Cardiovascular Disease: Recognition, Communication and Usual "Care" – Ref 289

with Malcolm Kendrick

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TRANSCRIPT

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Steven Bruce
Good evening! Great to have you with us this evening for what I think is going to be a really interesting 90 minutes of CPD. We often get orthopaedic consultants in, rehab specialists and we have practical demonstrations and that sort of thing, which of course, is very much akin to what we do in our own clinics. But this evening, I'm going to have a fireside chat as it were with somebody who I admire greatly and have done ever since I first came across his blog posts and I think it might have been the first of the books that he wrote, which is The Great Cholesterol Con, amongst others. And we'll talk about the books a little bit later on. This is Dr. Malcolm Kendrick, he has been on the show a couple of times before. He's made his name by criticising the pharmacological industry's drive to get everybody on statins, the general evidence surrounding cardiovascular care, and you might ask, what's cardiovascular care got to do with us in our practices? And I guess, we're going to see people who are worried about their cardiovascular health, we'll see people on various forms of medication and what Malcolm has to say this evening is going to be extremely useful, possibly very thought provoking, because as I say, he spent a lot of time pursuing the evidence. He knows the evidence really well. We're not talking here about someone who is an anti-vaxxer, or something of that sort. We're talking about somebody who is putting himself up against the bulk of medical opinion, it seems, on the basis of good quality evidence. So Malcolm, welcome. It's great to have you with us in the studio again, I'm really looking forward to this evening, and I know we'll cover stuff that we have done before. But I've just said, you're not the equivalent of an anti-vaxxer on the cardiovascular front, but you have got a court case brewing at the moment, I think, haven't you?

Malcolm Kendrick
Yes. Well, brewing, four years ago, The Mail on Sunday, wrote an article saying that myself and a couple of others were causing potentially hundreds of thousands of people to die, because we don't believe that statins are as effective as they're generally made out and also that they have more adverse effects.

Steven Bruce
Why would the Mail on Sunday do this? Because journalists aren't generally particularly experts in medicine. They're good at reading abstracts and sticking those into their headlines. But what provoked them to do this? Was there someone else behind it?

Malcolm Kendrick
Well, far be it for me to annoy lawyers listening. But no, I think they were doing a thing called fake science or a fake news series. And I think they've done a few other things and this was one of the things on their radar, but it's such a big subject in such a big area and there's such a lot of money and readers and people on statins, I think they just thought this is an approach. I mean, ironically, before this, they actually published articles on things that I'd written, they covered The Great Cholesterol Con, they covered other books. And in fact, they were thinking of covering my latest book, and then decided, no, they were going to take the reverse, which was: this isn't a good idea, this isn't good stuff, this is a maverick fool who should be crushed. And that's how newspapers work, they don't take positions other than, I suppose what they think is going to sell papers.

Steven Bruce
Which means they have to appeal to the widest popular beliefs rather than drive those beliefs.

Malcolm Kendrick
Well, they don't drive the beliefs. Interestingly, after the articles in the comment section, I think 95% were anti the article and anti the industry and pro what we had to say. So it possibly backfired.

Steven Bruce
Well, I was gonna say that possibly this could backfire in a big way on them, couldn't it? Because assuming that you win in your case against the Mail on Sunday, that will itself be big headlines.

Malcolm Kendrick
Well, probably won't be great big headlines. I'll do what I can to get people that I know and other journalists, but it's quite difficult because the Mail on Sunday associated newspapers are really the biggest newspaper group in the UK. If you're a journalist, it doesn't behoove your career to start going against what the Mail on Sunday has to say. So I'm not holding out huge hope.

Steven Bruce
Well, if you breathe, yeah.

Steven Bruce
We've mentioned your books, and I talked about The Great Cholesterol Con. Is it fair to say there's a progression here, The Great Cholesterol Con is about what is wrong with the cholesterol hypothesis, A Statin Nation is about what's driving us to be on statins. I think the guidelines are pretty much now that if you're over about 50, you're going to be found to be in need of statins.

Steven Bruce
And then the latest, The Clot Thickens, is, instead of the cholesterol hypothesis, there's an alternative, which has got some fairly decent evidence behind it.

Malcolm Kendrick
Yeah, I think it is. Well, it's a progression in that, a lot of people have said, well, if it isn't cholesterol, and if it isn't statins, then what is it? And I couldn't really answer that for a long time, because I didn't really know for sure.

Steven Bruce
Of course, there's a tendency, isn't there, if someone says to you, okay, if it's not this then what is it? And you say, I don't know, they say, well, you must be wrong then.

Malcolm Kendrick
Well, yeah, it doesn't give their thinking anywhere to go. It's like, yes, let's blow this up. And then where do you go? Well, there's nowhere to go. But I think the fascinating thing for me is that once I started looking into alternative ideas, which I've known about for some time, is how long they've been around. And how many people have proposed the idea that is the central idea in this book, and yet it's never taken off. I mean, it was first proposed 170 years ago in Vienna, all those years ago, and it didn't work. And it's been tried again, and again, and it's never grabbed the attention. I think more recently, because there's so much incentive and financial pressure to lower cholesterol and statins and a new cholesterol

lowering agent, that it's very difficult to go against it. But there was a long time when these things didn't exist. And yet still, the idea, the central idea, which you can go back into the history, it's like, there's a concept of the ghost in the machine. If you look back, you can see there was something in there and it's been there all the time. And yet somehow, it's just been kept in the background. So it's fascinating to read about these people have been pushing the central idea here for 170 years, and yet it's never stuck. It's just never happened. It's really fascinating why that happens.

Steven Bruce
And I've struggled with what you say in your books, because, of course, I read those books, and I forgot to mention Doctoring Data, which is another cracking read, because it's all about how the data has been manipulated to show whatever the pharmaceutical companies want it to show. And it's not the only book to show that either. But I struggle because I read your book, and I think, right, this works. And then the next week in one of the newspapers, or in one of the medical reports, there'll be this new study that shows that actually no, statins are good. And I think well is Malcolm wrong after all. I've emailed you in the past to say, Malcolm, what about this?

Malcolm Kendrick
Yeah, well, never think that. No, of course, it's very difficult to go against the tribe. An awful lot of this stuff that comes out, the problem is it sounds so plausible, but actually the reality of statins is that there's one organisation in in the world that holds all the data on statins. If you say this to people it's like a ha-ha, conspiracy theorist, go and check it out. And they're in Oxford in the UK.

Steven Bruce
Is that the Centre for Evidence-Based Medicine?

Malcolm Kendrick
No, no, it's different. That's also there, ironically. They're called the Clinical Trial Service Unit, and they run clinical trials. But actually, within that there's a thing called the Cholesterol Treatment Trials Collaboration. And they went to all the pharmaceutical companies and said, we will hold all the data on statins from all these competing companies. And we will have it and we will look at it and we will produce these reports. And no one else is allowed to look at it, no one else can see the data on statins, there's one group in the world hold all the data. When the Cochrane Collaboration sent someone to look at the data, they wouldn't let them look at it. And they hold all the data, they won't let anyone else see it. They do these reports. And upon these reports, rests everything. Well, no one else can do these reports, because no one else has got the data. And when they've been asked and pressurised, they say well, it's commercially sensitive information, and you can't see it and we signed agreements to say you can't see it. So this is to me, the antithesis of science, where science is supposed to be debate. It's supposed to be everyone gets to see the data. Everyone can review the data. Well, here, you can't, they've got it. They won't let anyone else see it. One group of people at Oxford University in the UK, that's it, no one else.

Steven Bruce
But that said, these are presumably, at Oxford University, are a bunch of well respected, impartial academics whose opinion we should trust?

Malcolm Kendrick
Well, I agree with certain of those statements. Well, of course, they're hugely respected. And they go and they speak, and they publish papers, and they do all this stuff. I'll just give you one example of how ridiculous some of the work there is. They looked at the use of statins in diabetes. And it is now widespread, if you've got diabetes, you must take a statin based on a study that they did. Now, in their study, there's been two studies directly done on statins and diabetes. That was the only thing it studied. Most of them have looked at other people and then gathered together the diabetic patients out of those studies, which you shouldn't really do, but they did it. And in it, when they did their analysis, they did not include the only two studies done on the use of statins and diabetes, they said, we have excluded these studies, because they wouldn't have made any difference to our results. Which is fascinating, because the only two studies that have been done specifically to look at statins and diabetes, found they had no beneficial effect. And yet the paper came out, which is basically statins are wonderful in diabetes. Everyone with diabetes should be on statins. And you look at that and think, how on earth can this be allowed to happen?

Steven Bruce
But hang on, you must be paraphrasing here because you can't say these studies would have made no difference if you haven't included them in the study surely?

Malcolm Kendrick
Well, that's not my paraphrasing. That's what they said in the paper itself. What you have to do in this world is you have abstracts, which are short things, like what does this paper show, you have some discussion. But then you have methodology, which no one reads because it's really, really boring. And you have the statistical analysis which no one reads because it's incredibly boring, usually incomprehensible. And then you have other stuff, it's all in there, but if you don't read the paper... I'll tell you a story about a paper which it's years ago it was written, and in the methodology section, the author had written, "If anyone reads this sentence and phones this telephone number, I will send them a case of champagne." No one ever phoned. And remember, this got through editorial review. This was published, no one even saw it, from the editorial perspective. No one ever phoned him. He said, no one ever phoned me. The reality is people don't read these papers properly. I do and it's down there. It's in black and white. "We did not...", I can't remember the exact words, "We did not include these two studies, as it would have made no difference to our results." The only two studies that have ever been done on the use of statins in diabetes. And these two studies were both completely negative. Now, you may think this is impossible to believe, surely there are people out there who must have noticed this and gone, you can't do that. But you come to do more and more of this stuff and you read it. I did a pro bono research into ME and CFS at one time, 650 pages of a NICE report, right? And I looked through the whole damn thing. There were tables where people had written this figure should be in table two, whatever. Anyway, there were editorial notes in it, this is a NICE report from which everyone bases how they treat, and no one had even read this. I think I'm the only person, apart from the person who wrote the thing in the first place, I'm the only person who's ever read that report ever. Ever.

Steven Bruce
It makes you think that perhaps for NICE, the aim of the exercise is to have a report, not to have a meaningful report that anyone does anything with?

Malcolm Kendrick
Well, I know that in the legal terminology it's like if you bombard people with so much stuff that they can't possibly read it, they just give up almost, like, oh, my God, and NICE do these enormous... I mean, in this report on ME and CFS, which we now call, anyway, whatever you call it, they decided to look at whether graded exercise therapy and cognitive behavioural treatment was beneficial, and they decided it was. And it was like 600 papers and just went on and on and on. But in the end, all the other papers were completely irrelevant, because they hadn't looked at this really, they'd looked at other endpoints and other things. There was one study in this entire paper of 600, that was to do with whether graded exercise therapy and CBT had a benefit on quality of life, which is the thing they were looking at. The study itself was done in Belgium it was on 200 people. And at the start, the two groups were differently matched. So one group had a higher quality of life than the other. In fact, the group that had the higher quality of life were the people who didn't get the treatment, the people with the lower quality of life were the people that did get the treatment. At the end of the study, the quality of life of both groups was the same. Now, any statistician will tell you, that's just regression to the mean. That means nothing happened in this study, the authors admitted, nothing happened in the study. And the entire NICE guidance was based on that one paper that was wrong. And when they went to the court, and I said, it's all based on one paper and the paper was wrong. And by the way, they got the nominator and the denominator upside down when they did the calculations. The judge said, I can't decide on this, this is scientific stuff. I'm just here to decide whether the process of doing the report was fine. Did they involve the stakeholders and blah, blah, blah, which they did, of course. And then they said the only people who can decide on whether this report is valid are NICE. I went, but they're the ones that did the report that was rubbish in the first place. It was just like, honestly, the grownups aren't out there. People just let this rubbish get through. And if you go, this is just rubbish, how can you allow a study on statins in diabetes to not include the only two studies ever done on statins in diabetes? Well, surely the editorial people should be going. hold on. This is this concept of peer review. At a conference in the States, we were discussing peer review. I hate peer review. I think it's the worst and stupidest thing. It's not the worst, stupidest thing, but it is a completely ridiculous concept.

Steven Bruce
In practice or in theory, or both.

Malcolm Kendrick
In theory, it's a good idea. Oh, yeah, get people to read it. But no one reads the bloody papers. I get asked to peer review all the time, by the way, and I peer review some things. And I look at the other peer reviewers comments, and I think, you haven't read this paper. You cannot have read this paper, if you're saying that. I don't do much peer reviewing, because I just think, oh God, I've got to read the bloody paper.

Steven Bruce
It must be incredibly time consuming. Presumably you've got to check their references actually add up to what they say they do.

Malcolm Kendrick
You have to check the references. You have to check the figures. I'm not very good at statistics. I mean, I understand statistics in a broad concept. But when someone says some equation that's 53 pages long and you think, I have no idea. I have some friends who are very good statisticians.

Steven Bruce
So I'm getting off the topic here to some extent, but I mean, medicine ought to be based on evidence, but actually, if the evidence is so difficult to find your way through or to sieve the good from the bad, how does it make progress? Well, you can tell us a little bit about that in cardiovascular terms.

Malcolm Kendrick
Well, you can read Richard Horton who published a paper, The Lancet published a paper on hydroxychloroquine. There was a big, huge debate about hydroxychloroquine at the start of COVID. And there's a group called Surgisphere, who said, we have this fantastic research and we've shown that hydroxychloroquine harms people and kills them. And the peer reviewers and the journal itself had let all that go through, it was only some other people, I think it was Australian researchers, who said, I work in that hospital and we never had any of these patients. So where the hell have they got the data from? Turned out they just completely made it up. They had completely made it up. And it got published in The Lancet. And Richard Horton said, well, how are we supposed to know if they made it up or not? Well, you can try asking a hospital or two, or something. It's your job, surely. And recently, just to scare people out there, the level of data fraud, I was just reading a paper, is at least 20% of data are just completely fraudulent now.

Steven Bruce
I'm sure it's the editor of The Lancet, and I presume it was Richard Horton, isn't he the one who said that you just can't trust medical evidence anymore?

Malcolm Kendrick
Well, I think he said, we don't know, how are we supposed to know? And you feel like saying, well, if you don't know, how does anybody know? There was a big monoblock thing. You know, the whole thing about Alzheimer's recently was based on amyloid beta amyloid plaques are the thing that build up in your brain and cause you to get Alzheimer's. Now, that was based, that entire hypothesis, which rules the world of Alzheimer's disease, was based on and they've now admitted it was fraudulent research. They just made it up. The Lancet have this and they've said, yeah, we're looking at it. No, here's direct evidence that they made up their results. Well, we're looking at it. No, get rid of it. Billions have been spent on this, huge amounts. A drug was recently approved in the United States, because it reduced beta amyloid plaque buildup to zero, in fact, so it got launched, it's hugely expensive. And they had no clinical data at all other than reduction of beta amyloid plaques. And when you looked at the data, some of the data, it showed that the dementia progression was more rapid in the treated group. So they're actually damaging and harming people, based on the assumption that the results on beta amyloid in Alzheimer's were true, when they were made up. Now I've become part of an organisation called Broken Science Initiative in the States, whether we'll be successful or not, it's to try and highlight the fact that this stuff is just being made up. I was looking at a paper on cholesterol lowering, not statins, a new drug. Where, as it turns out, 35% of the deaths in the study group, nobody knew what they died off. They didn't have a cause of death. But

they were sudden deaths. And they decided to assume they were cardiovascular deaths. No post mortems, they call them autopsies in the States, were done. So they basically just made up the data, they made it up. They're making it up. And if they can do that on these drugs, which are really high profile, and then people say, yeah, they made it up, and it's almost like, well? You're gonna say is all the data being made up? No, clearly, not all the data has been made up. There are really good researchers out there doing really good work. But there are other researchers out there specifically doing not very good work. And the regulatory authorities are almost just going, meh.

Steven Bruce
Which is sad. I've got lots of questions coming in and I want to save some of them until a bit later on, because I know we're gonna get on to these topics. So can you talk about, what is the current pathway for someone, which leads to their diagnosis of cardiovascular dysfunction of some sort? I'm not gonna say they've got cardiovascular problems, but they're told they have.

Malcolm Kendrick
Well, that's the trouble with science, you ask me a question like this and it's like, kaboom. But cardiovascular disease is, of course, a really wide spectrum and it includes many things. But what most people think of cardiovascular disease would be atherosclerotic cardiovascular disease, thickening of the arteries in your heart, your neck and around your body that reduce blood supply, and then can cause heart attacks.

Steven Bruce
and include strokes.

Malcolm Kendrick
Yeah. Oh, absolutely. So you can either have a heart attack or a stroke, and then obviously, you're going to be, you know, diagnosed with it. That tends to be where the diagnosis starts, you've had an episode, maybe you get angina, where you get pain because of lack of oxygen supplied to the heart. Other things can happen as well, it can damage your kidneys, it can damage your eyes, it can do all sorts of things, but generally, someone will have to have a symptom that will then be diagnosed. Not always, but that's sort of how it goes. So once you've had a symptom, you're called someone who has diagnosed heart disease. In the clinical trials, they would call that secondary prevention, you've had a primary event, we're trying to stop a secondary event. People who are treated before they have any diagnosed cardiovascular disease, that used to be called primary prevention, which is what most people are, we don't know you've got cardiovascular disease, but our risk calculator says you are at high risk of it. And they're now called low risk and high risk.

Steven Bruce
I suppose that's the population that I'm most interested in. Those are the ones who are going along and are going to be given some advice on how they avoid cardiovascular disease. And that's going to start with tests, which you're going to tell us about, I'm sure, and why would a GP test someone's cholesterol levels? Is that something you do as a routine?

Malcolm Kendrick
It's standard, it's routine. Well, in the UK they've got a thing called QOF, which is quality outcome framework. You get paid for doing things like measuring their cholesterol, measuring their blood pressure, measuring this, that and the next thing and you get paid for so doing, and if their cholesterol is here, you get paid for putting them on a statin. If your blood pressure's here, you get paid for lowering their blood pressure. If they've got diabetes, you get paid for putting them on diabetes medication and bringing their sugar down.

Steven Bruce
There are people who would say that's not a good model for healthcare.

Malcolm Kendrick
There are a lot of people who would say that's not a good model. And I would be amongst them. In fact, when QOF was coming in, I was part of the BMA negotiation committees, blah, blah, blah, and I threw myself on the tracks on this one and said, don't do it. And then the train ran me over and that was that. Because everyone thought this was going to be wonderful. It's based on evidence, it's fantastic. And the review on QOF is, it hasn't achieved anything at all. Nothing. In fact, all we can see is it might have caused some damage. This is not just me, it's been published in the BMJ and The Lancet, and da dee da dee da.

Steven Bruce
Is QOF still going?

Malcolm Kendrick
It's still going. It's gone in Scotland. Hurrah! People have been trying to get rid of it in England and Wales, but it's clinging on, a bit like Putin hanging on in Ukraine, we cannot give in otherwise it will demonstrate we were wrong about it all in the first place.

Steven Bruce
So given that you're going to be paid for measuring someone's cholesterol, what's the trigger point, when do you say, I'm going to measure your cholesterol? Is it as soon as they're 18?

Malcolm Kendrick
They keep changing the regulations, so I'll probably say something wrong here. But if you're a bloke, you'll get a cardiovascular screening thing done when you'r 55, think it is. Women at 60. And this testing will be done and they'll test your cholesterol and your blood pressure and blah, blah, blah, all the usual things, and then start treating you for various things. So that's kind of how it works.

Steven Bruce
And you're being paid to do this. And now you're being paid because, I mean, do what the current goal for cholesterol level is?

Malcolm Kendrick
Cholesterol's part of it. There's a thing called QRISK2, and 3, which is a risk calculator. You can go on the internet and type it, if you type in QRISK2 or QRISK3, it'll come up straight away. And it's basically, QRISK3 is the latest one, and it's 20 factors. Most GPs don't know this, but I separated them out and said, how many factors are they looking at? And so then it'll be weighted. So actually, you do not get your LDL level checked, by the way, this is not part of the calculation, LDL being the bad cholesterol. So it'll say, have you got diabetes, yes or no? Do you smoke, yes or no? How old are you? What sex are you? Are you from an ethnic minority? Which is a slightly trickier one. What is your postcode? There's another one. And you put all these in and then you press go, what's your blood pressure, da dee da dee da, and it will say your risk of having a cardiovascular event in the next 10 years is, whatever it is. And if it's above 10%, you will be advised to take a statin for the rest of your life. In the US it's 7.5%.

Steven Bruce
Do they use the same calculator?

Malcolm Kendrick
No, they use a thing called ASCVD, but it doesn't use as many factors. And they say, we tell everyone to take exercise and dietary stuff and blah, blah, blah, lifestyle things are first, but the reality is that never happens. They just want you on a statin and that's it, or if your blood pressure's high, you get your blood pressure lowered. If you've got diabetes, they'll lower your sugar level, and that's kind of about it, really.

Steven Bruce
There's a lot of people who will be very critical of GPs for doing that. But presumably a GP is seeing however many dozen patients a day at five minutes each and the simplest route is to say, the NICE guidelines say do this, that's what I'll do.

Malcolm Kendrick
Yeah, well, QOF is not quite the same. Let's not go down that route. Let's say it's NICE. And, yes, as a GP, if you don't do QOF, you will go bankrupt and lose all your money and you won't work anymore. Because you won't be able to make a profit. And if you don't make a profit, you can't pay yourself and if you don't pay yourself then you can't feed your children. So there's quite a lot of incentive to do this. It's not just cardiovascular, it's also other things that are not cardiovascular. But this is quite a major part of it all. So you get paid a lot of money for doing this. Anyway, you've probably gathered what my view is on this.

Steven Bruce
And I know it'll go down well with the audience, because, of course, everyone likes a bit of controversy. But also people like having it backed up with evidence. I know we would have got to this eventually, anyway, but Keith asked earlier on, did the statins cause weight loss and is that how they affect type two diabetes? I know that is covered in the The Clot Thickens.

Malcolm Kendrick
Well, no, statins can increase weight, can actually cause weight gain. In fact, there's quite a lot of studies that have shown that people take statins start to think, I'm protected, so I'm not going to do anything else.

They take less exercise, they do other unhealthy lifestyle things. And they make diabetes worse. It's actually a warning on the drug insert. People may develop diabetes taking statins, and there's biochemical reasons for that, which I have covered. But no statins will make diabetes worse, or they'll raise your blood sugar, they will not help with weight loss. That's not how they're supposed to work. The argument for statins in diabetes is, if you've got type two diabetes, we're not talking about type one here, you are at threefold increased risk of dying of cardiovascular disease, possibly higher. Now, statins reduce the risk of cardiovascular disease, therefore, all people with diabetes must take statins. It has nothing to do with your blood sugar level. That's not what they do. So whatever your blood cholesterol is, you will be advised to take a statin if you've got type two diabetes. If your cholesterol was one or point one, or zero, you'd be told to take a statin.

Steven Bruce
So do they have other effects than lowering cholesterol?

Malcolm Kendrick
Well, we've discussed this before. Yes, they do. I was just reading a paper showing that basically, statins have, last time I looked, I counted 38 off target effects of statins. All drugs do more than one thing. They all crash around the human physiology. The main benefit of statins, in such as they have, is that they are actually quite reasonably strong anticoagulants, around about the same strengths as aspirin. And that effect happens very quickly. So they have an anticoagulant effect, they stop blood clots. And as we know, drugs that stopped blood clots reduce the risk of heart disease. They also lower blood pressure, they do it through the same mechanism, probably won't discuss that here, but they lower blood pressure, they lower your blood clotting, and therefore these are probably the two main impacts that they have on reducing cardiovascular disease risk.

Steven Bruce
So this sounds contradictory, because now you're saying well, they do reduce cardiovascular risks, so therefore they are a good drug?

Malcolm Kendrick
Well, aspirin reduces cardiovascular risk, but there's a long argument about the adverse effects of aspirin outweigh the benefits, because the benefit is small and then the adverse effects are greater.

Steven Bruce
And with statins is that the same?

Malcolm Kendrick
Well, I believe that the adverse effects of statins are far greater. At the moment we've been given this message that statins cause no adverse effects. It's all a nocebo effect, in other words, we think they're going to cause an effect therefore they do. But that's based on this same research group in Oxford, essentially. Now, I have looked at more recent studies where they've been double blind, placebo, for whatever that means, crossover studies, where 43% of people who are given statins reported adverse effects, ranging from pretty minor to pretty major. And I've seen people die from taking statins, they can kill you. This is known. I'm not saying anything that is not known here. This is not controversial. Statins

can cause liver failure such that leads to death. It's not common, but it can happen. And statins can cause a thing called rhabdomyolysis, where your muscles basically dissolve. They break down, they head for the kidneys, because so much crap basically arrives at the kidneys, your kidneys fail, and then you die of kidney failure. Rhabdomyolysis has a 25% mortality rate. And statins cause it in one in however many hundred thousand people, doses, whichever metric you're going to use. So yes. You know, you say these things and people say, yes, but it's so rare it doesn't matter and you go, I've seen three people die from taking statins. Absolutely direct cause. I'm one GP. There's like 40,000 GPs in the country, if every one of them has seen three, that's 120,000.

Steven Bruce
To which I suppose the obvious question is, but how many people didn't die early because they were taking statins?

Malcolm Kendrick
Well, I know the answer to that question. In primary prevention, the answer to that question is zero. It doesn't prevent you from dying. They don't prevent you from dying.

Steven Bruce
They didn't prevent you from dying early, because obviously, nothing is going to prevent you from dying.

Malcolm Kendrick
That's true. You catch me.

Steven Bruce
No, I thought you were trying to catch me out.

Malcolm Kendrick
No, I'm not trying to catch you out. It's something I always say to people, you're gonna die, nothing will prevent you dying. It just depends how long they actually give you. A study by Christiansen in BMJ Open and they looked at this and said, well, how many extra days do you get? Whether that's statistically significant or not. And they found that if you took a statin in primary prevention, looking at nine of the major studies that they had, the increase in life expectancy was three days for over five years of treatment. So that's 0.75 days a year for taking a statin. Now, that is as beneficial as you can get. There's a group in America called NNT, which is Number Needed to Treat, who make the statement on their site, statins do not affect overall or cardiovascular mortality in primary prevention. 95% of people who are treated with statins are primary prevention, taking it without known cardiovascular disease.

Steven Bruce
I think you did say in, it might have been The Cholesterol Con, I'm not sure, that actually if you've had a prior cardiovascular event, then they can be beneficial. Is that still your opinion?

Malcolm Kendrick
Yeah. I do agree that they have shown some benefits in secondary prevention. But I mean, we're talking here about really minute amounts of time. In secondary prevention, the figure was 4.1 days of increased

survival, per five-year treatment. That's 0.8 of a day, a year. Now, you may think that's worthwhile. People think, oh, I'll live for an extra year. But remember, two things, what the statin promoters say is, yeah, well, obviously people are taking them for 30 years, and these benefits will get greater and greater. And what I would say is, well, you don't know that. And the other thing is, are they causing damage? If you did a study on people smoking cigarettes for five years, you would find no difference in overall mortality in the two groups. Does that mean that there's no danger or no damage? I've seen people who have become ghosts of themselves taking statins for 20 years. They just become a bit like Gollum in Lord of the Rings.

Steven Bruce
I don't want us to just go over stuff that we've talked about before. But I think some things are definitely worth emphasising. And one of the points you made on, I think the broadcast we did in Manchester, was that one of the reasons that the side effects, the adverse side effects, of statins are possibly not as great, it would seem, is that GPs don't ask the questions correctly. So if you say to somebody, "is your memory going?" or something like that, they're probably going to say, no, it's fine. But then their wife or their partner might say, no, he's been a lot worse.

Malcolm Kendrick
Absolutely. One of the things, going back in the world of cholesterol, was they noticed the first drugs that were given to lower cholesterol, this is 1970s, people were more likely to die of violent death, accident or murder or whatever, and they said, well, this, is this just a coincidence or is it a real effect? Well, if you go, you can find that 75% of criminals have got low cholesterol levels in their blood. Violent criminals have low cholesterol levels in their blood. And if you ask people who are on statins, about their sense of irritation and aggression and anger, if you ask those questions, every single one of them, or their close relative more likely, will say they've been almost impossible to live with since they've been taking these bloody drugs. I was doing an interview in my house with a Dutch crew, and I was talking about this. And there's a guy doing curtains in the back, and I was talking about this and he went, that's exactly what happened to my wife. She's become unbearable. She's so angry and irritable. Of course, it's not down as an adverse effect. No one will make those connections. But there's a researcher in the States, Beatrice Golomb, who's been looking at statin adverse effects for the last 40 years. And she says this is one of the primary things that she's noticed, is people become really irritable and angry about things, and when they stop, it goes away. Now, you can argue about why that happens. Mechanisms are there and potentially clear. 25% of brain's made of cholesterol, dry weight, it's essential for the production of synapses. It's just an essential neuronal function. And you knock that down, what's gonna happen in your brain? Well, it's not going to be good, is it? And I believe there is a huge amount of not done research out there demonstrating... And muscle pains and joints, you'll get this such a lot. Muscle pain, 40% of people. So if you're talking about this group, why is it important? Someone's getting muscle pain and joint pain and difficulty gripping and you say, are you on a statin? Well, let's see what happens if you stop it for a bit.

Steven Bruce
Again, I asked you this before, where do we stand as physical therapists in saying to a patient, well, try stopping your statin? It's outside our scope of practice.

Malcolm Kendrick
It is outside your scope of practice, but I think you can suggest, oh, I've seen a lot of people like this, maybe you want to go and speak to your GP?

Steven Bruce
Yeah. And I say to a lot of them, you might want to read one of these books.

Malcolm Kendrick
I mean, it's ridiculous, isn't it? You should be looking at causes of things. Here's a potential cause of a thing. And you're not allowed to discuss it.

Steven Bruce
Can I turn to a few of the questions? Pippa sent this one in earlier on, she says as someone with familial hypercholesterolemia, I'm staring down the barrel of statins, having been told that diet will play only a very small part in cholesterol levels. I've been taking plant sterols, a gramme a day, as well as omega oils and turmeric with curcumin, but haven't seen any real decrease in cholesterol levels. 8.8 at last check. I do 10,000 steps every day, as well as on the exercise front, and obviously try to eat healthily also, what else could people like her do to reduce their cholesterol level? Well,

Malcolm Kendrick
Well, you can take a statin, that'll reduce it. Or you can take one of the new injectable PCSK9 inhibitors, that will reduce it even more. Or what you could say, is what I would say to you, is stop worrying about it.

Steven Bruce
Familial hypercholesterolemia, tell us a bit about that though, because it is singled out, I think, as a group who are prone to cardiovascular disease, isn't it?

Malcolm Kendrick
Yeah, it is singled out. I've written a couple of papers on this. And the study where this comes from is obviously originally, it was Goldstein and Brown looking at, there's a thing called an LDL receptor, sits on all your cells, millions of them in your liver, and they pull LDL out of the bloodstream. LDL, low density lipoprotein, is what people are talking about when they're talking about cholesterol, in reality. So although it's called familial hypercholesterolemia, it's actually familial LDL-emia. The terminology is terribly stupid and confusing.

Steven Bruce
But basically, it's a genetic population who have high LDL.

Malcolm Kendrick
It's a genetic population, about one in 500 people have the heterozygous form of this. So there's different forms of it. About one in a million people have homozygous familial hypercholesterolemia and their cholesterol levels are like 40 and stuff and they die young of heart disease, it's like ah, proven it. But in the UK, we have a thing called the Simon Broome Register, where they've looked at people with familial

hypercholesterolemia, and monitored them over years and years to see what happened. Now, there is a small group of people who died young of cardiovascular disease with familial hypercholesterolemia. I think the total number out of the 1000s, it was eight. So we're talking minute numbers here. What they also found was after the age of 50, if you have FH, you live longer, and you're less likely to get heart disease. So to me, this is like saying, well, if you smoke before you're 50, it's going to kill you, but after 50 actually it protects you from lung cancer. Let's think that through again. So what we looked at was, this is the yellow fingers and lung cancer argument, again. It's that people who have yellow fingers are more likely to die from lung cancer. Yes. Why have they got yellow fingers? Because they smoke, it's not the yellow fingers causing the lung cancer. This is when you have, what's actually the causal agent that's going on here? Now, when you look at familial hypercholesterolemia, there are subgroups of people within this who have a blood clotting factor abnormality. Now, when they looked at twins, one of whom had the FH gene and had the high cholesterol, and the other one who didn't have that gene and didn't have the high cholesterol. They have the same risk of cardiovascular disease. So another gene, this is smoking. What you're looking at is yellow fingers, when you're looking at the cholesterol level, there's something else going on in there, that's actually causing heart disease, and that is blood clotting factor abnormalities. And you can show them, because I'm not going into the exact details of this, it'd take too long, but the LDL receptor itself, which sits on cells and pulls LDL molecules out of the bloodstream, also takes out factor eight, it has a very important blood clotting factor control issue with the LDL receptor. So this idea, what does the receptor do? Well, it takes LDL out. That's it. No, it does all sorts of other things as well, which are very important. And some people have this, and some people don't. And if you split the sections out 95% of people with familial FH, or however many it is, don't have this double gene, and 5% of them do. It's these 5% who are at risk. It's not because of the LDL, it's because of the clotting factors. By the way, she can go to her own doctor who will know none of this, understand it less, and will dismiss it completely out of hand.

Steven Bruce
That's where I was going with this because I know that, quite rightly, you've said you're not going to give medical diagnosis over the Internet to anybody who you haven't actually had in your treatment room and examined. So Pippa can't take this as her diagnosis or recommendation, so who should she go to, where she can get a reliable...?

Malcolm Kendrick
She can't, there's no one.

Steven Bruce
Where do you practice? You're in Manchester, aren't you? I don't know where Pippa is.

Malcolm Kendrick
There's no clinical practitioner that will even countenance this, even though the research shows that it is this. And everything shows that it is this.

Steven Bruce
So from what we're saying here, without having examined Pippa yourself, should she be somewhat reassured by what you've just said?

Malcolm Kendrick
I think she should be reassured that people with familial hypercholesterolemia live just as long as everybody else. Whether they die of cardiovascular disease... Go back, there was a study done in the Netherlands, ironically by one of the greatest cholesterol lowering proponents. And they look back through history and said, well, we know it's a genetic condition, so let's look back through history at people who died and what ages they died at, who we know will have had familial hypercholesterolemia. So, they went and looked at records from 1815, 1819, whatever. And what they found was that actually in the 1850s to about the turn of the century, people with familial hypercholesterolemia lived longer than the surrounding population from. 1900 to about 1960, they lived shorter, and from 1960 onwards, they are now living longer again. Now, the explanation for this is that LDL is quite a potent anti infective agent, it locks onto bacteria and viruses and stabilises them and then the immune system comes along and kills them. It plays a very important role. There's studies with rats, where you have rats with high LDL, you stick nasty substances into them, bacterial substances into them, and those with higher LDL, that if you ever heard of a thing called lethal dose fifty, at what dose do 50% of the animals die? The LD50 in those with higher LDL levels was eight times as high. Eight times as high.

Steven Bruce
This is only for bacteria, not viruses?

Malcolm Kendrick
That was only for bacteria. They are part of the immune system. Almost everything in the blood is actually part of the immune system when you look at it. Blood clotting factors are a key part of the immune system. And LDL is a key part of the immune system. And these these stick on to and basically stop them from being infected. And this research is well known, published and disbelieved by everybody to do with cholesterol. So you are less likely to die of an infectious disease if you have high LDL, it will protect you against infections, and a small proportion of people will have this clotting factor problem which is a problem.

Steven Bruce
Pip's come back in to say that it's very interesting, she was also identified as having a haemoglobin variant of no consequence, so she was told. Maybe she should look more into what that heamoglobin variant is?

Malcolm Kendrick
Well, pople with blood group O are less likely to die of heart disease, people with A or B are more likely to die of heart disease. This again, is an immune complex blood clotting issue going on here. It is fascinating when you start looking, everything connects to everything else in ways that you initially think they don't, but they do. Human physiology is just like, what, how has that ever happened? It's really fascinating. But the fascinating thing is that possibly FH was something that became more prevalent at a time when infectious diseases were wiping out so many people on this planet, because when people moved from the countryside to the cities, and the population was crammed together, and the might have had people dying to things like syphilis and TB and whatever, having an increased protective factor in your blood is probably quite a good thing to have. And that's why from 1900 to 1960, it actually didn't do any good, but once antibiotics came along. It's really fascinating, but don't get worried about it. There's a

guy in the States came up to me 10 years ago saying, my LDL, which is the bad cholesterol, is 18. And he said, I've been investigated for many years because they can't work out why I have no detectable heart disease. None. He's been scanned, he's been screened, he's had his arteries looked at in every possible upside-down way. I thought, well, maybe. And then he sent me a paper where he's been studied as a case history. Here's a man with the LDL, his total cholesterol would be about 25, of 18. No detectable heart disease. That's not just one by the way. I can give you example after example. Now the solution to this is apparently the experts go, oh, he must be being protected by something else. No, the solution is LDL doesn't cause heart disease. That's the obvious and easiest solution to your problem.

Steven Bruce
Something else is causing the heart disease.

Malcolm Kendrick
It's not LDL, it never was. It isn't, it can't be, it's impossible that it is.

Steven Bruce
So before we get on to what it might be, or what it is, let me ask you one more question because, I need to just scroll down first, and Robin sent this one in, I think yesterday, but was worried that he might not be here, but I'm told Robin is watching. So this is Robin. He's talking about Sally Norton's book Toxic Superfoods: How Oxalate Overload is Making You Sick and How to Get Better, and she says the blood vessels are prone to damage from oxalic acid and crystal accumulation which can lead to tissue degeneration, including cataracts, vision problems, and fatal brain aneurysm. Oxalate deposits are found in the arteries and in calcified arterial plaques. And the crystals are associated with blood vessel weakness, vasculitis, stroke and cardiac conduction abnormalities and arrhythmia. Could I ask you how significant you think oxalate damage is in heart disease?

Malcolm Kendrick
I'll quote my great mentor, who said it's fascinating why you find so many fire engines at the site of fires. They don't cause the fires. There's a lot of things you'll find associated with damaged arteries and all sorts of other parts of the body. Ask yourself the question, did they cause it? Or did it cause them? Oxidation and oxalic, the human immune system and also the clearing up system, uses superoxides to destroy bacteria and viruses. That's what microphages do. It also uses these to destroy damaged areas in the body. So if you have damage going on, your immune system goes in and oxidises the hell out of it, and then takes it away. Of course, if you don't get rid of all of it, what you've got left is an awful lot of superoxides kicking around. This is the body trying to heal itself. This is not the cause. This is somebody getting, as everybody does, cause and effect the wrong way round. And this is the same reason why the cholesterol hypothesis has lasted so long. What is the most important repair system in your body? It's cholesterol.

Steven Bruce
It is true is it, then, that if you've got cardiovascular disease, you are likely to have higher levels of cholesterol?

Malcolm Kendrick
No, it's not actually true at all.

Steven Bruce
So it's a very strange hypothesis.

Malcolm Kendrick
Well, that hypothesis began, because when people looked arteries, and atherosclerosis, thickenings and damaged areas or whatever you want to call them, they found that there were a high percentage of cholesterol in them, right? And then they said, well, where did this cholesterol come from? And the answer was, well, it must have come from the bloodstream, because where else can it come from? Which is a reasonable hypothesis. Therefore, the raised cholesterol that you find is the cause of the atherosclerosis. No, that's yellow fingers, and lung cancer all over again. This type of thinking is so prevalent in medicine, we find an abnormality and we decide the abnormality is the cause of the disease. We find beta amyloid plaques in the brain and decide that beta amyloid plaques are the cause of Alzheimer's. No, this is the body trying to repair itself, you idiots. We find cholesterol in arterial plaques. This is the body trying to repair itself. This is you getting it 180 degrees the wrong way around as per usual, you idiots.

Steven Bruce
My audience loves it when people get off the fence and they're fairly emphatic about their views.

Malcolm Kendrick
Well, I can't be more emphatic. This is just such a stupid idea that's caused so much damage, for so many years.

Steven Bruce
It must be doubly frustrating for you because as we already said, It's outside our scope of practice to advise people on what they do about their potential cardiovascular problems. But for you, trying to educate your fellow GPs and the rest of the medical world, because actually there's an awful lot of cardiovascular consultants, presumably, who sign up to the cholesterol hypothesis,

Malcolm Kendrick
They all do. Well, 99.99%

Steven Bruce
We'll move on to The Clot Thickens in a minute, but have there been occasions when you have sat down with the head of the unit at Oxford, is it Sir Rory...

Malcolm Kendrick
There was an occasion when I was supposed to be debating with him one time.

Steven Bruce
Rory Cox, is it?

Malcolm Kendrick
Collins.

Steven Bruce
Rory Collins.

Malcolm Kendrick
Where he pulled out. You can't debate anything anymore. Debate doesn't happen in science anymore. It's like, someone said, we should be playing tennis, but we're all playing golf, where we all just play our game and come to the end, where we should be banging it back and forward. But you don't get this bang, it is very difficult to get debate with anybody. They usually just say, do you know who I am? And that's it. Or they produce these enormous reports from the European Society of Cardiology, which had like 70 pages of why cholesterol causes heart disease, it's proven fact and then they selectively pick every fact that they can. Ironically, the man who runs the UK Biobank study is also Rory Collins. You may never have heard of the UK Biobank study, but it's this enormous study where they gathered genetic and other data about people to try and work out what's causing illnesses, which is, at least in theory, quite a good idea. Although if you're a pharmaceutical company, you get first dibs on all the information for the first five years or whatever it is. And they looked at cardiovascular disease in the UK Biobank study and said, well, what factors do we find increase cardiovascular disease? Number one was previously having had cardiovascular disease, big surprise. Number two is diabetes, essentially, big surprise. Smoking was pretty high up there. And you go down all these factors, and then they came to cholesterol. For each one millimole increase in cholesterol, the increased risk of cardiovascular disease is one. And one is basically, you or I would say. nothing, no risk, this is average risk. So there was no difference in cardiovascular disease death, with every one millimole increase in cholesterol, none. Zero. It was 1.01 and 1.02, which is essentially one and one is no increase in risk. So they produced a study. And it's in the BMJ about four years ago, and I read it and thought, there we go. You have seen no difference in cardiovascular risk, no matter what the cholesterol level is, nothing. Zero, zip, nada. Okay, so what do you say about this? They didn't even mention it in the abstract. They didn't mention it in the discussion. They didn't mention it in the results. They did the table, you had to go into like appendix 73, subsection four to find this table, but it was there. I wrote to them, of course, I didn't get a reply, saying, interesting, I noticed you found there was no increase in the risk of heart disease with an increased cholesterol level and what's your explanation for this? Do you have an explanation?

Steven Bruce
Simon, sent in a question a few minutes ago and Simon, I hope you'll forgive me for phrasing it this way. But it seems to me that what Simon is asking is possibly a very common response to what you were telling people because he says, do you think that cholesterol particle size has any relevance in this? Because he's read that it's not your cholesterol count matters, but what makes up that count. And I suspect that lots of people will turn to you and say oh, yes, but it's something else in the cholesterol.

Malcolm Kendrick
This is what I call throwing chaff into the air. You know, someone tries to shoot down an aeroplane, it throws chaff up. Well, essentially, yes. We started out with cholesterol, right. And then, oh, no, it's not cholesterol, it's low-density lipoprotein. Oh, no, it's not low-density lipoprotein, it's low density lipoprotein,

high density lipoprotein ratio. Oh no, it's the non HDL level that counts. And then we had light and fluffy LDL. And then we had small dense LDL, we still got all of these things, they still swirl around. And now we've got particle number, right? Well, what's the difference between a particle number and the total number of molecules? Explain this to me. Then they say it's not that, it's the apolipoprotein that's attached to the molecule that counts. And then now it's the ratio of... Guys, guys. Stop. It's got nothing to do with any form of cholesterol whatsoever. In fact, you have no cholesterol in your bloodstream anyway, it's all carried around in lipoproteins. Like people are in taxis. It's a bit like saying, how many people are there on the motorways? I don't know, they're all in cars. How much cholesterol you got in your blood? I don't know it's all inside lipoproteins. Oh, it's the particle, particle, what? What's the difference between the number of particles and the actual total number? Because they seem to be suggesting something here that stretches the possibility of of logic snapped beyond... every time you look at these things they go, ah, well it isn't that. The last time I looked at HDL, which is high density lipoprotein, I'll give you a little story about high density lipoprotein, it's supposed to protect against heart disease, because it sucks cholesterol out of plaques, takes it to the nearest LDL molecule, transfers it to that and it goes back to the liver, and it's taken out of the system. And they found a group of people living in Italy who had almost no HDL, and they had no heart disease. And they said, oh, right, they have a special form of HDL, which is specially protective, even though they haven't got as much of it. They called it ApoA-1 Milano. And they created ApoA-1 Milano in a laboratory, injected it into people and said, now they're atherosclerosis will disappear. And certain people became very rich on this because this technology was sold for a billion dollars to Pfizer. And Pfizer on some early results, by a couple of guys that I won't mention the names because otherwise I'll end up swearing at them, who said, this is amazing, the plaques disappeared, like snow on a dike or whatever. And then Pfizer did a study and they said actually, nothing happened. So this product kind of died. So particle size, particles, oxidised LDL, deoxidised LDL, it is nothing to do with LDL. You can flip it around in a million different directions, and they have and it still continues. I keep reading papers about oh, it's whatever form of LDL or it's the amount of esterified cholesterol within the LDL. No, you can't do this because it's nonsense. It is utter nonsense. It's the same thing, you're just changing the name and flipping it around and saying, oh, well, it's not this, it's that. No, it's none of these things. It's nonsense.

Steven Bruce
I've got a few other questions here, which are all asking variations on the cholesterol theme, is it low total cholesterol, is one of the questions here. But shall we just leave it that cholesterol has nothing to do with heart disease, as far as your research shows.

Malcolm Kendrick
Yeah, well, it has nothing to do with heart disease.

Steven Bruce
So, forgive me if I don't ask these questions specifically.

Malcolm Kendrick
No, no, I understand. You're trying to move people from something they've heard banged out for the last 30 years, by everybody, by the experts. How can this person possibly be right? How can they say that what they're talking about is right? How can they be right? Because the evidence says I'm right. There's

a drug out there called Repatha, otherwise called evolucumab, which lowers LDL by 60%. 60%. More than any statin. And the study, was a four-year study, and it was recently re-reviewed by a group restoring abandoned and incomplete trials. There is a group that do this. And they went back and reanalyzed the data from the trials and said, actually it's even worse than we thought. This drug reduces LDL by 60%, and in this trial over two years, the difference between the people that took it and the people that didn't take it was that there were 114 heart attacks in the people taking the Repatha and 80 in the people on the placebo. And the overall mortality went up as well.

Steven Bruce
That was statistically significant, was it?

Malcolm Kendrick
That was not statistically significant. But then statistical significance is another one of these...

Steven Bruce
Well it is an artificial measure, ain't it?

Malcolm Kendrick
Just measuring p-values. P-values and peer review are two ps we should be getting rid of. And anyway, more people died. Before statins came along there were other cholesterol lowering agents, clofibrate, that lowered not quite as much but a similar amount, increased overall mortality and cardiovascular mortality, and with overall mortality it was statistically significant. There's a whole bunch of other drugs that no one's ever heard of, they will never launch, they were called trapibs, four trapibs, euvacetrapib, torcetrapib, anyway. Billions were spent on reviewing these because they lowered LDL by as much as statins. In one case, they increased HDL by 130%. And none of them had any benefit on cardiovascular disease. In fact, one of them increased cardiovascular disease by 65%.

Steven Bruce
Which just added some weights to what you said earlier on, that if statins are beneficial, it's not the cholesterol lowering which is doing it.

Malcolm Kendrick
We have drugs that lower LDL more than statins, which have had no benefit on cardiovascular mortality. We have drugs that don't lower LDL at all that have a benefit on cardiovascular disease, like aspirin and various blood pressure lowering drugs and things like anticoagulants. And then we have statins that lower LDL and lower the rate of heart disease. So what does this tell us? It's not the lowering of cholesterol that is the thing. It can't be.

Steven Bruce
What is the thing, Dr. Kendrick?

Malcolm Kendrick
Well, the thing is something that people have been talking about for 170 years.

Steven Bruce
Just very quietly.

Malcolm Kendrick
17 years. 175 years now. So it's essentially when you look at it, the plaques, when you look at plaques, the thickenings in blood vessels. And I've had pathologist come up to me and say you're right, by the way, you know, this is what we are looking at. The idea is well, the original person was Carl von Rokitansky who looked at plaques in arteries in Vienna in the 1850s, and said, what I'm looking at are blood clots in various stages of metamorphosis and repair. He said that then. He was one of the first people ever to look at this under proper microscopic examination. And this is true, if you look at plaques, they are essentially blood clots in various stages of development, metamorphosis and repair. That's what they are. So you say, well, how can other people not have noticed this? Because what happens obviously in repair, if you cut your skin, you can get keloid in skin, especially with dark people, they develop these lumps, what you find in a keloid is not that there's been damage to the skin, i's just a big lump of thing. That's the body repairing itself, inappropriately in this case. Once the body starts to repair itself, what's in there looks nothing like what was in there originally. If you look at a blood clot after two weeks, there's not that much stuff that you'd definitely say was blood clot but there are things in there if you look at them closely enough. See, ironically, one of the things that was first seen inside atherosclerotic plaques was cholesterol crystals, actual crystals of cholesterol. So like sharp pointy things. They're not that long, there about...

Steven Bruce
Small, sharp, pointy things,

Malcolm Kendrick
Very small, sharp, pointy things. And that was what first directed people to think it's cholesterol, because they found that this was pure cholesterol, right? And you say, well, that's fine. Yes, it's there. I'm not gonna say it's not there. I'm not going to say that's not cholesterol, because it is. But you cannot make a cholesterol crystal out of the cholesterol you find in a low-density lipoprotein molecule, because you can only make cholesterol crystals out of pure cholesterol. And cholesterol is carried in low density lipoproteins as a thing called a cholesterol ester, which is attached end to end with a fatty molecule. That's a cholesterol ester. That's how it's carried about around the body. It's not carried free. It cannot be carried free. Chemically, it can't. So where do you get cholesterol crystals from if not LDL? The answer is there's only one tissue, or substance or whatever the exact term is, where you can find cholesterol of sufficient purity to create a crystal, and that is in the membranes of red blood cells. It's the only place in the body. And I could show you 100 papers, we know that the only place these crystals could have come from was red blood cell membranes. You can't make it out of LDL. So when you find cholesterol crystals, you know there's been red blood cells in there. They have to have been in there. So where do red blood cells come from? Well, you have red blood cells in clots. That's why if you cut yourself and you get a bleed, and then it forms itself into a scab, it's primarily dark red.

Steven Bruce
Perhaps we should have a drug to reduce red blood cells.

Malcolm Kendrick
There are people who say that if you reduce iron, you reduce the risk of heart disease, because they found that people who are anaemic are less likely to die of heart disease. It's not the iron. No, you don't want to make people anaemic. But red blood cells, again, it's amazing that they link in, red blood cells link to fibrin, which is the other part, and they attach to it. And then the red blood cells shrink into a sort of dodecahedronal shape and pull their blood clot really tight. Red blood cells are the tightener uppers of blood clots. Amazing. Anyway, you find red blood cells there, you find fibrin there, you find fibrin remnants. Where do you get fibrin from? There's two things that make up a blood clot. Well, there's lots of things that make up a clot, but there's two essential things. The platelets start it, they gather together, then red blood cells get drawn in, then fibrin forms around it like a fishing line. And then the whole thing goes skrch. And fibrin makes the clot really, really, really difficult to remove. And that's what holds it together. And if you find fibrin inside a blood vessel wall, where does it come from? Well, you're not going to form fibrin just spontaneously inside a blood vessel, it can only have come from a blood clot. So you've got the remnants of red blood cells, you've got the remnants of fibrin. Yes, you have cholesterol, and you have LDL molecules in there. So people have said. Unbeknownst to every doctor that I speak to, there is another form of LDL that floats around in the bloodstream. And it is identical to LDL except it has a protein attached to it. And this protein is called, sorry about these horrible names, aprolipoprotein A. And therefore the LDL molecule with this attached to it is called Lp(a), lipoprotein a. Everybody knows this exists, nobody really knows what it does. Well, the body doesn't produce stuff that has no function. The fascinating thing about Lp(a) is that when you have a damage to a blood vessel Lp(a) is attracted to it, sticks to the area of damage, forms very tight bonds with it and therefore plugs, is one of the original plugs for damaged to a blood vessel. And then the apolipoprotein A comes in, I just find this fascinating, other people maybe don't, but anyway. Apolipoprotein A, when a blood clot forms, all sorts of things get pulled in, it's like what? Anyway, one of the things that get drawn into every blood clot is a thing called plasminogen. Plasminogen is a pre-enzyme, it's not active. It's drawn into every single blood clot. I don't know how much it's on it. And, this is the amazing bit, if you want to blow up a blood clot, tissue plasminogen activator is a thing that's produced by the body. Tissue plasminogen activator comes to the clock. It locks in, it converts plasminogen to plasmin, and plasmin slices fibrin apart. And so the blood clot disintegrates.

Steven Bruce
This is the stuff they inject into people having a heart attack in hospital, isn't it?

Malcolm Kendrick
It used to be, they now do other things. If you're having a stroke, they'll give you tPA, it's called different things, and it busts the clot in your brain and stops the stroke from causing so much damage. Obviously, you don't want to give it to people who are having a bleeding stroke because otherwise it'll kill them. But if you're having a blood clot caused stroke in your brain, you give them tPA. So tPA, tissue plasminogen activator, activates plasminogen, plasminogen turns into plasmin, plasmin slices fibrin apart, the clot starts to be dissolved. Back in the story: Apolipoprotein A is identical to plasminogen apart from how it's folded at the end. So the tPA comes across an Lp(a) molecule, or the apolipoprotein A molecule, goes I'm going to activate you, and it goes, you can't activate me, I'm not plasminogen. So that clot does not dissolve fully, if at all. But of course, you then have this clot, which is stuck to the artery wall, and it's got tPA, it's got an Lp(a) in it, which is LDL by another name. And then what do you do with it? Well, you can

dissolve it around a bit, because if the clot started that size, you could reduce it to say that, whatever size. But you've still got to do something else with it, you can't let it break off and travel down the artery, because it will just get jammed somewhere further down the system. And could cause a heart attack or stroke, a smaller heart attack or stroke. So your body has to do something with this clot that's stuck to the artery wall. Now it can dissolve it so far, but then it runs across apolipoprotein A and it's stopped. Because obviously, if it could just keep dissolving it, all that would happen is you got a blood clot, it completely dissolved. And then you say, oh, my God, there's an exposed area. Another blood clot, dissolve, blood clot... Well, that is a stupid system, that won't work. So there's a bit of the clot that's closest to the artery wall that's been damaged, stays there and doesn't get broken down. That's the function of Lp(a). So then this thing that's sitting here has to get covered over by a new layer, a new endothelial layer, which is the layer that lines all arteries. And we know this is happens. One of the reasons why Rokitansky's idea was never accepted, because another chap called Virchow said, but these are underneath the endothelium, these blood clots are underneath the endothelium. How can a blood clot form underneath the endothelium, when blood clots form within the blood itself? And Rokitansky couldn't answer that question. So Virchow said, well, you're wrong, aren't you? And that was the end of Rokitansky's ideas. Rokitansky didn't know, because how would he know, that in our bloodstream float around endothelial progenitor cells, EPCs, and they're present in your bloodstream all the time and if they see an area of damage, they come across it, they stick to it, they grow into proper fully grown endohelial cells, and then at that point, everything's repaired. But you have a remnant blood clot stuck in the artery wall at that point. Now it's full of fibrin.

Steven Bruce
And that's causing a narrowing?

Malcolm Kendrick
It will cause a narrowing. Well, an initial one, and an initial one probably causes very little of a narrowing. But if you look at blood, if you look at plaques, and you chop them in half, you find a number of them, about 45% of them, it's like looking at tree rings, there's layer after layer after layer after layer after layer after layer after layer after layer after layer. You say well, what could have caused all these layers to have formed? Well, it's blood clot after blood clot after blood clot being shaved away and removed. Probably most of them are fully removed, but some of them will get stuck. And if you've got a stuck area, it's probably a vulnerable area, where you're more likely to get another blood clot. So these become focuses of blood clotting. And then blood clots build up and build up and build up and build up.

Steven Bruce
So I think we missed out a stage here, didn't we, because you were talking about blood clots and I'm thinking, well, why the hell is there a blood clot? We've got endothelial damage, but what's caused the damage? That surely is?

Malcolm Kendrick
So step back, you're not going to get a blood clot until you've damaged the artery wall, or the blood vessel wall, because there's no stimulus for a blood clot to form. Because your blood system enormously doesn't want blood clots forming all over the place.

Steven Bruce
So at last, this is where cholesterol comes in. It's bursting through the artery wall.

Malcolm Kendrick
Well, this is the idea, is that cholesterol bursts through the artery wall, through the endothelium. And then what? Well, it gets stuck inside the artery wall in some way. And then that's where it all happens. That idea might have some validity if you could get LDL through the artery, through the endothelium. Now, I've looked at this, this is the most complicated part of this, I'm not going to go into any great detail, but what I will say to you is, all arteries, the arteries of the size in which atherosclerosis develops, have actually got their own blood vessels to supply them with blood. They're called vasa vasorum, the blood vessels of the blood vessels. And they form a latticework around major blood vessels. And anything in the bloodstream can come into the vasa vasorum and then enter the artery wall from behind, including as many LDL molecules as you want. Because once blood vessels reach a certain very small size, which the size of a vasa vasorum, very small, they are no longer barriers to the movement of substances. Obviously, they can't be because otherwise nothing could move in and out of the bloodstream, and you'd just die. So they have what they call fenestrations, holes in them, gaps in them, and the basement membrane behind them starts to loosen off. So in your kidneys, for instance, you've heard of the glomerular apparatus? You've got all these blood vessels in this little cup, and they're capillaries. Well, clearly, this is the point at which all sorts of stuff leaks out, and then goes around your loop of Henle and all that. And if it couldn't leak out of here, then your kidneys couldn't work. So at the smallest level, blood vessels are leaky. But at a larger level, blood vessels cannot be leaky, because if you allowed everything to leak out of your major arteries into the tissue underneath, you would be dead almost instantaneously. Because your body would just fall to pieces. Now we know this because you've heard of Ebola? And Ebola kills you, and how does it kill you? It's called hemorrhagic fever, is the other word for it, you start peeing blood and stuff like that. Why does this happen? Because the Ebola virus, for reasons unknown, I don't understand why, is there are all these really tight junctions between all the cells in your body. And Ebola opens up these junctions, especially the junctions in your blood vessels. So it removes the tight junctions. And once it does this, all of the contents of the blood can go straight through the blood vessel wall into the surrounding tissue behind. And that's why you die of Ebola because it opens up the normal barriers in the endothelial cells and allows stuff to leak out. So from that perspective, unless you have opened up the barriers in the normal endothelium in the larger blood vessels, nothing can get through, that is not allowed to get through. The body very carefully regulates how these things work. And yet people say well, LDL is completely different, it just goes through. Well, why doesn't water go through? Why don't even smaller molecules go through? Why don't the endothelial cells just let anything go through? Because if they did, you'd be dead.

Steven Bruce
I got you started on a red herring there, didn't I? Because I cheekily said yes, it must be cholesterol, when I knew very well, you were going to tell me it wasn't. So what is causing the damage to the endothelium?

Malcolm Kendrick
Well, an endothelial cell is, say it's this size. Now, obviously the bloods flowing past them all the time and quite rapidly. Now, all endothelial cells also have got a thing attached to them called glycocalyx. Again, you ask 100 doctors, no one has any idea this exists.

Steven Bruce
This is the slippery stuff on fish?

Malcolm Kendrick
This is the slippery stuff on fish. You try and pick up a fish, not all fish, sharks don't do this, but the fish you catch normally, small fish, grab hold of it, straight out your fingers. Why? Because it's covered in glycocalyx, which is really slippery, doesn't let anything stick to it. And it also acts as a barrier to bacteria and viruses getting into fish. Glycocalyx is very important for not letting infections in. If you get too many fish together, like salmon farms, they bash into each other, they knock the glycocalyx off, they get horrible infections. So glycocalyx is an anti-infective, anti-clotting, it's got about 20 substances in it that are anticoagulant, it allows the blood to flow through really smoothly and fast and it doesn't allow anything to clot. If you damage the glycocalyx, then basically the endothelial cells are at risk. Things can either directly attack them, or bash against them, or do damage to them. And once you've damaged an endothelial cell sufficiently that they break off, you expose the underlying blood vessel wall. And when you do that, that's a red alert. A blood vessel, big blood vessel getting damaged, the body says, clot now, otherwise, you're going to bleed to death. So, if you damage the glycocalyx, if you damage the endothelial cells, you will get a blood clot forming on that point. Now it may be quite a small blood clot, usually is a pretty small blood clot. But we know this happens because if you get a healthy volunteer to smoke one cigarette and then you look at what happens when they do that. You can see the glycocalyx is damaged. You can actually measure destroyed and dying endothelial cells in the bloodstream. It's called microparticles. Microparticles are the remnants of dead endothelial cells. You smoked one cigarette and the microparticle level goes like this, the glycocalyx does this and endothelial cells die around your whole vascular system.

Steven Bruce
Which means clots are forming all around the vascular system?

Malcolm Kendrick
Clots must be forming all around. They're pretty micro clots. You might not even be able to see them with the naked eye. At the same time, luckily, the bone marrow goes, oops, things are happening to the endothelium. It stimulates it to produce more endothelial progenitor cells. So the repair troops come shooting out, find the areas, cover them over, sort them out. And these really small clots all over the place are essentially just repaired, almost completely probably. So if you smoke like one cigarette, yeah there will be damage, but it will be cleared up. You smoke 20 cigarettes, yeah there'll be damage, but it'll be cleared up. 40 cigarettes, there'll be damage, but it'll be cleared up. You smoke 40 cigarettes for 40 years, you're screwed. Because the body can only do so much repair. So, with heart disease, of course, if you smoke and you do nothing else, you're probably okay. You need to do other things. And the other thing that really damages endothelium and glycocalyx is diabetes, high blood sugar level strips the glycocalyx. So say it's supposed to be that thick, you get diabetes, it's that thick. And you can measure this, you can see it. You smoke as well, well, you're doubling your problems, aren't you? And this is why risk factors for heart disease are multiplicative. So you know, you do one thing wrong, you're probably all right. You do two things wrong, eeeeh. You do three things wrong... You do four things wrong, you do five things wrong, and you are in deep stumm. So people have to do, one of the things you do wrong is getting old, because as you get older, your repair systems don't work so well. So the things that you can get away

with when you're 20, when you're 50, you know, stop doing that. If you've got diabetes in the background and you smoke, and then there's other things that can cause damage. I was looking at all sorts of things that can damage the endothelium, what can I show damages that endothelium? We can show that smoking does and diabetes and these things. You can show things that people don't consider, lead, the heavy metal, which people say, hand on a second, what's that doing? How can lead damage the endothelium? Well, lead, if you inhale it, which we all used to do in exhaust fumes, gets into your lungs, goes through your lungs, because it's a micro particle, it's a nanoparticle actually, it's even smaller, it goes into your bloodstream and you can show it destroying endothelial cells. It's reckoned in the States, more people have died of heart disease from lead poisoning than have died from smoking. People say how does lead cause it? Well, because lead does the same thing as smoking. When you smoke nanoparticles in the smoke come out of your lungs, travel around your body and blow up your glycocalyx and your endothelial cells. So what else can cause it? Cocaine. People say how does cocaine cause heart disease? Well, if you snort cocaine, you know people snort cocaine? What happens is the middle of your nose falls apart. Why does the middle of your nose fall apart? Because cocaine causes a really intense vasculitis, it causes the blood vessels to inflame and die off. And that's why the middle of your nose falls apart, because once the blood vessels are gone. Once you've inhaled it into your lungs, it gets into your bloodstream. Once it's in your bloodstream, it causes an extreme vasculitis. And vasculitis just means inflammation of the vascular system. People who take cocaine, in an hour after taking cocaine, are 20 to 30 times as likely to have a heart attack in that period of time. It's like smoking except on steroids.

Steven Bruce
We are at the end of our show, which is extraordinary. I mean, the time just flies by and I've literally got three minutes left, but I'm gonna try, I'm gonna put you on a cross here between medical diagnosis and speed dating, because I've got a bunch of questions here. See what you think of these. What do you suggest for someone who has cardiovascular disease, what should they do to avoid early mortality?

Malcolm Kendrick
Well, it depends what's causing it. And this is the thing, I said there is no a cause, there just isn't "the cause of heart disease." I made a list once and it came to hundreds of things that can cause it. The important thing is to try and work out what it is for you. I'm talking to someone about setting up a clinic where we're going to be looking at these things in more detail. But essentially, what is it for you and it might be different for you than anybody else. You have to work out why it's happening to you, and what your risks are, and then what to do to mitigate them. I can't go through that at the moment, because it's like hundreds of things.

Steven Bruce
We're not here, you're not here, well, I'm not here to plug your book, you might be here to plug your books. I'm sure you're not. But I mean, there's a good start in reading those books, I'd have said.

Malcolm Kendrick
I have tried to say here are the X number of really the most important causes of heart disease and what you can do about them. If you get diesel fume inhalation or vehicle fume inhalation, so if you're next to big road and you're breathing in diesel particles, yes, they get through your lungs, they cause damage to

your blood vessels. So that might be your cause. I don't know with individuals. That's why it's so complex, really.

Steven Bruce
One very quick one, last one here from Specky. Specky says, she's been told by both a consultant and her GP that she needs to be on statins and clopidogrel for the rest of her life. A CT scan revealed what she is told is the result of a stroke that occurred at some stage in the past, therefore, she needs to be on those meds. Does that sound reasonable to you?

Malcolm Kendrick
No. Because you have to know what caused the stroke. You can have a stroke, because you've got a hole in your heart.

Steven Bruce
So it could be good advice, but it might not be.

Malcolm Kendrick
It could be terrible advice. What caused it? Is it blood clotting that caused it? A hole in your heart means clots that would normally get stuck in your lungs, travel through your heart and go up to your brain. And that's quite common, people call it cryptogenic, unknown cause stroke. Some people have strokes, they never know what caused it. But if you don't know what caused it, how can you know what to do to reduce your risk? You have to get down to the detail. What is it in your case? I don't know what it is in her case. And we don't do the proper screening. We don't do the proper screening in the NHS. So they come to the simplest conclusion, a statin and clopidogrel. Well, that might work for you, because it might be that those are the things. Well, the statin won't work. The clopidogrel might be effective. You might be getting the right treatment. I don't know. And neither do they.

Steven Bruce
Well, let's hope that that helps Specky in some way. I know she's not a smoker. Malcolm, thanks very much. I'm sorry, we've got some questions here. We've had over 500 people watching and just in case you were uncertain, everybody's loving it as much as I am. Literally I really can't recommend enough that you're go and have a look at these books. The Clot Thickens, the latest one, is a fantastic summary of what is likely to cause heart disease, would you say it's certain?

Malcolm Kendrick
It doesn't cover everything. But it covered hopefully 95% of the things that, on a population basis, these are the things.

Steven Bruce
But it answers the question, well, if it's not cholesterol, what could it be? Well, there's a very good, very well-reasoned argument in the book about what could cause heart disease. And I recommend these books to my patients as well, because they're the people who need to be reading them. So that when they go to their GP, they're armed with the information that you've just given us and so on. If I didn't ask your question, I'm really sorry, we have run out of time. I'm about to go to dinner with Malcolm. So I shall

try and put some questions to him over dinner and get the answers back to you in email either tomorrow or on Friday. So rest assured, I'll do my best for you. Just to look at what's coming up. We've got a case-based discussion on Wednesday the eighth and an evening broadcast on Tuesday the 14th, with Robin Lansman, which is going to be an interesting one about collaboration between practitioners. Lunchtime on the 16th of March, we've got Simeon Niel-Asher and Professor Bob Gerwin talking to us about, let me read this one out, myogenic thoracic outlet syndrome. And if you remember, Simeon and Bob are the guys who ran the intramuscular stimulation course here. Bloody good dry needling course, a fantastic dry needling course. People were emailing in afterwards for ages saying what great results they'd had with it. We've got one running on the 19th to the 21st of May. There are some places on that if you'd like them, go to the website or email Elaine, which is elaine@apmcpd.co.uk and get yourself on the course. I can't recommend it highly enough. And I just have to read this out as well, because there's quite a lot in this one. But I only got an email about this myself this afternoon. And it's about the EdACHe course, which is the study into headaches that we've done a broadcast on before. The course is now live. It's eight hours of CPD, it's made by osteopaths for all manual therapists and allied health care practitioners. And it's 20 short modules, most of them with quizzes, and you can just take one during your lunch break, and there's 10% off for the first 100 places. And nobody's told me how you sign up for that, but I will get that out in the email tomorrow or on Friday, as I've said. Failing that, just Google EdACHe, and I'm sure you'll come up with the right answers. Anyway, sorry I've had to rush that last bit. I hope you've enjoyed the show. Hope you've got lots of fantastic, fascinating information from this evening's show. And hopefully I'll see you again soon. Goodnight.