Statins: modelling study suggests lifespan benefits are not evenly distributed and that people may not choose the mathematically optimal option for benefit

A 3-part study has found that, according to a model based on UK population data, starting preventive therapy in people at risk of cardiovascular disease produces greater mean gain in lifespan in people aged 50–54 years than in older people (although quality of life was not modelled). It also suggests that the actual lifespan gain is not evenly distributed: most people gain no lifespan whereas a few gain a great deal, with a greater proportion of people benefiting among those at greater baseline risk. Finally, members of the public were asked to choose between the option of a 1 year gain in healthy lifespan for sure or a certain percentage chance (2%, 5%, 10%, 20% or 50%) to gain 10 years healthy lifespan. Although in each comparison the majority chose the option with the greatest mean gain, substantial proportions of people preferred the ‘sure thing’ over percentage options that offered a greater mean gain. This study should help to inform shared decision-making and elicitation of individual preferences, in terms of communicating risk in practice and in guideline development.

Overview and current advice

In its guideline on patient experience in adult NHS services, NICE recommends giving people both information and the support they need to make use of it so as to promote their active participation in care and self-management. This includes discussing the risks, benefits and consequences of the investigation or treatment options, clarifying what the person hopes these options will achieve and discussing any misconceptions with them. Similarly, in its guidance on supporting medicines adherence, NICE recommends involving and supporting people in decisions about medicines. For example, in its guidance on lipid modification, NICE recommends that any decision to initiate statin therapy should follow a discussion with the person about the likely benefits and possible harms of this approach. To support such discussions, NICE has produced a patient decision aid relating to statins for primary prevention of cardiovascular disease.

The decision aid looks at the effects of statins on cardiovascular events but not the risk of death from any cause. People’s perspectives on that question were examined in a UK study, discussed in a previous medicines evidence commentary. Participants were asked to imagine an ‘ideal’ tablet that had no side-effects, was available at a negligible cost, needed no prescription or medical supervision and could be started or stopped at any point without problem. The authors ascertained the minimum benefit, in terms of increase in lifespan, which people felt they would have to see to offset the inconvenience of taking such a tablet every day. There was a wide variation in results. Although about
34% participants would take the medicine if it would increase their lifespan by less than 1 month, about 1 in 8 people (12%) would take the medicine only if it would increase their lifespan by 10 years or more. Similar results were obtained when the results were stratified by participants’ age or sex.1

New evidence

In a 3-component study, researchers first used modelling to estimate the average effect on life expectancy (mean lifespan gain) associated with the use of a statin, depending on a person’s age, sex, systolic blood pressure, total cholesterol and smoking status.2 The modelling used data for England and Wales from the Office of National Statistics and the QRESEARCH database. The model assumed a 30% relative reduction in risk of cardiovascular (but not non-cardiovascular) mortality as a result of taking a statin. They found that, although baseline risk increases with age, this does not translate into a greater mean lifespan gain with increased age at initiation of intervention. In fact, for any combination of cardiovascular risk factors, the potential lifespan gain from initiation of intervention decreases with increasing age of initiation. For example, among non-smoking men without diabetes whose total cholesterol is 5 mmol/l and systolic blood pressure is 140 mmHg, mean lifespan gain from starting treatment at age 50-54 years is 7.4 months. For men with the same cardiovascular profile starting therapy at age 80-84 years, mean lifespan gain is 4.2 months. This is explained by the risk of death from non-cardiovascular causes increasing with age.

Secondly, the researchers modelled the distribution of lifespan gain among individuals at different levels of cardiovascular risk, since, by the play of chance, some people will gain more than average and some will gain less. The researchers estimated that benefit was not distributed in a classical normal distribution. The great majority of people gain no extra lifespan but in the minority that do gain, their increase is much more than the group average increase in lifespan. For example, for a 50-year-old, non-smoking man without diabetes with average cholesterol and blood pressure, mean life expectancy gain is 7 months after starting preventative therapy. However, among 100 such individuals, 93 gain no extra lifespan, but the remaining 7 men gain a mean of 99 months (8.25 years). The modelling found that among those who gain lifespan, the amount gained is very similar in groups with higher and lower baseline risk. What differs greatly between these groups is the proportion of people who benefit, with more people in the higher risk group benefiting thus increasing the mean lifespan gain.

It is important to note that this is not a gain in lifespan in addition to the average life expectancy of the group, but a gain over what the modelling suggested would have happened to that individual person if they had not taken the statin. The model is an attempt to examine the question ‘how much longer would this individual [modelled] person have lived if they had avoided the fatal cardiovascular event that they would otherwise have had but which, in their case, was prevented by statin therapy?’

Finally, the researchers asked 396 members of the general public in London, Leicester and Newcastle for their preference for a certainty of a 1-year gain in healthy lifespan or a percentage chance of a 10-year gain in healthy lifespan. The mean age of participants was 40 years, 55% were male and 4% had had a myocardial infarction or a stroke. Each respondent was randomly allocated to 1 of 5 versions of the survey questions in which the percentage chances of the larger gain were 2%, 5%, 10%, 20% and 50%.

In classical economic terms, the expected utility of these probabilities of a 10-year gain in lifespan are 0.2 years, 0.5 years, 1 year, 2 years and 5 years respectively, hence the ‘sure thing’ of 1 year extra lifespan is a better prospect than the 2% or 5% chances, and the 20% or 50% chances are better bets than the sure thing. Of course, no individual person actually gains 0.2, 0.5, 2 or 5 years – that is simply the average gain. Another way of presenting, for example, a 20% chance would be to say ‘out of 100 possible futures for you, 20 of them involve you living 10 years longer than you would have done
otherwise, and 80 of them involve you living no longer than you would have done otherwise; but we can’t say which of those possible futures will actually come to pass.’

Actual numbers are not reported in the paper, but a graph shows that in every pair of options, most people chose the option with the greater expected utility. That is, more people chose the sure thing than the 2%, 5% and 10% chances, and more people chose the 20% and 50% chances than the sure thing. However, the graph suggests that about 40% of people chose the sure thing instead of the 20% chance and about 15% of people chose the sure thing instead of the 50% chance. The precise wording of the questions and the way the options were presented to participants are not reported and so the extent to which mathematical aptitude (the ability to calculate expected mean benefit) influenced people’s choices is not clear.

The authors discuss some of the limitations of their study. They used data from large meta-analyses of statins and, as is usual, assumed that risk reduction was constant for all baseline levels of risk and all time periods. They also discuss the inevitable limitations of the assumptions about life expectancy inherent in any modelling exercise. An accompanying editorial also notes that the model treats the risks of cardiovascular and non-cardiovascular as independent of each other, when this is not the case3. This is linked with another limitation: the study authors used official statistical data on causes of death drawn largely from death certificates, in which a proximal cause of death is designated in section 1 of the certificate and other contributing diseases are designated in section 2, but only the section 1 cause is usually reported as the cause of death. The editorialist points out that although the death of a person with, for example, angina might be statistically coded as being primarily cardiovascular or non-cardiovascular depending on the circumstances, the reality is that such a person dies from the accumulated physiological burden of multiple disease processes rather than the linear progression of each pathology individually. The model also does not consider time without disability, which is important both for quality of life and also because of the effect of disability itself on risk of death. Nevertheless, the editorialist concludes that these limitations are unlikely to change the general direction of the study findings.

Commentary

Commentary provided by Dr Richard Lehman, Senior advisory fellow in primary care, Cochrane UK, Oxford

Here is a richly innovative paper which challenges us to think differently about how we conceptualise and communicate risk with individuals. This lies at the heart of what clinicians need to do in order to share decisions with patients. It also lies at the heart of how guideline developers need to approach the evidence in every clinical area and for each intervention, because the central message of this study is that one size seldom fits all.

Initially the authors looked at the evidence for the overall benefit of statins for the prevention of cardiovascular disease. This is unusually well established from numerous well-conducted randomised trials, and is generally summarised as the number-needed-to-treat. But then they looked at the distribution of this benefit within the trial populations, and found that it was very unevenly distributed. And since the key events are massive and binary, this really matters – you either die, have a heart attack or a stroke, or you don’t. We can’t say that for every patient we give a statin, there will be some degree of benefit. For the great majority there will be none at all, while for a few it will prolong life for years. This is illustrated by some neat infographics showing that the NNT is not evenly spread out like honey melting on buttered toast. It is more like a mountain range at the edge of a wide plain.

We know that real people are not rational gamblers, carefully weighing the numbers and the odds and all reaching the same conclusion. Much depends on the way the decision is presented, and even more depends on whether it is a small benefit evenly distributed or a massive benefit for a few. The National
Lottery makes almost every contributor a few pence poorer and a few contributors very rich. The statin situation is similar, except in a negative sense. While you are alive, you can never know if you are a winner.

The authors carried out a brief survey of how people react to this way of conceptualising risk. Again, the distribution of responses was far from uniform. When we actually allow free-living individuals to make their own decisions, they will never turn out exactly the way we predict, or necessarily the way we want. But this is the way we have to operate in the real world. Millions of unopened packets of medication attest to the fact that people already often decide for themselves.

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**References**


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