



Efficacy of Lowering Low-Density Lipoprotein Cholesterol in Older patients: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

Baris Gencer, MD; Nicholas A. Marston, MD, MPH; KyungAh Im, PhD; Christopher P. Cannon, MD; Peter Sever, PhD, FRCP; Anthony Keech, MD; Eugene Braunwald, MD; Robert P. Giugliano, MD, SM; Marc S. Sabatine, MD, MPH.

TIMI Study Group, Division of Cardiovascular Medicine,
Brigham and Women's Hospitals, Harvard Medical School,
Boston, MA, USA.

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Background

- Numerous RCTs with statins and non-statins established that lowering LDL-C reduces CV risk.^{1,2}
- However, relatively few older individuals (≥75 years) were studied and there is uncertainty of benefit-to-risk ratio in the elderly.³
- Practice guidelines assign lower level of evidence and strength of recommendations in older compared to younger patients.⁴

¹ CTTC. *Lancet* 2010;376:1670-81.

² Silverman MG et al. *JAMA* 2016;316(12):1289-97.

³ Chou R et al. *JAMA* 2016;316:2008-24.

⁴ Grundy SM et al. *Circulation* 2019;139: e1082-143.



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Methods

- MEDLINE and Embase searched from 2015-2020.
- Key inclusion: RCT of LDL-C reporting CV outcomes of lowering therapies recommended by 2018 ACC/AHA guidelines.¹
- Data compared in patients aged <75 vs \geq 75 years.
- Primary endpoint: Major Vascular Events (composite of CV death, MI or UA, coronary revascularization or stroke).
- HR or rate ratio normalized per 1 mmol/L (38.67 mg/dL) difference in LDL-C for each trial.
- Random-effects meta-analysis used to account for trial heterogeneity in lipid-lowering therapies (statins vs. non-statins), follow-up duration, and study population (with vs. without established atherosclerotic CV disease).

¹ Grundy SM et al. *Circulation* 2019;139: e1082-143



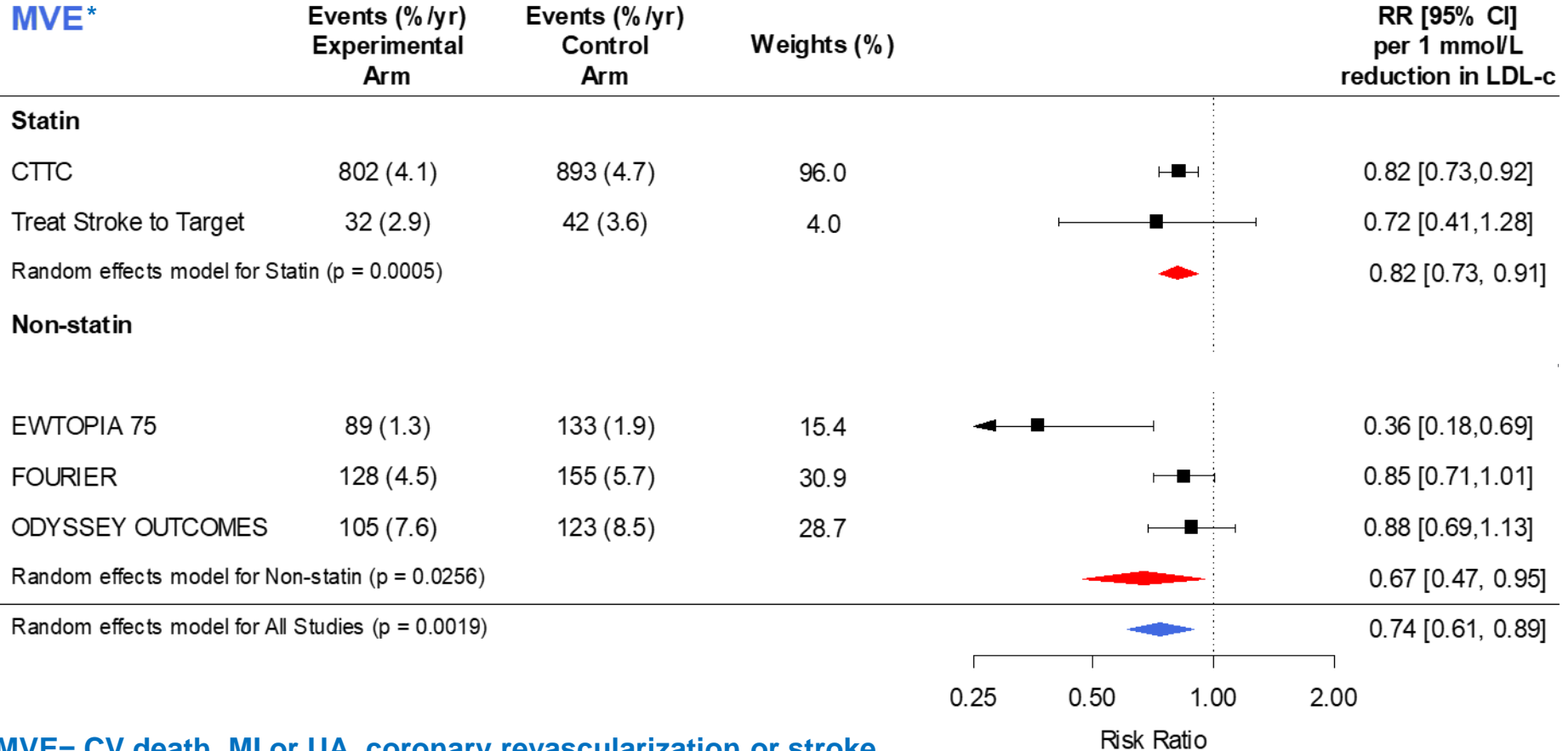
Baseline Characteristics

Trials	Older Patients	Population	Mean Age	Female, %	Experimental Arm	Control Arm	Δ LDL-C mmol/L	Median F/U (yrs)	Major Vascular Events
Statin									
CTTC* (n=24)	11,108	Mixed	NA	NA	Statin or more intensive statin	Placebo or less intensive statin	0.9	4.9	1,695
Treat Stroke To Target	642	Secondary	NA	NA	Target LDL-C <1.8 mmol/L	Target LDL-C 2.3-2.8 mmol/L	0.8	3.5	74
Non-statin									
IMPROVE-IT	2,798	Secondary	80	33.8	Ezetimibe+ Simvastatin	Placebo+ Simvastatin	0.4	6.0	1,017
EWTOPIA 75	3,411	Primary	81	74.4	Ezetimibe	Usual care	0.4	4.1	222
FOURIER	2,526	Secondary	78	33.6	Evolocumab + statin	Placebo + statin	1.3	2.2	283
ODYSSEY	1,007	Secondary	78	45.5	Alirocumab + statin	Placebo + statin	1.0	2.8	228
Total	21,492	Mixed					0.9 (0.4)	3.3 (2.2-4.6)	3,519

*Cholesterol Treatment Trialists' Collaboration included 24 trials of statin vs placebo or more vs less intensive statin



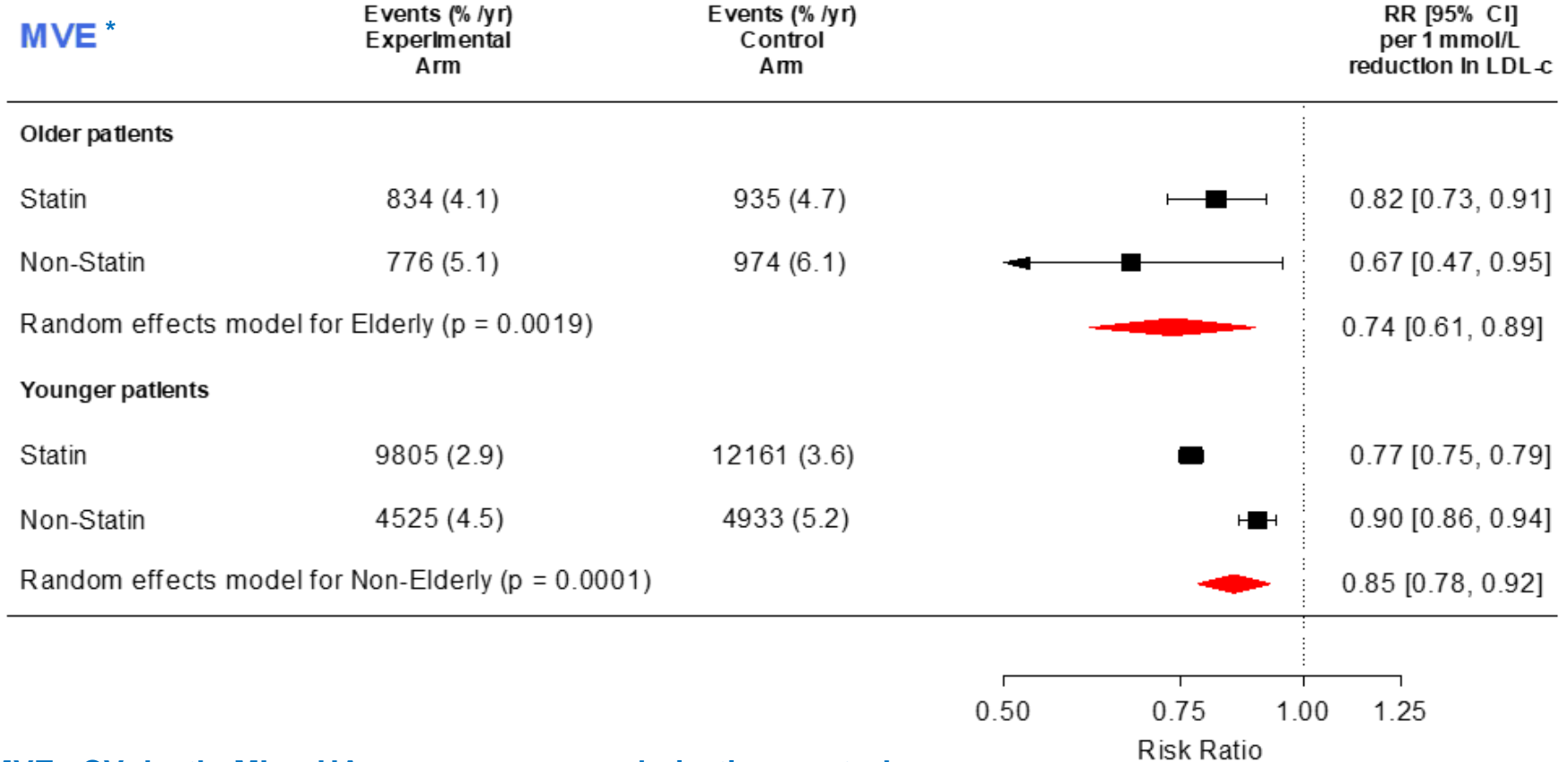
Effect of LDL-C lowering on the risk of major vascular events in older patients



*MVE= CV death, MI or UA, coronary revascularization or stroke



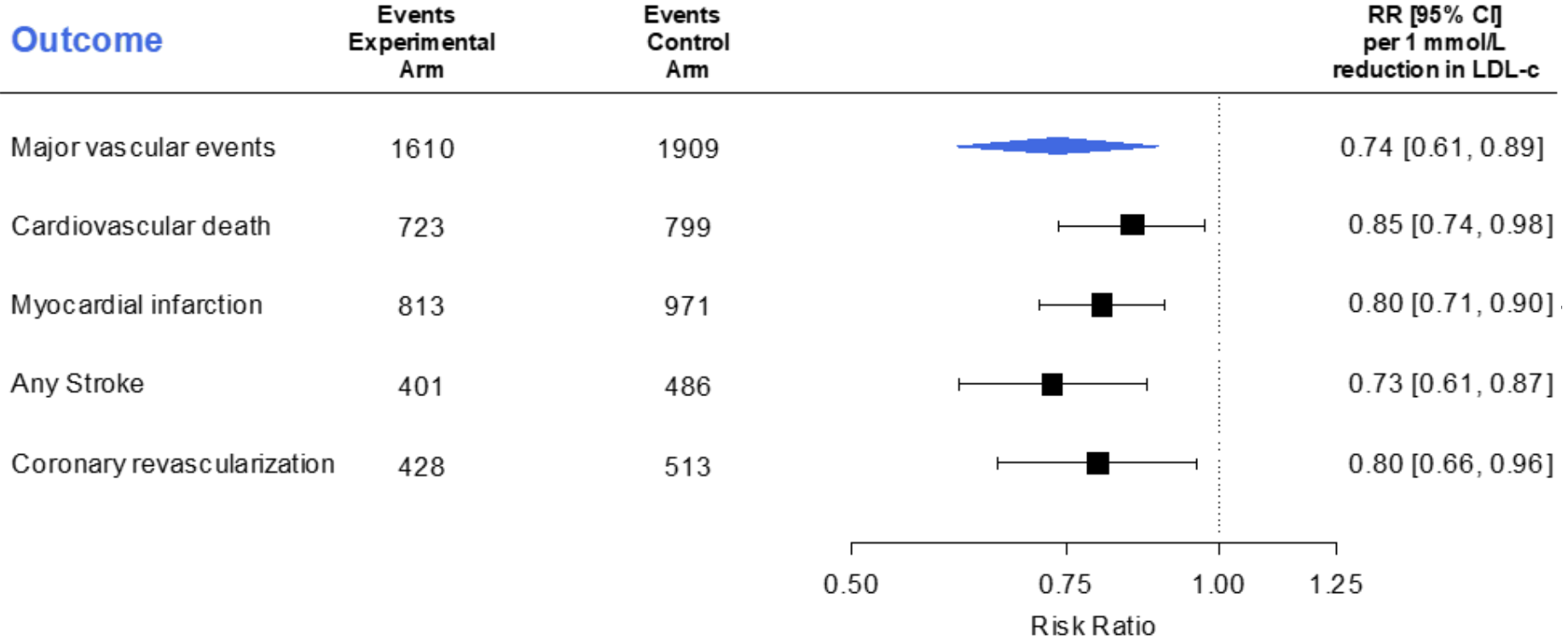
Effect of LDL-C lowering on the risk of major vascular events in older vs. younger



*MVE= CV death, MI or UA, coronary revascularization or stroke

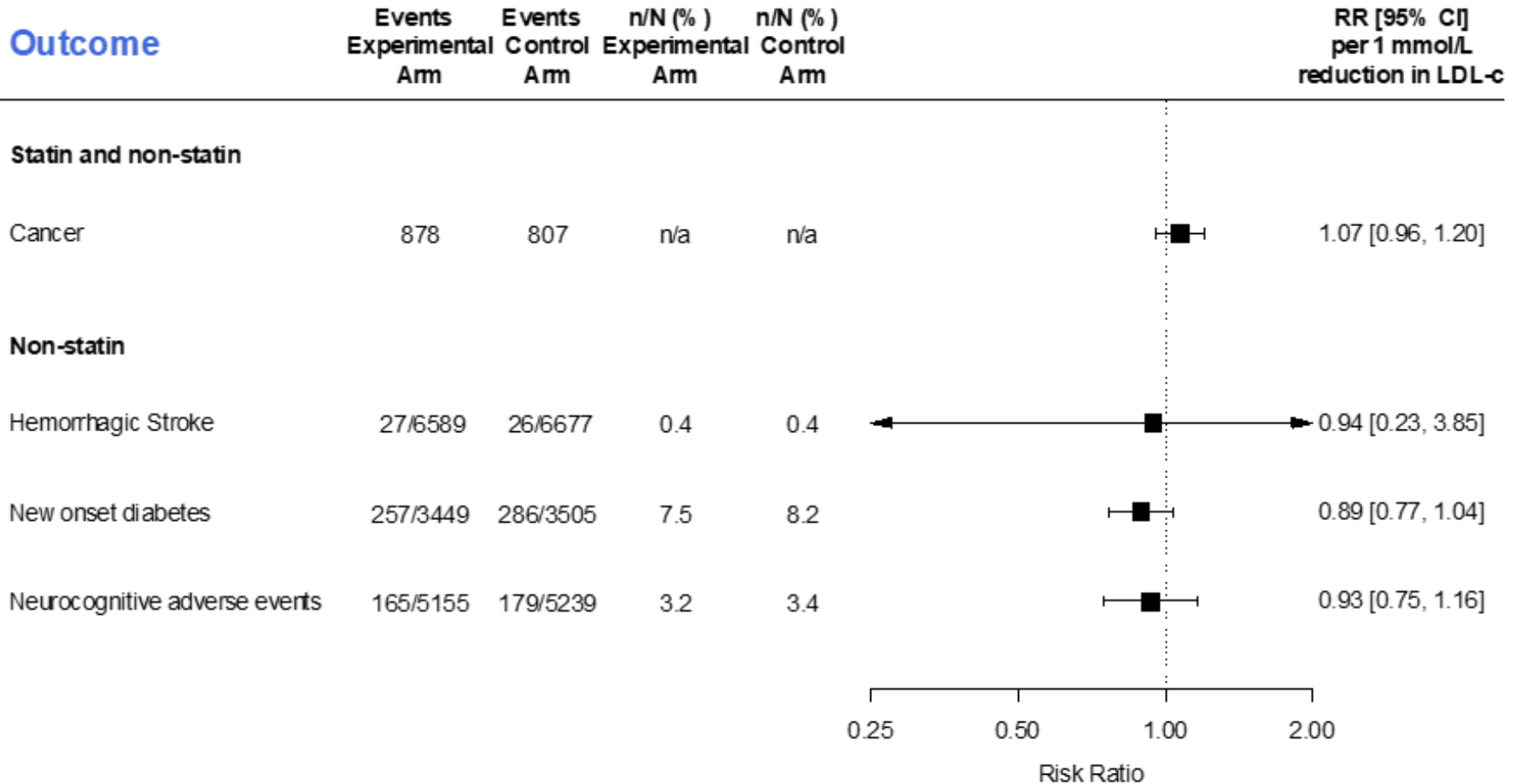


Effect of LDL-C lowering on the risk of individual efficacy endpoints in older patients





Effect of LDL-C lowering on the risk of safety endpoints in older patients





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Conclusion

- In patients aged 75 years and older, lipid-lowering was as effective in reducing CV events as it was in patients younger than 75 years.
- These results should strengthen guideline recommendations for the use of lipid-lowering Rx, including non-statin Rx, in older patients.

THE LANCET

Efficacy and safety of lowering LDL cholesterol in older patients: a systematic review and meta-analysis of randomised controlled trials



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