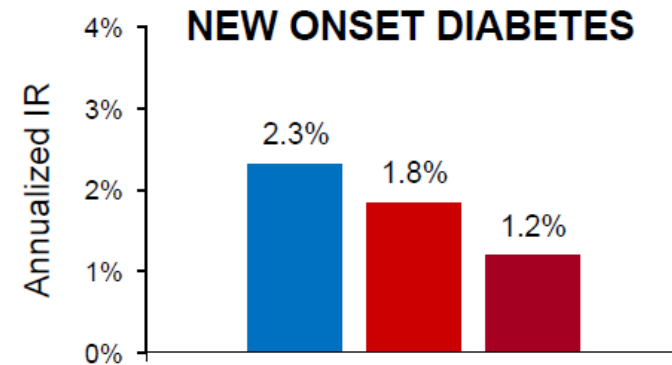
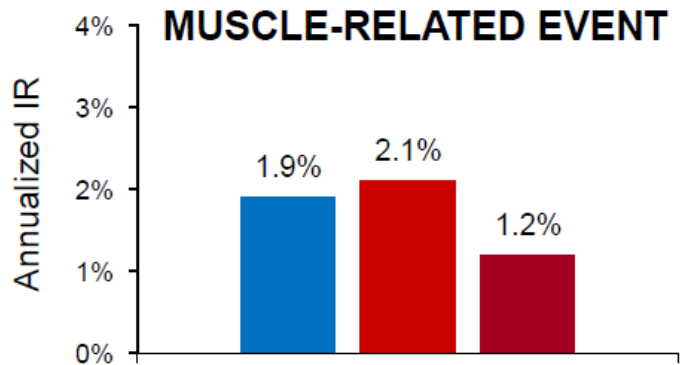
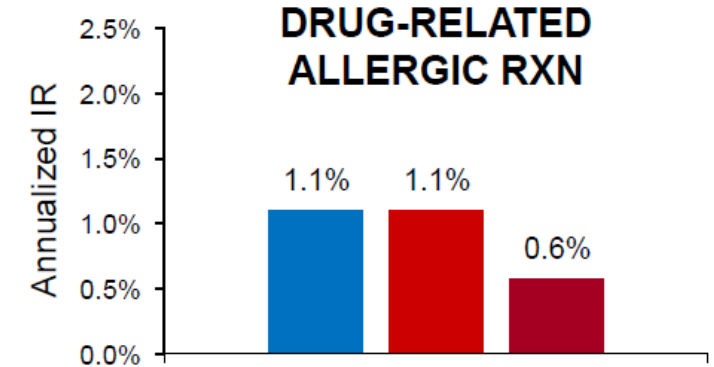
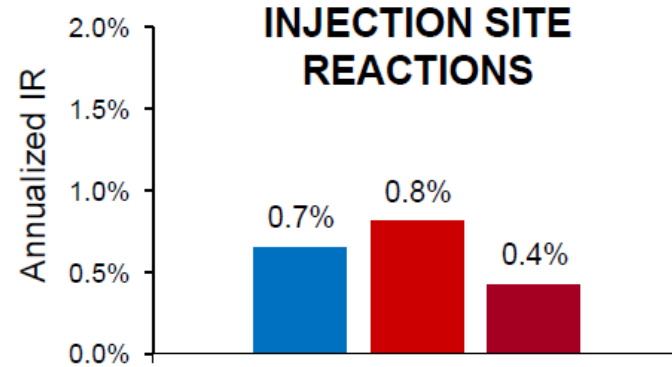
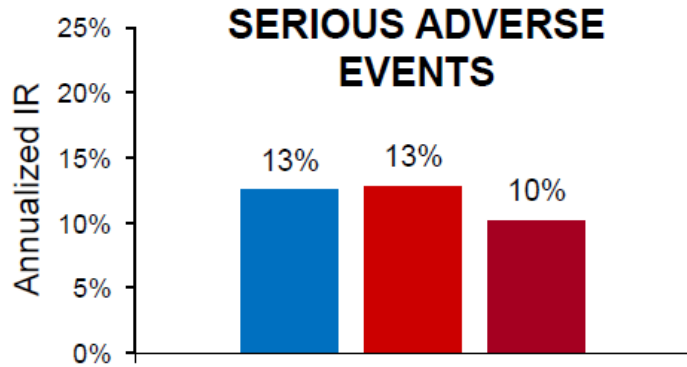
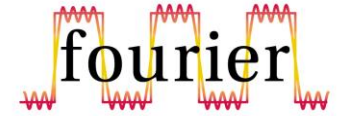


Key Secondary Efficacy Endpoint



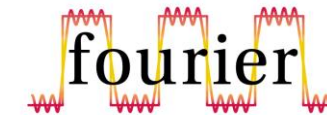


Results of FOURIER-OLE - Safety





Evidence Gap



The optimal achieved LDL-C level with regards to cardiovascular and safety outcomes in the long term remains unclear.





Objective



To explore the relationship between achieved LDL-C levels and the occurrence of long-term adverse cardiovascular and safety outcomes, down to very low (<20 mg/dL) achieved LDL-C levels.





Methods

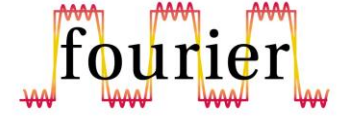


- **Patients divided into 6 categories based on achieved LDL-C**
 - Used LDL-C at 4 wks in FOURIER (or 12 wks in OLE for pts who transitioned from placebo -> evolocumab)
 - LDL-C bins: <20, 20-<40, 40-<55, 55-<70, 70-<100, and ≥ 100 mg/dL
- **CV outcomes**
 - Primary: CV death, MI, stroke, coronary revascularization, or hospitalization for unstable angina
 - Key secondary: CV death, MI, or stroke
- **Safety outcomes**
 - Serious adverse events, muscle-related events, new-onset diabetes mellitus, cataract-related adverse events, neurocognitive events, hemorrhagic stroke, malignancy, and non-CV death





Methods (cont'd)



- Examined trends in baseline characteristics
- Annualized incidence rates and 95% confidence intervals were calculated for all cardiovascular and safety outcomes
- Multivariable models adjusted for baseline characteristics associated with achieved LDL-C, including age, BMI, sex, race, current smoker, prior MI, prior non-hemorrhagic stroke, history of diabetes, history of peripheral arterial disease, high-intensity statin use, ezetimibe use, and participation in OLE.





Cohort & Follow-Up

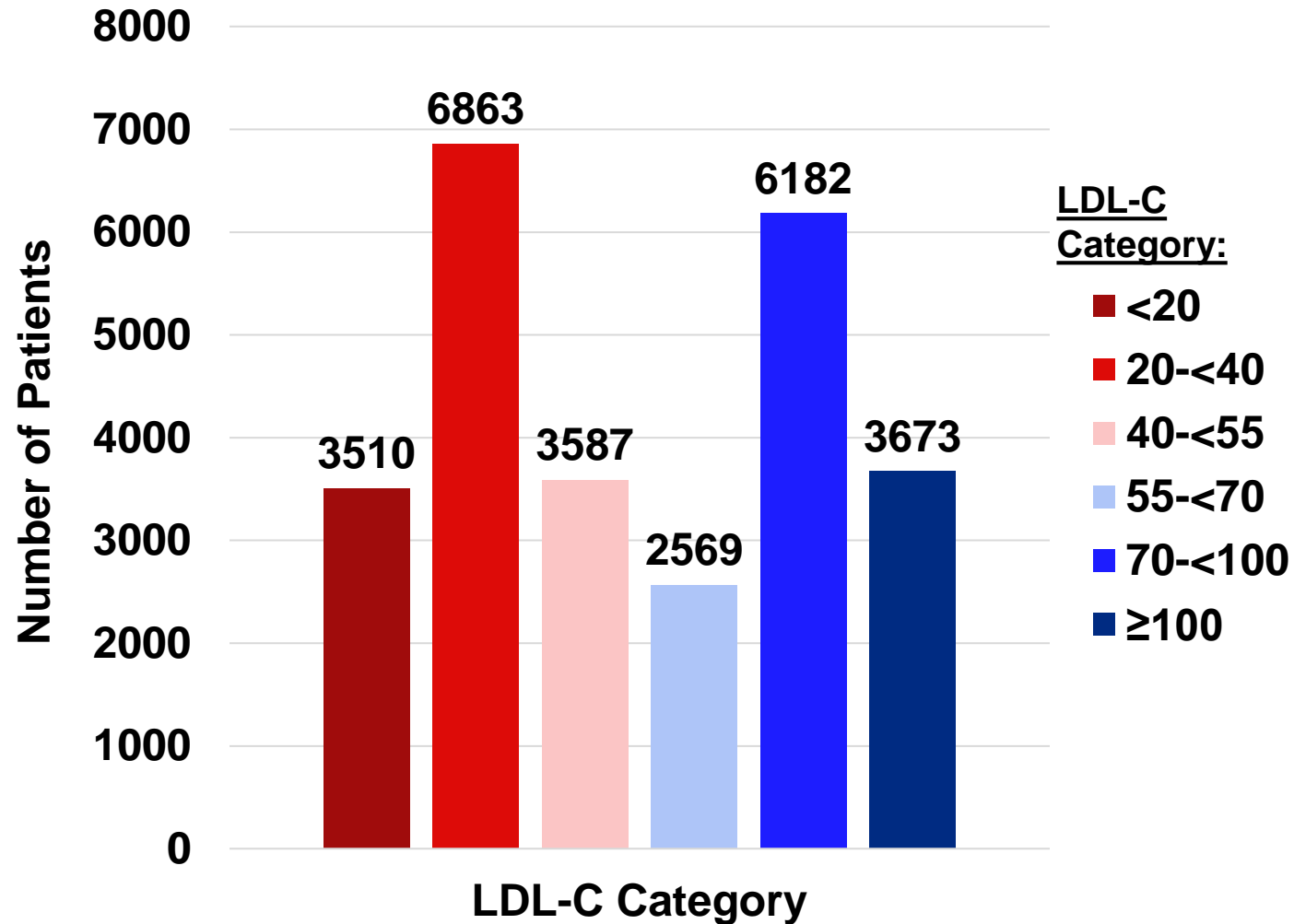


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- 26,384 patients with achieved LDL-C levels in FOURIER and/or FOURIER-OLE
 - 19,960 patients in FOURIER alone with a median follow-up 2.0 years
 - 6,429 patients also participated in FOURIER-OLE with median follow up 4.9 years
 - Including FOURIER & FOURIER-OLE, maximum follow-up 8.6 years



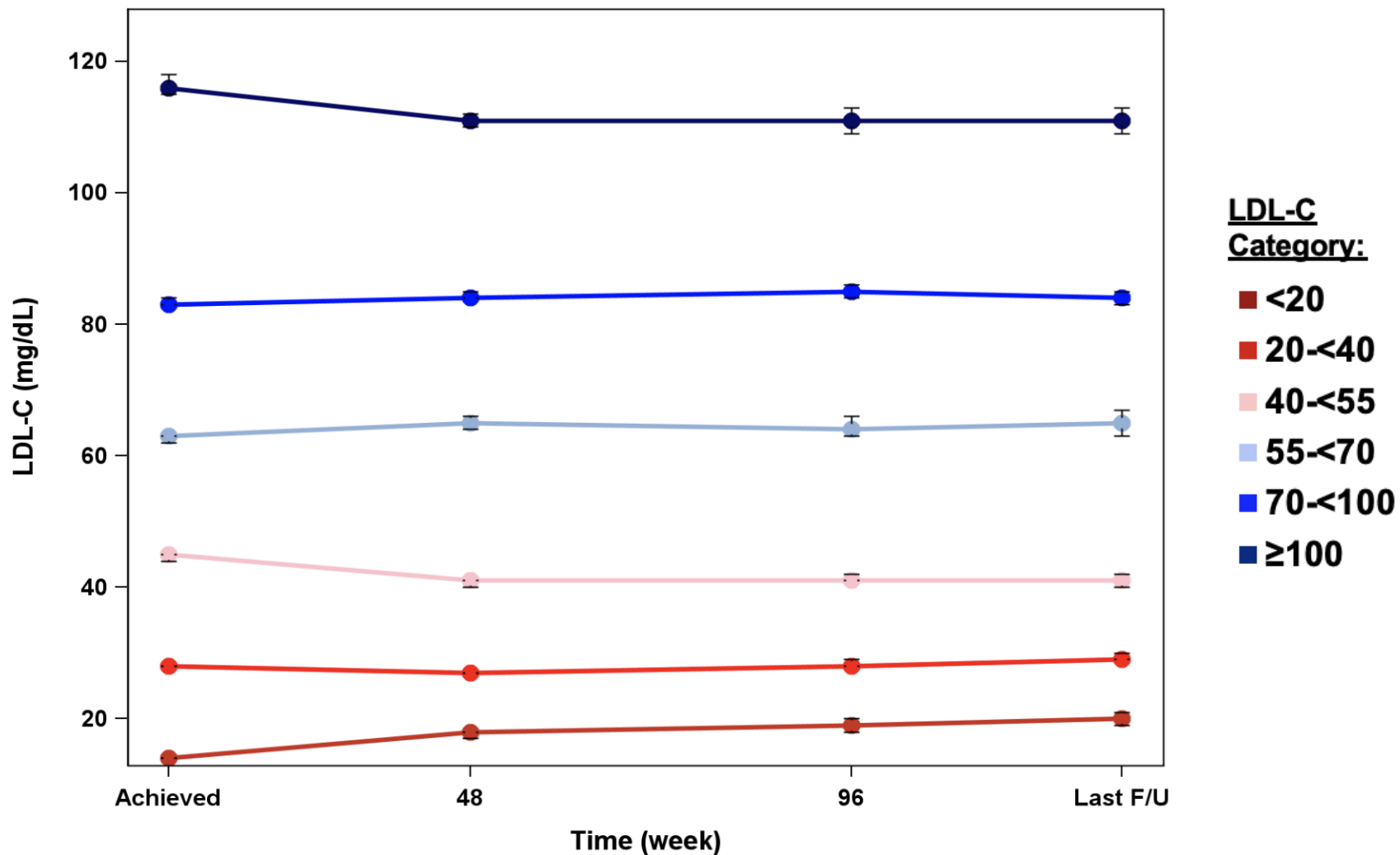


Achieved LDL-C Categories



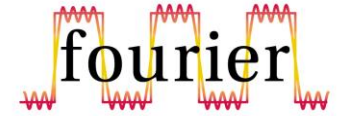


Achieved LDL-C Over Time





Baseline Characteristics by Achieved LDL-C



	Achieved LDL-C level (mg/dL)						P _{trend}
	<20	20-<40	40-<55	55-<70	70-<100	≥100	
Age, mean (SD), yrs	63.5±8.7	63.2±8.8	61.6±8.9	62.0±9.3	62.7±9.0	61.2±9.0	<0.0001
Male	83.7%	78.9%	71.4%	71.4%	74.6%	70.7%	<0.0001
BMI, mean (SD), kg/m²	28.4±4.4	29.1±4.7	30.3±5.7	30.1±5.7	29.4±5.3	29.5±5.1	<0.0001
White race	84.0%	87.4%	87.0%	82.2%	82.5%	86.1%	0.0003
Prior MI	82.2%	81.6%	81.0%	79.3%	81.7%	79.9%	0.037
Non-hemorrhagic CVA	18.9%	18.3%	18.8%	19.7%	19.8%	20.8%	0.0019
Diabetes mellitus	34.9%	33.9%	40.6%	42.0%	35.8%	35.6%	0.051
Current smoker	26.6%	26.2%	28.0%	28.9%	28.7%	32.6%	<0.0001
High-intensity statin	65.8%	69.1%	72.5%	69.6%	68.2%	71.4%	0.0043
Baseline LDL-C, median (IQR), mg/dL	82 (75, 94)	90 (79, 103)	95 (81, 112)	85 (74, 107)	90 (81, 102)	115 (101, 137)	<0.0001

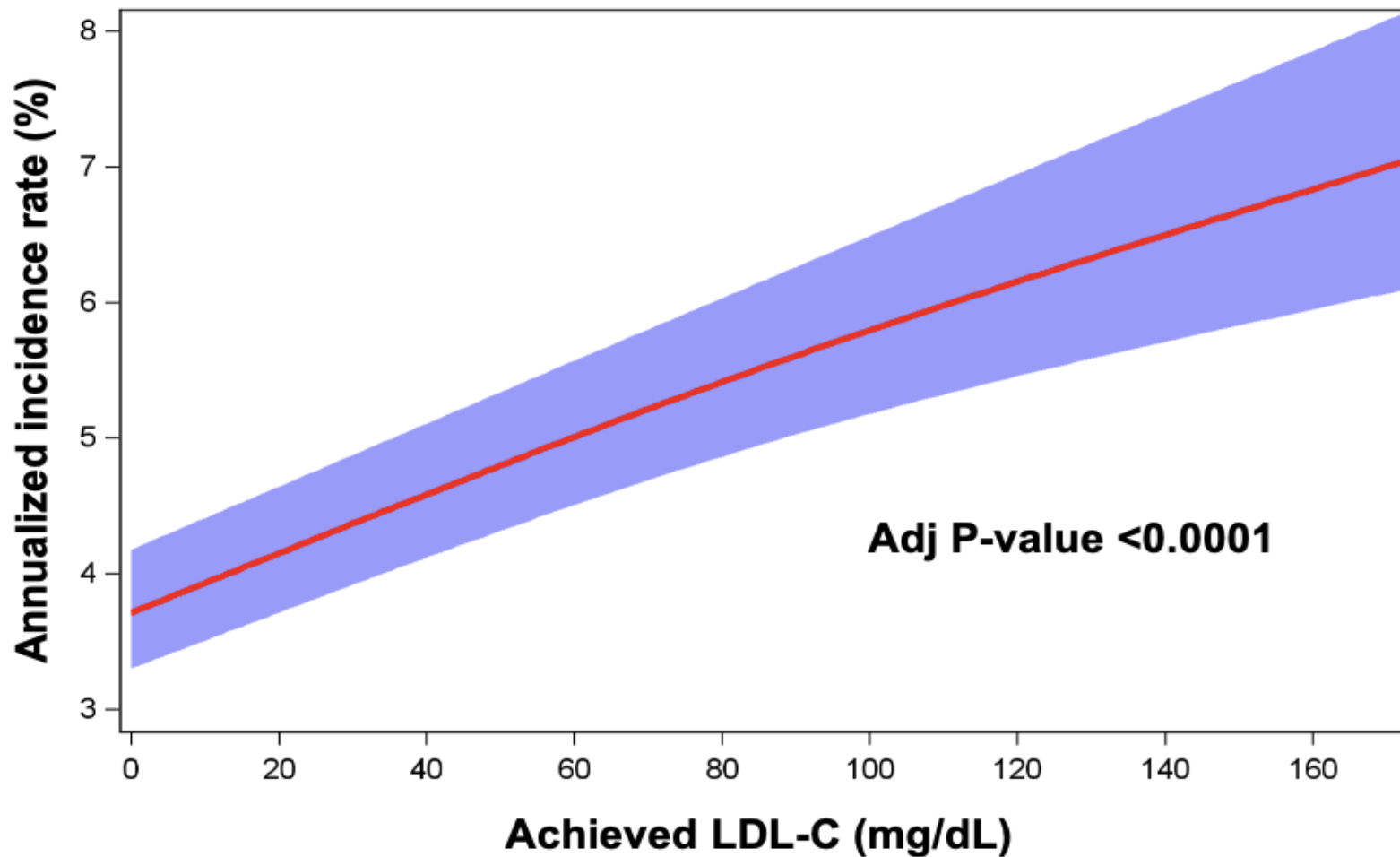




CV Outcomes and Achieved LDL-C



Primary endpoint: CV death, MI, stroke, coronary revascularization or hospitalization for unstable angina

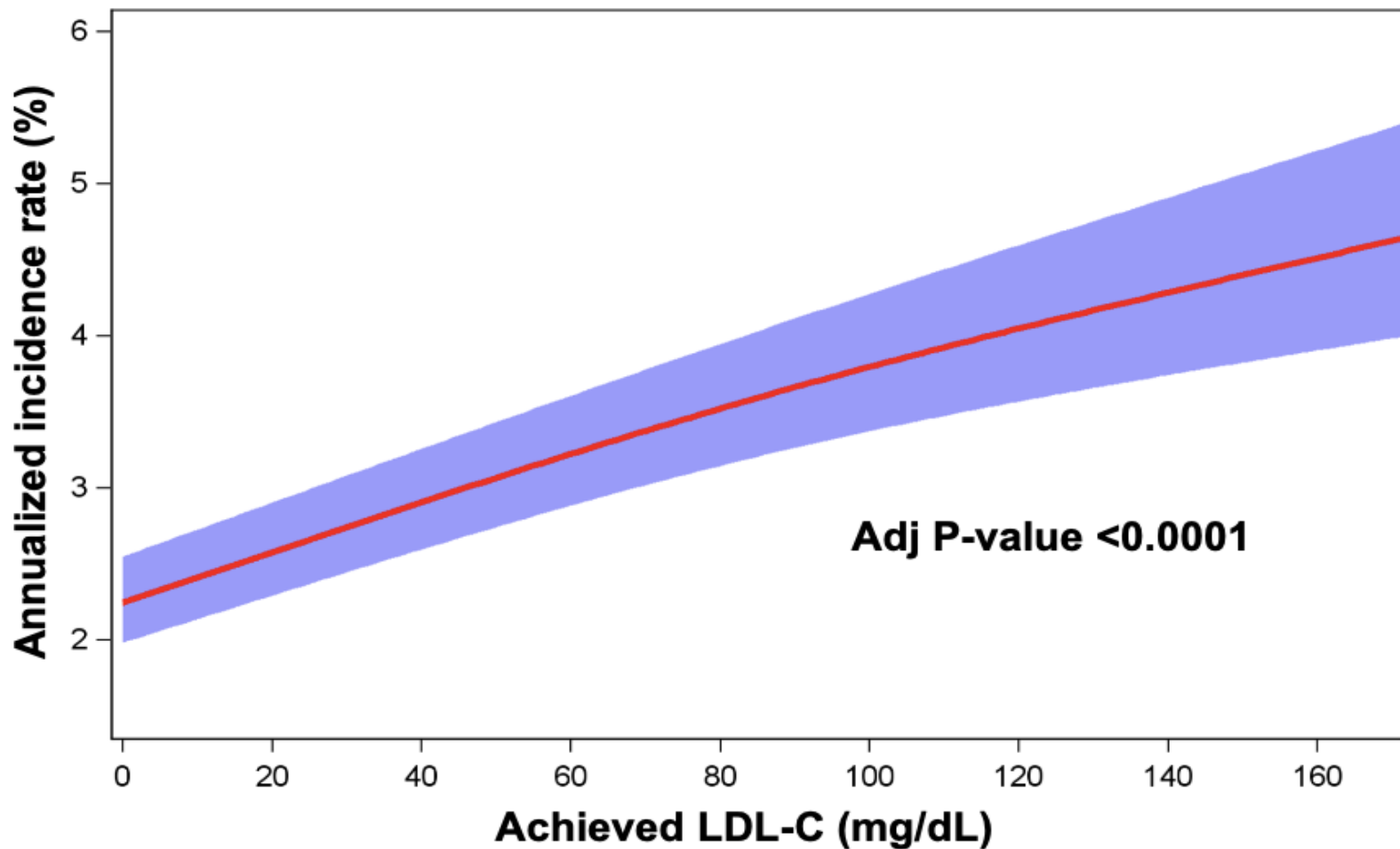




CV Outcomes and Achieved LDL-C

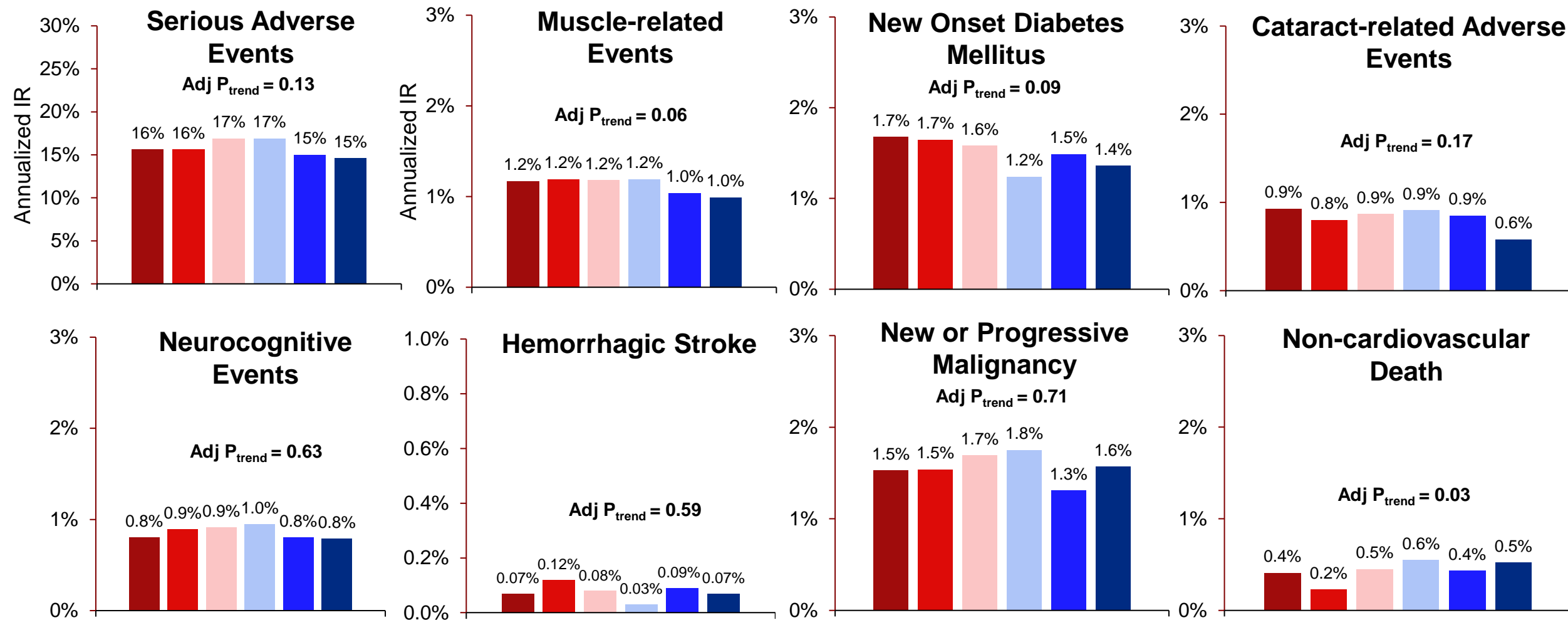


Key secondary endpoint: CV death, MI, or stroke

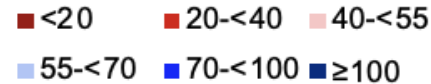




Safety and Achieved LDL-C



LDL-C Category:

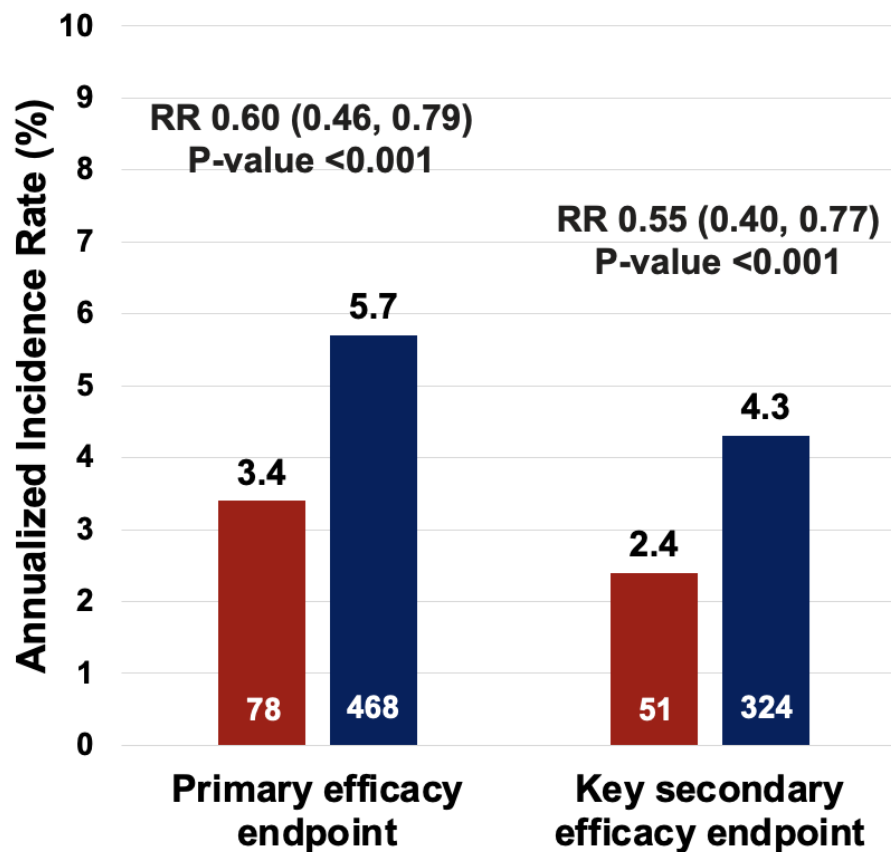




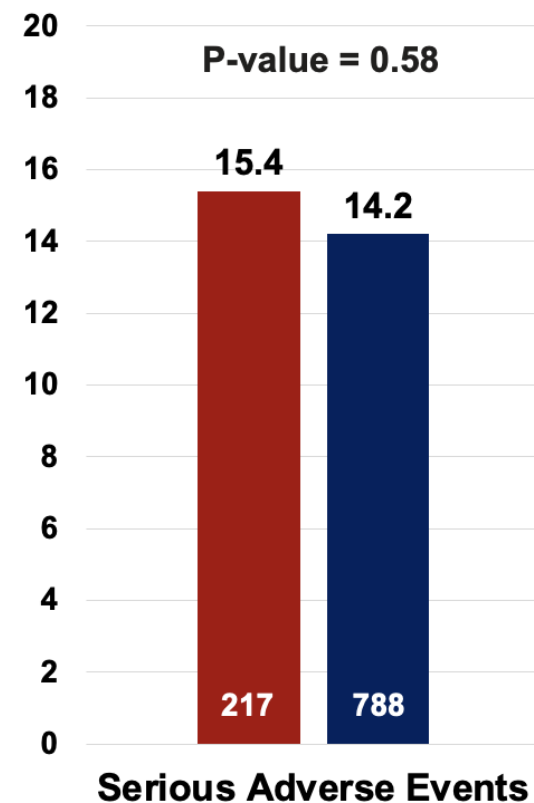
MACE & Safety w/ LDL-C <10 vs ≥100 mg/dL



A. Cardiovascular Outcomes

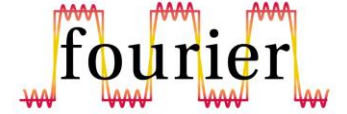


B. Safety





Limitations

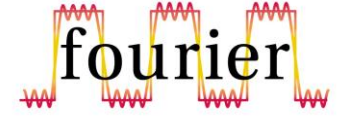


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- All patients enrolled in FOURIER had stable ASCVD with baseline LDL-C ≥ 70 mg/dL and non-HDL ≥ 100 mg/dL on GDMT, and thus findings may not be applicable to all patients in general practice
 - Comparisons based on a post-randomization variable and, despite multivariable analysis, may be subject to residual confounding





Summary & Conclusions



- Monotonic relationship between lower achieved LDL-C levels, down to very low LDL-C levels <20 mg/dL, and a lower risk of cardiovascular events up to 8.6 years of follow-up
- No serious safety concerns with low LDL-C during the extended follow up period
- **Altogether, these data suggest that targeting a very low LDL-C level is both effective and safe for patients with atherosclerotic cardiovascular disease**

