NARRATION

We've been told that medications to lower cholesterol will save lives.

Professor Beatrice Golomb

We repeatedly hear from patients that their doctors tell them, 'If you don't take this, you will die.'

NARRATION

Over 40 million people worldwide take drugs to lower their cholesterol. But now there's evidence that the majority of them won't benefit.

Professor Rita Redberg

None of those people are less likely to die.

NARRATION

I speak to doctors accusing the drug companies of distorting the evidence about the drug's side effects.

Dr John Abramson

Of course they're going to try to minimize the adverse events 'cause that will increase the sales of their drugs.

Professor Beatrice Golomb

In its effect it's certainly scientific fraud, and in its effect it's organized crime.

Dr Maryanne Demasi

So how do these drugs work? And are they really safe? I've come to the United States to investigate how drugs to lower cholesterol came to be the most widely prescribed drugs in the history of medicine.

NARRATION
The '80s saw the debut of a new weapon in the battle against heart disease - a novel class of drugs called 'statins' that lowered cholesterol like no other medication before them.

**Dr Ernest N Curtis**

They were heralded as... Nirvana. The next great thing. Because all of a sudden, now you're getting 30-40% reduction with statins, which was huge. And this was great news to the people who were pushing the cholesterol theory, because they said, 'Aha! Now we don't have to settle for these piddling little amounts anymore - we can really show how important cholesterol is by knocking it way down.'

*Man, in advertisement*

...medical information comes along that say you may need to get...

**NARRATION**

In the US, influential TV ads like this use popular actors to boast the enormous potential of these drugs.

*Man, in advertisement*

Crestor, along with diet, can lower bad cholesterol by up to 52%.

**NARRATION**

But the reality is - lowering your cholesterol with medication doesn't guarantee you won't have a heart attack.

**Professor Rita Redberg**

The marketing concentrates on the fact that you can lower your cholesterol as if that was the end in itself, which it is not. Cholesterol's just a lab number. Who cares about lowering cholesterol unless it actually translates into a benefit to patients?

**NARRATION**

Over the decades, drug companies have had an enormous vested interest in statin drugs.

**Dr Ernest N Curtis**

It's the most profitable group of drugs in the history of the world. Something like $15 to 25 billion, with a 'B', per year, spent on these drugs. So that's higher than the gross national product of many countries around the world.

**Dr John Abramson**

Lipitor is the bestselling drug in history. So in terms of cost, total sales of Lipitor have been in the range of $140 billion since it came on the market in 1996.

**NARRATION**
Statins work by disabling a critical step early in the formation of cholesterol.

**Dr Jonny Bowden**

There's a pathway that produces cholesterol in the body. You could think of it like a tree. So, we've decided collectively that one of the branches of this tree is bad, meaning cholesterol. So we've decided that the best way to get rid of that branch is to cut the tree off at the root.

**NARRATION**

Statins inhibit this enzyme, which is also required for essential molecules like Coenzyme Q10. Nutritionist Dr Jonny Bowden says CoQ10 is essential for optimal heart muscle function.

**Dr Jonny Bowden**

This is partly, we believe, why so many side effects have to do with lack of energy, muscle pain - because Coenzyme Q10 is so vital. So what's the irony of giving people a drug to reduce something that probably doesn't even have that much to do with heart disease, that also reduces one of the molecules that's most necessary for heart health? How insane is that?

**Dr John Abramson**

It's assumed that the cholesterols a toxic substance in your body and getting it as low as you can is a good thing. Well, cholesterol is the organic molecule that's most common in your brain, by weight. It's in every cell wall. It's the precursor of many of the hormones in our body. It's an enormously complex molecule. And to think that you can radically pull this out of the body and not have consequences is just... it's ridiculous, it's such bad science.

**Dr Maryanne Demasi**

It's been about 30 years since statins were first introduced as the new blockbuster drug in heart disease. And millions of people around the world are being prescribed these medications. But many are concerned that the benefits of these drugs have been grossly exaggerated.

**NARRATION**

Professor Rita Redberg is a world-renowned cardiologist. She says, barring a genetic condition, the only people who live longer by taking a statin are those that have already had a heart attack or stroke.

**Professor Rita Redberg**

Valve's working great.

**Patient**

That's good.
Professor Rita Redberg

Yeah.

NARRATION

And of them, only a very small number will benefit.

Professor Rita Redberg

One or two people in a hundred will benefit from taking a statin. What people don't understand is that means the other 98 will get no benefit at all. It's not going to reduce their chance of dying.

NARRATION

But this hasn't limited their use. These drugs are now being widely prescribed to relatively healthy people - those without diagnosed heart disease. And Dr Redberg warns most of them won't benefit.

Professor Rita Redberg

For healthy people, even people that have a lot of risk factors. So they might have high blood pressure, they might smoke, they might have diabetes. The data is not there to suggest that those people are better off taking a statin. No, I don't think it's a wonder drug.

NARRATION

But Dr David Sullivan disagrees. He says all the risk factors should be considered equally, including cholesterol.

Assoc Prof David Sullivan

If you want to mount these arguments about not treating the cholesterol, you've got to take the responsibility of saying it's not necessary to treat these other risk factors either. I would certainly encourage people who are considering cessation of treatment for perceived side effects and so forth to discuss it with their doctor.

NARRATION

In 2012 there was an interesting turn of events. The CTT collaboration, a highly regarded group of researchers, reanalyzed all of the old data with different methods and concluded that statins were effective for the wider population. The report was subject to harsh criticism, but it's still the data that many cardiologists turn to. The media jumped on board and reported that everyone over the age of 50 should be taking a statin to reduce their risk of heart disease, even if you had normal cholesterol. But Professor Redberg says there's a downside.

Professor Rita Redberg

None of those people are less likely to die. So you can take a statin for many, many years and you're just as likely to die as if you had not taken a statin.
Dr Maryanne Demasi

Unless you've already been diagnosed with heart disease, then taking a statin won't help you live longer. It may reduce your risk of a cardiovascular event, but it may also increase your risk of developing something else, like diabetes. Either way, taking a statin won't extend your life span.

NARRATION

Dr Abramson says cardiologists are so focused on how these drugs prevent blood vessel disease they often overlook the other problems caused by statins.

Dr John Abramson

People are more than their cardiovascular system, and what we really want to do is improve people's overall health, longevity and the risk of serious illness. If you look at overall health, we haven't done anything for them. Now, do people want to take a statin to trade one cardiovascular event for some other very serious illness - in other words, no net benefit - and expose themselves to the risk of harm from the statins? Do you want to do that? I think it's a bad deal. If somebody has a particular fear of heart disease and says, 'Look, I don't care if I get diabetes, I don't care if I have muscle symptoms, I don't care if I can't exercise the way I want to exercise, I do not want to have heart disease,' fine, take a statin. But understand that that's why you're taking a statin, not because it's going to improve your overall health.

NARRATION

Cardiologist Dr Ernest Curtis says the absolute benefit of statins is so minor that it's unlikely to be because of their ability to lower cholesterol. He says statins probably work through other mechanisms.

Dr Ernest N Curtis

It seems very likely that the amount of reduction that they saw with the statin agents could easily be due to its effect on the blood clotting, and possibly the anti-inflammatory effect, and have nothing to do with the cholesterol.

NARRATION

Dr Golomb has scrutinized the data, and she's even more skeptical about the value of these drugs, especially in women.

Professor Beatrice Golomb

Right now the evidence has not supported benefit to women, even if they have heart disease, in terms of mortality and all cause morbidity. It has not shown benefit to elderly, even if they have heart disease. In fact, in the 4S trial, there was a 12% increase in mortality in the women in that group who were assigned to statin rather than placebo. So the evidence really doesn't support that the benefit is the same for women and for men. And on top of that, women are at higher risk of complications from statins.

Dr Maryanne Demasi
Should women take cholesterol-lowering medication?

**Professor Beatrice Golomb**

In general, no. Now there may be exceptions. Medicine actually does have an element of art. And if women are from a family with severe familial hyperlipidaemia, where a lot of people are dying from heart disease in their 30s and 40s, that's a group where I would say there is an art.

**NARRATION**

There are now calls for patients to give written consent before taking a statin.

**Professor Beatrice Golomb**

If you do plan to give statins to women, to elderly, to people at low risk, they should sign a consent form saying they understand that they're receiving a drug that will not extend their life, but will only shift the cause of death. I think patients have a right to know that before they agree to take on a medication.

**NARRATION**

The National Heart Foundation of Australia agrees that people are being prescribed statins unnecessarily.

**Dr Robert Grenfell**

I would agree that there are people in Australia today who are being treated for cholesterol where their cardiovascular risk is not high. And you have to question whether they should in fact actually be on that.

**NARRATION**

A report estimated around 75% of people taking statins are in the low to moderate risk category, and, according to these researchers, that means up to 30 million people are taking a drug that won't offer them the benefit of living any longer.

**Edward**

My doctor pointed out that my cholesterol levels were high and that I should take some sort of medication to reduce the cholesterol level.

**NARRATION**

There was nothing wrong with Edward's health, apart from his high cholesterol. He took his doctor's advice and began taking a statin.

**Edward**

After about two weeks I was having a difficult time walking in the daytime, and at night I had trouble sleeping, my legs ached. I was definitely experiencing a memory loss. I didn't feel that I could recall things as clearly as I did before I was taking the statin.
Statins have a long list of side effects - like muscle weakness, memory loss, and, in rare cases, a potentially fatal condition called rhabdomyolysis, where muscles break down and cause kidney failure. Edward decided to stop taking his medication.

Edward

I started feeling better after about three weeks to maybe a month afterwards.

Dr Maryanne Demasi

How long did it take for you to get 100% improvement?

Edward

100% better took from the time I stopped taking the statins, it took six months.

Professor Rita Redberg

They feel like they're in a fog, they can't get out of their chair - side effects that go away when they stop their statins. And I have patients come in and tell me they'd rather be dead than keep taking the statin.

Professor Beatrice Golomb

Some of them tell us that their doctors fire them as patients if they discontinue their statins, which I really wonder about the ethics of. Some of the people that we hear from also say that their doctor didn't believe them, that their problem couldn't be due to statins, and based on how patients perceive it, badger or bully them into resuming or continuing the medication. That's not an acceptable way for medicine, as a system, to be run.

Assoc Prof David Sullivan

In alerting patients to some undesirable possibilities, and, in fact, maybe even through the power of suggestion, lead them to believe that they're experiencing those particular issues, which they would then blame on the drug when in fact it might be arising from other factors.

Dr Maryanne Demasi

Their imagination?

Assoc Prof David Sullivan

Um, look, I'd be reluctant to... I think a lot of these things aren't imagined. I think there are days when you can feel more of a muscle ache than others, and it can be age, it can be all sorts of other things.
Dr Golomb makes a stunning accusation about why she believes some doctors in the US may push their patients to take statins.

**Professor Beatrice Golomb**

I think they often intentionally hide those risks because there are often physician incentives that benefit the physician for having more patients on statins. So it pits physician self-interest against patient benefit. This particular woman contacted me, and she had left the practice that she was at because they insisted that at least... I believe it was 80% of her patients be on statins. This has actually been written up in media as something that is actually considered legal and acceptable. I can't see any way in which that's acceptable. I'm literally the only researcher I know who studies this class of drugs who has a policy not to take money from industry.

Statins are meant to be lifelong medications, but Dr Curtis says we don't know about the long-term side effects.

**Dr Ernest N Curtis**

The studies that have been done have generally been just a few years in duration. The long-term effects may not show up for many years. It may take many years for a cancer that develops to make itself manifest. Because cholesterol is so important in the brain, could it contribute to dementia when someone gets older if you lower their cholesterol? We don't know. Again, how would we be able to tie that to the drug? So all of these concerns about the unknown long-term side effects are very serious, in my opinion.

Harvard Doctor John Abramson is an expert in litigation involving drug companies. He says we're not being told the whole truth about the dangers of these drugs.

**Dr John Abramson**

We're told over and over again that statins are extremely safe. And when you look at the results of the clinical trials, you would conclude that they are safe. Problem is that the clinical trials are not designed to pick up all the side effects.

The CTT collaboration, for example, use mostly drug company data, and report very low levels of muscle side effects from statins. But when you look at the side effects in the general population, it's 100 times higher.

**Dr John Abramson**

Are the trials lying? No. I just don't think they ask the right questions. Why don't they ask the right questions? It's not in the interest of the drug companies to ask the right questions. So, it's creating the impression that the drugs are safe.
Another complication with clinical trials is that drug companies don't recruit volunteers that reflect the typical patient on statins.

**Dr Robert Grenfell**

The problem with the study design is that we exclude people with chronic disease or other comorbidities. We exclude people who are very old or very young, and we'll certainly exclude people with other types of risk factors or diseases that may interfere with the metabolism of the drug. So we often get a skewed picture of what the side effect profile is.

**Professor Beatrice Golomb**

The fraction of people with problems in my sort of real-world, on-multiple-medications, etc clinic is far higher. And I would say that in that sample it really seems in the order of a third of patients that develop problems.

**Professor Rita Redberg**

There are a lot of ways that one can manipulate data in a trial. Trials do what they call a washout period, and what that means is before they choose the people that are going to be in the trial, they give everybody the drug, and the people that have side effects get excluded from the trial. And they say that so people aren't uncomfortable when they are in the trial. But of course it takes out all the people that have side effects, and that's very commonly done in drug trials.

**Dr Maryanne Demasi**

So the side effects would be grossly underestimated.

**Professor Rita Redberg**

Yes, it would definitely grossly underestimate the number of people that have side effects. They're not as safe as they're made out to be, no.

**Professor Beatrice Golomb**

In its effect, it's certainly scientific fraud, and in its effect it's organized crime. It's always difficult to allege intent, but it is clear that manipulation of evidence subjects many people to treatments that those people should never have been subjected to.

**Dr John Abramson**

I think there is criminal activity that goes on. And I think when drug companies act in ways that misrepresent information that leads to harm, they ought to be held responsible, just like any other individual or organization that conducts itself in a way that leads to harming other people.
Drug companies have a history of illegal activity. This is just a sample of the billions of dollars they incur for things like fraud and bribery in any given year. In the ‘80s, when President Reagan came into office and slashed funding to the national institutes of health, it left a gaping hole for private industry to move in. Nowadays, around 85% of trials are funded by drug companies. A review concluded that if a drug company paid for a trial, it was 24% more likely to report the drug was effective and 87% less likely to report the drug's side effects.

Dr John Abramson

There is a sense that science is science, so it doesn't matter who pays for it. And yet because the research is privatized, the fundamental purpose for which it's conducted has changed. It's not to improve the public's health - it's to fulfill the fiduciary obligations of the sponsors and create an opportunity to maximize profits instead of improve the public's health.

Dr Maryanne Demasi

Some might say that that's a rather cynical view of how science works.

Dr John Abramson

To say it's cynical that commercial sponsorship of science taints the science is just totally naive. It's silly. Business is in business. Their job is to make money. We ought to be clear in our public discourse that to say we've got a bias in commercially sponsored research is neither cynical, nor paranoid, nor impolite - it's a fact. So let's just accept it as a fact and stop being naive at our own expense.

But, if big pharma doesn't pay, it will have to be the taxpayer.

Assoc Prof David Sullivan

A drug now costs about $2 billion to develop. The success rate of drugs is very low. You know, is the public purse going to be willing to shell out, in advance, $2 billion for a drug which it doesn't know the likely outcome of?

Dr Maryanne Demasi

Arguably, the biggest ethical issue in science is that drug companies withhold unflattering results. So, in the end, what we're presented with is a distortion of the data.

Two of the three major drug companies declined to comment. AstraZeneca denied these allegations, stating that all their trials are publicly available. But in 2010, the drug-maker reportedly paid a half a billion dollars to settle a class action after being accused of burying information about the increased risk of diabetes seen with their widely prescribed anti-psychotic drug, Seroquel.
Dr John Abramson

I spend a lot of time as an expert in pharmaceutical litigation, and one thing you learn is that you can't possibly know what's going with that drug unless you have access to the corporate hard drives. If you want to know the truth about a drug, you need to have subpoena power or, in litigation, discovery that gets you into those corporate hard drives. Because without getting into the corporate hard drives, it's impossible to know what the real benefits and the real risks of those drugs are.

NARRATION

Even the definition of 'high cholesterol' keeps changing. In 2004, a US panel of experts decided to lower the threshold of cholesterol, which sparked outrage amongst many doctors.

Professor Rita Redberg

More and more people think they have high cholesterol even though they don't have high cholesterol.

NARRATION

By changing the definition, it meant that millions more people became eligible for statins, and these thresholds were adopted by many countries around the world.

Dr Ernest N Curtis

Has this been on the basis of any scientific data? Absolutely not. Absolutely not, no evidence whatsoever, just the theory that less is better. You're creating more patients, you're creating more people who now have something to worry about where they didn't have anything before.

NARRATION

But Dr Sullivan insists this was a good decision.

Assoc Prof David Sullivan

I think what we actually started off with was maybe appropriately conservative targets which were really not in the patients' best interest. So the likely outcome is a further reduction in targets.

Dr Maryanne Demasi

More cholesterol lowering.

Assoc Prof David Sullivan

Yep, I think that's absolutely to be expected.

Dr Maryanne Demasi

The decision to lower the threshold of cholesterol was a controversial one. An investigation into the matter revealed eight out of nine panel members had a direct
conflict of interest after declaring financial ties to the companies that manufactured statins.

**Dr John Abramson**

We don't have independent reviewers evaluating the data and making independent recommendations. You might ask, 'Am I accusing these people of selling their opinion because they're getting paid by the drug companies?' No, I'm not. I'm not accusing anybody of bad faith. But the people the drug companies choose to pay are people who advocate the use of their drugs, and have standing and presence and reputation that will enhance the sales of their drugs.

**Dr Maryanne Demasi**

So do drug companies seek out doctors to be their mouthpieces?

**Dr John Abramson**

Drug companies clearly seek out what's called key opinion leaders. These are people with a national reputation who can create the street knowledge for practising physicians, that this is the way things should be done.

**NARRATION**

There is ample published literature showing that doctors who receive money from drug companies have more favorable attitudes and prescribing habits towards that drug.

**Dr John Abramson**

There's no question that doctors are influenced by drug companies. And I hate to say it, but drug reps showing up in nice suits and fancy women's clothes without much medical education play a significant role in what doctors think. Now, there's no reason for doctors to be getting their information from drug reps, my goodness. The drug rep's job is to increase the sales of the drugs they represent. Doctors need to take some responsibility. They need to do their best to get independent knowledge, and they need to put political pressure on their governments to get the clinical trial data unsealed so they can know what the clinical trials really showed.

**NARRATION**

Many doctors feel obliged to follow the guidelines, even if they don't agree with them.

**Dr Ernest N Curtis**

They have to worry about malpractice suits if they don't follow the guidelines. An opposing attorney could make them look very bad in court by saying, 'Well, doctor, do you think you're smarter than this national group of recognized experts?' And this is a factor that's impelling doctors to follow the guidelines.

**NARRATION**

The push to lower cholesterol in the wider population continues.
Dr Maryanne Demasi

A group of doctors published an article claiming that statins could counter the effects of eating a burger. They suggested that statins be handed out as free condiments, just like ketchup.

Professor Rita Redberg

Because it gives people that false reassurance that it's OK if you eat this food that is not good for your health, because then you're going to take this pill that is going to make it OK. And that's very attractive, but it is a fallacy, it's just not true. And it's still bad for your health to eat processed foods, eat trans fats and have a regular diet of fast food hamburgers.

Dr Maryanne Demasi

And the absurdity doesn't stop there. Here in the US, it was even suggested that statins be put in the public water supply.

Dr Ernest N Curtis

I think this idea of handing out statins willy-nilly to everybody is totally irresponsible. You're talking about a drug with potentially toxic side effects, and a drug whose quote 'beneficial effect' is extremely small, and whose benefit can be achieved with much less toxic drugs and even with some non-drug treatments.

Dr John Abramson

We're missing the message: that health rarely comes out of a bottle. Exercise and a Mediterranean-style diet is the best way to prevent heart disease. I think virtually everybody agrees with that. Now, it's very clear that when you look at the effects of exercise, they're far more powerful than statins. Moderate exercise, exercising the equivalent of two hours of brisk walking a week, adds about two years to your life compared to not exercising that much. Two years. Now, for statins for low-risk people? No benefit in longevity. So do you want to exercise, which is going to add two years to your life? Or do you want to take a pill that's not going to lengthen your life and has the risk of side effects? It's craziness.

Dr Maryanne Demasi

Until the science of clinical trials can break free from commercial interest, then decisions about our health rest in the hands of big business.

Researcher: Dr Maryanne Demasi

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