Reduction in Ischemic Events, Including Cardiovascular Mortality, with Icosapent Ethyl in Patients with Prior Myocardial Infarction: REDUCE-IT PRIOR MI

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Disclosures

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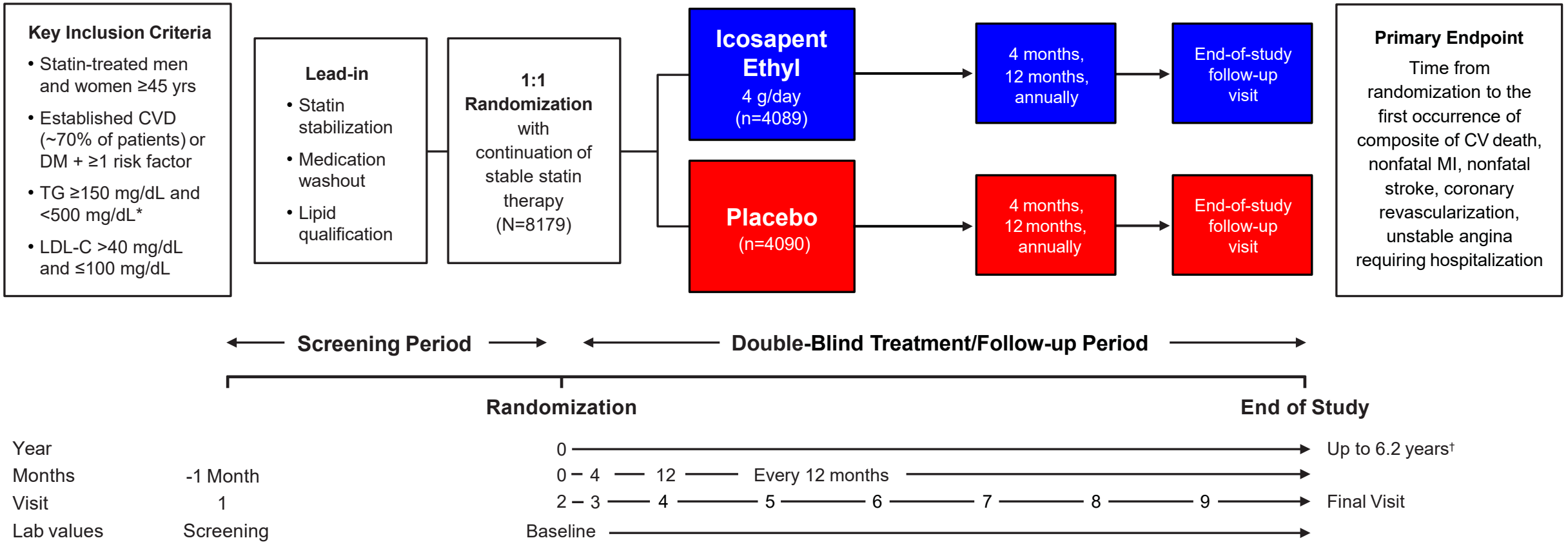
REDUCE-IT Design



*Due to the variability of triglycerides, a 10% allowance existed in the initial protocol, which permitted patients to be enrolled with qualifying triglycerides ≥135 mg/dL. Protocol amendment 1 (May 2013) changed the lower limit of acceptable triglycerides from 150 mg/dL to 200 mg/dL, with no variability allowance.

†Median trial follow-up duration was 4.9 years (minimum 0.0, maximum 6.2 years).

Bhatt DL, Steg PG, Brinton EA, et al; on behalf of the REDUCE-IT Investigators. Rationale and design of REDUCE-IT: Reduction of Cardiovascular Events with Icosapent Ethyl–Intervention Trial. *Clin Cardiol.* 2017;40:138-148. ClinicalTrials.gov number, NCT01492361.

Primary and Key Secondary Composite Endpoints

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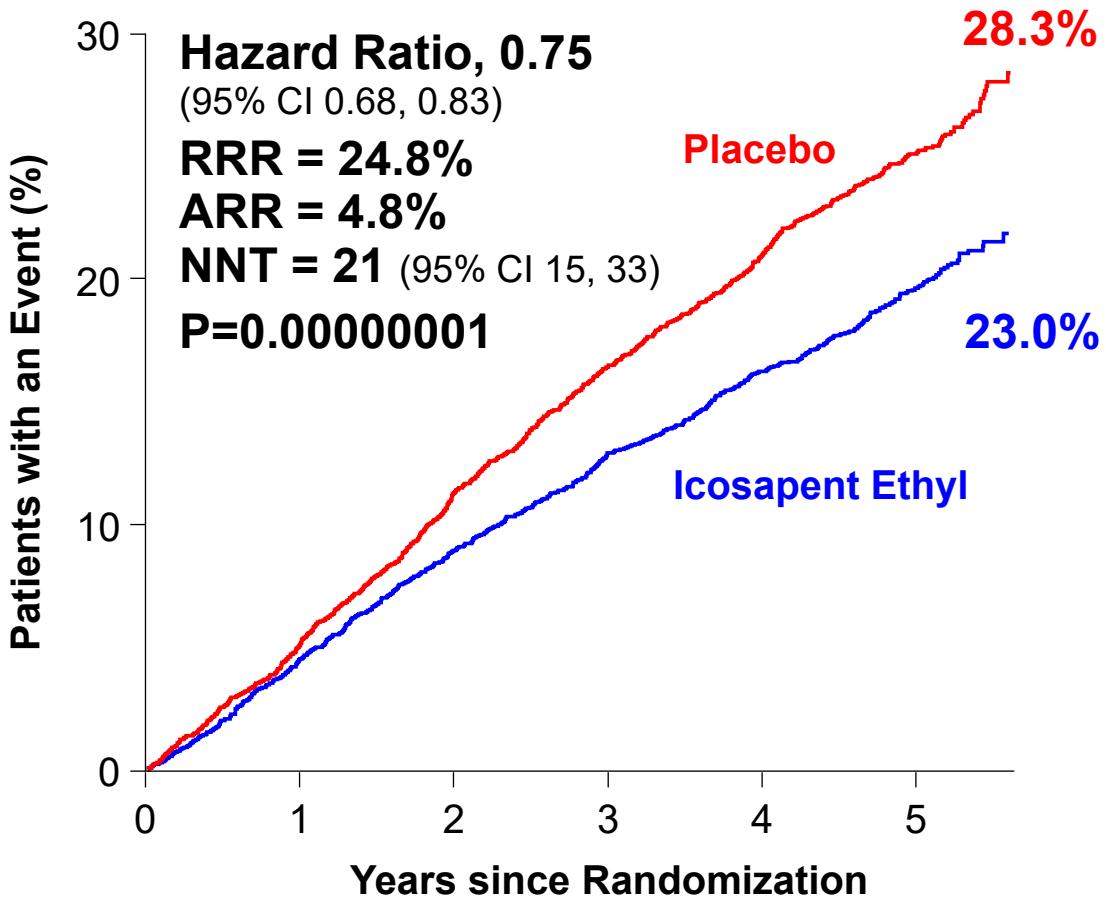
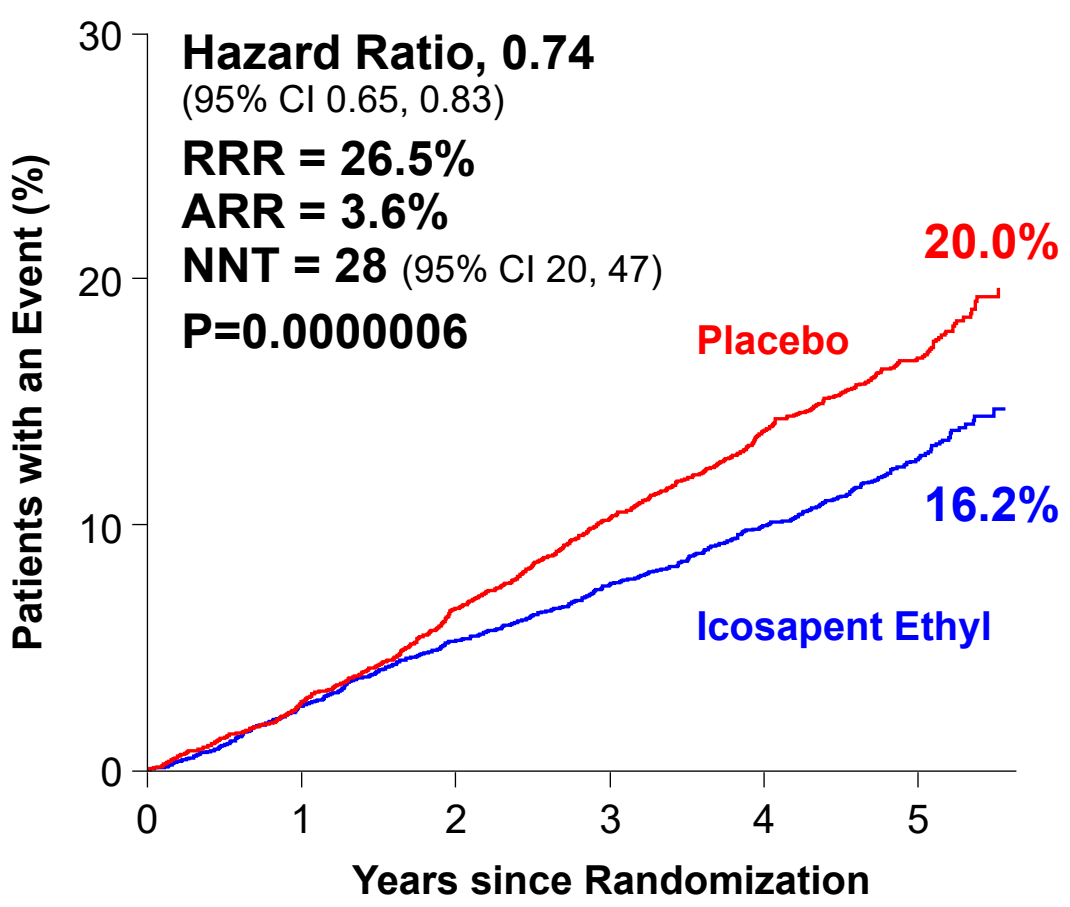
Primary Composite Endpoint:

CV Death, MI, Stroke, Coronary Revasc, Unstable Angina



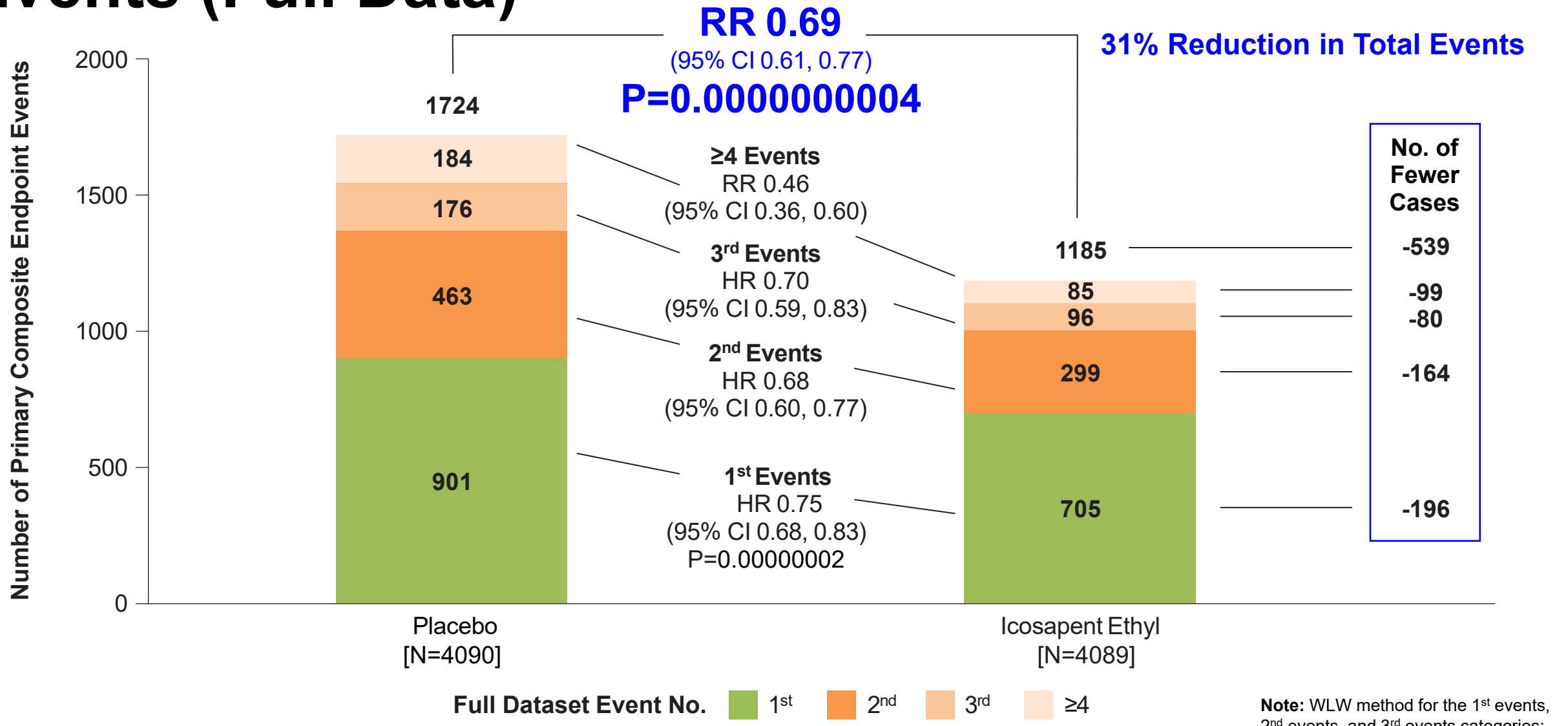
Key Secondary Composite Endpoint:

CV Death, MI, Stroke



Bhatt DL, Steg PG, Miller M, et al. *N Engl J Med.* 2019; 380:11-22. Bhatt DL. AHA 2018, Chicago.

Primary Endpoint First and Recurrent Events (Full Data)



Note: WLW method for the 1st events, 2nd events, and 3rd events categories; Negative binomial model for ≥4th events and overall treatment comparison.

Bhatt DL, Steg PG, Miller M, et al. *J Am Coll Cardiol*. 2019;73:2791-2802. Bhatt DL. ACC 2019, New Orleans.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Baseline Medications in Patients with Prior MI

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Medication Taken at Baseline, n (%)	Icosapent Ethyl (N=1870)	Placebo (N=1823)	P-value
Antidiabetes	638 (34.1)	628 (34.4)	0.83
Antihypertensive	1813 (97.0)	1771 (97.1)	0.73
Antiplatelet	1690 (90.4)	1645 (90.2)	0.89
One Antiplatelet	1143 (61.1)	1092 (59.9)	0.45
Two or More Antiplatelets	547 (29.3)	553 (30.3)	0.47
Anticoagulant	197 (10.5)	178 (9.8)	0.44
Anticoagulant + Antiplatelet	79 (4.2)	71 (3.9)	0.61
ACEi or ARB	1449 (77.5)	1448 (79.4)	0.15
ACEi	1041 (55.7)	1039 (57.0)	0.42
ARB	425 (22.7)	427 (23.4)	0.62
Beta Blocker	1580 (84.5)	1517 (83.2)	0.29

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First and Total Primary and Key Secondary Endpoints in Patients with Prior MI

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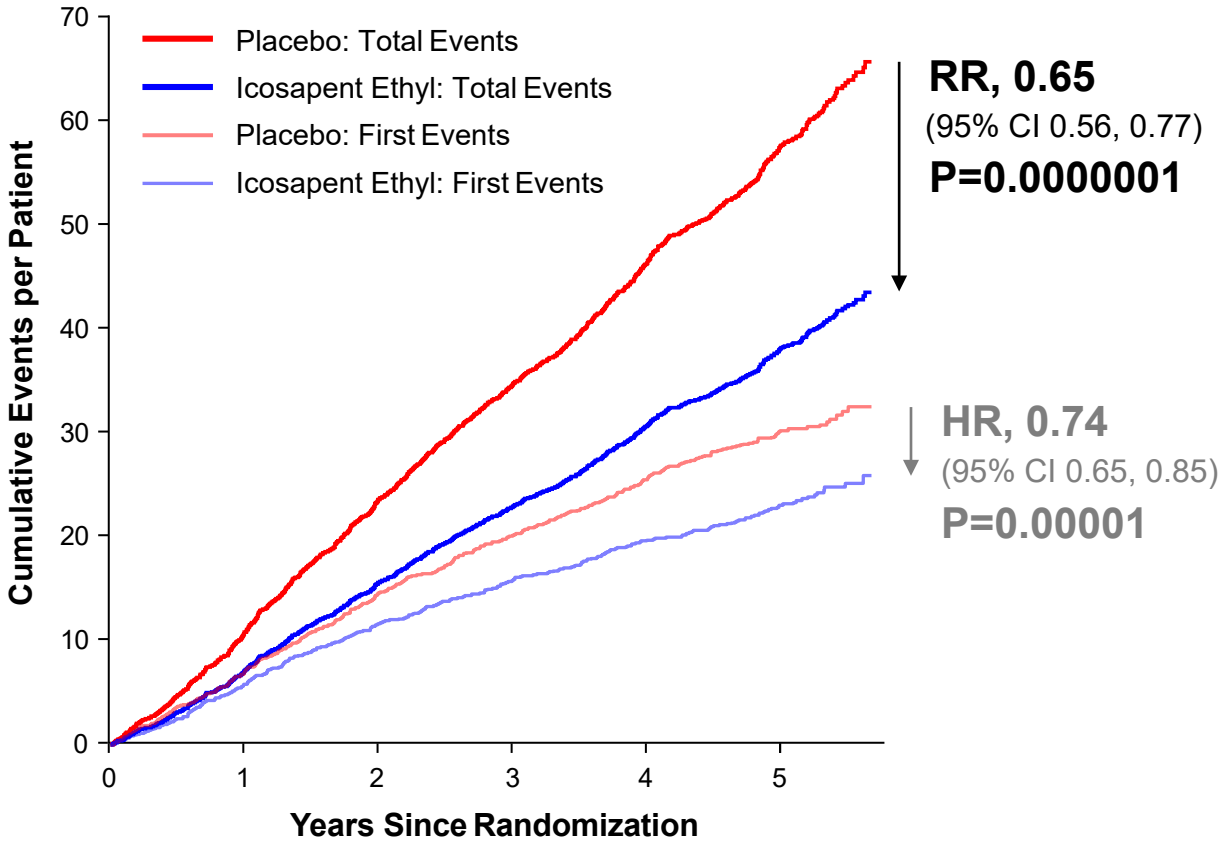
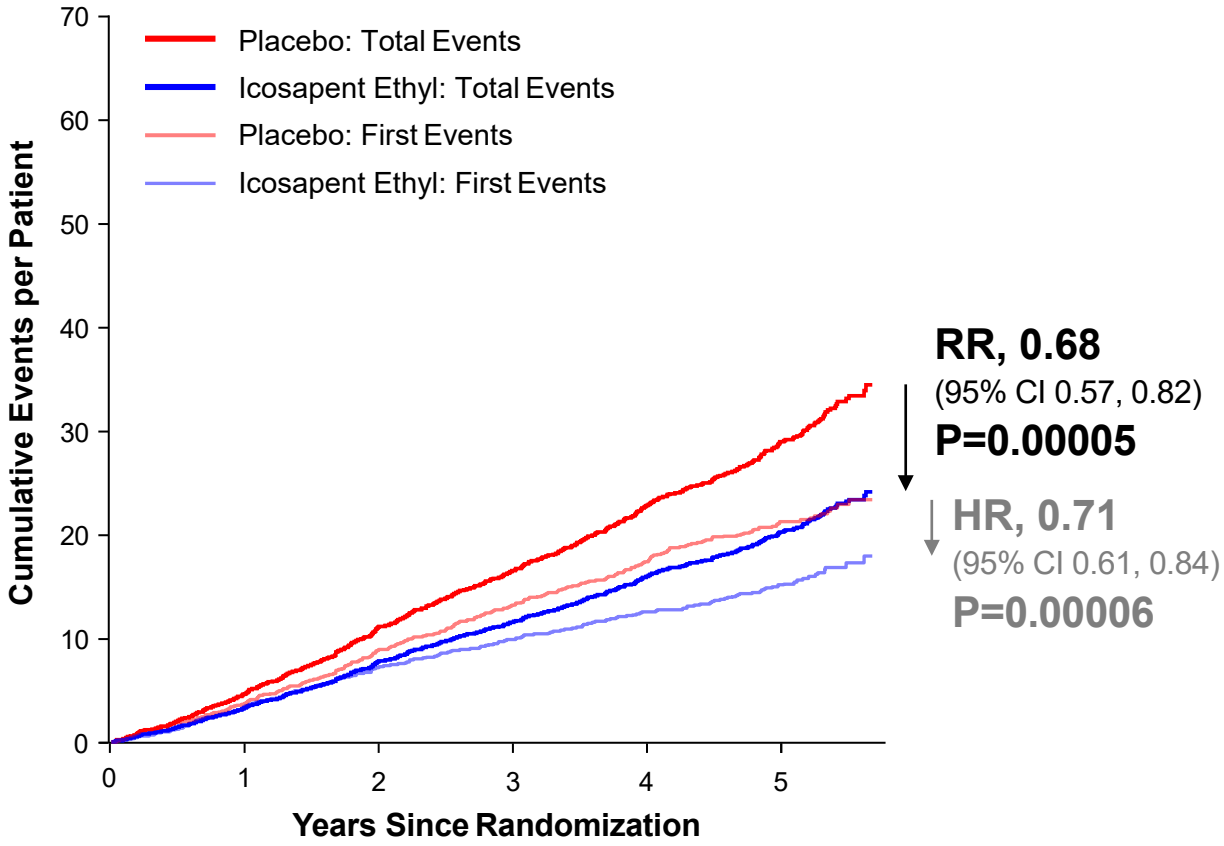
Primary Composite Endpoint



Key Secondary Composite Endpoint



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Prespecified Hierarchical Testing in Patients with Prior MI

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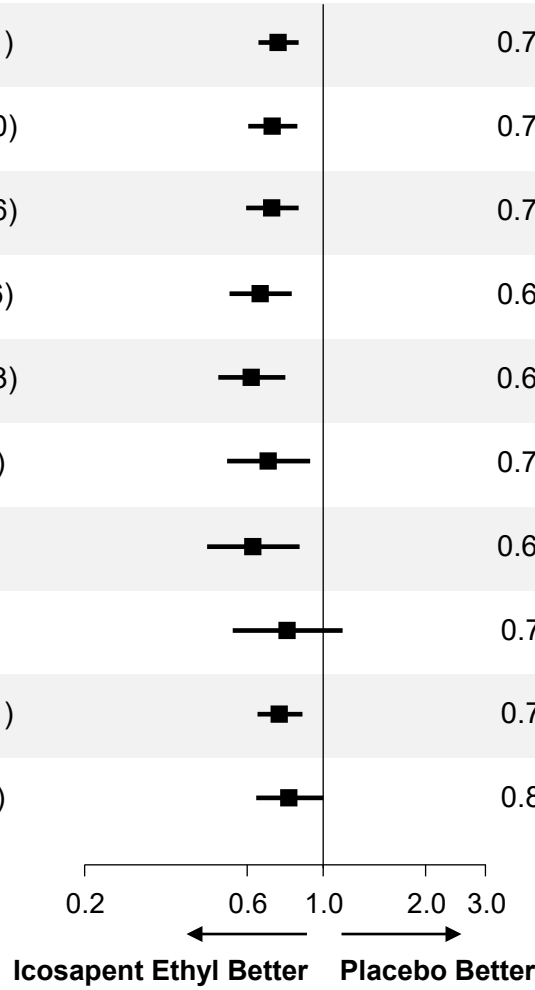
Endpoint	Icosapent Ethyl	Placebo	Icosapent Ethyl vs. Placebo	P-value
	n/N (%)	*n/N (%)*	*HR (95% CI)*	
Primary Composite Endpoint	378/1870 (20.2)	475/1823 (26.1)	0.74 (0.65, 0.85)	0.00001
Key Secondary Composite Endpoint	248/1870 (13.3)	328/1823 (18.0)	0.71 (0.61, 0.84)	0.00006
Cardiovascular Death or Nonfatal Myocardial Infarction	215/1870 (11.5)	285/1823 (15.6)	0.71 (0.60, 0.85)	0.0002
Fatal or Nonfatal Myocardial Infarction	147/1870 (7.9)	211/1823 (11.6)	0.66 (0.53, 0.81)	0.00009
Urgent or Emergent Revascularization	124/1870 (6.6)	188/1823 (10.3)	0.62 (0.49, 0.78)	0.00003
Cardiovascular Death	84/1870 (4.5)	116/1823 (6.4)	0.70 (0.53, 0.92)	0.01
Hospitalization for Unstable Angina	65/1870 (3.5)	99/1823 (5.4)	0.63 (0.46, 0.86)	0.003
Fatal or Nonfatal Stroke	51/1870 (2.7)	62/1823 (3.4)	0.79 (0.55, 1.14)	0.21
Total Mortality/Nonfatal Myocardial Infarction/Nonfatal Stroke	292/1870 (15.6)	367/1823 (20.1)	0.75 (0.64, 0.87)	0.0002
Total Mortality	136/1870 (7.3)	163/1823 (8.9)	0.80 (0.64, 1.00)	0.05



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Hierarchical Testing in Patients with Prior MI by Prior Coronary Revasc

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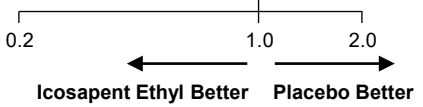
Endpoint	Icosapent Ethyl	Placebo	Icosapent Ethyl vs. Placebo	P-value	Int. P-value
	n/N (%)	*n/N (%)*	*HR (95% CI)*		
Primary Composite Endpoint	378/1870 (20.2)	475/1823 (26.1)	0.74 (0.65, 0.85)	<0.0001	
Prior Coronary Revascularization	305/1469 (20.8)	384/1423 (27.0)	0.73 (0.63, 0.85)	<0.0001	0.75
No Prior Revascularization	73/401 (18.2)	91/400 (22.8)	0.78 (0.57, 1.06)	0.11	
Key Secondary Composite Endpoint	248/1870 (13.3)	328/1823 (18.0)	0.71 (0.61, 0.84)	<0.0001	
Prior Coronary Revascularization	196/1469 (13.3)	255/1423 (17.9)	0.72 (0.60, 0.87)	0.0005	0.86
No Prior Revascularization	52/401 (13.0)	73/400 (18.3)	0.70 (0.49, 1.00)	0.05	
Cardiovascular Death or Nonfatal Myocardial Infarction	215/1870 (11.5)	285/1823 (15.6)	0.71 (0.60, 0.85)	0.0002	
Prior Coronary Revascularization	169/1469 (11.5)	223/1423 (15.7)	0.71 (0.58, 0.86)	0.0006	0.89
No Prior Revascularization	46/401 (11.5)	62/400 (15.5)	0.73 (0.50, 1.07)	0.10	
Fatal or Nonfatal MI	147/1870 (7.9)	211/1823 (11.6)	0.66 (0.53, 0.81)	<0.0001	
Prior Coronary Revascularization	125/1469 (8.5)	176/1423 (12.4)	0.66 (0.53, 0.83)	0.0004	0.83
No Prior Revascularization	22/401 (5.5)	35/400 (8.8)	0.62 (0.36, 1.05)	0.07	
Urgent or Emergent Revascularization	124/1870 (6.6)	188/1823 (10.3)	0.62 (0.49, 0.78)	<0.0001	
Prior Coronary Revascularization	110/1469 (7.5)	163/1423 (11.5)	0.63 (0.49, 0.80)	0.0001	0.70
No Prior Revascularization	14/401 (3.5)	25/400 (6.3)	0.53 (0.27, 1.02)	0.05	
Cardiovascular Death	84/1870 (4.5)	116/1823 (6.4)	0.70 (0.53, 0.92)	0.01	
Prior Coronary Revascularization	55/1469 (3.7)	79/1423 (5.6)	0.66 (0.47, 0.93)	0.02	0.60
No Prior Revascularization	29/401 (7.2)	37/400 (9.3)	0.79 (0.48, 1.28)	0.33	
Hospitalization for Unstable Angina	65/1870 (3.5)	99/1823 (5.4)	0.63 (0.46, 0.86)	0.003	
Prior Coronary Revascularization	57/1469 (3.9)	88/1423 (6.2)	0.61 (0.44, 0.86)	0.004	0.79
No Prior Revascularization	8/401 (2.0)	11/400 (2.8)	0.65 (0.26, 1.63)	0.36	
Fatal or Nonfatal Stroke	51/1870 (2.7)	62/1823 (3.4)	0.79 (0.55, 1.14)	0.21	
Prior Coronary Revascularization	39/1469 (2.7)	46/1423 (3.2)	0.81 (0.53, 1.24)	0.32	0.87
No Prior Revascularization	12/401 (3.0)	16/400 (4.0)	0.76 (0.36, 1.61)	0.48	
Total Mortality/Nonfatal Myocardial Infarction/Nonfatal Stroke	292/1870 (15.6)	367/1823 (20.1)	0.75 (0.64, 0.87)	0.0002	
Prior Coronary Revascularization	233/1469 (15.9)	290/1423 (20.4)	0.75 (0.63, 0.89)	0.001	0.96
No Prior Revascularization	59/401 (14.7)	77/400 (19.3)	0.74 (0.53, 1.04)	0.08	
Total Mortality	136/1870 (7.3)	163/1823 (8.9)	0.80 (0.64, 1.00)	0.05	
Prior Coronary Revascularization	98/1469 (6.7)	120/1423 (8.4)	0.77 (0.59, 1.01)	0.06	0.64
No Prior Revascularization	38/401 (9.5)	43/400 (10.8)	0.87 (0.56, 1.35)	0.54	



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Cardiac Arrest and Sudden Cardiac Death in Patients with Prior MI

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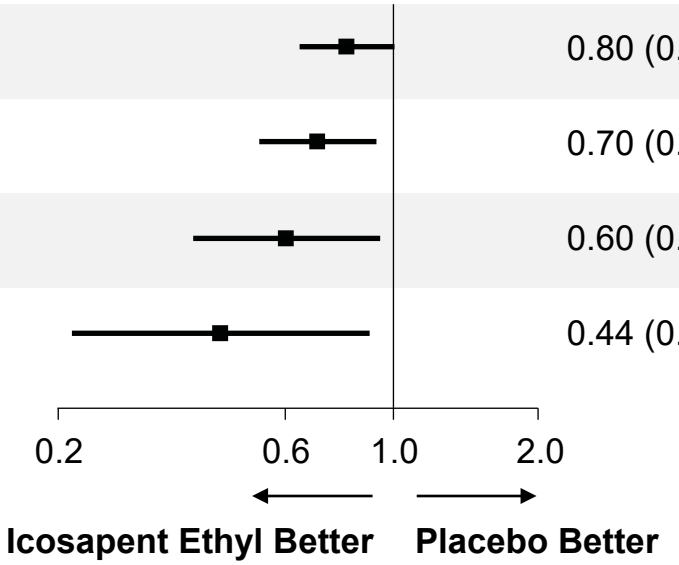
Endpoint	Icosapent Ethyl	Placebo	Icosapent Ethyl vs. Placebo	P-value
	n/N (%)	*n/N (%)*	*HR (95% CI)*	
Total Mortality	136/1870 (7.3)	163/1823 (8.9)	0.80 (0.64, 1.00)	0.05
Cardiovascular Death	84/1870 (4.5)	116/1823 (6.4)	0.70 (0.53, 0.92)	0.01
Sudden Cardiac Death	31/1870 (1.7)	50/1823 (2.7)	0.60 (0.38, 0.94)	0.02
Cardiac Arrest	11/1870 (0.6)	24/1823 (1.3)	0.44 (0.21, 0.89)	0.02



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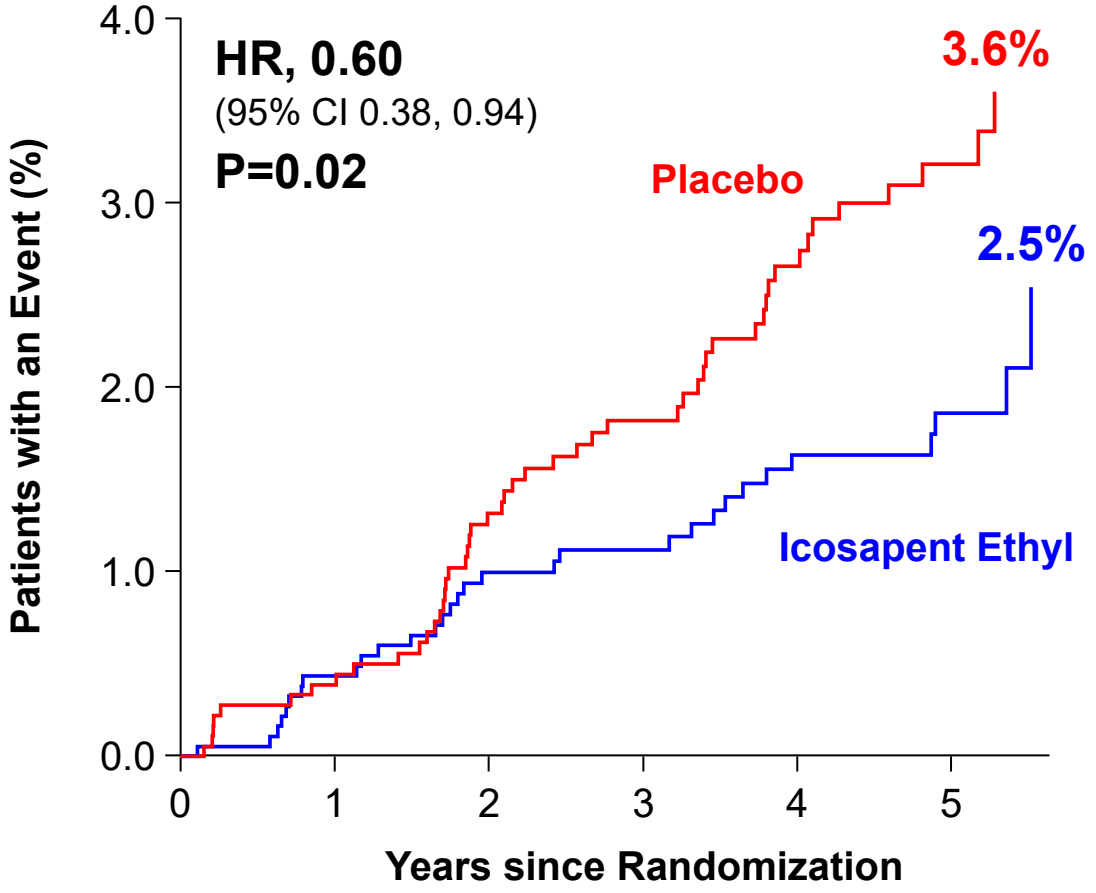
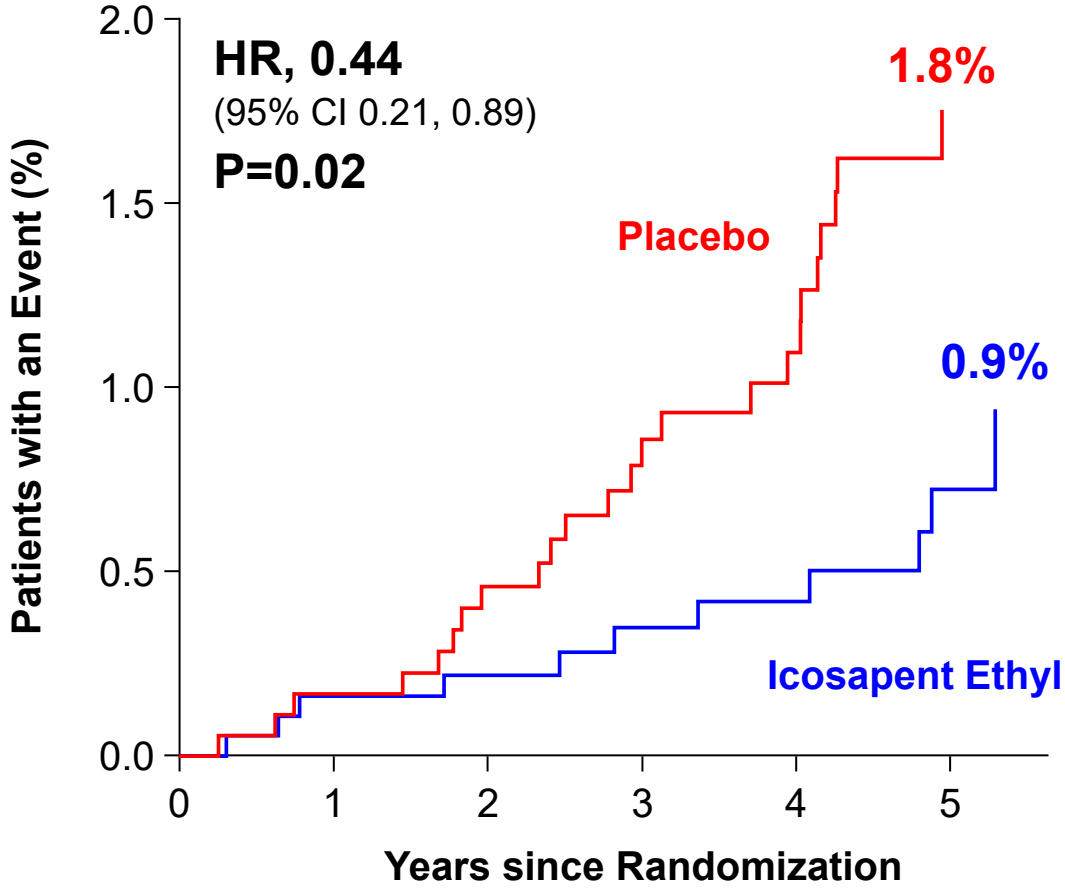
Sudden Cardiac Death



Cardiac Arrest



Results consistently statistically significant by ~ 4 years

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Safety

Safety was generally consistent with the full study.

No differences were observed between icosapent ethyl and placebo in overall tolerability or adverse events in patients with prior MI.

More bleeding occurred with icosapent ethyl vs. placebo in patients with prior MI.

More atrial fibrillation/flutter occurred with icosapent ethyl vs. placebo.

Limitations

These data include both prespecified and *post hoc* analyses.

REDUCE-IT was designed and powered for the primary composite endpoint; it was not powered for subgroup analyses.

Enrollment was not stratified by prior MI.

Conclusions

Icosapent ethyl 4 g/day significantly reduced first and total primary endpoints by **26%** and **35%**, respectively, in patients with prior MI.

Icosapent ethyl led to robust reductions across the prespecified hierarchy of endpoints, including reductions in the key secondary endpoint, MI, CV death, sudden cardiac death, and cardiac arrest.

The benefits of icosapent ethyl in patients with prior MI were consistent in those with or without a history or prior revascularization.

Icosapent ethyl provides substantial cardiovascular risk reduction in the high-risk **REDUCE-IT** population, with consistent and significant benefits in patients who have experienced a prior MI.


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