

# Let them eat cake, butter, cream ...(cholesterol and heart disease)

by Jerome Burne

*For decades the advice has been to cut cholesterol and protect your heart. Now some doctors think it makes no difference*

There is almost no connection between the amount of cholesterol in your blood and your risk of a heart attack. Not only that, if you don't already have heart disease, you probably won't live any longer if you bring your cholesterol level down. Finally, statins, the cholesterol-reducing drugs we are all being urged to take, are of little use to women.

These are just a few of the highly controversial claims being made by a loose network of researchers, known collectively as the Cholesterol Skeptics, who are mounting a direct challenge to one of the cornerstones of public health policy - the notion that reducing cholesterol saves lives at risk from heart disease. Any doctor will tell you that if your cholesterol level is higher than five (millimoles per litre) that you should bring it down, probably through taking one of the statins family.

According to the Cholesterol Skeptics, however, this will not only involve the NHS in a massively increased drug bill when many cheaper options are available, but will only benefit men who already have a heart condition. Can such views, which fly so directly in the face of the entire medical establishment, have any basis in fact?

The proponents certainly make some challenging points. For instance, they say that there is precious little evidence that a longer life results for those millions of people who for years have dutifully taken their drugs and endured cholesterol-reducing diets. In fact, a number of trials have found that, even though the number of deaths from heart disease does fall when cholesterol is reduced by a range of means among patients in primary care - that is, at GP level - there is often an increase in the overall death rate from other causes.

Writing in the British Medical Journal (BMJ) at the end of last year, for instance, Rebecca Warburton, a professor at the University of Victoria in Canada, reviewed studies of statins and concluded: "Statins in primary prevention have not consistently reduced the incidence of myocardial infarction [heart attack] or stroke. Other studies have even found that over the age of 50, reducing cholesterol increases the death rate.

The notion that cholesterol is linked to heart disease goes back to the middle of last century, along with the idea of bringing cholesterol levels down with a low-fat diet to protect the heart. But both of these ideas have been strongly challenged. For example, plenty of studies show that only 50% of people who develop heart problems have high cholesterol, while a study in the BMJ in 2001 found no link between changing fat in the diet and heart disease.

"At a global level the link with cholesterol and heart disease is far more tenuous than is generally supposed," says Malcolm Kendrick, a GP from Cheshire who is the most active Skeptic in Britain. "For instance, in Russia at the moment, heart attack rates are rising dramatically but their cholesterol levels are the reverse of what we see in the US and the UK. They often have high levels of the so-called "good" HDL cholesterol and low levels of the "bad" LDL, but they still keel over from heart disease."

Even in the west the link is pretty thin according to Joel Kauffman, a professor at University of the Sciences in Philadelphia. A review he did of statin use last year pointed out that what does correlate with high cholesterol is age, a major factor in heart disease. "When you correct for age," he concluded "there is almost no correlation between high cholesterol and heart disease."

This challenge comes at a time when the government, the medical profession and the pharmaceutical industry are united in their approval of cholesterol-reducing drugs. Government figures out last week, for instance, show that heart attack deaths are declining and part of the credit for this is given to statins.

This month the New England Journal of Medicine is due to publish the results of a large trial reporting that the heart patients who reduced their cholesterol down as far as two, had a 16% drop in their risk of experiencing such "vascular events" as heart attacks and strokes. One of the cholesterol-reducing drugs, Lipitor, is among the best-selling prescription drugs in the world with sales worth \$16bn. The message from this trial is likely to be that when it comes to cholesterol "you can't go too low".

So what are the Skeptics basing their apparently highly idiosyncratic challenge on? At this point it is worth making clear the difference between primary care - your GP prescribing statins because he considers you have a raised risk of heart disease - and secondary care, which you get after a heart attack in hopes of preventing another one. Even the Skeptics generally agree that the studies show that taking statins after you have obviously got heart disease can reduce your chances of a further attack.

"But the fact that bringing down cholesterol can help some male heart patients," says Kendrick "doesn't mean it's going to protect otherwise healthy people whose cholesterol is over five. Since the average level in the UK is 5.7, that is an awful lot of people."

But what about trials showing that statins reduce the risk of heart attacks and strokes by a quarter among healthy volunteers? That sounds impressive. But how impressive, say the Skeptics, depends on how you work out the percentages. Heart attacks among healthy people are quite rare, so the actual percentage of people having a heart attack while on statins is just 3% compared to 4% on a placebo. That is indeed a drop of 25% but it is also a mere 1% fewer heart attacks over five years, which is not quite so wonderful. In Sweden official advice is to reserve statins largely for secondary care.

If pushed, experts in favour of aggressive cholesterol reduction may well admit that the value to women is less clear. That is because, although women tend to have higher levels through life, they develop heart disease 15 to 20 years later. An increasing number of doctors are putting post-menopausal women on statins to protect their hearts now that HRT has been discredited. Is this wise?

A resounding "no" was the answer from an analysis of five statin trials conducted by a team of researchers at the University of British Columbia (UBC) in Canada and published last year. Stressing that only 28% of the participants were women, the team concluded: "The results do not support the use of statins by women without heart disease."

The UBC group also raised new queries about side effects. Statins are generally described as safe and well tolerated. But the same report concluded that although patients on statins had a 1.4% lower rate of heart attacks, this was cancelled out by a 1.8% rate of "serious adverse events associated with the drug", including cancer. That, they say, is almost

certainly an underestimate since only two of the trials provided details of any serious side effects. The researchers said they had asked the drug producers for the missing data but received no reply.

To an outsider what is curious about this debate is that both sides are using the same data; much of the disagreement is based on how you interpret it. But that is not all that is going on. Two recent developments have given a big impetus to the Skeptics. The first is the huge surge in the popularity of the Atkins diet. So far the results seem to show that eating a diet high in fat doesn't automatically result in a rise in cholesterol. This strikes at the roots of the cholesterol hypothesis," says Kendrick - though the jury is still out on the long-term effects of an Atkins-style diet and bigger trials are ongoing. Another aspect of the Atkins argument is that a diet high in carbohydrates, especially refined carbohydrates such as sugar, damages arteries in the long run.

A key factor in developing heart disease, say the Skeptics, is inflammation. This is the defensive reaction produced by the body when it feels under attack, the redness that flares up round a cut or bruise. An inflamed point on an artery makes it more likely that plaque will form.

In the past two years, two major studies have found that the amount of inflammation in your body is a better indicator of your heart-attack risk than your cholesterol level. Inflammation is measured by something called C-reactive protein (CRP). Some claim such findings make the cholesterol hypothesis redundant. This could supply an answer to the question raised by the Skeptics' challenge: If cholesterol reduction isn't that beneficial, why do the drugs reduce the number of heart attacks? Probably, say the Skeptics, by reducing inflammation.

The body produces inflammation via a number of complicated pathways many of which involve a molecular switch known as NF kappaB and recent studies show that statins are pretty effective at dimming NF kappaB. However this is what a number of other effective heart treatments also seem to do, such as aspirin and omega three fatty acids found in fish oils, not to mention garlic and vitamin E.

If this turns out to be what is going on, and trials are under way to test the idea, this seems likely to shunt cholesterol reduction into a small corner of the overall picture of heart disease and allow statins to be marketed as "inflammation fighters". Other ways of reducing your C-reactive protein level include stopping smoking, losing weight and exercising.

The cholesterol hypothesis is unlikely to be abandoned in a hurry, given the weight of financial and political muscle behind it. But the Skeptics have raised questions that could ultimately have an impact on the way we think about heart disease.

Visit the Cholesterol Skeptics website at [www.thincs.org](http://www.thincs.org).