

# FOURIER

Further cardiovascular Outcomes Research with  
PCSK9 Inhibition in subjects with Elevated Risk  
Outcomes by age and sex

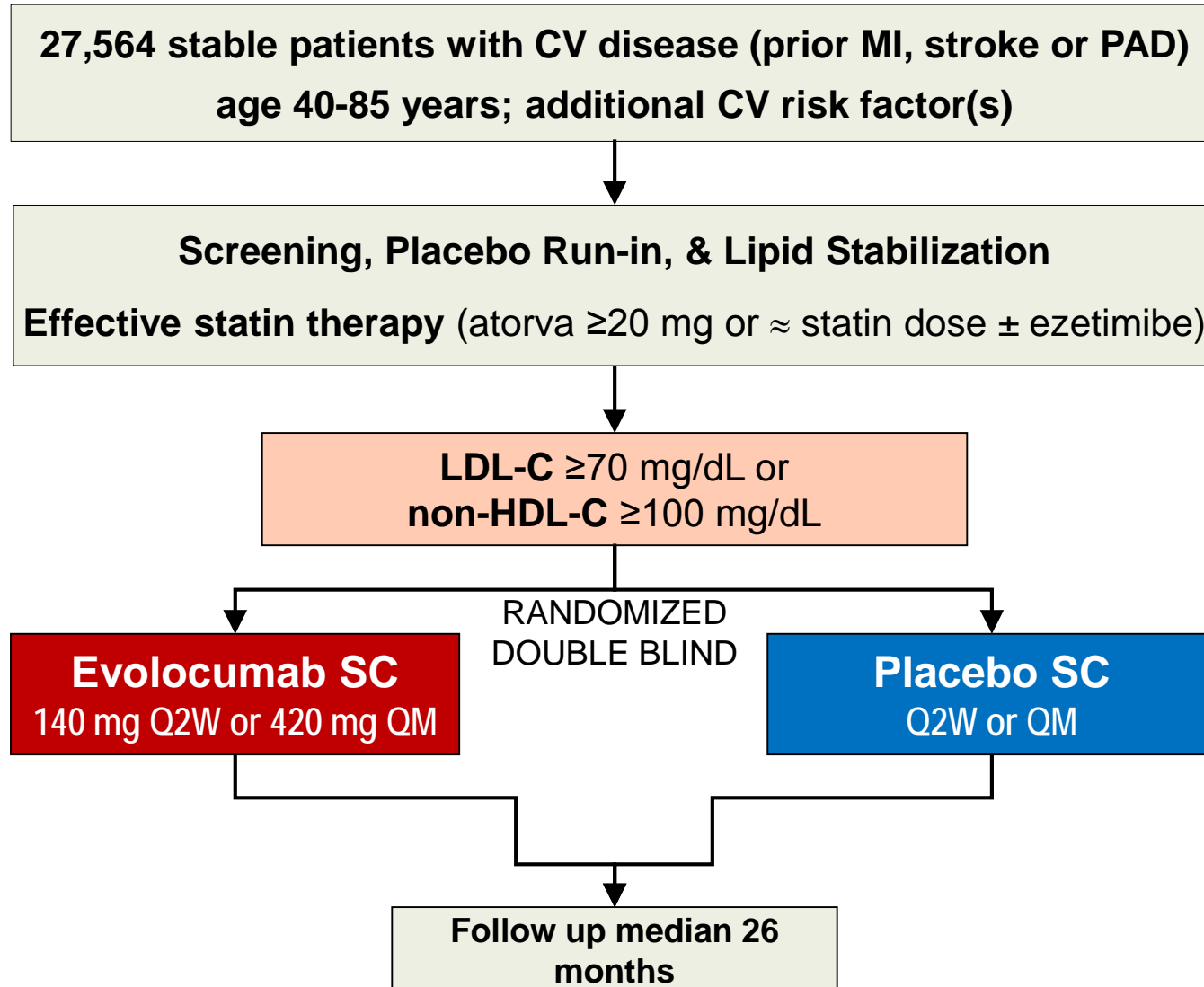
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for the FOURIER Steering Committee & Investigators

# Disclosures

Recipient of research grants and consulting fees from Amgen and Pfizer Inc.

# Trial Design



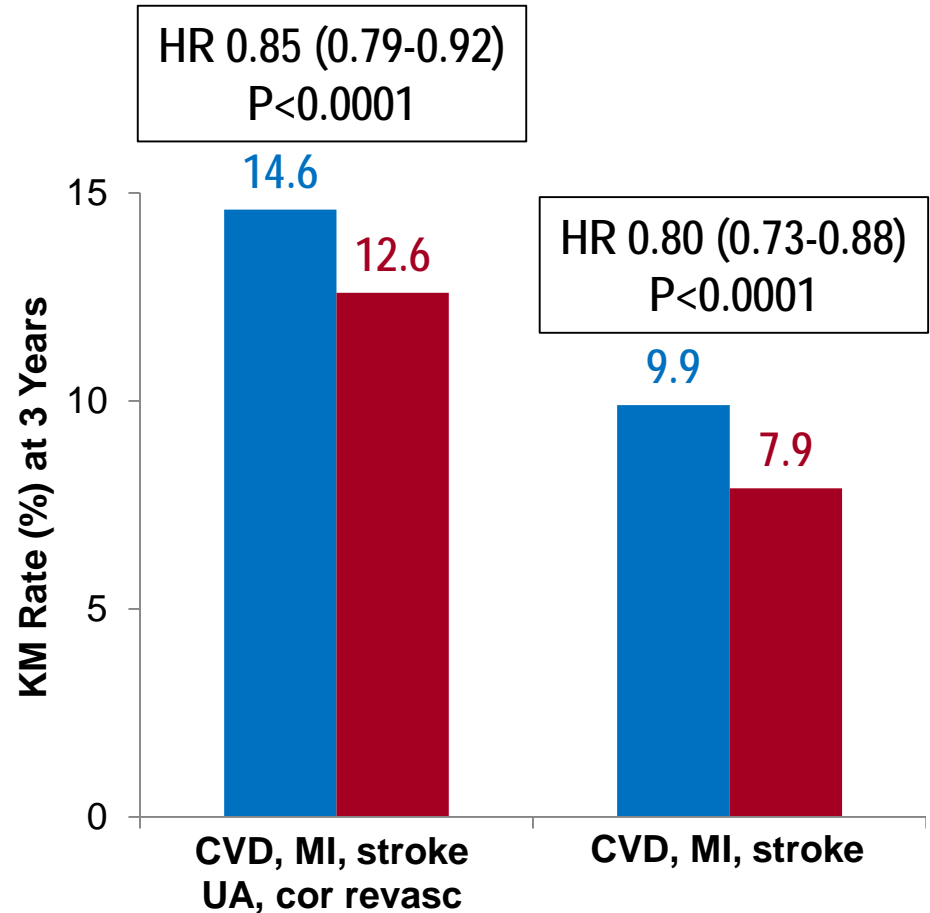
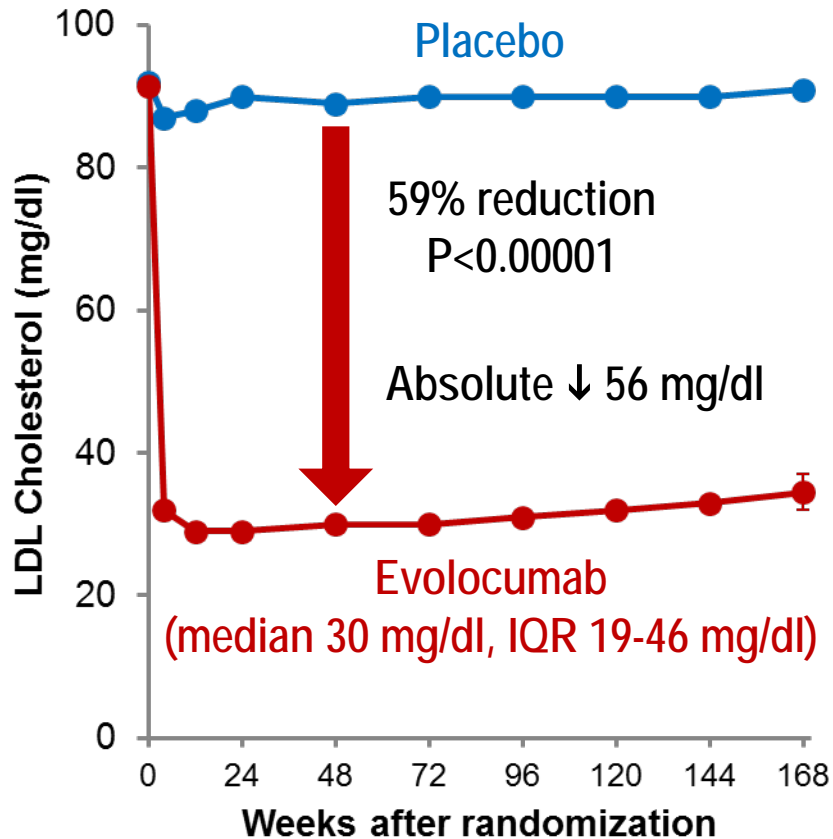
# Baseline Characteristics

Characteristic	Value
Age, years, mean (SD)	63 (9)
Male sex (%)	75
<b>Type of cardiovascular disease (%)</b>	
Myocardial infarction	81
Stroke (non-hemorrhagic)	19
Symptomatic PAD	13
<b>Cardiovascular risk factor (%)</b>	
Hypertension	80
Diabetes mellitus	37
Current cigarette use	28

} Median time from most recent event ~3 yrs; ~¼ within 1 yr

# 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



# Analyses by Age and Sex

# Rationale

There is evidence that the benefits of lipid-lowering with statins may be attenuated in the elderly population and concerns have been expressed about the risk benefits in women versus men.

Observations in clinical practice demonstrate that despite evidence for the overall benefits of lipid-lowering, elderly patients and women are frequently undertreated.

# Methods

- Efficacy analyses were conducted in the ITT population based on time from randomization to the first event.
- Hazard ratios and 95% confidence intervals were generated with the use of Cox proportional hazards models with stratification factors (screening LDL and region) as covariates.
- Analyses by age and sex were a prespecified subgroup analysis for the FOURIER trial
- Tests for subgroup heterogeneity were conducted by including an interaction term in the model.
- Given the exploratory nature of the analysis, a P value  $<0.05$  was considered significant.



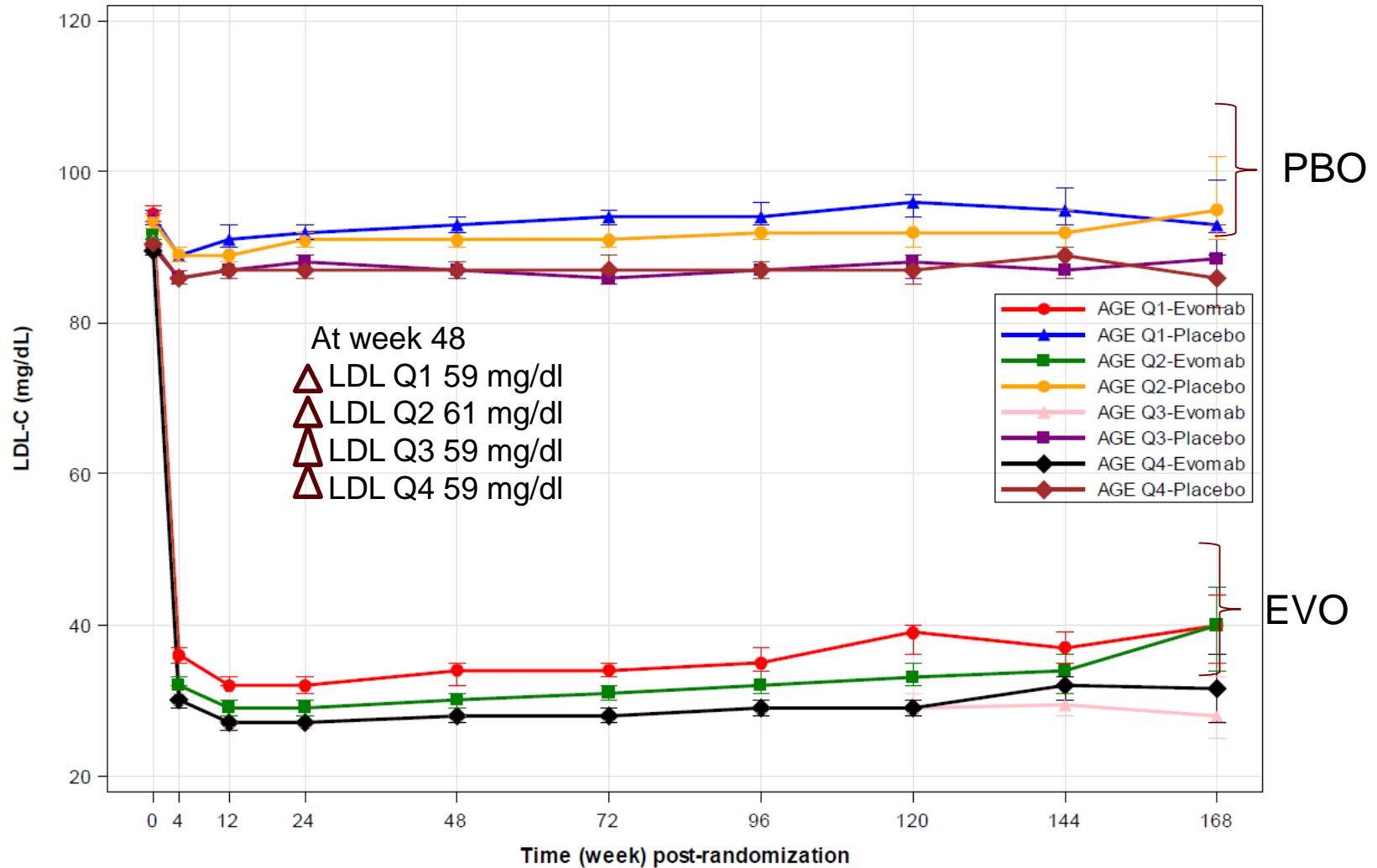
# Baseline Characteristics by Age Quartile

Characteristics	Q1	Q2	Q3	Q4	P-value
	<56y (N=7122)	56 - ≤63y (N=7154)	>63 - ≤69y (N=7055)	> 69y (N=6233)	
Age (yrs) mean	50.8	60.0	66.4	74.2	
Male sex	80%	77%	75%	69%	<.0001
Weight (kg) - mean	89.4	86.5	84.4	80.1	<.0001
Type of atherosclerosis					.
Myocardial infarction	86%	81%	80%	77%	<.0001
Non-hemorrhagic stroke	15%	20%	20%	24%	<.0001
Peripheral artery disease	9%	15%	14%	14%	<.0001
Hypertension	74%	82%	81%	84%	<.0001
Diabetes mellitus	35%	41%	36%	35%	<.0001
Current cigarette use	45%	39%	18%	9%	<.0001
High intensity statin use	75%	73%	67%	62%	<.0001
Median lipid measures					.
LDL cholesterol - mg/dl	94	93	91	90	<.0001
Total cholesterol - mg/dl	169	169	167	166	<.0001
HDL cholesterol - mg/dl	41	43	46	48	<.0001
Triglycerides - mg/dl	145	139	129	121	<.0001
Lipoprotein(a) - nmol/liter	38	36	37	37	0.57

# Baseline demographics by sex

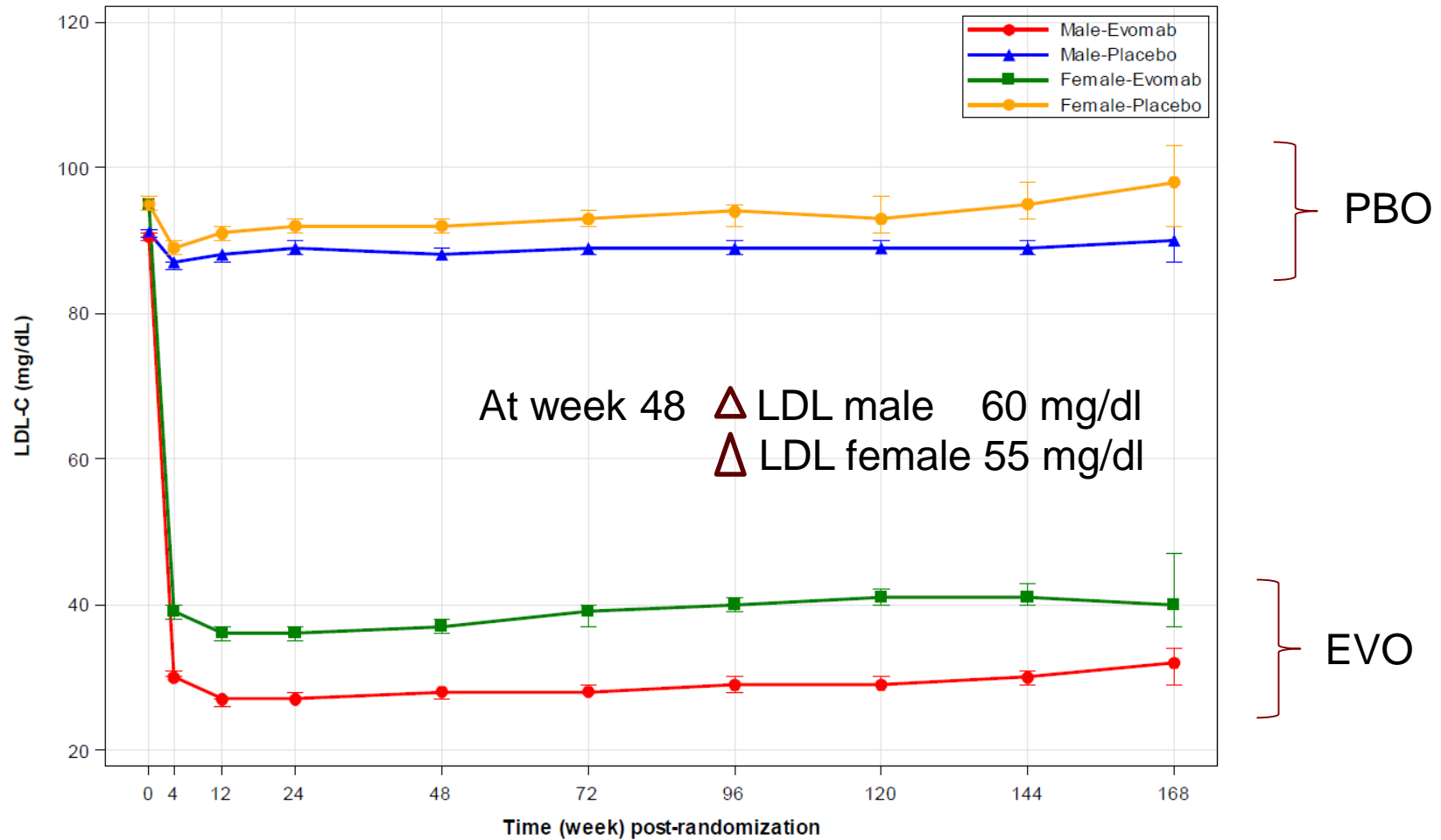
Characteristic	Male (N=20795)	Female (N=6769)	P- value
Age – yr, mean	62.0	64.1	<.0001
Weight – kg, mean	88.1	76.7	<.0001
Type of atherosclerosis			
Myocardial infarction	84%	71%	<.0001
Non-hemorrhagic stroke	7%	27%	<.0001
Peripheral artery disease	13%	15%	<.0001
Hypertension	79%	85%	<.0001
Diabetes mellitus	35%	40%	<.0001
Current cigarette use	29%	25%	<.0001
High intensity statin use	69%	69%	0.94
Median lipid measures			.
LDL cholesterol - mg/dl	91	95	<.0001
Total cholesterol - mg/dl	165	176	<.0001
HDL cholesterol - mg/dl	42	49	<.0001
Triglycerides - mg/dl	133	134	0.16
Lipoprotein(a) - nmol/liter	34	51	<.0001

# Similar Absolute Reduction in LDL-C with Evolocumab Regardless of Age



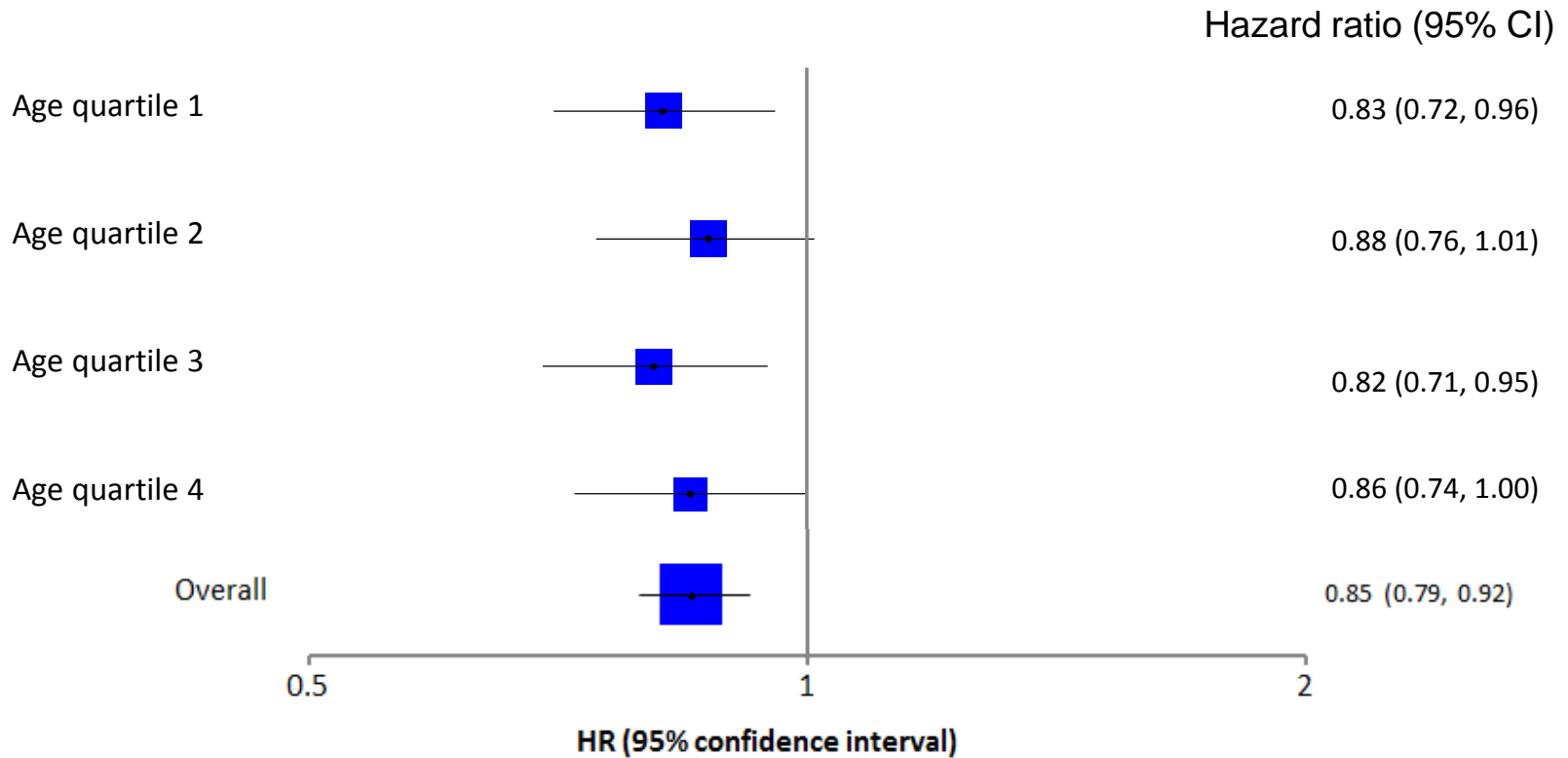
Q1 <56y, Q2 56-≤63y, Q3 >63-≤69y, Q4 >69y

# Similar Absolute Reduction in LDL-C with Evolocumab Regardless of Patient Sex



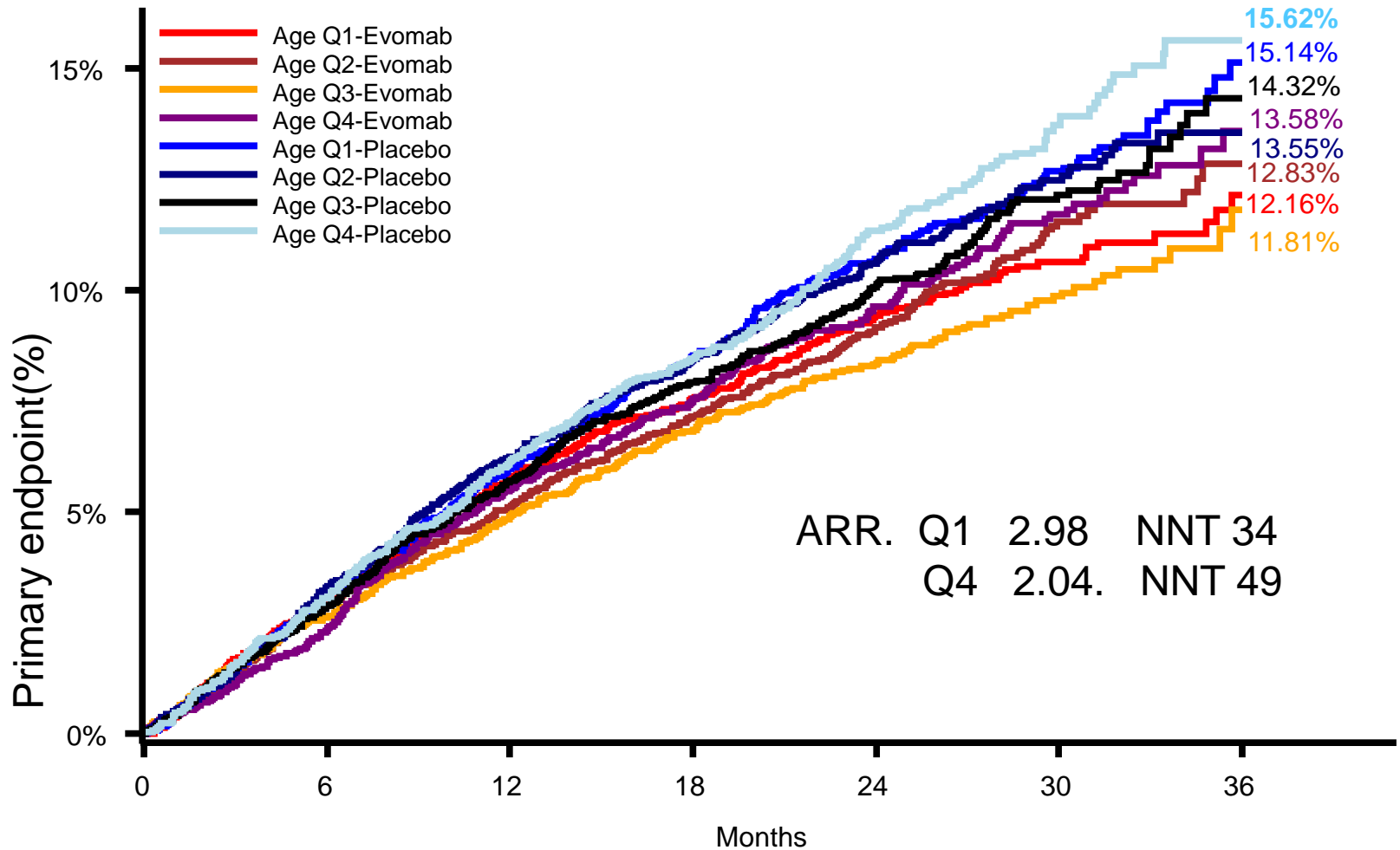
# The efficacy of evolocumab stratified by age

FOURIER Primary endpoint  
(CVD, MI, stroke, hosp for UA, coronary revasc)



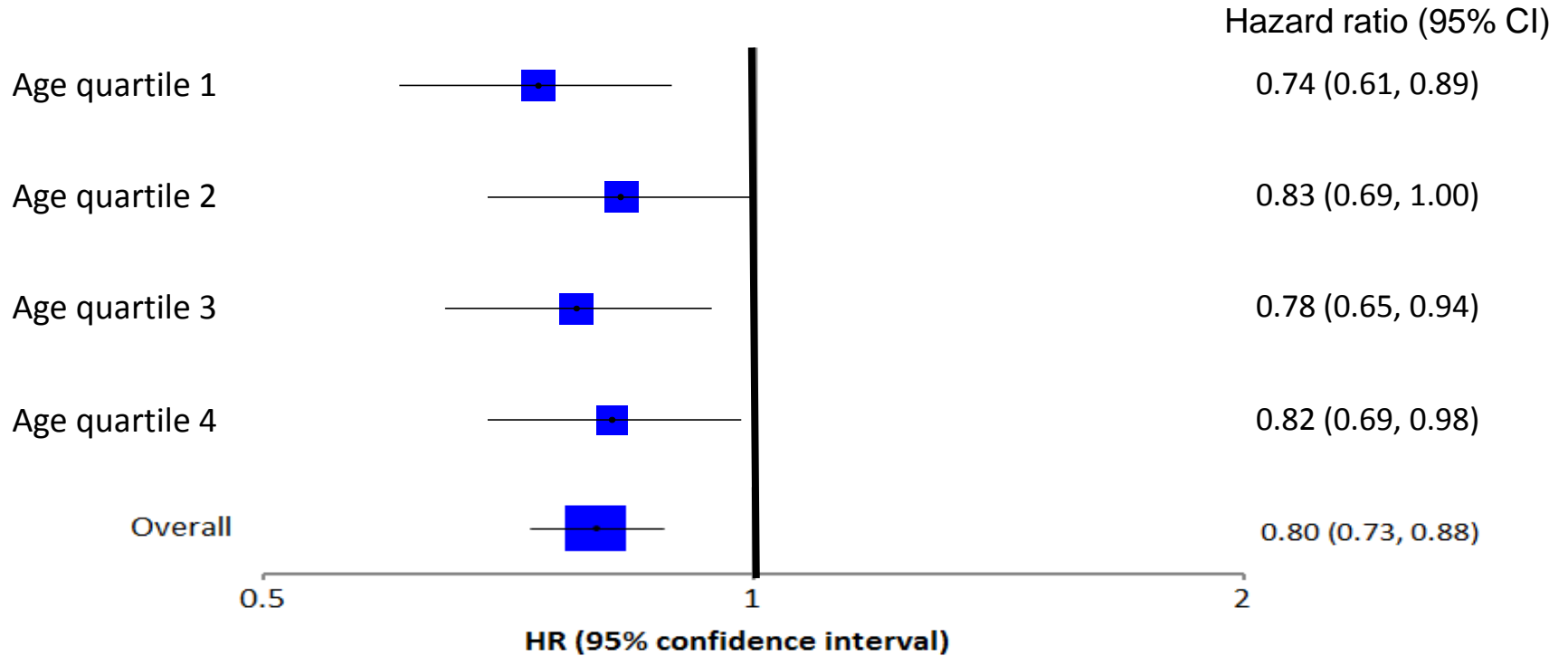
p interaction 0.908

# Primary endpoint stratified by age quartile



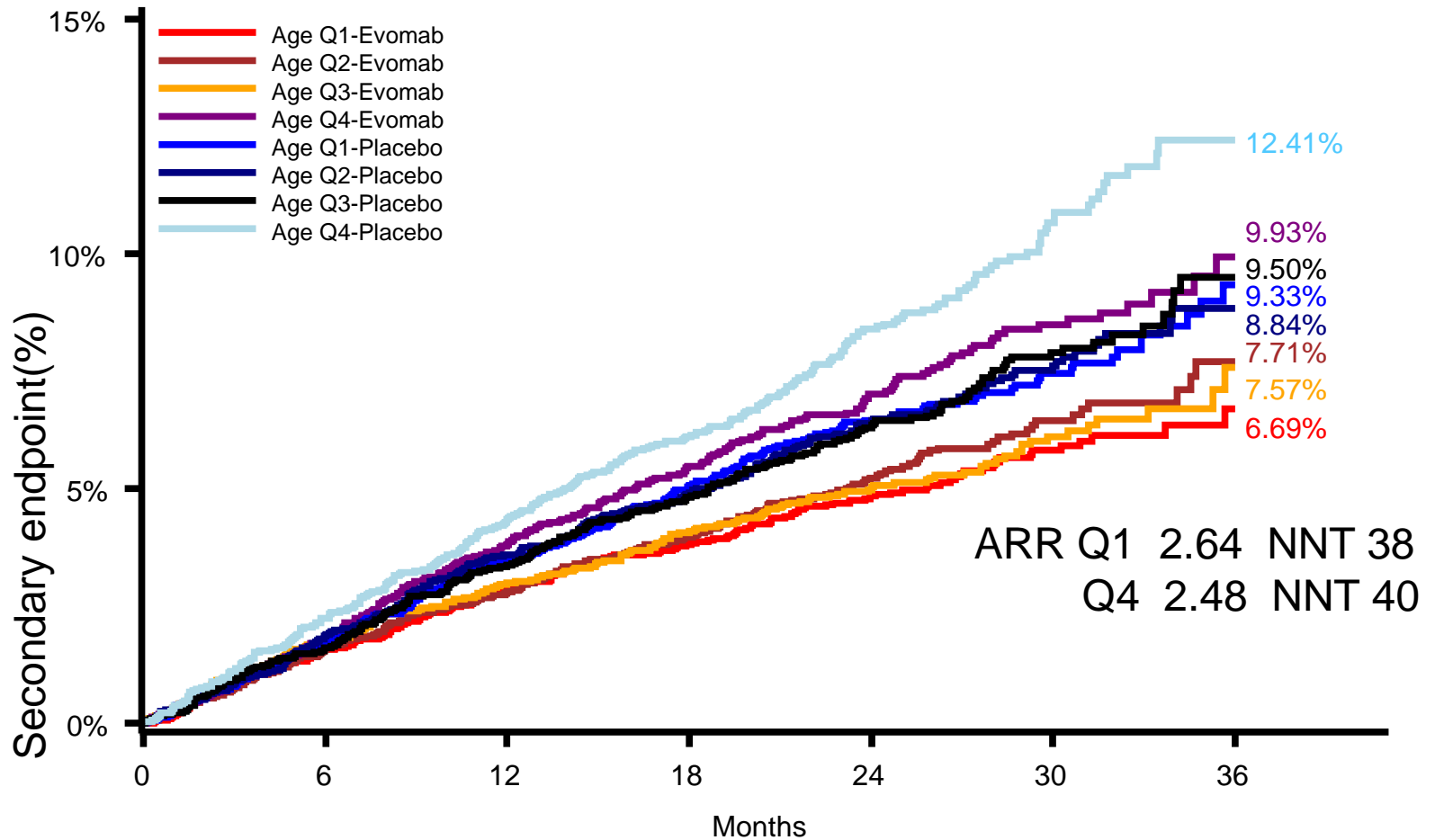
# The efficacy of evolocumab stratified by age

FOURIER Key Secondary endpoint  
CV death, MI or stroke



p interaction 0.813

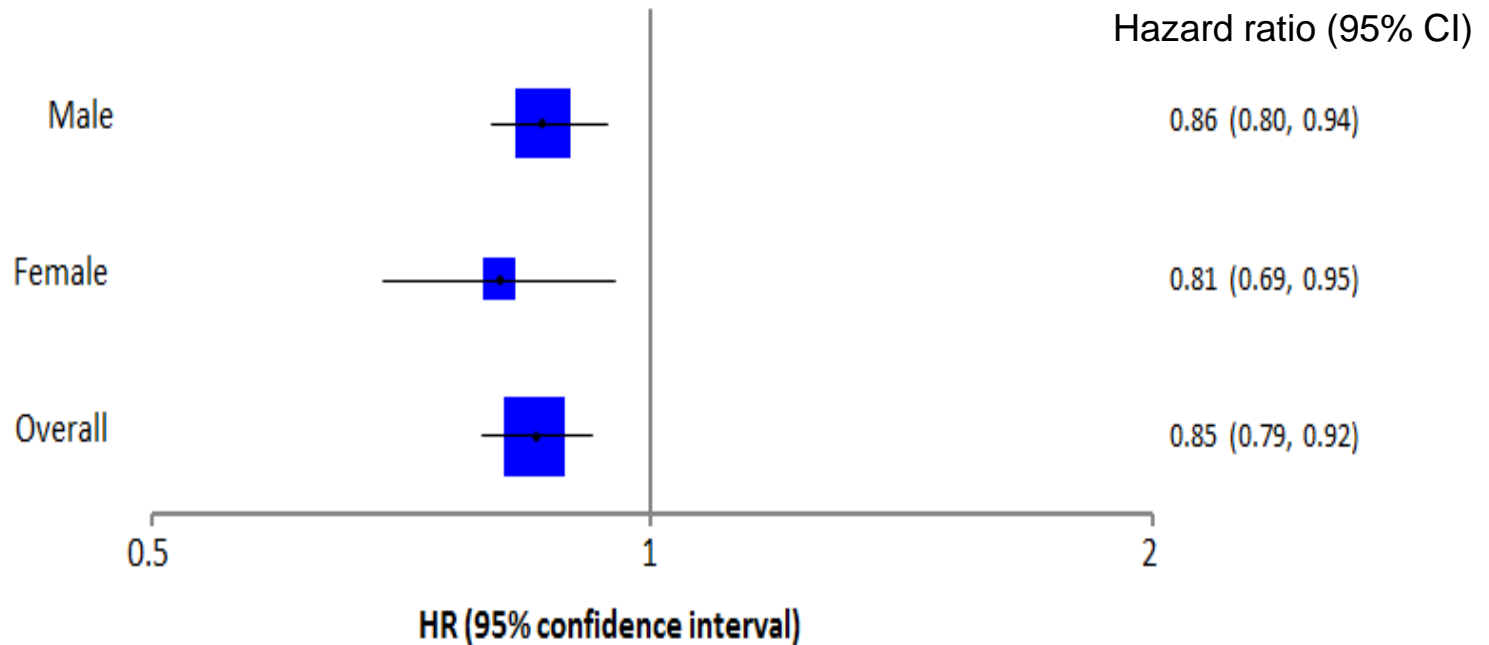
# Secondary endpoint stratified by age quartile





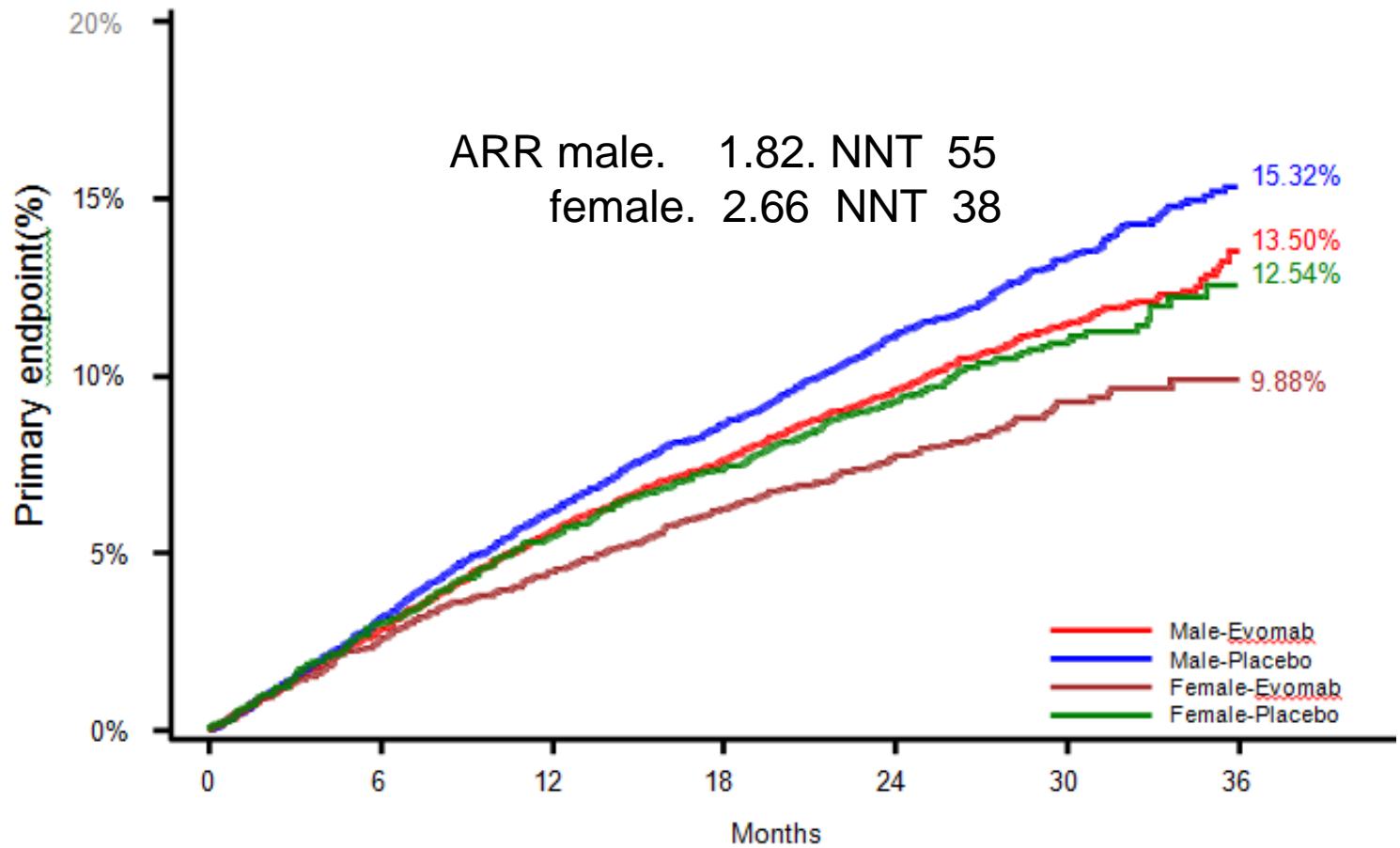
# The efficacy of evolocumab stratified by sex

FOURIER Primary endpoint  
(CVD, MI, stroke, hosp for UA, coronary revasc)



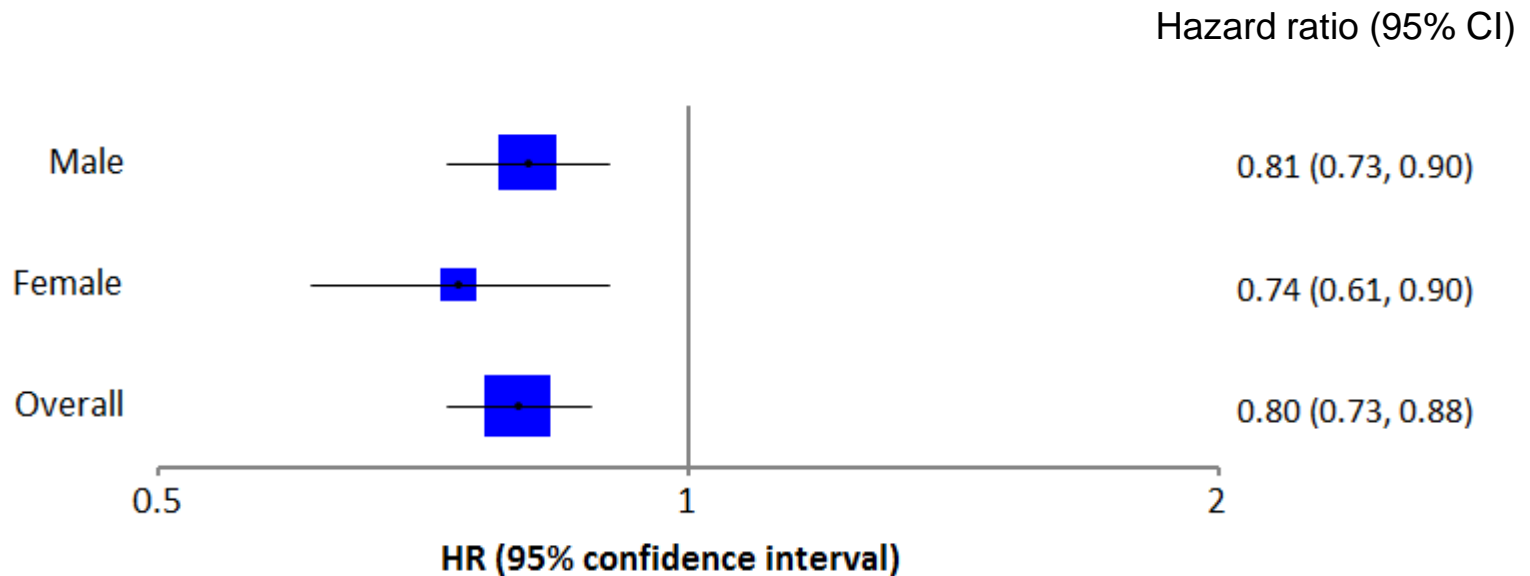
p interaction 0.477

# Primary endpoint stratified by sex



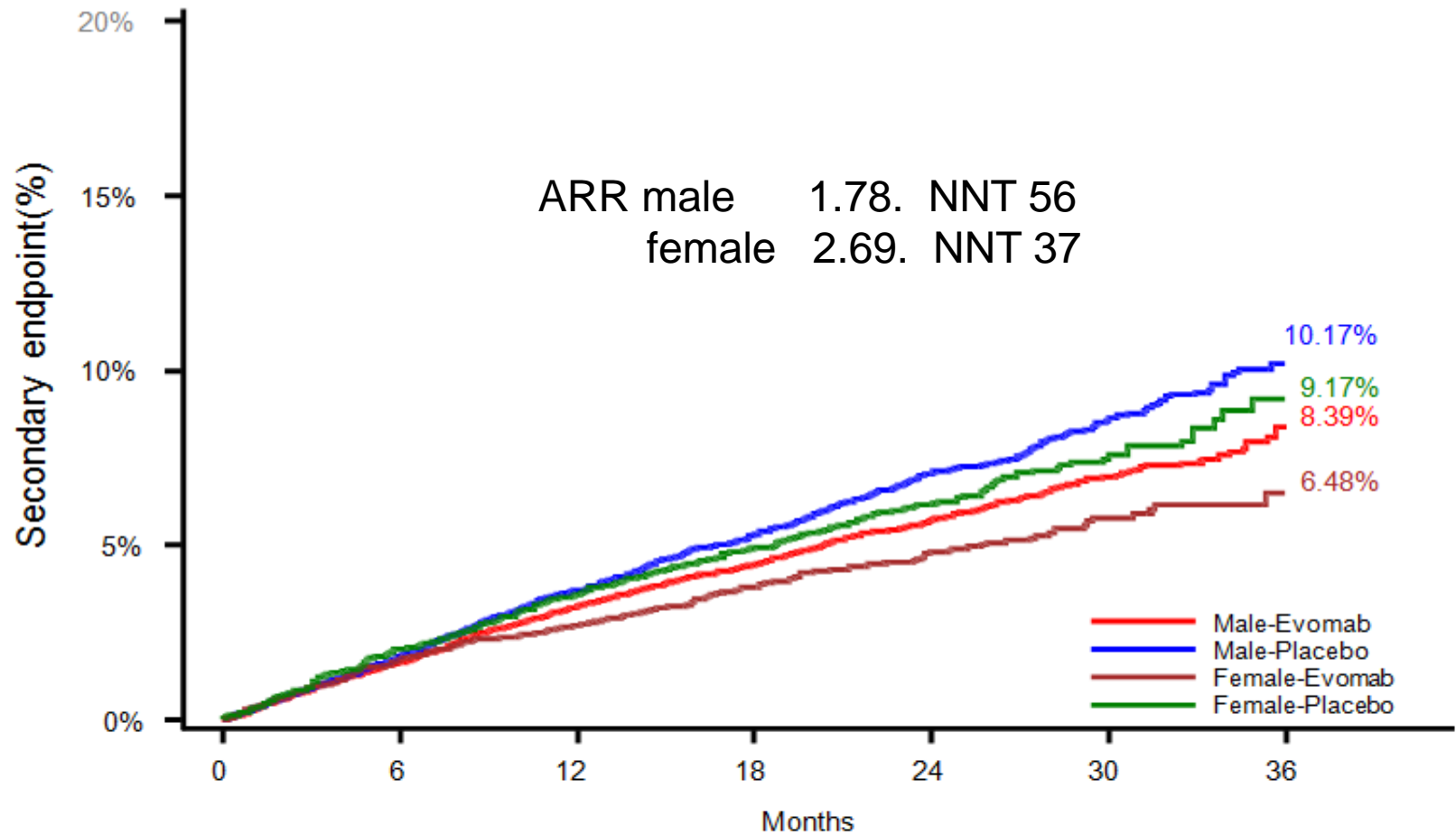
# The efficacy of evolocumab stratified by sex

FOURIER Key Secondary endpoint  
CV death, MI or stroke



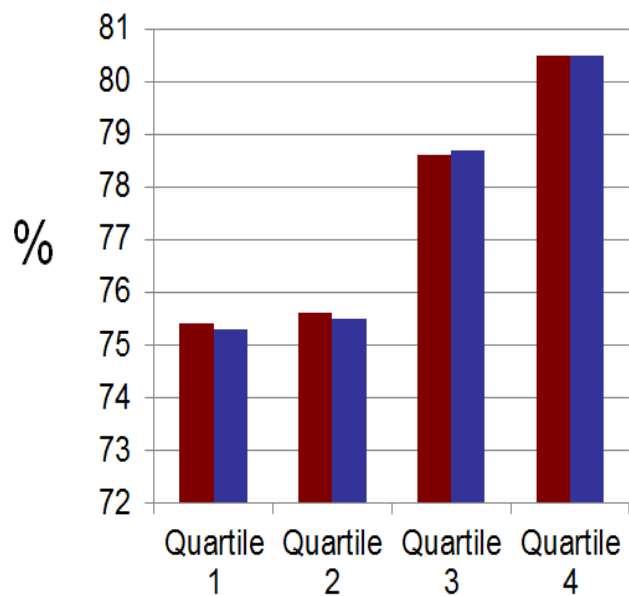
p interaction 0.436

# Secondary endpoint stratified by sex

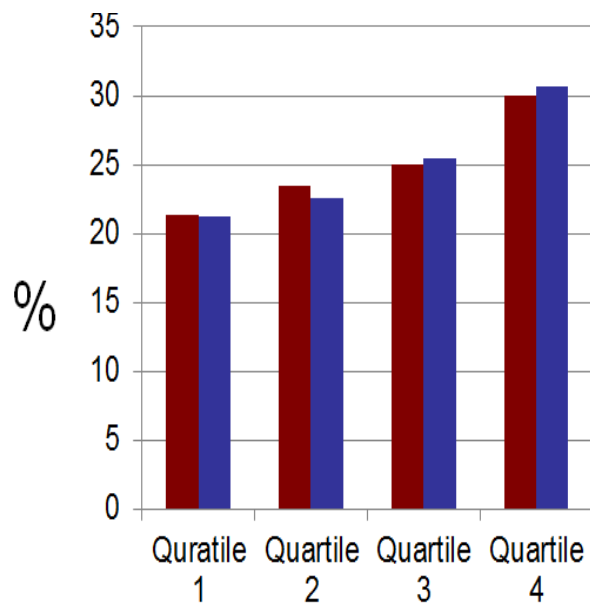


# Adverse events by age quartile and treatment allocation

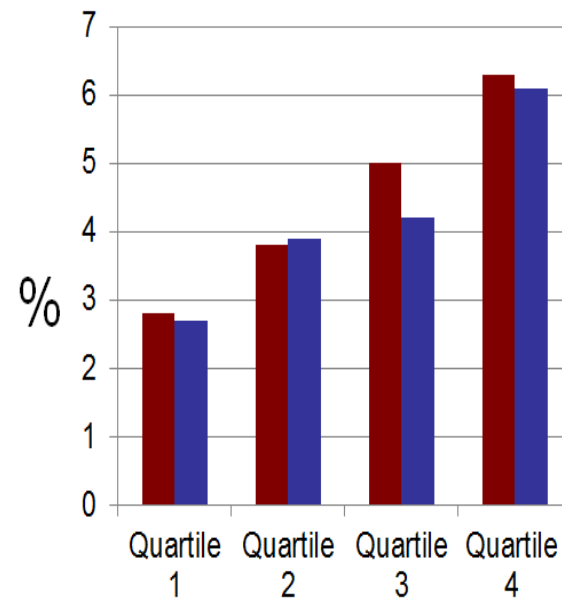
All Adverse events



Serious adverse events



Discontinuations



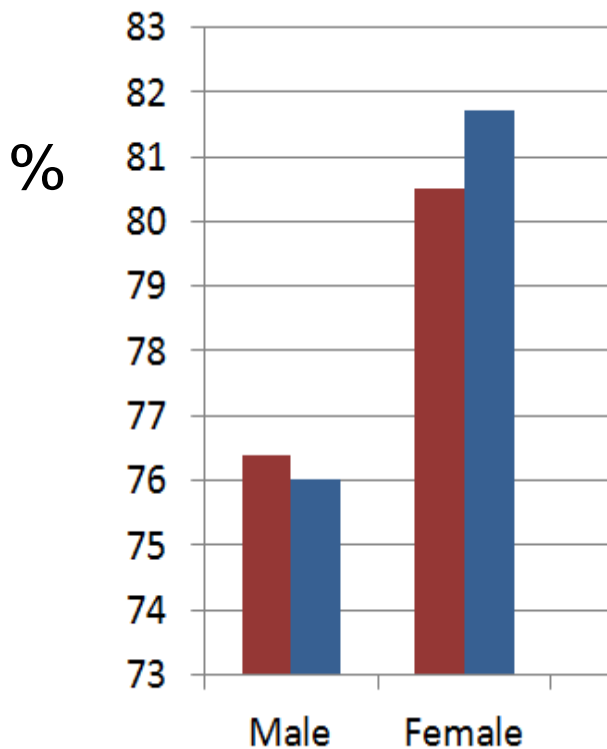
placebo



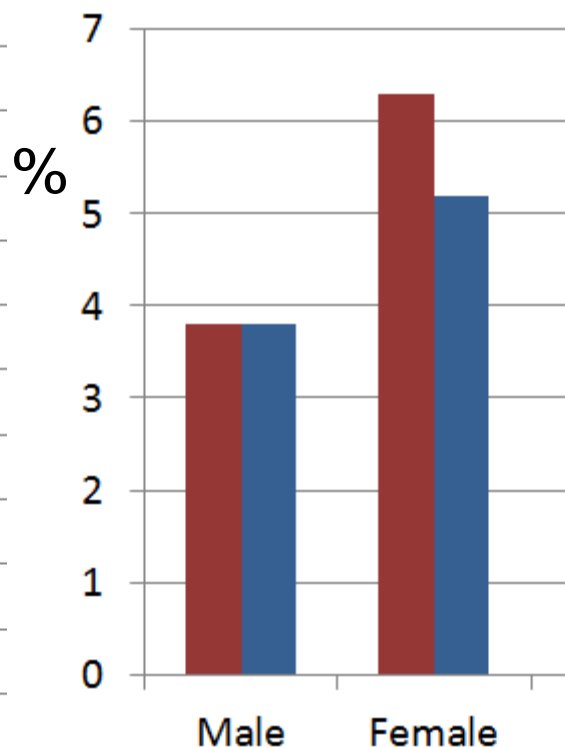
evolocumab

# Adverse events by sex and treatment allocation

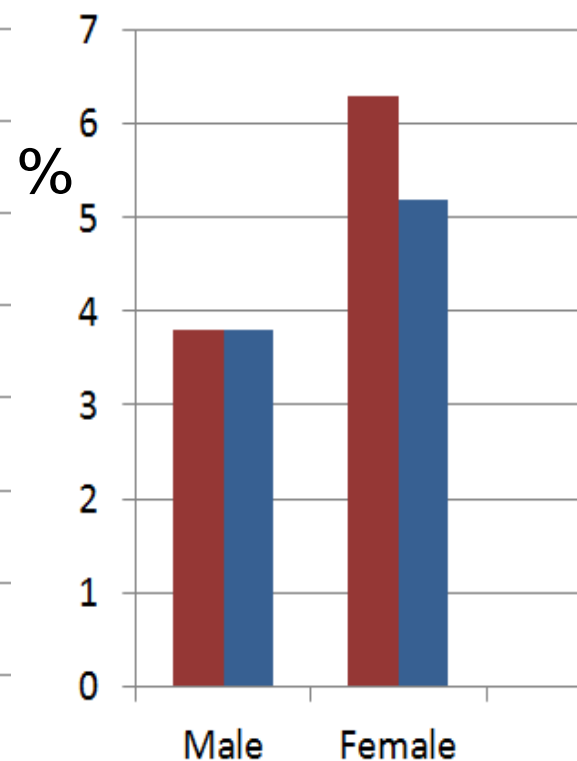
All adverse events



Serious adverse events



Discontinuations



evolocumab



placebo

# Summary and Conclusion

The results of the FOURIER Trial clearly demonstrate that in both sexes and across a wide age range of patients with established CV disease, the efficacy of evolocumab in reducing CV events is maintained.

Despite some differences in reporting of adverse events in men and women, and across the age range, there were no differences in those reported by those assigned evolocumab or placebo.

The current results provide new evidence that lowering LDL-cholesterol with evolocumab confers CV outcome benefits irrespective of age and sex.