



Statins:

LIFE SAVERS or BIG PHARMA CON?

The risks, the benefits and the conspiracy theories.

Some claim they're nothing but a con, marginally effective drugs foisted on the public by pharmaceutical companies out to make a profit at the expense of our health; others say they are so effective in the fight against cardiovascular disease that they should be added to our drinking water.

We're talking about statins, one of the most widely prescribed classes of drug in the world – and one of the most controversial.

Statins are prescribed to millions of people to help lower their cholesterol levels. While

their benefits have been widely debated for some time now, the contention around them kicked into overdrive recently thanks to the UK National Institute for Health and Clinical Excellence's (NICE) recommendation that the cardiovascular disease (CVD) risk threshold for prescribing statins should be halved from 20% to 10%, meaning these drugs are poised to be much more widely prescribed.

While no-one really disputes that statins are beneficial for people who've already had a heart attack or stroke (called 'secondary prevention'), it's the doling out of these drugs to healthy people who are believed to be at high risk of developing heart disease that's causing all the ruckus.

Detractors oppose the 'medicalisation' of people who are not ill, and also cite grave side effects – muscle pain, liver damage, memory loss, diabetes – as reason enough to avoid the drugs. On top of that, some doctors have claimed that the link between cholesterol and cardiovascular disease (CVD) is pure fiction. As one vascular surgeon memorably said in the UK's *Telegraph*: 'High total blood cholesterol or high LDL levels no more cause heart attacks than paramedics cause car crashes.'

On the other side of the debate, doctors and heart health experts – indeed, the majority of medical health practitioners – say that the bulk of evidence suggests that high cholesterol is a valid risk factor for cardiovascular disease, that the side effects of statins have been vastly exaggerated, and that they are a safe and effective means of lowering cholesterol and thus saving lives.

As with Buddha's path to liberation, the truth lies somewhere in the Middle. We try to answer some of the most pressing questions, with the help of experienced experts.

WHAT ARE STATINS?

Statins are a class of drugs that act on the liver to reduce LDL* cholesterol levels in the body – and slightly increase your body's production of HDL** cholesterol. This is believed to reduce the risk of heart attack and stroke.

(* **LOW-DENSITY LIPOPROTEIN, OFTEN REFERRED TO AS "BAD" CHOLESTEROL, ALTHOUGH THIS IS SOMEWHAT OF AN OVERSIMPLIFICATION**

** **HIGH-DENSITY LIPOPROTEIN, OR 'GOOD' CHOLESTEROL**)

WHO TAKES THEM?

Hundreds of thousands of South Africans take them every day. According to Health24, current estimates of the number of South Africans on statin medication range from 380 000 to perhaps a million or more. Statins are usually prescribed for secondary prevention of CVD

(i.e. if you've already had a heart attack or stroke, statins can help prevent a second 'event', as doctors like to call it), as well as for primary prevention in individuals who are at high risk of developing CVD (i.e. if you haven't yet had an 'event', but perhaps have risk factors for heart disease such as diabetes, high cholesterol, high blood pressure, excess weight etc.).

DOES HIGH CHOLESTEROL LEAD TO HEART DISEASE?

This question is at the heart of the debate around statins. Dr Dirk Blom of the Division of Lipidology at the Health Sciences Faculty at the University of Cape Town says that

the perception people have of 'grease clogging up your arteries, like a drain gets clogged if you pour oil down it', is misleading, and that the processes leading to blocked or damaged arteries [atherosclerosis] are far more complex.

Simply having elevated LDL cholesterol levels, for example, is not a clear-cut sign of increased CVD risk, say statin sceptics like family physician Dr Gail Ashford.

'In South Africa, we measure LDL-c (or LDL concentration), which is a poor indicator of oxidised LDL particles. Heart attacks are linked to oxidised (damaged) LDL particles. It is possible to have high LDL-c but be at low risk for heart attack. It is also possible to have many unhealthy, oxidised LDL particles but a normal or low LDL-c. For this reason, the LDL-c does not correlate well with risk for heart

attack, and half of people who have heart attacks will have a normal LDL-c. We are measuring the wrong thing. We need to measure the number of LDL particles, and not a concentration of particles. This test is not freely available in South Africa, but there

is a surrogate test available here – called the Apolipoprotein B – which will tell you whether your particle number is high (and worrying) or not (reassuring).'

'Nobody is disputing that atherosclerosis is a very complex process,' says Dr Blom. 'Small LDL particles are usually oxidised, and a bit more dangerous. They penetrate artery walls more easily, and they may generate more inflammation. But that doesn't discount the larger

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particle LDL being a risk factor for heart disease. It is still a problem.’

Inflammation has been fingered as a far more accurate predictor of atherosclerosis than cholesterol levels. Blom cites an experiment in which rats’ immune systems were manipulated – i.e. their inflammatory response was suppressed – and they were then given LDL cholesterol. The rats had far less atherosclerosis than another group of rats with a normal immune system, proving what an important role inflammation plays in heart disease. ‘In fact therapies that modify the immune system and suppress the inflammatory response are currently being tested in human trials to see whether they can lower the risk of heart attacks or strokes when combined with statins.’

‘Where we differ,’ he continues, ‘is by saying that LDL cholesterol is still an important part of the atherosclerosis process, and often an initiator of the inflammation in the vessel wall. This is what some dispute. Of course LDL isn’t the only factor in predicting risk of atherosclerosis: Blood pressure, inflammation, smoking, glucose levels... All of these things matter, but so does LDL cholesterol. And LDL happens to be one element for which we have very effective treatment – statins – that has been shown to save lives.’

WHAT ARE THE SIDE EFFECTS OF STATINS?

The comments sections of online articles written about statins are often filled with accounts by readers of the severe side effects (memory loss, fatigue, depression, muscle pain) they experienced while on statins – which disappeared when they stopped taking the pills.

However, the evidence suggests

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these side effects are far less common than many claim: ‘This didn’t come through strongly in the studies on statin side effects,’ says Dr Blom. ‘If you put people in a trial and they don’t know if they’re taking a statin or not, a fair amount of people experience symptoms even when they’re not on medication.’

This is what’s known as the ‘nocebo’ effect – the ‘evil twin’ of the placebo effect – a kind of misattribution of symptoms. ‘The phenomenon of people getting unpleasant symptoms simply because they expect to is fairly well-documented,’ said British medical doctor, academic and author of *Bad Pharma* Ben Goldacre recently in a column in *The Guardian* UK.

‘All drugs have side effects,’ adds Johannesburg general practitioner Dr Jonathan Witt. ‘If you want drugs exempt from these then you need to drink water. Medical science simply cannot follow anecdotes and personal opinions; it has to follow the best available scientific evidence at any given time. NICE and ethical medical practitioners do as such. Unfortunately some people (a small percentage of those who actually take statins) will suffer from side effects related to statins. Muscle pain is a one of the more common side effects which can be combated by changing the statin the patient is on. In a small number of cases the side effects cannot be overcome and patients will not tolerate them. It is important to understand that tens of millions of people take these drugs

worldwide without any issue. The package inserts of statins, or any other drug for that matter, clearly state the potential side effects. The public should do themselves a favour and read the package insert of aspirin – even the most effective, useful and seemingly harmless drugs can be dangerous.’

There IS an increased risk of developing type 2 diabetes in statin-takers, albeit a small one (and it usually occurs in people ‘who were heading in that direction anyway’, according to Dr Blom), so it’s a good idea to discuss any concerns with your doctor.

As for cancer, several meta-analyses* have found no relationship between statin treatment and increased risk. It is also thought to be highly unusual for a patient to develop symptoms of liver damage due to taking statins, though new guidelines recommend a baseline liver test before taking statins.

(*A META-ANALYSIS STUDY IS A RE-ANALYSIS OF MANY STUDIES ON ONE SUBJECT.)

CAN WE TRUST STUDIES FUNDED BY PHARMACEUTICAL COMPANIES?

It makes sense to be suspicious of research that is funded by a source that has a vested interest in the outcome. As Dr Blom puts it, pharmaceutical companies are not charities – they’re about making a profit in the final analysis. But that doesn’t automatically mean research funded by statin manufacturers is untrustworthy, says Dr Witt.

‘Even if funding does originate in part from pharmaceutical companies, this does not make sound clinical or scientific findings untrue. The methods by which studies are performed, especially randomised

control trials*, makes it difficult to skew evidence, and the process to publish such evidence in peer-reviewed journals means that any conspiracy theory of “Big Pharma” controlling the narrative is just that – a conspiracy theory.

‘Another point is that drug companies, as conspiracy theorists point out, are in the business of making money. But they actually do this by making good, effective products. The belief that a marketing machine and unethical doctors worldwide are the reason why statins are so commonly used is frankly farcical and baseless.’

Dr Blom also weighs in. ‘Do the trials always answer the questions we’d like them to answer? No, because the pharmaceutical industry is not going to deliberately design a trial that’s going to make their drug look bad. But they ARE very strictly regulated. The best test you can do is to test your drug against a placebo – i.e. nothing – and if your drug performs, that’s a pretty clear-cut indication of benefit for the patient. And not all drugs that enter clinical trials perform as expected – these drugs are of course not approved and are never marketed and cost the pharmaceutical company several hundred million dollars in lost development costs.’

It is concerning, however, that many pharmaceutical companies do not offer free access to all their data, and only release certain information. ‘There is a site called ALLTRIALS.net that is encouraging companies to hand over all their data to be accessed freely,’ says Dr Ashford. ‘This includes benefits and adverse effects of drugs. Roche recently handed over the data around their flu medicine Tamiflu, which has now been exposed as a drug which was really not terribly effective. I suspect that should Pfizer and the like hand

over their data about the statins, we would also get a shock about the benefits vs side effects.’

(* RANDOMISED CONTROLLED TRIALS ARE THE GOLD STANDARD OF CLINICAL TRIALS.)

WILL STATINS HELP YOU LIVE LONGER?

Research into primary prevention has found that statins will reduce your risk of dying from a heart attack or stroke – but it doesn’t necessarily follow that you’ll live longer. It’s a bit of a contradiction, certainly, because while research finds that you’re less likely to die of a heart attack or stroke on statins, there is little evidence to suggest that statins reduce ‘all-cause’ mortality (death from any other cause).

‘Part of the problem is that the duration of most studies is relatively short,’ says Dr Blom. ‘Three to five years, perhaps. And you may not be observing people long enough to see a reduction in the cardiovascular death rate in primary prevention.’

A useful way to consider the benefit of statins is to ask: how many people need to be treated for one person to benefit? (This is referred to as NNT: the number needed to treat.) The answer, according to Dr. David Newman of Mount Sinai Medical Center in New York, is 60. About 60 people need to be treated with statins for five years to prevent one heart attack. For strokes, that number jumps to 268. Of course, this is just an average – the true NNT will be different for each patient, according to their risk profile.

Some take this to mean the drug is ineffective, or that the benefits are insignificant, while others infer the opposite, and feel the drug should be more widely prescribed. What if, for example, you happen to be that one person out of 60 who avoids a heart

attack by taking statins?

‘Even if you take a statin and it brings your LDL cholesterol down to a level that we would consider good, you could still be at risk of having a heart attack,’ says Blom. ‘Your risk has been reduced, but not removed. You can never really bring your risk down to zero.’

Essentially, he says, it’s more of a philosophical question than a medical question. ‘It really depends on what level of risk you are prepared to accept.’

WHAT SHOULD I DO IF I’M EXPERIENCING ADVERSE EFFECTS?

‘Go back to the doctor who prescribed the medicine,’ says Dr Witt. ‘Your doctor didn’t go to medical school for all those years and work as hard as they have just so that they could make you suffer. Every doctor I know wants the best for their patients. If the symptoms are minor and you feel it may be too early to go back to your doctor, or if this is not possible, then give it some time and see if the perceived side effects resolve. If not, you may require a different statin or may not be able to take these drugs.’

IN CLOSING, PERHAPS DR GOLDACRE PUT IT BEST:

‘Some people get a bit melodramatic about statins, as if they’re being forced down our throats: the evidence shows they reduce your risk a bit if you’re at high risk of a heart attack; they’re less helpful – but still a bit helpful – if you’re low risk; and if you decide you don’t want to take them, after being apprised of the evidence, well, that’s easy: don’t take them.’

[SOURCES: THE AMERICAN HEART ASSOCIATION WWW.HEART.ORG]; PHOTOGRAPHS: GALLO IMAGES/GETTY IMAGES