



## Medicines Evidence Commentary

commentary on important new evidence from Medicines Awareness Weekly

Published: December 2018

### Cardiovascular disease: statins for primary prevention in older people, with and without diabetes

A Spanish [observational study](#) assessed the benefit of starting statin therapy for primary prevention in participants aged 75 years and older. A statistically significant reduction in cardiovascular disease (CVD) and all-cause mortality was observed in participants aged 75-84 years with type 2 diabetes, but not in people without diabetes or older than this. NICE guidance and patient decision aids support shared decision-making between people and their health professional about whether to start taking a statin.

#### Overview and current advice

The NICE guideline on [lipid modification](#) recommends using the [QRISK2](#) risk assessment tool to assess risk in people up to and including 84 years of age and subsequently their need for lipid-modifying treatment. People aged 85 years or older should be considered at increased risk of CVD because of age alone, without using QRISK2, and particularly those people who smoke or have raised blood pressure. For these people, QRISK2 does not provide any additional information and could underestimate their risk of CVD, leading to inappropriate treatment, as outlined in the NICE quality standard on [cardiovascular risk assessment and lipid modification](#).

NICE also recommends that the decision whether to start statin therapy for primary or secondary prevention of CVD should be made after an informed discussion between the health professional and the person about the risks and benefits of statin treatment. This should take into account additional factors such as potential benefits from lifestyle modifications, informed patient preference, comorbidities, polypharmacy, general frailty and life expectancy. NICE has produced a [patient decision aid](#) to help a person considering statin therapy for primary prevention weigh up the possible advantages and disadvantages of the different options.

The NICE interactive flowchart on [CVD prevention](#) collates all related NICE guidance and associated products in a set of interactive topic-based diagrams. See the Clinical Knowledge Summary on [lipid modification - CVD prevention](#) for a general overview of prescribing considerations.

#### New evidence

A [retrospective cohort study](#) by [Ramos et al.](#) (2018) assessed the effectiveness of statins started for primary prevention of CVD in participants aged 75 years and older, using data from the Catalan primary care system ([SIDIAP](#)) covering 274 primary care practices. Data from 46,864 participants aged 75 years or older (mean age 77 years; 63% women) with at least 1 visit recorded in the 18 months before July 2006 was included. Participants with an existing clinical diagnosis of CVD, type 1

diabetes, considered to be frail and those who had received lipid-lowering treatments in the previous 18 months were excluded.

Between 2006 and 2007, statin therapy was initiated in 6,558 participants aged 75 to 84 years (of whom 1,756 had type 2 diabetes) and 944 participants aged 85 years and older (of whom 201 had type 2 diabetes). The mean systolic blood pressure was 137 to 141 mmHg, the mean total cholesterol was 5 to 6 mmol/L and few participants were smokers (12%). Most participants (78%) were started on [moderate intensity statins](#). The study outcomes were total mortality and fatal and nonfatal CVD (a composite of fatal and nonfatal coronary heart disease and stroke). Among participants aged 75 to 84 years who had type 2 diabetes, statin initiation was associated with a reduced risk of all-cause mortality (adjusted [hazard ratio](#) [adjHR] 0.84, 95% CI 0.75 to 0.94) and fatal and nonfatal CVD (adjHR 0.76, 95% CI 0.65 to 0.89). New statin initiation was not associated with a [statistically significant](#) reduction in all-cause mortality and the risk of fatal and nonfatal CVD in participants *without* type 2 diabetes aged 75 to 84 years (adjHR 0.98, 95% [confidence interval](#) [CI] 0.91 to 1.05; and 0.94, 95% CI 0.86 to 1.04, respectively).

In participants initiated on statins at the age of 85 years or older, there was no statistically significant reduction in risk of all-cause mortality or fatal and nonfatal CVD; neither in those without type 2 diabetes (adjHR 1.00, 95% CI 0.90 to 1.11 and 1.00, 95% CI 0.80 to 1.24, respectively) nor in those with type 2 diabetes (adjHR 1.05, 95% CI 0.86 to 1.28 and 0.82, 95% CI 0.53 to 1.26, respectively).

There was no statistically significant effect of statins on the risks of cancer, haemorrhagic stroke or diabetes. No cases of hepatotoxicity or myopathy were recorded among statin new-users.

## Commentary

### Commentary provided by NICE

With an increasing focus on reducing problematic polypharmacy, especially in older people, the findings of this study are certainly interesting. The [relative risk reduction](#) among people with diabetes aged 75 to 84 years (24%) is not out of line with that seen in the CARDS [randomised controlled trial](#) (RCT) of atorvastatin 10 mg daily for primary prevention in people with type 2 diabetes aged 40 to 75 years at study entry: 37%, 95% CI 17% to 52% ([Colhoun et al, 2004](#)). However, it does raise questions about the initiation of statins for primary prevention after the age of 75 years.

The number of people aged over 85 years with diabetes in whom statin therapy was started was small, possibly reducing the [power](#) of the study to detect a significant difference. For primary prevention of CVD, NICE recommends use of a [high intensity statin](#). The majority of people in this study were treated with a statin of [moderate intensity](#), possibly limiting the effectiveness of the intervention. The study also provides no information on adherence or continuing or discontinuing statins in older people who started them at a younger age.

It is important to consider whether the findings from this Spanish study can be translated to the UK population given the differences between the UK and Catalan population, exclusion of people with an overt risk factor for frailty and recruitment of people without CVD and relatively well controlled lipid levels and blood pressure which may have resulted in a healthy user survival bias.

This study emphasises that the choice to take a statin is a highly preference sensitive decision. We should continue to embed shared decision making into practice and ensure the potential benefits and risks of initiating statin therapy are discussed, enabling people to make informed decisions about their care. The authors calculate an annualised [number needed to treat](#) (NNT) of 306 for all-cause mortality among people aged 75 to 84 years with type 2 diabetes, when statins are initiated in this age group for primary prevention of CVD. Putting that another way, and assuming a constant hazard, for every

1000 such people who take a moderate intensity statin for 5 years, about 16 avoid dying from any cause as a result, and 984 live or die just as they would have done if they had not taken a statin.

## Study sponsorship

This project was supported by clinical research grants from the Ministerio de Salud, Spain's Ministry of Science and Innovation through the Carlos III Health Institute, co-financed with European Union ERDF funds (Network for Prevention and Health Promotion in primary Care), the Red de Investigación Cardiovascular and Miguel Servet Contract CP12/03287) and by the Departament de Salut, Generalitat de Catalunya, Agency for Management of University and Research Grants.

## References

Colhoun H, Betteridge D, Durrington P, et al (2004) [Primary prevention of cardiovascular disease with atorvastatin in type 2 diabetes in the Collaborative Atorvastatin Diabetes Study \(CARDS\): multicentre randomised placebo-controlled trial](#) Lancet 364: 685–96

Ramos R, Comas-Cufi M, Martí-Lluch et al. (2018) [Statins for primary prevention of cardiovascular events and mortality in old and very old adults with and without type 2 diabetes: retrospective cohort study](#). BMJ 2018; 362:k3359

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