



Medicines evidence commentary

commentary on important new evidence from medicines awareness weekly

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Cardiovascular effect of discontinuing statins for primary prevention in people aged 75 years

A cohort study from France found that previously adherent people who stopped taking statins for primary prevention of cardiovascular disease at about 75 years of age were more likely to be admitted to hospital with a cardiovascular (CV) event than those who kept taking their statin. This is to be expected given the known effects of statins on the risk of CV events. Although the reasons for people stopping their statin were not recorded, they may well have included multimorbidity and limited life expectancy or frailty. The NICE guideline on [multimorbidity](#) recommends that healthcare professionals should discuss with people in such circumstances whether they wish to continue treatments recommended in guidance on single health conditions that may offer them limited overall benefit. Although some may wish to continue, others may decide that doing so is not in line with their goals and informed preferences, and this choice should be respected.

Overview and current advice

The NICE guideline on [multimorbidity](#) notes that the management of risk factors for future disease can be a major treatment burden for people with multimorbidity; they should be carefully considered when optimising care. It recommends thinking carefully about the risks and benefits of individual treatments recommended in guidance for single health conditions. In particular, it recommends taking into account the possibility of lower overall benefit from continuing treatments that aim to offer prognostic benefit, particularly in people with limited life expectancy or frailty. The pros and cons of treatment should be discussed with the person alongside their preferences for care and whether they wish to continue such treatments.

An American [randomised controlled trial](#) (RCT) found that discontinuing statin treatment in people with advanced, life-limiting illness may not adversely affect clinical outcomes and may improve some important patient orientated outcomes, such as quality of life and reducing overall medication burden. This study was discussed in a NICE medicines evidence commentary on [medicines optimisation: discontinuing statin therapy in palliative care](#).

The NICE pathway on [cardiovascular disease prevention](#) brings together everything NICE has said on cardiovascular disease prevention in an interactive flowchart. The NICE key therapeutic topic on [lipid modifying drugs](#) summarises the evidence base and was updated in September 2019.

New evidence

A large French retrospective [cohort study](#) of 120,173 people, who turned 75 between 2012 and 2014, used data derived from the French national health insurance claims database to examine the association between discontinuing statin therapy and hospitalisations for cardiovascular events ([Giral et al. 2019](#)). Participants had no history of cardiovascular disease and had been adherent to statins for at least the previous 2 years, but no other inclusion or exclusion criteria were applied. This is in contrast to the American RCT discussed above, which included only people with clinician-estimated life expectancy of 1 year or less. Discontinuation was defined as not having a statin prescription for 3 consecutive months. The cohort was divided into those who discontinued statin treatment (14.3%) and those who continued statin treatment (85.7%). The reasons for stopping statin treatment were not recorded, but factors associated with discontinuing statin treatment were female gender and diagnoses of dementia or cancer.

During the mean 2.4-year follow-up (maximum 4 years), 5,396 people were admitted to hospital for a cardiovascular event. After adjustment for confounding factors, discontinuing statin treatment was associated with a [statistically significantly](#) increased risk of admission for a cardiovascular event ([hazard ratio](#) [HR] 1.33, 95 % [confidence interval](#) [CI] 1.18 to 1.50). At 4 years of follow-up, the adjusted cumulative incidence rate of admissions for cardiovascular events was 10.1% (95% CI 8.8 to 11.3%) in people who had discontinued statins and 7.6% (95% CI 7.3 to 7.9%) in people who continued statins.

Subgroup analyses of the baseline characteristics, gender, antihypertensive use and comorbidity all found significant associations of discontinuing statin treatment with cardiovascular outcomes after adjustment for confounding. However, in people with diabetes at baseline there was no significant association between discontinuing statin treatment and cardiovascular event admissions (adjusted HR 1.14, 95% CI 0.89 to 1.44).

This [observational study](#) may be subject to many confounding factors. Although considerable effort was made to control for confounding, some residual confounding may remain. For instance, the reason for stopping statins was not recorded and it was not possible to take this fully into account. It is of note that stopping statins did not show a statistically significant effect among people with diabetes (who, generally speaking, are at higher cardiovascular risk and so would have more to gain from statin therapy). The study was based in France, where prescribing practices, lifestyle and environmental factors may differ from the UK. Furthermore, the study was exclusive to people aged 75 years therefore the findings may not be applicable to other age groups.

Commentary

Commentary provided by Professor Richard Lehman, Professor of the Shared Understanding of Medicine, University of Birmingham

This study suggests that French people who discontinue statins at the age of 75 are about a third more likely to get cardiovascular events and die sooner. This shouldn't come as a surprise. For more than a decade, we've known that statins reduce cardiovascular events by about the same proportion (roughly 20–30%) regardless of initial risk.

Mortality benefit is usually assumed to be the best kind of benefit. But there's a trade-off to be made, especially when it comes to medicines that reduce the risk of future disease. Perhaps the biggest question raised by this paper is why almost 15% of people who had previously been very diligent in taking their statins (or at least getting prescriptions) stopped taking them – was it a matter of choice in some, and what were the other reasons? Some older people may feel – rightly or wrongly – that their statins are contributing to the muscle aches and weakness of old age. Others might want to reduce the number of medicines they are taking. For yet others, avoiding a cardiovascular death – instead of

death from some other cause, or some long term mental or physical disability – is no longer such a priority.

This observational study triangulates well with the existing evidence about statins, but also raises issues about what we are trying to accomplish with these drugs. They give people slightly better odds in the lottery of life, by sparing some from myocardial damage or stroke. We may feel that this is a population benefit. The offer should be there, but we shouldn't be surprised if some people don't take it up.

Declaration of interests:

Professor Richard Lehman declared no interests.

Study sponsorship

None declared.

References

Giral P, Neumann A, Weill A et al. (2019) [Cardiovascular effect of discontinuing statins for primary prevention at the age of 75 years: a nationwide population-based cohort study in France](#). European Heart Journal 0: 1-10

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