An American randomised controlled trial found that discontinuing statin therapy in people with advanced, life-limiting illness may not adversely affect clinical outcomes and indeed may improve some important patient orientated outcomes, such as quality of life and reducing overall medication burden. Despite some limitations, this study supports the NICE medicines optimisation guideline that recommends shared decision making and an individualised approach to treatment choices.

Overview and current advice

Statins are prescribed to reduce the risk of cardiovascular disease; in most people there is no anticipation of symptomatic benefit. The NICE guideline on lipid modification recommends that the decision whether to start statin therapy should be made after an informed discussion between the clinician and the person about the risks and benefits of statin treatment, taking into account additional factors such as informed patient preference, comorbidities, polypharmacy, general frailty and life expectancy. However, there is no specific advice on the timing, safety or risks of discontinuing statin therapy other than for intolerance.

People with advanced, life-limiting illness may require an increasing number of medicines. In this situation, consideration could be given to the continued appropriateness of medicines previously prescribed for preventative purposes; the General Medical Council provide guidance on assessing the overall benefit and risks of treatment options towards the end life. The NICE guideline on medicines optimisation offers best practice advice on the care of all people who are using medicines and also those who are receiving suboptimal benefit from medicines. It discusses the importance of shared decision making and an individualised approach to treatment choices including how safe the medicines are, how well they work for the person and how appropriate they are. The Academy of Medical Royal Colleges, which represents all medical royal colleges in the UK, is also launching a Choosing Wisely programme in collaboration with other clinical, patient, and NHS organisations with the aim of changing clinical practice with regard to interventions or tests of questionable value. This programme, developed in the US and Canada (www.choosingwisely.org) and described by Malhotra et al1 rebalances discussions between doctors and their patients about the potential risks and benefits of tests and interventions, including the acknowledgement that sometimes, doing nothing might be the favourable option.
New evidence

An American randomised controlled trial (RCT) considered the clinical impact and safety of discontinuing statins in people with advanced, life-limiting illness. The multicentre, parallel-group, unblinded, pragmatic trial recruited 381 adults receiving a statin for 3 months or more for primary or secondary prevention of cardiovascular disease from 15 palliative care research sites in the USA. Participants had advanced, life-limiting illness (clinician estimated life expectancy of 1 month to 1 year and recent deterioration in functional status), a mean age of 74 years and were taking a number of medicines other than statins (mean 11.6). Approximately half the participants (49%) had a diagnosis of cancer, 58% had cardiovascular disease and 69% had received statins for more than 5 years. People were excluded if, in the treating physician’s opinion, they had active cardiovascular disease or were at sufficient risk of active cardiovascular disease to warrant continuing statin therapy.

Participants were randomised to either discontinuing (n=189) or continuing (n=192) statin therapy and were monitored monthly for up to 1 year. Allocation was concealed and analysis was by intention-to-treat. Median follow up was 18 weeks (median of 10 weeks for people who died during the study). The primary outcome (which was changed part-way through the trial) was the proportion of deaths within 60 days of enrolment. Discontinuing statin therapy was considered to be non-inferior to continuing therapy if the upper limit of the 90% confidence interval (CI) for the difference between groups in this proportion was less than 5%. Secondary outcomes focused on safety concerns and person-centred outcomes, and included survival, time to first cardiovascular event, quality of life (scored using a validated participant questionnaire), symptoms (measured using a validated assessment scale), number of non-statin medications and statin-related adverse effects.

The proportion of people who died within 60 days was not statistically significantly different between the groups (23.8% in the discontinuation group compared with 20.3% in the continuation group, 90% CI 3.5% to 10.5%, p=0.36). However, non-inferiority was not achieved because the upper CI for the difference was greater than the pre-specified non-inferiority margin of 5%. There was no statistically significant difference between the groups in time to death (p=0.60; mean survival 30 weeks in total study population), time to first cardiovascular-related event (p=0.64; only 6.3% of the total study population had such an event), physical symptoms (p=0.18) or statin-related adverse events (p=0.71). However, quality of life was statistically significantly higher in the discontinuing statin therapy group (mean 7.11 compared with mean 6.85 on a scale of 0 to 10, p=0.04). The total number of non-statin medications was also statistically significantly lower in the discontinuation group (10.1 compared with 10.8, p=0.03).

The authors highlight the strengths of this study as being its pragmatic design involving a population with a broad range of life-limiting diagnoses from multiple settings, making it generalisable to ‘real world’ practice. Limitations include the unblinded design of the RCT, the change of primary end point part-way through the trial and more people in the discontinuation group being cognitively impaired (27% compared with 17%, p=0.02). People were also only included in the RCT if they and their clinician were willing to discontinue statins. This may have biased the results as people with a similar prognosis in ‘real world’ clinical practice may not be agreeable to discontinuation. The study was not sufficiently powered for survival and involved a relatively small number of participants which could also have affected the validity of the results.

Commentary

Commentary provided by Medicines and Prescribing Centre

This study provides comparative RCT data for discontinuing or continuing statin therapy in people who were not expected to live longer than 1 year. The investigators selected this population because
Evidence from large clinical trials has shown that benefits of statins are seen at the earliest after 2 years of therapy. Despite the limitations highlighted, the findings of this study suggest that stopping statins at the end of life may not be harmful and indeed may improve some important patient orientated outcomes, such as quality of life and reducing overall medication burden. However, the overall differences between the 2 treatment groups are small and the clinical significance is unclear. Previous validation of the McGill quality of life (MQOL) questionnaire suggests that a difference of 2.6 in MQOL total score is similar to changing a bad day into a good day; a difference of 1.5 is similar to changing a bad day into an average day and a difference of 1.1 is similar to the difference between an average and a good day. The average MQOL difference (discontinuation or continuation of statin) in this study is only 0.26, but on an individual basis this difference may be important.

This study supports an individualised approach to stopping or continuing preventative treatment in people with limited life expectancy. The accompanying commentary by Holmes et al suggests a particular strength of the study is the inclusion of people for whom clinicians ‘would not be surprised if they died within the next year’ which is a simple measure to understand and replicate. As Holmes et al point out, people’s preferences at the end of life are particularly relevant and in this study many eligible people initially selected declined to participate. A barrier to initiating those difficult conversations with people near the end of life is appropriate timing of the intervention. Holmes et al suggest that use of the ‘surprise’ question is a pragmatic approach to this clinical problem.

This study is discussed in an accompanying special communication article on inappropriate polypharmacy and discontinuation of drug therapy in older people and in palliative care settings.

**Study sponsorship**

This RCT was funded by a grant from the US National Institute of Nursing Research and was further supported by the US Veterans Affairs Health Care System.

**References**


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