TPWKY – Ep 218 – Cholesterol 2

[00:00:00]

EW: "I was born into a rural farming family in northern Japan, where I lived for 17 years with my extended family, including grandparents, parents, three brothers, and two sisters. My grandfather, who had an interest in medicine and science, was a great home teacher to me. Thanks to his influence, at the age of eight, I dreamt of becoming a scientist. After finishing high school in Akita, I entered Tohoku University's College of Agriculture in Sendai in 1953. As a student, I was deeply impressed by the knowledge that antibiotics had saved the lives of many patients with infectious diseases. I received a PhD degree from Tohoku University in 1966. At this point, I became interested in cholesterol biosynthesis. I eventually studied from September 1966 to August 1968 at the Albert Einstein College of Medicine in New York. At that time, coronary heart disease was the main cause of death In the United States. The number of people with hypercholesterolemia, a precursor to coronary heart disease, was said to exceed 10 million. My experience of living in New York made me realize the importance of developing a cholesterol-lowering drug. After coming back to Tokyo in 1968, Sankyo Research Laboratories gave me an opportunity to work on a project of my own choosing. I speculated that fungi like molds and mushrooms would produce antibiotics that inhibited HMG-CoA reductase. Compactin seemed to be a wonderful gift from nature."

EAU: I to know everything more that you're about to tell

EW: You, you will, you will. So that was excerpted from actually two different articles written by Akira Endo, who was the father of statins. He, uh, discovered the first statin. And, um, he has written about this in multiple different places, but this was from two papers, one from 2008 and one from 2010. And we'll have them in our show notes. But, um, yeah, I loved, I love just like, I'm still amazed at the logic link leap that it took. Yeah.

EAU: I want so much more of that, of like, what was he thinking and

EW: Yes,

EAU: these things together? And like, I wanna know it all. 'cause I'm re I'm really, I'm really excited for this episode. Erin, should we

EW: I know. Yeah, me too. Me too. Um, It's gonna be great. Hi, I'm Erin Welsh

EAU: And I'm Erin Allmann Updyke.

EW: this is, this podcast Will Kill You

EAU: Welcome to Cholesterol part

EW: part two.

EAU: we

EW: Statin. Boogaloo. Yes.

EAU: Good one. Yeah.

EW: Um, yeah. To this. So if you didn't listen to last week's episode, you really should because it'll give you some great foundation for understanding why cholesterol does what it does in our bodies and why certain levels of different types of cholesterol mean disease.

EAU: I know that we are biased, but I think it's a great episode,

EW: I do too.

EAU: listened to it, check it out. And

EW: Yeah.

EAU: we're gonna build on so much of that and talk about how we deal with high cholesterol

EW: Yeah.

EAU: Out how to deal with it and, it's gonna be really great.

EW: Yes,

EAU: But

EW: is.

EAU: it's quarantine time,

EW: It is. Once again, we are drinking plaque attack again. Are we attacking plaque as plaque attacking us? Yes.

EAU: of both. Mm-hmm.

EW: Yes, plaque.

EAU: plaque attack?

EW: It's, it's a pretty, it's a pretty delicious, straightforward, nothing to do with cholesterol,

EAU: Mm-hmm.

EW: It's blueberries, smashed with lemon juice and, uh, club soda and simple syrup and mint. I have it written down and yet it's like not, I just didn't pull it up. So

EAU: we'll post the full recipe on our website, thispodcastwillkillyou.com on our social medias, which include, um, Instagram and Blue Sky and, um, Facebook and TikTok. I don't know if it's there on TikTok though. Listen, just follow

EW: just follow us. Yeah.

EAU: we're up to.

EW: Absolutely you will. Yeah. Uh, you can also see a little bit of what we're up to by going to our website, thispodcastwillkillyou.com. It's got y not, not, not quite, but like it's

EAU: Not quite, but

EW: got resources, right? It's got lots. We've got all of the papers we use for all of our episodes. It's got links to our bookshop.org affiliate page, uh, music by Blood, mobile, links to merch, links to Patreon. It's got a firsthand account form a contact us form. Things that you can explore.

EAU: Everything we could think of is there.

EW: Yeah.

EAU: Thank you to everyone who has rated and reviewed and subscribed on your pod [00:05:00] catcher or YouTube of choice. We appreciate

EW: We do. I know. We know there are so much media out there that you could consume, and so it means truly, it means so much to us. It feels surreal that you're choosing to spend any time with us at all. Thank you.

EAU: they listen, I'm like, to me, to

EW: What?

EAU: really.

EW: Yeah. It's incredible. It's incredible. Thank you.

EAU: Okay. Erin, tell me this guy and how he came up with statins and everything else. Okay,

EW: Absolutely. Let's take a quick break and we'll do all of that.

Last week, I took us through the story of cholesterol and how it earned its reputation as a major cause of cardiovascular disease. Over the course of about seven decades, from the 1910s to the early 1980s, researchers put the pieces of the cholesterol puzzle together using a wide range of studies. We had experimental ones like Anitschkow's atherosclerotic rabbits. There were analytical ones, epidemiological ones like the Framingham heart study, genetic ones, and mechanistic ones like Brown and Goldstein's, Nobel Prize winning work, uh, characterizing the LDL receptor. Lots of different studies. Lots of different lines of evidence.Yes, yes. And this week I'm gonna pick up with the final piece of this puzzle, cholesterol lowering drugs and some of the controversy that surrounds them. By the 1970s, much of the cardiology world, like researchers, physicians and institutes, they saw the link between cholesterol and cardiovascular disease as a done deal.

This is established. Okay, now let's proceed from here. But that knowledge didn't reach beyond that realm of experts, and many physicians remained either skeptical or oblivious to this new knowledge. So for example, a a 1983 study of internists in the US showed that 50% did not recommend any therapy including diet for cholesterol lowering unless levels were over 300.

EAU: Fascinating. In the, in like the mid eighties

EW: 1983. Yeah.

EAU: Wow.

EW: Yeah. It just, it also shows how quickly things have shifted.

EAU: Yeah.

EW: Yeah.

EAU: W and which is so interesting also 'cause I just think about, like we've talked about before, how slow change is in medicine and like there are plenty of people today who were probably practicing in the eighties, like getting trained in the eighties,

EW: Yep.

EAU: that Oh, it's just so interesting.

EW: Yeah. Yeah. It is, it is really interesting. And I think it, it also, like okay, for you today this I, I wanted to, to share more of these numbers because I think it'll come as a real, like double take. Yeah, exactly. So, um, of that, of those 50% who wouldn't recommend any therapy unless, oh, over 300, nearly half said no therapy unless levels were over 340 and 27% of those, said that they would never recommend drug treatment under any circumstances

EAU: for cholesterol.

EW: For cholesterol. Yeah. So what? What would it take for high blood cholesterol to be seen as a pressing public health issue?

EAU: Mm-hmm.

EW: At least among all medical professionals, if not the general public

EAU: Yeah.

EW: An available treatment and evidence that intervention worked. Those two things would emerge at nearly the same time in the early 1980s.

EAU: Erin, I don't wanna interrupt you because I'm loving this, but as a side note, you know what? We should do an episode on

EW: Tell me,

EAU: evidence-based medicine

EW: yeah. Okay.

EAU: 'cause that is a really new thing.

EW: Wait, wait, wait. What do you mean by that? It's a really new thing.

EAU: I mean, the idea that we should only make recommendations for things if we

EW: Oh,

EAU: to support them a relatively new concept in the history of medicine, and it would be really

EW: the humoral theory has tons of support, Erin.

EAU: So anyways,

EW: Sorry.

EAU: to

EW: No, we should definitely do, we should definitely do that. I, we have had ideas to do things like randomized control trials as well, and

EAU: know

EW: just like, yeah. Other,

EAU: of a list.

EW: we have such a long list. It's, it's great. It's a, it's a good problem to have. Okay,

EAU: is, we're in the eighties.

EW: in the eighties,

EAU: of people are like, nah, dude, gimme some evidence.

EW: Right? And the cardiologist or the, the cardio cardiology research, people are like, oh my God, we're this, we're in trouble. We're in trouble. Okay. So we needed, uh, treatment and proof that any sort of intervention worked, whether it was the treatment or just lowering cholesterol, that that led to actual results.

EAU: Right.

EW: Those two things, a treatment and proof of intervention would emerge at nearly the same time in the early 1980s. So at the [00:10:00] National Institutes of Health, Plans had been underway since 1970 for a large scale study that would measure the impact of cholesterol lowering drugs on cardiovascular disease.

EAU: Okay.

EW: Previous studies had shown that high, high blood cholesterol levels overall correlated to higher rates of heart attacks. But the next step was showing that lowering those levels would then lead to fewer cardiac events.

EAU: We know that there's this positive correlation between high levels and bad outcomes. Can we change that

EW: we change that? Can we do something? 'cause then that would also suggest it would be a very great evidence for causation.

EAU: causation.

EW: Yeah,

EAU: Yep.

EW: The coronary primary prevention trial was designed to do exactly that, show this line of causation. The study enrolled, uh, 3,800 men, aged 35 to 59 with high total blood cholesterol, so 265 or higher, and they were to be followed for at least five years. The treatment group was supposed to take a cholesterol

lowering drug. Cholestyramine. Statins weren't yet approved at this point, and all participants were instructed to follow a cholesterol lowering diet.

EAU: Okay.

EW: Knowing what we know today about the link between cholesterol and cardiovascular disease, a trial like this would not be conducted in the same way where you would withhold drugs from one group,

EAU: Right?

EW: But at the time, the evidence was not as firm, especially for medication, and so that's why it went forward. By the early 1980s, after an average of seven years follow up for each participant, the results were in and they were unambiguous. Lowering blood cholesterol in high risk men reduced the risk of heart attack. Those who took. Period. Those who took the full TR dose of treatment had a 35% reduction in total cholesterol and a 49% decline in the rate of cardiac events. But even those who didn't follow the treatment to a T like the, the cholestyramine had lowered cholesterol and fewer heart attacks. Now the study was not perfect, but when the results were published in 1983, it led to a moment of reckoning for the field. Like it was no longer enough to simply acknowledge that this relationship exists, something had to be done about it,

EAU: Right.

EW: and that something was to be decided at the 1984 NIH Consensus Development Conference. So there was a panel of experts at this conference who came up with a set of guidelines for what would be considered high or low blood cholesterol, um, age, uh, for certain ages and how that fell out. And also diet and exercise recommendations for how to reduce cholesterol. They also advocated for a nationwide educational program in which general practitioners, as well as the general public, were taught about the importance of cholesterol.

EAU: I love that.

EW: Yep. This conference had a substantial impact over the next decade with the percentage of physicians pointing out LDL as an important marker for the risk of heart disease. That increased from 1986 to 1995. From 34% to 75%,

EAU: So like in 1986, only like

EW: 34% said LDL is important. Yeah.

EAU: and then 90. Okay.

EW: 95, and then it was 75% in 1995. Yeah.

EAU: than before.

EW: Better than before. At the time that the panel was making these recommendations, there still wasn't really a good cholesterol lowering medication available. So the one that they had used in the study, cholestyramine, came in a sandy powder, which you had to mix into water and consume throughout the day. So you had to consume 24 grams a day, was like the goal in the study, which was like six packets of, of this or something like that,

EAU: no one's

EW: which so was, it was quite a heavy lift and it was made even more daunting by the GI upset that it caused in many, you know, bloating, diarrhea, constipation, stuff like that. So there was clearly a need for a safe, effective, and easy medication to lower cholesterol. Fortunately, researchers were well underway in their quest for such a wonder drug

EAU: Okay.

EW: In 1971. The, uh, firsthand account provider for this episode, Dr. Akira Endo was working as a research biochemist at the Japanese pharmaceutical company, Sankyo. When he got an idea, Endo had long been fascinated with Alexander Fleming's serendipitous discovery of penicillin.

EAU: Hmm.

EW: And after a research stint in New York, he had become intrigued by this problem of hypercholesterolemia. And he figured that, okay, if, if fungi produce antibacterial compounds like penicillin to compete with other fungi, it's not like they produce it because they're like, oh, humans could use this.

EAU: No.

EW: They

EAU: Right,

EW: Right. It's part of the, the ecology of this, of Penicillium. Mm-hmm. Then it's possible that they would produce other types of [00:15:00] compounds that would interfere with, or help them compete against fungi in other ways, such as maybe a compound that interferes with cholesterol production.

EAU: because cholesterol is so essential for life. Fascinating.

EW: There,

EAU: just was like, bro, Fleming did this once.

EW: did this. Maybe there's something. Yeah.

EAU: 'cause cholesterol is so important,

EW: Yeah,

EAU: what?

EW: and he was, I mean, part of the thing too, he was like, he was like, fungi is all I knew, so I, that's where I looked.

EAU: huh.

EW: But it also like that that logic is very clear, but it had no direct support from any studies, like there was penicillin and the fact that we found other antibiotics through this sort of like, oh, this thing is producing this thing that kills this bacteria or this, uh, fungi in the environment, but like, yeah.

EAU: think of it for, for use on cholesterol, like

EW: Yeah.

EAU: that's so interesting that his brain just did that

EW: Right. Yeah. And. He found it.

EAU: right.

EW: He found it. Yeah. I mean, so it, it took a while. It took two years. He and his colleagues over that time screened 6,000 strains of microbes searching for a

compound with cholesterol lowering properties. It's like searching for a needle in a haystack, really. And the first hit on this was less of a needle and more of a crochet hook. Uh, but the second was exactly what they were looking for. The compound came from the mold, penicillium citrin, which another pen, another penicillium. And they named it Compactin, also known as Metastatin later on. Yeah. And this was the first statin?

EAU: Wow.

EW: So over the next several years, endo and other researchers at Sankyo tested compact in safety, efficacy, and commercial viability and other pharmaceutical companies got wind of this, like Merck, who was like, can we get a sample of that and see what's going on? And then they were like, how did you find this? Well, we're gonna look for our own statin. In the same way they had to kiss way fewer frogs only 18 before they found their prints in Lovastatin in 1978

EAU: oh. Competition.

EW: Competition. Yeah. And then there's some, there's like a lot, there's so much more to the story of like statin production, statin approval, statin testing and stuff like that. Um, which I will have some papers there if you want to dig more into that.

EAU: Okay.

EW: But essentially there were some early trials in animals that hit some hiccups, but then those were smoothed out trials in humans. Then went forward in the early 1980s and results were striking. People with high cholesterol saw their LDL levels drop dramatically after taking the medication with few side effects.

EAU: Hmm.

EW: But did this drop translate to protection from cardiovascular disease?

EAU: Right.

EW: You betcha.

EAU: Yeah.

EW: betcha.

EAU: Yeah.

EW: Yeah. So there was one study sponsored by Merck who was testing out their statin found a 42% decrease in death rate in those taking a statin. This is the second generation statin Simvastatin.

EAU: Simvastatin,

EW: Yeah.

EAU: It today. Wow.

EW: Yeah. Statins look to be the next blockbuster drug and soon every pharmaceutical company wanted in on the action.

EAU: course.

EW: And by the last year of the 1980s, three statins were approved and available on the market.

EAU: Wow.

EW: The following decade, saw new statins and an expansion in their use, which allowed for large scale clinical studies, not just ones headed by pharmaceutical

EAU: Mm-hmm.

EW: who were trying to get their drug approved.

EAU: Great.

EW: Um, I also just can't believe how recent it all is.

EAU: I really did not realize that

EW: Yeah.

EAU: in the last 40 years,

EW: Yes,

EAU: the 1980s. That's really wild.

EW: Is wild. And I think it also is part of the reason why there's been such controversy. I,

EAU: Hmm. It is

EW: my thought.

EAU: though, Erin, because there's so, there's newer, newer, newer drugs

EW: I know.

EAU: have way less controversy surrounding them,

EW: I know

EAU: just like, what?

EW: I, there's a lot. There's a lot. And we're gonna, we're gonna get into it in a second.

EAU: Yeah.

EW: Yeah. Um, but these studies, these large scale studies that were done, not just by pharmaceutical industry, they conclusively and consistently showed that statins were lifesaving drugs and that they had earned their blockbuster status. Across the board, statins led to a 25 to 30% reduction in LDL, coronary artery disease and death from cardiovascular disease. In the 40 or so years since statins have been on the market, death from cardiovascular disease has dropped by over 75% in many industrialized countries. Statins are a major tool in that fight, along with big advancements in medicine, lifestyle modifications, and diagnostics. [00:20:00] But of course the story doesn't end here.

EAU: Mm.

EW: The potential benefits of statins are enormous, both at a population and individual level, especially with cardiovascular disease being the leading cause of death in many countries. But increasingly, the benefits of these drugs are not

realized because people aren't taking statins when it's recommended that they do. Why is that?

EAU: Why.

EW: Why? As it turns out, it's for many different reasons. A couple of recent papers looked into the issue and they presented some themes that they found and why people either refused or discontinued statins. There were, you know, practical and logistical considerations. So concern about taking multiple medications, polypharmacy burden, financial barriers, uh, you know, having to drive to the clinic to get low cost statins, things like that.

EAU: That's so annoying

EW: It's really grim. I know.

EAU: especially in this country, be high cost,

EW: It should not be a barrier and there should be, you know, by mail, et cetera. Yeah,

EAU: yeah.

EW: yeah. Um, pregnancy and breastfeeding is another sort of practical reason or preferring lifestyle modifications over a daily pill. Like, I'm not gonna be able to take a pill every single day. I'm gonna forget that.

EAU: Right.

EW: There were also preconceptions about side effects or impact on someone's identity. So people reported negative side effects, or a fear of negative side effects. And others felt that taking statins was like giving up, that it signified sickness and that they didn't wanna be on a medication for the rest of their life. They didn't wanna be dependent on this drug for health.

EAU: Yeah.

EW: And then there was another big reason, or another big theme was mistrust in medicine and kind of a lack of understanding or belief in the drugs and how they worked.

EAU: Yeah.

EW: So some questioned their utility. Like, I have high cholesterol. The doc says I have high cholesterol, but I don't feel bad. Statins doesn't make me feel any different, or it makes me feel worse.

EAU: this side effect that came from it,

EW: Yep.

EAU: and, and I didn't feel bad to begin with.

EW: Exactly.

EAU: Why would I be on a medicine forever?

EW: Mm-hmm. Um, people didn't also understand how statins lowered cholesterol, so it was just sort of like, well, I don't understand how they work, so I don't know that they do work. And many people also questioned the motives of doctors in prescribing the medication. Like, big Pharma has a hand in this, and they felt that over-prescribing was an issue, especially with levels being revisited every so often and being like, now we recommend that you're, you know, you didn't recommend this last year when my LDL was the same.

EAU: exactly

EW: Yeah.

EAU: We need your LDL to be less than 70. Now we need it to be less than 55 now. Yeah. Without, without a good explanation. They just updated the guidelines in March of this year. So they're changed yet again.

EW: Right. So there's this sort of fear of like diagnostic creep. Is that happening with cholesterol and statins or is there evidence to support this shifting of the levels and the recommendations, but often with all of these different reasons? Um, there was, it was a combination of things that led people to either refuse statins or stop taking them. Within two years, roughly 40% of people who were taking them for primary prevention and 25% of people on statins for secondary prevention end up stopping the medication.

EAU: Hmm.

EW: So, to say that these negative attitudes towards statins are worrisome, I think is quite an understatement. It could have serious, even fatal consequences. So what do we do about it? The first step is understanding why, you

EAU: Yeah.

EW: Are these attitudes, these beliefs coming from? Many of the reasons that people give for not taking or discontinuing statins can be attributed in part to misinformations or or negative beliefs promoted across social media. When statins first came on the market in the late 1980s, the cholesterol heart disease link had not yet been fully embraced by the general public. And in fact, there were some highly publicized front page stories written by vocal deniers, controversy sells, consensus doesn't.

EAU: Mm-hmm.

EW: And so all of a sudden you go to the doctor, your doctor is telling you you should take this drug for your cholesterol. But just that morning you read how the cholesterol heart disease link is overblown so that big pharma can rake in the dough and get people on meds for life. Why would you do this?

EAU: Yeah.

EW: And it would take years after statins were introduced to put together those big data sets that show the life-saving benefits of the drugs and the relatively low rate of side effects. And so doubt has really been sown into statins from the very beginning, along with a mistrust in how the pharmaceutical industry is involved. And I get it, like there is some truth to this involvement, especially early drug trials being designed by [00:25:00] pharmaceutical companies. Many researchers in this area hold BO PO board positions or received funding from these companies or have a patent for these drugs. And they're trying, you know, like there is, there are financial ties that are undeniable.

EAU: a hundred percent. A hundred percent. And

EW: Yeah.

EAU: Like in today's day and age, not just with pharmaceutical companies, also with radiology companies and imaging companies and

EW: yes.

EAU: And so as our guidelines shift to incorporate more of these, like it is very valid to question these conflicts of interest, whether they are real or perceived like they matter.

EW: They matter. They do matter. And I, I think that this is, like you said, as these, as these guidelines are shifting, there's these questions around like, who, what's, what's behind these guidelines? Is there evidence for it, et cetera.

EAU: Mm-hmm.

EW: At the same time, decades of statin research, these drugs have been around for. Almost 40 years.

EAU: now.

EW: Yeah. Decades of research have proven the value of statins and that research is not solely conducted by industry, but large scale work being done across the globe, not just within pharmaceutical sectors in the United States, but across the globe. And while, yes, of course, pharmaceutical companies love a drug that someone has to take for long periods of time, many statins today are available in a generic form, and so they're not as profitable as they once were. In any case, your primary care doc is not getting a kickback from prescribing these drugs. They simply don't want you to die from heart disease.

EAU: Uh, it's so true, Erin.

EW: That's true. It's true. Okay. Another big reason that people cited was side effects, including, or specifically muscle symptoms. This is one of the top reasons that people stop taking or never start taking statins. Side effects are real and important to take seriously because they can truly impact quality of life. But the story of side effects when it comes to statins is complicated. Until 2001, there were very few reports of tolerability or safety concerns for people taking statins. But that year a statin, rivas statin was removed from the market due to safety concerns specifically for rhabdomyolysis, which occurred at a rate of 0.01% in people taking it

EAU: Okay.

EW: Promptly after its removal from the market. All information sheets included warnings about all for all statins.

EAU: statins.

EW: Included warnings about muscle symptoms and physicians counseled patients to report muscle aches as an early warning sign of rhabdomyolysis. This issue was highly publicized as it should have been. You know, this is a potentially serious side effect, and so let's you know, make sure you look out for this. And many patients who felt muscle aches often would interpret them as myopathy or go to their doctor with concerns about myopathy. They would stop taking statins and their symptoms improved, which reinforced the belief that these statins might be dangerous.

EAU: the cause of that

EW: The cause of that, right? And certainly these muscle symptoms were and are real, but there is also something called the nocebo effect that seems to be at play here, at least to some degree. So the nocebo effect is the opposite of the placebo effect. It's anticipation of negative symptoms that leads you to experience them. Studies on statins have shown that when both researcher and patient don't know whether someone is getting medication like statin or placebo, both control and treatment groups experience similar rates of muscle aches,

EAU: Hmm.

EW: suggests that it might not be the statins themselves directly responsible for those symptoms.

EAU: Right,

EW: At least in all cases. The symptoms are absolutely real. The nocebo effect does not mean that it's all in your head. You're experiencing these symptoms. They just might not always be caused by the drug itself.

EAU: It's not like there's a direct mechanistic link between the drug that is directly causing that muscle symptom necessarily.

EW: Right. But it could be, it could like, and so this is where it's really, really tricky to tease apart both for patient and provider. And so it might be just like, feel like the easiest course to go, I'm just gonna stop 'cause I don't wanna feel this way. I don't wanna, I'm worried about this and this is hurting my quality of life. I'm going to stop. Other research has also shown that people who are exposed to more negative stories surrounding statins and side effects are more likely to discontinue use.

EAU: Mm-hmm.

EW: I think that what's also at play here is, and we kind of touched on this, is that we don't feel high cholesterol. Like we don't feel any different when our cholesterol is low.

EAU: Mm.

EW: But we do expect a lot of the time that the medications we take will make us feel different. Will, we're supposed to feel better from these medications.

EAU: supposed to feel

EW: Something. Something. Yeah. And so it makes sense that if you read horror stories about side effects of statins [00:30:00] that abound on the internet, you're predisposed to expect that those bad outcomes will happen to you. And what doesn't help this is that there's a vast amount of misinformation and disinformation about statins circulating on social media and generative ai. There is a motive for people to be spreading some of this disinformation. So in fact, there was a recent study that showed that many generative AI models when Fed prompts asking about statins, especially if those prompts were leading, sort of like, what can I take? That's Yeah,

EAU: evidence of these side effects with statins? Like those kinds of questions.

EW: yeah. Or like, um, what should I take that's safer than statins? Like, what, what natural products should I take that are, that's safer than statins?

EAU: okay.

EW: But many of these models gave inappropriate and inaccurate answers.

EAU: doesn't surprise me at all.

EW: Right, right. The sheer amount of misinformation that's out there and just sort of the overall decline or disregard of expertise that's happening around the globe.

EAU: Yeah.

EW: Uh, there. And then there are the people who are very vocal in their opposition to statins that at the same time are telling you, don't go on statins, buy my red yeast rice supplement instead,

EAU: Erin

EW: buy this diet book. Or they're trying to make money off of you in some way. You know, subscribe to my substack that says, you know, day one diet with me and we You'd throw away your statins. Yeah. Yeah. And that the thing is like, I also understand why that's appealing when you've been dismissed by your physician or your physician is saying, it's not the statin causing this, just like that simply across the board. Or if you can't even afford to go see a doctor,

EAU: right.

EW: This, this information is, is out there and that is filling. A, a hole that you want that is filling a need.

EAU: taken seriously for

EW: Yes. Yeah.

EAU: I went to my doctor with these concerns and you were totally dismissed. Or they were like, oh, fine.

EW: Right.

EAU: not fine if I'm having symptoms. Right.

EW: Yeah. And I mean, again, like all of this, I think what it, what it does is it speaks to a need to more closely examine the side effects that people report. Not just muscle symptoms, but the other side effects that people report and how best to address them, how best to measure them. How can we make it so that people can take drugs that will lower cholesterol and potentially save their lives.

EAU: Yeah.

EW: So again, what do we do about it? And I think that as a start, we can look at the reasons people take statins. So that same systematic review that I mentioned earlier also showed many people have positive sentiment towards these drugs. They trust their efficacy. Like, look how much my bad cholesterol dropped and my good cholesterol rose. They report that their health anxiety has eased thanks to the drugs reporting an an enhanced peace of mind.

EAU: hmm.

EW: And they view them also as a way of taking control and ensuring a better, healthier future, rebrand these drugs for what they are. Heart attack prevention. Stroke prevention, a way to extend your life, your quality of life, and spend more time with the people you love, accomplishing all the things you want to do. These drugs might not make you feel any better instantaneously, but they will make it more likely that you're around to feel and do things 10 years from now,

EAU: Mm-hmm.

EW: Having high cholesterol, it doesn't mean that you have failed. It should not be seen as shameful as something that you should hide or feel embarrassed by. And taking these medications should make you feel like you're taking agency over your own life. Prevention is always harder, especially when the threat, like a heart attack, doesn't seem imminent or is so scary that you're like, I have to think that this won't happen to me.

EAU: Right, right. I can't, I can't put my mind in that place.

EW: Yes, but that denial, it really does not serve us well. And so with that, Erin, I'm gonna turn it over to you to tell us about how statins actually work and where things stand with cardiovascular disease around the globe today.

EAU: I would love to.

So knowing that statins have made such a huge impact or has the have the potential, at least to make such a huge impact on disease, we first need to understand a little bit more about how they work. So I wanna go through not just statins, but the strategies overall that we use today to lower LDL Cholesterol specifically. How these strategies work. And then I wanna wrap up by giving us all like a reminder of why lowering cholesterol is so important by looking at atherosclerotic heart disease kind of across the globe. Okay.

EW: Mm-hmm.

EAU: And so the first thing to know is that while statins are, because of how long they've been around and because of how strong the evidence is, that they are [00:35:00] extremely effective, not just at lowering that cholesterol, but actually at preventing heart attack, stroke, and death. They are a mainstay of therapy today for cholesterol management. But they are not, the only thing that we have, and the first thing that is always recommended across the board is diet and lifestyle changes.

EW: Yeah.

EAU: And the thing is that we do have really decent data as far as like nutrition data goes, which we all know is,

EW: It is rough. Yep.

EAU: We do have decent data that lifestyle changes can work for a lot of people, but the problem is that we also know that total cholesterol and Your LDL cholesterol. So the, the packages of LDL cholesterol not entirely driven by your diet. They're not

EW: Yeah.

EAU: Driven by how much exercise you're getting, right? There are a lot of different things that go into determining what your cholesterol levels are and whether they are high or whether they're low, and one of the big things is our genetics. You talked in last week's episode, Erin, about familial hypercholesterolemia. This is one, or really kind of like one group of disorders that can seriously contribute to elevated cholesterol, especially LDL cholesterol. But it's not the only one. There are a whole bunch of other genetic contributions, whether that's multiple genes or things that we don't even know yet. Right. Genes that we haven't even discovered yet that are associated with the like ratios and amounts of cholesterol. Whether that's because these genes affect how we recycle cholesterol, whether they affect how much cholesterol we produce in our liver, or whether like in familial hypercholesterolemia, they affect our LDL receptors and how good our cells are at taking that cholesterol out of our bloodstream.

EW: Right.

EAU: So all of these things are going to play a role as well as our dietary factors and our lifestyle factors, and so that is usually the first thing that any physician is going to recommend if someone's cholesterol is elevated, is, can we bring this down by reducing or stopping smoking if you smoke, because that has a huge effect. Lowering the amount of alcohol that you drink, which is gonna help to lower your cholesterol levels. Switching out saturated fats in your diet for unsaturated fats, right? Switching out animal products for plant products. These are the kinds of dietary changes that we have good data to say that not only do they reduce your cholesterol levels, but they also can actually prevent cardiovascular disease. We have that data

EW: yeah,

EAU: but for many people that isn't sufficient. And so that is when it is recommended that medication is actually used. Right? it's because somebody can't or doesn't want to change their diet or exercise, or they can't increase physical activity, or they are literally already doing the most

EW: yeah.

EAU: it's still not enough, and that happens So, so, so often.

EW: And I think it's like, this is where I feel like It can feel like I have failed or I thought I was trying my best to do all these things and still it's not working and it's like that. That's okay. Like this is not your No, you're not a failure of to, yeah.

EAU: No, it's, that's so true, Erin. Like I, I see people in clinic all the time that this happens to, and I just say blame your parents like it's probably your genes. Okay, so

EW: let's talk about what are

EAU: some of the big medicines that we use and how do they actually work? Why are they working? All right.

EW: Yes,

EAU: Statins. So statins block an enzyme in our liver called HMG-CoA reductase. The CliffNotes version is that this particular enzyme, HMG-CoA reductase, this one is the rate limiting step in cholesterol synthesis in your liver. That enzyme is necessary in our liver, for our liver to make cholesterol. And remember, our liver is making over 50% of the cholesterol floating around in our body,

EW: so you have, you have more HMG COA reductase, then you have more cholesterol floating around in your body. If you reduce that reductase, that enzyme, then you have less collect cholesterol.

EAU: it goes even further than that.

EW: Okay.

EAU: Because what happens is that by blocking this enzyme in particular, because it is the rate limiting step, meaning it's like the slowest one in the daisy chain, right? When you're moving stuff into a house, um, we dramatically reduce, not just like a little bit, do we reduce how much cholesterol your liver's making. You're dramatically reducing, like putting a huge brake on how much cholesterol your liver can make. [00:40:00] And because all of our cells still need cholesterol. Our cells have to get better at taking cholesterol out of our bloodstream. So they actually upregulate those LDL receptors, those Velcro sticky hands on the surface of their cells that capture our LDL cholesterol floating around in our bloodstream. So it's not just that, oh, we're not making as much cholesterol, it's that we're not making as much cholesterol and our body cells still need cholesterol, so they start vacuuming it out of our bloodstream at really high rates.

EW: beautiful.

EAU: Isn't that cool?

EW: Oh, yeah,

EAU: I love that. There's also some interesting evidence that statins also might have a little bit of like an anti-inflammatory effect as well.

EW: yeah,

EAU: we talked in last week's episode about how important inflammation is in the process of atherosclerosis or in the process of that cholesterol actually forming a plaque in your bloodstream. Inflammation is an integral part of that, and so there's some thought that there's also an anti-inflammatory effect of statins, though we don't fully understand that mechanism there.

EW: Mm-hmm.

EAU: So that's how statins work and they're incredibly effective. Erin? There was a meta-analysis from 2016 that was really interesting, so it's kind of old now,

EW: Yeah.

EAU: at over 50 different studies that looked at all the different possible interventions that we had at that time,

EW: Okay.

EAU: All of the like randomized control trials of those different interventions and the effect of lowering LDL cholesterol on cardiovascular disease risk by these different interventions. Okay. We had 25 trials on statins. 25 of them compared to only four diet trials

EW: Huh.

EAU: Compared to only two at the time on PCSK-9 inhibitors, which I'll get to in a second one on Ezetimibe, which is another medicine that we use. And so what that means is not only do we have so much data on their effect, it also means that our confidence intervals on just exactly how effective they are, are really narrow for statins. we know, like without a doubt, that statins are extremely effective at lowering our LDL cholesterol and at reducing the risk of adverse cardiovascular events,

EW: So is that what, what did that study show the meta-analysis show In terms of like the, by the numbers impact.

EAU: So by the numbers, statins are the most consistent. Diet is a, is has a slightly less effect, but still a significant effect. PCSK-9, which I'll get to in a second, have the greatest effect. They lower lDL cholesterol the most and they reduce your risk the most, but the confidence intervals are super wide.

EW: Okay.

EAU: At least at that time we just didn't have as much data on them.

EW: right,

EAU: Um, yeah. And then the other ones are in between, but statins are like, like pound for pound I guess. I don't know if that's right. But like incredibly effective and like just so much good data to support

EW: right. We're really dialed in on, on how statins work and how well they work.

EAU: Yeah.

EW: there, what are the differences between different types of statins?

EAU: Great question. So different types of statins, a lot of the difference is in their potency. So some statins can lower your LDL cholesterol to a much greater degree than other statins. The exact of like why? Uh, I don't know. Okay. Um, but that means that we have statins that vary in what we call their intensity. And by intensity we mean how much, by what percentage are we lowering your LDL cholesterol. So if I can give you a medicine that's gonna lower your LDL cholesterol by at least 50%, that's considered a high intensity statin regimen. And if it's by less than 30%, then that's considered a low intensity regimen. And then there's intermediate in between.

EW: Okay. Okay.

EAU: Okay. Or moderate. Um, there's also differences in like some of them are more lipophilic, so they're more like fats and some of them are more hydrophilic, so they're more like, they act more like proteins and that they're more like soluble in water.

EW: Hmm.

EAU: Um, and so that might differ in how much they build up in different tissues in your body. there's not great data that says that one is more or less likely to cause side effects than the other. And that's the

EW: Huh?

EAU: briefly talk about

EW: Yeah. Yeah.

EAU: an important part of the statin story. you mentioned it as well, Erin. It is not the case that side effects don't exist.

EW: Right.

EAU: Any medication, any therapy really has the potential to cause side effects. like you mentioned, Erin, the most cited side effect that causes people to stop taking a statin medication is muscle symptoms. And that's a really general term.

EW: Yeah.

EAU: Often muscle pain or muscle aches, or sometimes muscle weakness.

EW: Mm-hmm. Mm-hmm.

EAU: Now there's also other things like gastrointestinal side effects or, uh, liver enzymes can increase, which is usually transient and can be completely reversed, either by going down on the dose or stopping the statin. But muscle [00:45:00] effects are like the, the big one. Right. And there was a recent meta-analysis that looked at. Data from randomized controlled trials from over 150,000 people and 23 different studies that were comparing either statins versus placebo or different intensities of statins, so that high intensity versus low intensity therapy. what they found is not that muscle symptoms were never reported by any means, but that by comparing all these different regimens, what they estimated was that less than 10% of all of the reports of muscle symptoms could actually be directly attributed to statins themselves. Does that make sense?

EW: I think so. So the, it's not talking about the rate of side effects that happen, but

EAU: Mm-hmm.

EW: how much of those side effects are statins directly responsible for causing, and is this based on like, do we understand a mechanism?

EAU: Oh, such a good question. We don't,

EW: Okay.

EAU: don't, because the vast majority of these, even the side effects that could be attributed to statins are considered mild. A lot of people actually will continue their statin and the, of people who report symptoms after the first year actually goes

EW: Yeah.

EAU: usually in that first year of therapy. Realistically, it's usually within a first few weeks or months of starting a statin medicine that people are more likely to have effects directly related to the statin.

EW: Mm-hmm.

EAU: Um, but no, we don't understand exactly the mechanism, but most of them are mild and they do not result in actual damage to the muscle tissue or myopathy.

EW: Right, right.

EAU: that does not mean that they can't ever, right. There are more serious events like rhabdomyolysis and and that is estimated to occur about four excess cases per 10,000 people if you're on a high intensity statin

EW: Okay.

EAU: there's only four, but like some people get rhabdo, that has nothing to do with statins.

EW: Right,

EAU: So statins will call it four excess cases for every 10,000 people on a high intensity statin.

EW: Is it more common? Okay. You were about to say.

EAU: Yeah. And one per 10,000 on less intensive. So it

EW: Okay.

EAU: Up like the chances of side effects and the chances of more severe side effects go up with intensity. So sometimes just going down from a high intensity regimen to a lower intensity regimen takes away side effects entirely for people, and that's enough. And then you're

EW: Yeah.

EAU: some benefit, just maybe not quite as much as you were on a high intensity regimen.

EW: Okay. Question about that meta-analysis. You said that 10% of the side effects experience are directly attributable to statins. What is the 90%? Where does that get attributed to?

EAU: I dunno,

EW: Okay.

EAU: don't, we don't have an answer to that. Just

EW: paper didn't suggest

EAU: No Uhuh,

EW: any, answers. Okay.

EAU: I mean, some of it, they're like, is it just aging? Is it just nocebo

EW: Right?

EAU: bunch of different possible things? Um, but not like a clear answer. No,

EW: Hmm. And so this was like by looking at people who are on placebo are still experiencing these side effects and we don't know what's causing that. Okay. Okay.

EAU: looking at like, how many excess cases, how many

EW: Yes.

EAU: will you get? Um, it was estimated like 11 reports of muscle pain or weakness per 1000 people on statins in that first year were from statins.

EW: Okay.

EAU: It's 11 per 1000.

EW: Right. It's tricky. It's really, really tricky.

EAU: Because it's not that these symptoms are not real, right? And, and if you are one of those people who has that severe side effect, right? One of four per 10,000,

EW: Yeah.

EAU: a very real effect for you. And so it, it is always a tricky thing to balance because when we are talking about treating and preventing, especially when

we're talking about preventing cardiovascular disease, we are talking both about population level reductions in risk, and we're also talking about an individual risk benefit calculation, right?

EW: right.

EAU: so, and those are not the same calculations on a population scale versus on an individual scale.

EW: Yeah.

EAU: And yeah. It doesn't help when people's symptoms are completely ignored

EW: Mm-hmm.

EAU: They're told, oh, it's absolutely not from this. Or when they're told from wellness influencers online that this medication that they've been on safely for 10 years is now causing the symptoms that they're having.

EW: Yeah, yeah, yeah, yeah.

EAU: I see all the time.

EW: I mean, I think that what is a real challenge too is like, how do you balance saying, okay, these are real symptoms. You are experiencing this, this is very real. Is and deciding is this caused by the statin? Is this not caused by the statin? Are you going to be someone who is the 0.001% are, and then it's like, what? Even if these side effects are not directly, directly caused by the statin, they're still impeding your ability to say exercise, or [00:50:00] something like that. And so it's

EAU: is gonna

EW: just

EAU: your health.

EW: right. It's a mess. I'm very curious to hear suggestions on how to, how to approach this.

EAU: I don't know, like, I really think that what it always has to come down to is a good relationship with a physician or provider that you trust,

EW: Yeah.

EAU: Who knows you, who you know, who can explain these things to you. And like, it's why I don't think AI can take over for all doctors, Erin, but maybe that's my bias.

EW: but I think it, it is the way that medicine is going and like the, and has been trending in the last 20 years, more expensive, shorter visits,

EAU: yep.

EW: more video visits that don't always necessarily feel like you're having a connection with someone.

EAU: Right.

EW: It all is just standing in the way of forming these relationships.

EAU: know 'cause they're the most important thing in my biased opinion. Okay. But we have more options too. Some

EW: Yes.

EAU: have side effects from statins or they're just like, no, I will not take a statin. Cool. Don't worry. We have other options now,

EW: Yeah.

EAU: And I'm not gonna go through every single one, but I'm gonna call out two that are probably like the two biggest groups that we use. One is called Ezetimibe, and this is a drug that blocks a protein that's in the cell membranes of our guts and our bile ducts.

EW: Hmm.

EAU: what this does is it blocks the amount of cholesterol that we are absorbing and reabsorbing. So this one, it doesn't have as huge of an effect by

EW: Okay.

EAU: But it can still lower cholesterol often by like 10%. We're talking LDL cholesterol. It can lower you. So that's not nothing to shake a stick at.

EW: Um,

EAU: let me talk about the one that people are so excited about and that I said multiple times, that is a nonsense word called PCSK-9

EW: PCSK -9 inhibitors. Yes.

EAU: PCSK-9 is the shorthand name for a protein that I'm not gonna tell you the name of because I don't know it. It's too long. But this is a protein that our liver makes. It's really interesting. Its job, this protein is to degrade, breakdown LDL receptor proteins. Okay? So this protein is kind of like an anti recycler of

EW: Okay.

EAU: Of this receptor. Who usually collects the LDL in our bloodstream? Okay?

EW: Yeah.

EAU: Why does this protein do

this?

EW: Yeah.

EAU: I don't know right now, but that is what it does. So if you can block this this

enzyme this protein

then you will have more LDL receptors available to be reused and recycled to be collecting our LDL cholesterol in our bloodstream. Ah.

EW: So this is like a Velcro glove thief. This, this protein. And so if you stop it,

EAU: Exactly. It's a Velcro glove thief.

EW: the Velcro gloves are numerous and available to catch all those tennis balls of LDL.

EAU: I really like this analogy by

EW: It's a really good analogy. I'm, I am. Yeah.

EAU: Thanks. You know, I don't always come up with good ones, so

EW: I mean, the best I could do is Bill Buckner, so you know.

EAU: Enjoyed that so much more than I can say. Um, yeah, so that is how PCSK-9 inhibitors work. The, the main group, like there's a couple different medicines that we use that are mostly monoclonal antibodies. Um, they're really interesting 'cause a lot of times, like they're not a, a pill that you have to take every day. like an injectable medicine that you take every week or two weeks, depending on the medicine. There's also something called Inclisiran, is, uh, a small interfering, RNA molecule. Okay. That binds to this proteins, PCSK nine's, mRNA, and degrades it. So it's also affecting that same system. It's just not blocking the receptor itself. Ah, isn't that so cool?

EW: Wow.

EAU: And the data on all of these medicines that affect PCSK nine, it is incredibly strong. So we talked about that, that meta-analysis from 10 years ago or so. PCSK nine inhibitors reduce your LDL drastically

EW: Mm-hmm.

EAU: and can drastically also reduced cardiovascular events, especially in people who are very high risk, meaning people that we are doing secondary prevention

EW: Right.

EAU: Already have, you know, cardiovascular disease, who have maybe already had a heart attack or a stroke and we really need to lower that cholesterol. Or people who are just very high risk, right? So in those populations is mostly where it's been studied. And so cardiologists love this medicine. biggest issues are, as with all new drugs, especially ones that are fancy things like siRNA and monoclonal antibodies, they're expensive as heck.

EW: Mm-hmm.

EAU: In this country, we also just don't have nearly [00:55:00] as much data on them as we do for statins. So the error bars on their benefit is still messier,

EW: It's just a messier.

EAU: they still have a really good effect.

EW: Do we have information about side effects?

EAU: That's a great question. I should have looked into it more. There definitely can be side effects, uh, but I honestly just did not do a good job of looking into

EW: Okay.

EAU: as much. So I back to you on that.

EW: Okay. Uh, and then I have a question sort of like about lowering. So we, we've talked about lowering and the importance of, of having lower levels, but there is such a thing as too low. What are consequences of that?

EAU: That's a great question. I don't have a number for you.

EW: Okay.

EAU: what the data shows is that the higher your individual risk of cardiovascular disease, right? Because cardiovascular disease is not only cholesterol.

EW: no, no.

EAU: I hope that I have made that clear. It is not by any means only cholesterol, but lowering cholesterol is one of the big ways that we have to reduce the chances that you're going to develop or have really bad outcomes, like a heart attack or a stroke or death from cardiovascular disease. so what we know is that the higher your individual risk based on all of your other risk factors, age, whether or not you smoke, how much alcohol you drink, your BMI, your blood pressure, whether you're on a blood pressure medicine, your

kidney function, based on all of those things, the higher your risk, the lower we need to push your cholesterol to really lower your risk of

EW: Ah, okay. Okay.

EAU: people who are very high risk in the newest guidelines, people who are very high risk, the recommendation is to reduce their LDL to less than 55. And that's very low. And

EW: Yeah.

EAU: seen any bad outcomes from that, meaning we haven't found a number that is too low for those people who are very high

EW: Okay. Okay.

EAU: But for other people, we haven't necessarily shown that there is a benefit to pushing them that low.

EW: Okay.

EAU: for most other people, the recommendation is gonna be either less than 70 or less than 100, depending again on what your risk is of cardiovascular disease development.

EW: Huh.

EAU: Yeah,

EW: So prolonged use of statins or like longtime use of statins. Basically, if your blood, cholesterol is high enough that you need to be on a statin or you are prescribed a statin, you,

EAU: lipid lowering

EW: or something like that, you are on that regimen for the rest of your life.

EAU: Often.

EW: Okay. Okay.

EAU: Yeah. Um, that, that, 'cause again, that's the data that we have. Right.

EW: Right.

EAU: And we'll talk in a second about how much atherosclerosis is, is a disease of, of long term. Right.

EW: Yeah,

EAU: not a, it's not a short, it's not the rabbits that just get it in a week or two.

EW: yeah.

EAU: A long-term disease kind of a thing. And so that is why it requires long-term management

EW: Plaques weren't built in a week, just like Rome wasn't built in a week or whatever. Yeah.

EAU: Isn't it a day?

EW: Probably,

EAU: Okay,

EW: with like sayings like that. I cannot remember them. I mix my metaphors constantly.

EAU: I love it. Um, I wanna just briefly like, um, shout out is not the right word.

EW: Highlight,

EAU: Rage,

EW: right? Sure. Okay, sure.

EAU: Um, because there, there is a lot out

EW: Right.

EAU: on like, oh, alternative types of medicines, lower cholesterol.

EW: Mm-hmm.

EAU: And I'm not talking about lifestyle interventions like diet and exercise changes. We already talked about those. They have decent evidence, they're an important part of this. But one of the things that some people use or claim to have a benefit in lowering cholesterol are phytosterols, right? Those are plant-based cholesterols, it is possible based on some like observational data that consuming high levels of these plant-based cholesterols or plant-based sterols might decrease LDL cholesterol, especially when you look at people on like vegan diets who have quite a lot of phyto sterol consumption or who are taking other, you know, additives of phytosterols. But we have no randomized control trial data on these the data that do exist, what's really interesting is that they seem to be most effective when they're consumed with meals. Meaning when you're getting it from foods rather than just a

EW: Supplement,

EAU: an addition. And of course, as we talk about so often on this podcast, Erin, there are no regulations on supplements, whether we're talking about phytosterols or other nutraceuticals. And one of the big ones out there for cholesterol is red yeast rice, you mentioned it, Erin. The mechanism of the compound produced by this yeast that's grown on rice is that it blocks [01:00:00] HMG coa, reductase.

EW: It's a statin,

EAU: a statin. Okay.

EW: because it's coming from a, it's extracted from a plant, plants produce different levels of these things, and so you have no idea how much you're getting. And so it can be dangerous. You could be on very low dose, non-existent dose versus inten, inten, high intensity or whatever.

EAU: And most brands in studies that have looked at this have no detectable levels of that actual compound. Right. There's no regulation on the composition of those particular supplements. There's no regulation on how much of that compound, like you said, the yeast is actually gonna produce

EW: Right?

EAU: So there's batch to batch variation, there's brand to brand variation, and at the end of the day, it's an unregulated statin.

EW: It's unregulated.

EAU: yeah, and, and I don't want to make that sound like, oh, well pharmaceutical companies are just the best thing ever,

EW: Right. No. No.

EAU: They're not, and it's also not the case that our guidelines might not be subject to some degree of bias, because, like you mentioned, of the conflicts of interests that exist within cardiology and within

EW: Right.

EAU: I mean all fields of medicine, realistically. A good number of the authors and the people who are involved in the peer review process for the newest dyslipidemia guidelines in the US have financial conflicts of interest, not just with pharmaceutical companies, but with imaging companies, with genetic testing companies. And that doesn't mean that all of our data that we have that is so strong isn't real or isn't strong, but it just muddies these waters even more. And it,

EW: Yeah,

EAU: creates this gap where people can really exploit that uncertainty.

EW: totally, totally.

EAU: It's really, really a bummer because atherosclerotic heart disease, including heart attack and stroke, kills an estimated 19 million people worldwide every year, as of the 2023 Global Burden of Diseases study.

EW: Wow. Yeah.

EAU: an estimated 600 million people are living with cardiovascular disease right now.

EW: Mm-hmm.

EAU: Every across the globe, cardiovascular disease is the leading cause of disability adjusted life years. In some countries it is a third to 40 to 45% of all deaths.

EW: That's wow.

EAU: In this country, the estimated costs to healthcare are in the hundreds of billions of dollars. And an estimated 80% of this disease is due to modifiable risk factors. And cholesterol this relationship between LDL cholesterol and cardiovascular disease is so incredibly clear, and it is something that we really have the potential to treat.

EW: Yeah. Yeah.

EAU: So it's uh, it's such a huge bummer that there are so many people who do not have access to this.

EW: Mm-hmm.

EAU: And it's not just older adults. I think that we think of cardiovascular disease as something that only happens to older people. But the more that we look at and study the like, pathogenesis of cardiovascular disease, the more we understand that especially cholesterol is a long-term exposure that increases your risk.

EW: Yeah.

EAU: So having exposure to higher levels greater than a hundred of LDL cholesterol, especially greater than 160 younger in life and for longer periods, increases your risk more than if it just goes up over time, if that makes

EW: Yes, it does make sense.

EAU: And it's estimated that 12 to 13% of young adults have dyslipidemia in this country.

EW: Wow. Yeah.

EAU: a

EW: It's not a small amount. Yeah.

EAU: It's estimated that in the US if everyone based on guidelines who was recommended to be on medicine to lower their cholesterol, was actually on a medicine for this, like a statin, we could prevent 1 million cardiovascular disease events like heart attack, stroke, and death in 10 years, a million.

EW: Whoa.

EAU: Okay.

EW: That's a lot.

EAU: And that's just in the US where we have much better access. In low and middle income countries. It's estimated that only one in 10 people who would be recommended to be on some kind of medicine to lower their cholesterol are actually on a medicine

EW: Yeah.

EAU: they don't have access. Right. so

EW: That's a lot. It's a lot. Erin.

EAU: It's a lot. Um, but there is, I just think it's one of those situations where medicine has come so far, right? And the data that we have is so strong, but it's also not all just one thing. And I think that that is where some of the kind of confusion and uncertainty and doubt can come [01:05:00] from right? Because we look at cardiovascular disease events over time, they're still going up, right?

EW: Yeah.

EAU: these great medicines, but they're still going up.

EW: Yeah.

EAU: Um, and that's because it is so many other things that play into it. So this was not an episode just only about cardiovascular disease, but

EW: No.

EAU: cholesterol overall, and that

EW: right.

EAU: is what I have to say, Erin.

EW: It is really complicated and it's so recent, and I think that's what contributes a lot to this. And it does go to show that you can have the data, you can have the treatments, you can have the, uh, like all of these different facets of in support of this, and that's not enough. And so figuring out that gap, what will make, what will be enough? How do we actually either get the treatment to people who need it? How do we actually develop better treatments? Whatever it is, how do we address those gaps where we're clearly failing?

EAU: Yeah.

EW: Yeah.

EAU: it's a great question, Erin.

EW: Hopefully someone figures it out

EAU: Yeah. If you wanna read so many papers

EW: many.

EAU: got all of this information, we can tell you.

EW: We can tell you. Um, I also want to shout out real quick too, that they're speaking like on, on the subject of misinformation and social media, wellness influencers, uh, health influencers, stuff like that. There is next week's book club episode is an interview with, uh, Deborah Cohen. It's a book called Bad Influence, and it's really a fascinating conversation. Definitely tune in. There's a whole, we have a, a little bit about statins in there, so check it out.

EAU: Yeah.

EW: But papers for this episode. Okay, I have a bunch more, again, I'll shout out again that Steinberg series from 2004, an interpretive history of the cholesterol controversy, then by Ju et al. from 2018, patient beliefs and attitudes to taking statins. And then by endo, a gift from nature, the birth of statin. So that's the person who.

EAU: Oh, I

EW: Came up statins

EAU: let me tell you where you can learn more. Um, I really liked a paper by Silverman et all from JAMA 2016. Um, that was the association between lowering LDLC, which is LDL, cholesterol and cardiovascular risk reduction among different therapeutic interventions, a systematic review and meta-analysis.That's the one that has really great graphs, honestly, on like with the error bars and the risk reduction. Loved it. Um, I have links to the newest guidelines as well too. The study looking at the, like, overall risk of cardiovascular disease and heart attack was from the, uh, journal of American College of Cardiology from 2023, and that was the one of the global burden of disease studies. So we have that one. Um, there's also that 2022 paper by wreath etal in the Lancet that was the effect of statin therapy on muscle symptoms an individual participant data, meta-analysis of large scale randomized double-blind trials. But honestly, so much more there, Erin.

EW: Truly, truly.

EAU: everyone can check it out on our website, this podcast kin you.com under the episodes tab.

EW: Thank you to Blood Mobile for providing the music for this episode and all of our episodes.

EAU: Thank you to Leanna and Tom and Mark and Jessica and everyone at xact. Right. For everything that you do to make this podcast possible.

EW: Thank you. Thank you. Uh, and thank you to you listeners, subscribers, watchers, et cetera. We appreciate you engaging with this podcast so much. I know it sounds so clinical when I say that, but what I mean is like anyone who is like follows us on social media, whatever, any, anyone, it is, it truly means everything.

EAU: it

EW: you.

EAU: Thank you. And thank you as always to our patrons for your support over on Patreon. It means like it. I can't believe that you're supporting us there.

EW: Truly. Yeah.

EAU: really means a lot.

EW: Until next time, wash your hands.

EAU: You filthy animals.