Association of statin use in older people primary prevention group with risk of cardiovascular events and mortality: a systematic review and meta-analysis of observational studies

K. Awad¹, M. Mohammed¹, M.M. Zaki¹, A.I. Abushouk², G.Y.H. Lip³, M.J. Blaha⁴, C.J. Lavie⁵, P.P. Toth⁴, J.W. Jukema⁶, N. Sattar⁷, M. Banach⁸

¹Zagazig University, Zagazig, Egypt; ²Cleveland Clinic Foundation, Cleveland, United States of America; ³Liverpool Heart and Chest Hospital, Liverpool, United Kingdom; ⁴Johns Hopkins University School of Medicine, Baltimore, United States of America; ⁵Ochsner Medical Center, New Orleans, United States of America; ⁶Leiden University Medical Center, Leiden, Netherlands (The); ⁷University of Glasgow, Glasgow, United

Kingdom; ⁸ Polish Mother Memorial Hospital Research Institute, Lodz, Poland

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Background: Current evidence from randomized controlled trials on statins for primary prevention of cardiovascular disease (CVD) in older people, especially those aged >75 years, is still lacking.

Purpose: We conducted a systematic review and meta-analysis of observational studies to extend the current evidence about association of statin use in older people primary prevention group with risk of CVD and mortality.

Methods: PubMed, Scopus, and Embase were searched from inception until March 18, 2021. We included observational studies (cohort or nested case-control) that compared statin use vs non-use for primary prevention of CVD in older people aged \geq 65 years; provided that each of them reported the risk estimate on at least one of the following primary outcomes: all cause-mortality, CVD death, myocardial infarction (MI), and stroke. Risk estimates of each relevant outcome were pooled as a hazard ratio (HR) with a 95% confidence interval (CI) using the random-effects meta-analysis model.

Results: Ten observational studies (9 cohort and one case-control study; n=872,845) fulfilled our criteria. The overall combined estimate suggested

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that statin therapy was associated with a significantly lower risk of all-cause mortality (HR: 0.86 [95% CI: 0.79 to 0.93]), CVD death (HR: 0.80 [95% CI: 0.78 to 0.81]), and stroke (HR: 0.85 [95% CI: 0.76 to 0.94]) and a non-significant association with risk of MI (HR: 0.74 [95% CI: 0.53 to 1.02]). The beneficial association of statins with the risk of all-cause mortality remained significant even at higher ages (>75 years old; HR: 0.86 [95% CI: 0.81 to 0.96]) and in both men (HR: 0.75 [95% CI: 0.74 to 0.76]) and women (HR: 0.85 [95% CI: 0.72 to 0.99]). However, this association with the risk of all-cause mortality remained significant only in those with DM (HR: 0.82 [95% CI: 0.68 to 0.98]) but not in those without DM.

Conclusions: Statin therapy in older people (aged \geq 65 years) without CVD was associated with a 14%, 20% and 15% lower risk of all-cause mortality, CVD death and stroke, respectively. The beneficial association with the risk of all-cause mortality remained significant even at higher ages (>75 years old), in both men and women, and in individuals with DM, but not in those without DM. These observational findings support the need for trials to test benefits of statins in those above 75 years of age.

Outcomes	No. of studies		HR (95% CI)	I-squared	Chi2, p
All-cause mortality	9		0.86 (0.79 to 0.93)	90	< 0.0001
CVD death	4		0.80 (0.78 to 0.81)	0	0.6
Stroke	8	- - ;	0.85 (0.76 to 0.94)	61	< 0.0001
MI	5		0.74 (0.53 to 1.02)	85	< 0.0001

Subgroup	No. of studies	Statins	No statins		HR (95% CI)	I-squared	Chi2, p	P value for interaction
Age								0.76
65 to 75 years	3	40189	215321	- -	0.84 (0.81 to 0.88)	0	0.54	
≥75 years	8	107874	572867	i	0.88 (0.81 to 0.96)	91	< 0.0001	
≥80 years	3	34225	171357		0.84 (0.79 to 0.89)	83	< 0.0001	
≥85 years	2	9735	56104		0.88 (0.79 to 0.99)	87	< 0.0001	
Sex								0.14
Men	4	59194	325360		0.75 (0.74 to 0.76)	0	0.60	
Women	4	6265	55723		0.85 (0.72 to 0.99)	48	0.12	
Diabetes								0.38
Yes	3	17594	49080		0.82 (0.68 to 0.98)	85	< 0.001	
No	5	48984	358144		0.92 (0.77 to 1.10)	95	< 0.0001	

Statins better No statins better

Figure 1. Results of the meta-analysis