Statins need no introduction. Although almost unknown 20 years ago, these drugs now are taken by about 1 billion people worldwide. They are popular for good reason: They are easy to take; have minimal side effects; are easy on the wallet; have a measurable biochemical effect; and, importantly, have outstanding clinical benefits for those who take them.

Statins can reduce the risk for cardiovascular (CV) events by 30% or more. They also work across the board—in people with diabetes as well as those without. One question that has remained, however, is whether statin treatment is appropriate in the young diabetes patient or in those at low CV risk.

To address this question, two eminent speakers were invited to debate the issue at the recent annual meeting of the European Association for the Study of Diabetes. The title of the debate was "Statins for All?"[1]

Dr Sattar: Not for the Drinking Water

Dr Naveed Sattar from Glasgow made the unusual move of opening his arguments for the "no" position with a sweeping statement in favor of statins. For those who are not familiar with Dr Sattar's work, it was his landmark paper in the Lancet that alerted the medical community to the adverse diabetogenic effects of statins.[2]

In this debate, however, Dr Sattar wanted to deliberately part with his past image, so he was clear and unequivocal about the clinical importance of statins. He drew attention to a glowing new report on the safety of statins[3] and then reminded everyone of the "fantastic scientific evidence" behind statins as successful agents in the prevention of CV disease.[4-7]

Dr Sattar seemed committed to the statins cause, but he also wanted to draw a line of caution: "Statins are not for the water."

As clinicians, we have excellent clinical guidelines to follow, and we should not venture outside current recommendations, Dr Sattar said. He was not willing to give statins the benefit of the doubt in patients who are at low CV risk. Serious side effects, such as myositis and rhabdomyolysis, should not be discounted just because they are rare or uncommon.

"They do occur," he insisted. Statin-induced muscle pain and discomfort are commonplace, real, and debilitating for those who suffer from it. However, he was at a loss to explain the findings of a recent report exonerating statins in most of the cases of statin intolerance.[8]

Dr Sattar provided a list of patients for whom he said he would not prescribe statin therapy. High on that list was patients with diabetes who are younger than 40 years (unless, of course, they had CV risk factors or diabetic complications). The benefits of using statins in such cases were practically "negligible."

Dr Sattar gave an example of an otherwise healthy 36-year-old patient with newly diagnosed type 2 diabetes. The calculated benefit of treatment with statins instead of waiting until the patient reached 40 years of age amounted to an extra few months of life expectancy.

The second group on Dr Sattar's list was all patients with prediabetes, even if they had coexistent CV risk factors. Statins could tip the individual into a full-blown diabetes state, with all the known repercussions (emotional, medical, and financial) associated with a formal diagnosis of diabetes. Dr Sattar argued that in the long run, it would be better to pursue lifestyle modification than use statins in people with prediabetes.

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Elderly persons made up the third group whom Dr Sattar would exempt from statin therapy. The older patients become (> 75 years), the more likely they are to die of something other than CV disease, he said. Dr Sattar was also categorical about...
patients in heart failure and those on renal dialysis treatment, saying that "statins simply do not work" in such cases.

To complete his list of "no statins," Dr Sattar added terminally ill persons and those with dementia.

The guidelines got it absolutely right, he concluded: Let's not pick on the very old or the young. Let's focus instead on the mainstream patient population, using statins judiciously for the right person at the right time.

Ray: A Remedy for All Seasons

When it was his turn, Dr Kausic Ray from London wasted no time in launching a mock counterattack on Dr Sattar. How can we trust someone who has done the greatest damage to the name and reputation of statins to become a fan of these agents in today's debate? he asked, receiving chuckles from the crowd.

Dr Ray then turned more serious, emphasizing that most patients who experience CV events are not in the highest-risk category, but rather in the low- and intermediate-risk categories. So, why not simply lower the risk threshold for intervention in order to reach the majority of patients who are at risk for CV disease?

This should make sense to anyone, given the safety record of statins and the substantial CV benefits expected from statin treatment, he said. Dr Ray gave examples of several international societies that have lowered the 10-year CV risk threshold recommended for intervention.

Dr Ray's next point was that the risk calculation method itself is imprecise and sometimes unhelpful. He gave an example of a 25-year-old man with elevated cholesterol in whom CV risk was apparently impossible to calculate. Should we leave such a young person without treatment, given that atherosclerosis is a process that begins at birth and continues throughout life?

To further his argument on the need to intervene early, Dr Ray gave another example of a 35-year-old woman who was not diabetic but who smoked and had hypertension and elevated cholesterol. Without intervention, such a patient would probably live until she is 71 years of age before experiencing a heart attack or stroke. However, if all risk factors were treated, that age would increase to 85 years, giving the patient an extra 14 years of life without a major CV event.

Dr Ray explained that it was not age so much as the number of years of exposure to a risk factor that mattered to CV outcome. He showed evidence of a continuous relationship over time between such risk factors as hypertension and CV death.

Unfortunately, no lipid trials have been done specifically in young people, so we have to settle for evidence drawn from randomized "experiments of nature." Observational research conducted in people with genetic variants of low-density lipoprotein (LDL) cholesterol showed that the risk for coronary heart disease is substantially lower in those exposed to lower LDL cholesterol beginning early in life than those who receive cholesterol-lowering therapies later in life.[9]

Placebo-controlled trials have shown muscle symptoms to be nearly as common in the placebo-treated patients.

Dr Ray then turned his attention to people with diabetes. He listed a series of intervention trials that had shown benefits of statins in the general diabetes population.[7,10] However, no statin trials were done specifically in diabetes patients younger than 40 years or in those with type 1 diabetes. The best evidence at hand is a pooled meta-analysis of patients with type 1 diabetes that showed similar CV benefits for both types of diabetes.[11]

Dr Ray believes that statins are safe. Placebo-controlled trials have shown muscle symptoms to be nearly as common in placebo-treated patients.[12] He presented excerpts from a recent publication reiterating the safety profile of statins and the potential dangers to patients if treatment is stopped prematurely.[3]

Dr Ray concurred with Dr Sattar's view on the lack of benefits in people with severe heart failure and those on renal dialysis treatment. He also preferred to avoid statins in elderly patients but did not completely discount the option, especially if they are fit and interested. "If they get symptoms, they can always stop the drug," he said.

This Observer's Thoughts

I walked into the debate session hoping to have at least one question settled in my own mind, which was whether or not to offer statin therapy to diabetes patients younger than 40 years. There have been many moments at the clinic when I have paused and pondered what to do in such a case.

I walked out of the hall much closer to an answer, and with a whole lot of information I did not know before.

First, I did not realize that statins had caused so much controversy and debate in the United Kingdom. Both experts thought
that the media were to blame for “getting it wrong.” A bitter scientific feud continues to escalate.\[^{13}\]

Unfortunately, when professionals bicker or medical facts become openly contested, it is usually the patients who end up suffering. I believe that the true winner of this saga will not be the one who gets to have the last word, but the one who is first to put an end to the story.

This lively debate was as entertaining in style as it was scientific. The two speakers could not be more different in terms of spoken accents and styles of presentation. For those who are familiar with British social norms and politics, the debate seemed to me like a showdown between a dogged trade union leader and a consummate local politician.

Overall, I liked Dr Sattar’s list of patients for whom it might be unwise or unrewarding to prescribe statin therapy. However, I struggled with his nonlenient stance on young diabetes patients. To be fair, he was absolutely right about the absence of scientific data to support the use of statins in this group. However, the reality on the ground might be different.

Clinically, we are seeing an increasing number of patients with type 2 developing coronary heart disease in their 30s and 40s. In one study, 13% of young patients with type 2 diabetes developed CV disease before the age of 40 years.\[^{14}\] Obviously, urgent studies are needed in the young type 2 diabetes population.

Dr Sattar made a very valid point when he called for aggressive treatment of patients with moderate or high CV risk. Unlike what happens in clinical trials, adherence to statin therapy is a problem in the real world.\[^{15}\]

Dr Ray adopted a generally commonsense approach: If a drug works so well under most circumstances, if it prevents serious complications, and if by most accounts it represents a safe and cost-effective intervention, then why not offer such a successful therapy to the remaining eligible patients? It is a very appealing argument, but one that is built largely around circumstantial evidence.

The example of the 35-year-old nondiabetic woman with multiple CV risk factors was an interesting one. If we were to recalculate the benefit related to the use of a statin alone, the patient would have lived until 75 years of age (instead of 71 years without a statin) before experiencing her first heart attack or stroke. Would it be worthwhile for this young woman to start taking statin therapy every night for the next 40 years to delay the onset of a CV event only by a few years late in her life?

Incidentally, it was very strange to watch each speaker use the risk calculator method to shrink or expand someone else’s lifespan to suit his point of view. As someone in the audience later pointed out, risk calculation might not be the best or most accurate way to estimate quality-of-life benefits.

Finally, I was hoping to pick up a few hints from the distinguished chairman of the debate, Dr John Betteridge, about his personal views on the subject. Unfortunately, he remained absolutely neutral throughout the debate. Nor did he call on the audience to take a vote at the end of the session.

With no one else to turn to for a second opinion, I struck up a conversation with a member of the audience as we all marched outside. As it turned out, this woman had exactly the same risk profile as the woman described by Dr Ray. In fact, she was attending the debate precisely because she wanted to make up her mind about whether to take statin therapy or not.

I eagerly asked for her verdict on the debate. “I found Dr Ray’s argument slightly more convincing, but I’m still not ready to take a statin,” she replied.

Obviously, both our speakers had won.

Let's Hear Your Verdict

Assuming that the patient has a neutral opinion on statins, would you consider prescribing statin therapy to a relatively healthy 35-year-old patient with type 2 diabetes?

- Yes
- No
If your patient on statin therapy is experiencing muscle pain, would you:

- Recommend discontinuation of statin medication
- Convince the patient that statins are an unlikely cause of symptoms and encourage continuation of treatment, on the basis of recently proposed recommendations\textsuperscript{16}

References


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