Atorvastatin for primary cardiovascular prevention reduces major events but not disability-free survival in older adults

30-second summary:

Treatment with atorvastatin 40 mg for primary prevention of cardiovascular disease reduced a composite of cardiovascular risk by 30% over 5.9 years in community-dwelling adults over age 70 years, according to this double-blind, randomised, placebo-controlled trial published in the *New England Journal of Medicine*. There was no significant difference in risk of death, dementia or physical disability between those treated with atorvastatin or placebo, whereas myocardial infarction and coronary revascularisation rates were almost halved. During the study, nearly 10% and 20% of the atorvastatin group and placebo groups, respectively, started or switched to another open-label statin, which interferes with the intention-to-treat results reported. Serious adverse events occurred in 2.7% of both the statin and placebo groups, with musculoskeletal, hepatobiliary and diabetes-related adverse events more common in those taking atorvastatin. Discontinuation was common, with "unwillingness" and "reason unknown" being twice as common as "side-effects" as the reason for discontinuation across both groups.



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Debate continues around the benefits and side-events of statins for primary prevention of cardiovascular disease in older adults. Although each 1 mmol/L reduction in LDL-cholesterol has been demonstrated to reduce the risk of major cardiovascular events by 22% in one year in those at high risk, data suggest reduced significance at higher ages, with *"less direct evidence of benefit among patients older than 75 years who do not already have evidence of occlusive vascular disease"* (Cholesterol Treatment Trialists' Collaboration, 2019), whereas other studies demonstrated no reduction in benefit in those aged 70 and over compared with those under 70 years (Andersson et al, 2023).

The present study

The STAREE (STAtins in Reducing Events in the Elderly) study was a double-blind, randomised, placebo-controlled trial conducted in general practice in Australia. Results were presented at the European Society of Cardiology congress in August 2026 and published in the *New England Journal of Medicine*.

Zoungas and colleagues treated 9971 community-dwelling adults aged 70 years and older (>40% aged over 75 years), with no history of cardiovascular disease, dementia or diabetes, with atorvastatin 40 mg or placebo. Mean participant age was 74.7 years, and just over half of the participants were women (51.9%). The two primary composite endpoints were:

- 4-point major adverse cardiovascular events (MACE): cardiovascular death, non-fatal myocardial infarction or stroke, or coronary revascularisation.
- Death from any cause, dementia or persistent physical disability (to assess the effects on disability-free survival).

Results

Results were only presented as "intention-to-treat"; thus, everyone initially enrolled was included in the results even if they discontinued atorvastatin or switched statins during the study or were in the placebo group and received open-label statins.

After a median of 5.9 years, treatment with atorvastatin 40 mg achieved around a 38% reduction in LDL-cholesterol (close to the 40% reduction recommended for primary prevention), compared with a 13% reduction in the placebo

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Table 1. Comparison with other statin studies recruiting older people (Zoungas et al, 2026).

Study	Trial drug	Mean age of participants	Cardiovascular benefit compared with STAREE
PROSPER (Shepherd et al, 2002)	Pravastatin 40 mg	75.4 years	Lower
JUPITER (Ridker et al, 2008)	Rosuvastatin 20 mg	66.0 years	Similar
HOPE-3 (Yusuf et al, 2016)	Rosuvastatin 10 mg	65.7 years	Similar
Cholesterol Treatment Triallists' Collaboration (2019) meta-analysis	Various	Groups aged 71–75 years and >75 years included	Lower

group (as nearly 20% of the placebo group received open-label statins during the study but remained in the group).

The risk of 4-point MACE was significantly reduced in atorvastatin recipients. A primary event occurred in:

- 297 participants in the atorvastatin group (10.9 events per 1000 person-years).
- 412 participants in the placebo group (15.5 events per 1000 person-years).
  - ➤ Hazard ratio (HR): 0.70 (95% confidence interval 0.61–0.82; *P*<0.001).

Subgroup analysis showed no significant benefit in women, or in participants with well-controlled blood pressure, lipids and weight at baseline.

The risk of the composite of death from any cause, dementia or persistent physical disability was not significantly reduced, with events occurring in:

- 637 atorvastatin recipients (21.6 events per 1000 person-years).
- 676 placebo recipients (23.0 events per 1000 person-years).
  - ➤ HR 0.94 (95% confidence interval 0.84–1.05; *P*=0.25).

Other secondary endpoints with significant reductions, statin versus no statin, included:

- Composite of cardiovascular death and myocardial infarction: 8.6 vs 11.7 events per 1000 person-years (HR 0.73).
- Myocardial infarction (fatal or non-fatal): 2.9 vs 5.9 events per 1000 person-years (HR 0.57).
- Coronary revascularisation: 4.0 vs 7.0 events per 1000 person-years (HR 0.57).

Risk of fatal or non-fatal stroke did not differ significantly between the groups.

Serious adverse events occurred in 2.7% of each group, with musculoskeletal, hepatobiliary and diabetes-related adverse events more common in those taking atorvastatin. Statin discontinuation was more common than in previous statin trials:

- "Participant unwilling" was the commonest reason given: 15.6% and 16.2% in the statin and placebo groups, respectively.
- "Adverse effects or unacceptable side-effects": 7.2% and 6.1%, respectively.

Nearly 10% of the statin group and almost 20% of the placebo group received open-label statins. For those in the treatment group, this meant their study drug was stopped and replaced with an alternative statin. "Per-protocol" results examining only those who continued the study drug were not reported.

Conclusions and comparisons

After 5.9 years, treatment with atorvastatin 40 mg achieved a 30% reduction in MACE events but subgroup analysis showed no significant benefit in women or participants with well-controlled blood pressure, lipids and BMI at baseline, although this was not highlighted in the paper. There was no significant reduction in the composite of all-cause death, dementia or persistent physical disability, or in the individual components of this, in any group.

Substantial numbers discontinued statin treatment during the study, reinforcing the need for support to encourage treatment persistence. There was significant open-label statin use in both groups: close to 10% in the atorvastatin group and almost 20% in the placebo group.

Study limitations included a largely white population, recruitment during the COVID pandemic and the fact that the trial findings cannot be generalised to older adults who are more frail or have more underlying conditions.

Comparison of these results with those of other statin studies recruiting older people is detailed in *Table 1*.

Implications for practice

We support an ageing population. Today, although lifespan is being maintained, albeit with impact from deprivation, health span is

decreasing, largely as a result of chronic disease and underlying obesity. Older people metabolise drugs differently to younger people, and many take several medications, increasing the risk of adverse reactions and drug interactions.

Some studies and guidelines encourage lipid-lowering therapy for primary prevention of cardiovascular events in people of all ages and risk levels, especially if they have type 2 diabetes, but guidance is inconsistent (see previous *Diabetes Distilled*). This study aimed to take a broader view, assessing not just the impact on cardiovascular disease but also whether statins would contribute to improved disability-free survival and independence in community-dwelling adults over the age of 70.

As with any clinical study, when considering whether the results should inform our decision-making, we need to consider the population recruited and those who achieved benefits, and how well they match the person sitting beside us. In this case, participants were community-dwelling adults aged at least 70 years with no history of cardiovascular disease, diabetes or dementia at baseline. This suggests a population who were independent and at the fitter end of the spectrum, albeit in an age range where such adverse outcomes are highly likely.

Education and shared decision-making regarding primary prevention with statins will help people decide whether the 30% reduction in cardiovascular benefits without any change in disease-free survival is important to them. It is, however, important to note the subgroup findings that women and those with well-controlled blood pressure, BMI and lipids did not gain significant cardiovascular benefits. For us as clinicians, these results add to our ability to provide a randomised controlled trial-informed answer to the question: "Should we recommend initiating statins for primary prevention in those over 70 years?"

Practice points

1. In this study, atorvastatin 40 mg offered significant benefit for primary prevention of cardiovascular disease in community-dwelling men aged over 70 years.
2. However, while the risk of major adverse cardiovascular events was reduced, overall disability-free survival rates were not significantly reduced compared with placebo.
3. Shared decision-making can help older people weigh up benefits versus side-effects for all drugs, including statins.
4. These findings cannot be generalised to older adults who are more frail or have more underlying conditions.

Andersson NW, Corn G, Dohlmann TL et al (2023) LDL-C reduction with lipid-lowering therapy for primary prevention of major vascular events among older individuals. *J Am Coll Cardiol* **82**: 1381–91

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Zoungas S, Wolfe R, Moran C et al; STAREE investigators (2026) Atorvastatin, cardiovascular events, and disability-free survival in older adults. *N Engl J Med* **395**: 1259–272

Atorvastatin, cardiovascular events, and disability-free survival in older adults

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