

Transcript

Dr. Kendal Williams (Host): Welcome everyone to the Penn Primary Care Podcast. I'm your host, Dr. Kendal Williams.

In this podcast, we seek to engage internists and other experts in the common and practical questions that primary care physicians face every day. If you've listened to our other podcasts, we're doing a series primarily starting with the stuff that we do most frequently. And one of the things left out and in the list of things that we've talked about is lipids. So, we wanted to bring in some expertise in lipids today to talk about cholesterol management and other lipid management in the primary care setting.

Here with me today is Dr. Daniel Soffer. Dr. Soffer's a practicing General Internist. He's a Penn lifer. He attended medical school at Penn and trained at Penn. He sees his own primary care patients in the Media practice, but also as a key member of the preventive cardiology and lipidology team at Penn, seeing patients in that capacity at both Radnor and at Perelman in the city. Dan, thanks so much.

Daniel Soffer, MD (Guest): Kendal, thanks so much for having me. I'm really looking forward to having this conversation with you. By the way you left out that I also went to Penn undergraduate.

Host: So you truly are Penn lifer

Dr. Soffer: Truly a lifer.

Host: Dr. Gregory Troutman is new to the podcast. And we're really honored to have Greg on because he is the first resident on the podcast. Greg is a second year primary care resident at Penn. He's currently doing his CCU rotation, so he is seeing the end stages of all the processes that we're trying to prevent in this podcast. Greg, thanks for coming on.

Dr. Gregory Troutman (Guest): Yeah, thanks so much for having me. And hopefully there's many more residents to be involved down the road.

Host: Greg also has a special interest and extra training in clinical lipidology, has done cardiovascular research and plans to go into this field.

So, Greg, I know you have a special interest and probably know more than me, so, which is true of many residents I've found over the years. So, really happy to have.

In preparation for this session, Dr. Soffer sent me a case that captures many of the key points in lipid management. And we're basically just going to start with that case. And then we're going to parse through various elements. We have a little outline here in front of us, of the various areas we want to address, but we're going to talk through each aspect. So, let me present the case first.

This is a 56 year old overweight man with a BMI of 32 who has seen to Dr. Soffer's clinic for a second opinion regarding statins versus no statins. So, his current lipid panel looks like this. His total cholesterol is 238. Triglycerides are 176. His HDL cholesterol is 38. His LDL is 165. His ten-year risk by the atherosclerotic disease calculator is 11% and he had a calcium score done that also, that was 56.

So let's go, you don't have to memorize all those numbers if you didn't catch them the first time we're going to go back through them.

But Dan, let me just start with you. You sent me this case for a reason, right? What were some of the aspects that you thought were good to discuss?

Daniel Soffer, MD (Guest): Well, this guy has a lot of the common features that we see in a regular medical practice, a great primary care case, because he has mild elevations of almost everything, but nothing severe of anything. And so, we're taught early in our training that single risk factors cause cardiovascular disease. And it's really the accumulation of mild elevations of these risk factors that tends to accumulate and contribute to the cardiovascular disease. And so this gentleman is not obese. He's not hypertensive. He doesn't have a severe lipid disorder. He doesn't have diabetes. But he has features of all of these things that contribute.

I guess I didn't give the blood sugar in this, but he has features that suggest that he's on the continuum of accumulated risk due to multiple risk factors combined, but no severe abnormalities in any one of them. And so I liked that idea because these are the kinds of patients that we see every day who walk around and are told, you know, your risk is significant over the course of a lifetime. You should eat less and exercise more and come back in six or 12 months and five or 10 years later, that's all they've ever been told until they show up. And now they're on the service that Greg is taking care of in the CCU, and we missed opportunities to help them.

Host: So when I talk to patients about this, and I'm curious just to hear what the two of you do. I explain this process as biological corrosion of your pipes, right? And I say, listen, you know, pipes carry blood. If they get corroded that corrosion flicks off, blocks the pipe. That's what heart disease and strokes are all about.

And, we want to prevent that process and I go over with them and I say, okay, it's hypertension that causes it. It's high lipids, diabetes, smoking and just your age. Right. So those are the major risk factors right Dan?

Dr. Soffer: Yes. And so, you know, I think it really is important and I actually like to draw pictures. Greg has worked with me in the clinic and I can't remember if he saw me drawing these pictures for my patients, but it's the same picture we draw in the foundations of lipidology course. And when I'm teaching with the residents to let them know about the impact of the LDL particle or they, APO B containing cholesterol particles that contribute to atherosclerosis, right? That's the foundational building block for plaque in the arteries, but all of these other features contribute to the progression of atherosclerosis.

And I remind my patients that, in order to have a heart attack, 98% of the time, you have to have significant atherosclerosis beforehand. And I, I'm not sure it's 98%. I think only about 2% of heart attacks occur due to other causes. So, heart attacks are essentially due to atherosclerosis. So, when we're talking about atherosclerosis formation, I want them to know that all of these things contribute to atherosclerosis formation, but you don't have to have a diagnosis of any of them to have significant atherosclerosis.

Host: One of the questions that I was asking myself thinking through this is with those five risk factors, what percentage of the total amount of risk of atherosclerosis is explained by that? Right. So, there was a study, the INTERHEART study back in 2004, it was a case control study, but it seems to be cited quite a bit that large international study that showed that, those five risk factors essentially, you know, were explaining about 90%, it seems of atherosclerotic disease.

There's a couple of things that they picked up in that study that I'm not sure we see even obesity and some other elements, but I think it's those. It really is those five, isn't it Dan that causes most of what we see, if not all.

Dr. Soffer: Yeah, those are the major risk factors that increase the hazard ratio for cardiovascular events by close to two or more. And there's other risk factors that move the needle a little bit too. But when they do, they have an impact in populations where the hazard ratio is only increased by much smaller amount.

So don't amount to be major cardiovascular risk factors. But I really want to stress the point, Kendal that you can have atherosclerosis and not have hypertension and diabetes or severe cholesterol disorders or smoking. All those things contribute, but they're not necessary antecedents for the presence of atherosclerosis or for heart attacks.

Host: So getting back to this case, Greg, what struck you about that particular cholesterol panel? Is there anything that you found significant about it?

Dr. Troutman: No. And I think exactly to Dr. Soffer's point, it's someone who has a few low risk factors. And I could imagine meeting this patient in the office and I'm feeling kind of proud of being a nonsmoker, of not having hypertension, being non-diabetic and feeling that overall their health and ASCVD risk is pretty well managed.

But I think it's interesting to kind of pick apart. I think one thing I'd want to know if this is a fasting or non-fasting panel in the context of the slightly elevated triglycerides, I'm seeing kind of a low normal, but a little low HDL that shows some room for improvement and maybe it could be indicative of exercise status outside of the clinic.

And then really notably I think the LDL of 165 again, as Dr. Soffer said not anything that makes us lean towards like a familial or genetic lipid disorder, but something that is a marker of risk for this patient.

Host: And that LDL is 165. So it's not over 190, right. This isn't an automatic treatment. Right. If somebody had, came into you with an LDL of over 190, you'd basically be looking at a statin right away, even if they were 32 years old. Right?

Dr. Troutman: Yeah, correct.

Host: And let's just talk about HDL. We know it's an independent well, a low HDL is an independent predictor for heart disease, but there doesn't seem to be a ton that we can do about it. Right. Dan, I mean, in terms of medication wise, it's just exercise.

Dr. Soffer: Yeah, HDL is super interesting. I mean, I've colleagues who have spent their entire careers looking at HDL cholesterol metabolism, you know, it really looked like it was as an independent risk marker is one of the most powerful markers of cardiovascular risk we have as an independent variable. It turns out though, it's far more interesting and it has to do with what HDL is.

And what we see reported on a lipid profile is the HDL cholesterol content, but HDL is a very complicated particle. We don't have to get in deep into the science here, but the HDL particle is loaded with all kinds of proteins that turn off atherosclerosis primarily, but have other roles throughout the body and the immune system and other features.

And so the actual particle itself is very athero protective and the cholesterol content of HDL particles in the blood, generally reflects the health of the HDL particles and how well they protect against

atherosclerosis, which is why they're a real good marker. But they're directly, if the HDL cholesterol is directly affected by the triglyceride content.

And when you look at HDL cholesterol as an independent marker, it loses a lot of its predictive value, when you factor in triglyceride level and remnant cholesterol. And if you look at genome wide association studies and for determination of the impact of HDL cholesterol, the genes that regulate HDL cholesterol do not have a close association with cardiovascular risk, even though epidemiologically, the HDL cholesterol is a fantastic marker of cardiovascular risk. So it's very complicated. It's a good marker.

We learned over the last decade that therapeutics for HDL cholesterol, like niacin and CETP inhibitors are not effective therapeutics for reducing cardiovascular risk. And so HDL cholesterol is not a target for therapy. It's simply a marker of the general metabolic health, oftentimes the same things that control triglycerides, at the extremes, when the level's less than 30 or greater than 80 milligrams per deciliter, it's a great marker of inherited defects or inherited variants that affect HDL metabolism. And those are the ones that are not necessarily associated with cardiovascular risk.

In the norm, like in this gentleman, an HDL cholesterol 30 is a good marker that he's at greater risk for cardiovascular disease, but it's not going to be the target of therapy. It's just a marker.

Host: So if somebody does an exercise program, loses 20 pounds, is doing aerobic exercise five days a week and their HDL goes up to 50. It's really, the HDL is simply reflecting, they're in better metabolic health than they were before. It's not the independent thing that's going to be causing them to be, right?

Dr. Soffer: Yes. Yeah. That's really well said. So they've definitely improved their health. They've probably reduce their cardiovascular disease, but it's not necessarily because their HDL cholesterol went from 38 to 50.

Host: So let's talk about the LDL particle then, right. And by the way let's step back and just say because this is going to come up later, the difference between APO lipoprotein B and lipoprotein A, which get people confused, but this'll be, maybe you can sort of figure those into your answer about the LDL particle. What are we looking at with the LDL particle?

Dr. Soffer: All right. I'll try not to get too lipid wonky here. So, all of the circulating lipoproteins are either containing as their main protein, either APO lipoprotein B or APO lipoprotein A1 with a capital A. Okay. So I'm already getting a little wonky because I'm throwing out capital versus lowercase a and the main distinction here is that the APO B containing lipoproteins are atherogenic and APO A1 is the principal APO lipoprotein found on HDL particles and HDL particles do not contain APO B.

So all of the other lipoproteins in circulation have APO B. And that includes chylomicrons from the intestines, VLDL particles from the liver, and LDL, which is a metabolic product of VLDL metabolism also contains APO B.

So all of those APO B containing lipoproteins contribute to atherosclerosis. Whereas HDL tends to be a protective particle that protects against atherosclerosis. In the circulation and unless your triglycerides are super, super high, the predominant circulating APO B containing lipoprotein is always LDL, even in people who have high triglycerides, even in people who have very high LPA little a, which we'll talk about in a little, in a minute, I guess. And so, all of the variation in almost all of the atherogenicity from the lipids is going to be due to the LDL particle.

We estimate how much LDL is in circulation by using an LDL cholesterol level. Since these are spheres and they contain fat, you can estimate how much LDL there is by measuring the cholesterol that's in there. Am I, are you following me so far? Cause I know I threw out some technical stuff and I wanted to keep it as clinically relevant as possible.

Dr. Troutman: And this was one of my questions for you too Dr. Soffer is especially, even from the resident trainee perspective, this is something where there's different coursework and certification and ways to kind of dive deep into the science to fully understand this.

What are your strategies for communicating this to patients? You kind of mentioned using some visual cues and drawing things out, but especially for this patient who seems just from the one-liner I'm coming in for a second opinion, kind of concerned and invested and might be wanting some of that nitty gritty to figure out whether or not starting a medication is really right for him. What are your strategies for conveying kind of this complex?

Dr. Soffer: Perfect. So, you know, the real practical aspects of this. So, the first thing is, I would actually not dive in too deep with the lipid profile. Kendal, I think you're falling into some of the trap I think a lot of our patients fall into. And I think a lot of clinicians fall into also, which is focusing too much on the lipid profile in terms of assessing the cardiovascular risk.

And so this is a gentleman who has features of cardiovascular risk that even if you didn't know his specific lipid details, you might think he was at risk anyhow. And if you skip down past his lipid profile and you see that his coronary artery calcium score is 56. Then you know that regardless of what his lipids are, right this moment or what they were a month ago or five years ago, or 10 years ago, whatever he's been doing for the last 56 years, he's developed far more atherosclerosis than most men, the same age.

I didn't include this number here with the calcium score of 56, but he's around the 75th percentile for a man his age. So, he has more calcified atherosclerosis than three quarters of all men, the same age, which tells me that over the course of his lifetime, he's highly likely to have a serious cardiovascular event. Since more than a quarter of men go on to have cardiovascular events in their lifetime. His calcium score of 56 is not super high. And so his short-term risk, his five-year risk for a cardiovascular event may not be super high, but he has strong indications that he has significant atherosclerosis and would benefit from therapies that reduce atherosclerosis. And so I don't see this as a lipid case. I see this as an atherosclerotic cardiovascular disease risk case, and that's how I think of treating most patients with statins, unless they have severe lipid derangements, so a very severe hypercholesterolemia or some other lipid derangement.

Does that make sense to think about it in those terms?

Host: Oh, absolutely. For me it does. Greg?

Dr. Troutman: Yeah, completely. And I think, especially from the trainee perspective, we're so used to kind of getting all the data and trying to interpret what's the best next test to order and how to interpret. And it's helpful to take a step back and look at the big picture instead of getting caught in the weeds.

Dr. Soffer: Once you've established that the person has significant cardiovascular risk, then you want to just make sure that they're taking advantage of all the things that can reduce their risk. And so all of those things, including the things that you all counsel your patients on you know, on a regular basis.

This gentleman should be taught to follow a healthy diet and should be taught exactly what that is. He should be told that regular physical activity and exercise is good for him, that maintaining a healthy body weight will help optimize his health in the long run. He shouldn't be smoking and we should do everything we can to make sure he's not a smoker, that we should maintain excellent blood pressure control, whether it's with medicine or not with medicine.

I know you talked about that with Jordy Cohen in a previous podcast. And those are the things that pertain to everybody who comes into your office. They don't have to be just people at risk for atherosclerotic cardiovascular disease or people with disease.

Those are the interventions that we know are critical. The things that are specific and that include pharmacotherapy for management are going to be whether to initiate a statin or not, whether to use antiplatelet therapy or not. And whether to use any of the other pharmacotherapies that we use to address ASCVD in our patients.

And typically I know we think about using medicine only in people if their risk qualifies them. But, you know, I think that's true when there's a really tough side effect profile or a high expense from a medication. But I think it's important to talk about the different medicines that we have at our disposal, because we know that we can reduce this patient's risk with some of those medicines.

And so, of course, first and foremost, the medicine that we use is statin drugs. That's the class of drug that's been around the longest. Statins have been around since 1987. There are seven different statins. They vary in potency and in their ability to lower LDL cholesterol. They have slightly different pharmacologic characteristics, different drug interactions, and the like. And different potency at LDL cholesterol lowering is probably the most important differentiating characteristic and they have slightly different costs. But in 2021 atorvastatin and rosuvastatin, the two most potent LDL cholesterol lowering therapies are both available as generics and really should be first-line in anybody who's starting on a statin in 2021. There's very little reason to use any other statins. There are some rare circumstances where we think about using some of the other statins, but it's really going to be one of those two because of their significantly improved potency for LDL cholesterol lowering and the side effect profile is excellent.

And we can talk about the perceived side effects and the actual side effects. That could be a whole other podcast if you wanted, but it's a drug class that's very well tolerated. That's extremely safe. That's evidence-based for a wide range of cardiovascular risk and that's very inexpensive. And so the entry point for statin drugs should be very low.

Greg probably knows that I sort of joke that if you walk near me I'm willing to prescribe a statin for you. And I'm only half joking when I say that. There really should not be that much discussion about who can get a statin cause pretty much almost everybody can get a statin. And the question is who should get a statin and who must get a statin and that's where the guidelines differentiate, and give us some guidance on how strongly we should be recommending it to our patients. Not necessarily whether we should recommend it, but how strongly we should recommend it.

Host: So, let me just start with that, because I know we do want to get back to statins and the specifics of statins, and you've touched on some of the questions, Dan, that when I poled my colleagues about, hey, what do you want them to ask Dr. Soffer on this podcast? There were a couple that came in about these statins, but I want to just go back review the criteria more specifically.

So, you know, the ACCH and the USPSTF both of them say anybody with prevalent atherosclerotic disease as manifested by stroke, heart attack, PAD, those folks should be put on statins at really at

whatever age they're manifesting that. And then the second category are people who are over 40, who are diabetic. They should be placed on a statin. And then next category are people who are over 40, but have an atherosclerotic 10 year risk that is greater than 10% or seven and a half percent. It depends on which guideline you follow. But one of them says seven and a half percent. The other says 10%. Is that correct Dan?

Dr. Soffer: Right actually, so both the diabetics and for the risk group, it's between the ages of 40 and 75 years old, that they qualify for a statin at least a moderate intensity statin, and in the risk group, if your risk is greater than at least seven and a half percent, but could be considered as low as 5% if you have other risk factors or risk enhancing factors, I should say.

Host: So to your point, I think, the case we have is 56. If you plug his numbers into the ten-year risk calculator, it comes up at 11%. Right? So by both guidelines, he should be on a statin clearly right.

Dr. Soffer: Yes, exactly.

Host: And you find, I assume that atherosclerotic risk calculator to be useful in making these decisions?

Dr. Soffer: You seem to have hesitated a little bit when you, well you hesitated, when you asked that question. Cause you know that I, I rec I could recommend it for anybody.

Host: Yeah. Cause I'm thinking in my head, you know, he's probably got it in his head. I mean, you could, as you said, you, you're sitting on a bus. Right. And you're pointing people out who

Dr. Soffer: Right.

Host: Right.

Dr. Soffer: Yeah. You can wing it.

Host: Yeah. But I mean, when we're sitting there and we're having to have conversations with patients. Sometimes the, having the backing of the risk calculator is helpful, be able to sell it.

Dr. Soffer: Yeah. This is sort of a funny story that I remember from 20 some years ago when I was at a lecture by a JD MD who was talking about how not to get sued. Have you ever been to a lecture like that where someone teaches a medical community, how to you know, optimize their medical legal risk? And one of the things he said was there are no laws in medicine. And then he said, he corrected himself. He said, except for guidelines. The guidelines are the minimum standard.

And now that was back in the 1990s, even. And that was before the true minimum standards set forth by the 2013. And then by the 2018 ACCHA multi society, cholesterol guidelines, where it's really the minimum standard. It's not the best you can do or aspirational. It's the minimum standard that if you don't even do this, that you're not even performing the minimum standard.

And in this JD MDs lecture, that would be an actionable offense if something bad were to happen.

And so that's something to keep in mind. It's really the minimum standard. And so using that as your guideline to determine whether to recommend a statin, you should keep that in mind. And remember, the risk calculator is really thought of as the conversation starting point. You can say to this patient, hey Mr. Smith, I've gone through your medical history and you appear to have a moderate cardiovascular risk over

the next 10 years. And what's not listed here is what his lifetime risk or his 30 year risk is. And it's going to be certainly greater than 50%. And we have an opportunity right now to change your future by giving you treatments that can really improve your outcomes. And in addition to all of the lifestyle measures that we've just talked about, I'd also like to offer you some medication and that's how the medication should be thought of.

Host: Yeah. And you know, it's a cumulative process. Back long ago, I was asked to do a journal club presentation and I chose the West of Scotland study, which is one of the initial epidemiological studies showing the value and it was pravastatin at the time, which is not a very potent statin. And what was very interesting in that study is that I don't remember the time windows, but they were, people were on it for a year, I believe, or something to that effect. And then they had follow-up, five, 10 years later and you know, many people had gone off their statins, but they still showed benefit down that time.

So there was something about initiating the process early, kind of like a sort of analogy that came to my head at the time was that it's like pruning a tree. You know, when you turn it a certain way, you turn the branch a certain way at a certain stage of its development, it's going to grow that way. And so I think to your point, getting on this early, because down the line, it's going to have much bigger effects.

Dr. Soffer: Yeah, that's a really good point.

Dr. Troutman: I think, especially for this case I appreciate you brought up point that his short term risk is kind of low, but there's a high 10 year and probably even 30 year risk. And I think it's interesting to think of this as a canary under the curve, and trying to explain that to patients as well, especially if this is someone who's coming in with some potential statin hesitancy, trying to emphasize that this is a medication that will help reduce risk over the long-term.

And if he is still leaving with questions, and not feeling kind of ready to take the next steps in this care, there's still chances to kind of maximize his preventative care down the road and that this isn't a once and done conversation.

Host: So I want to circle back to calcium scoring because this comes up in primary care and we talked about it here, but we presented it right with a case, but oftentimes patients are coming in, they have their lipid profile. I have to tell you, I don't order a lot of this test. And the reason is, because most of the patients that I would consider ordering it in should really just be on a statin. And so I just ended up having that conversation with them, but I want to talk about what it is and how you use it. So how do you use it, Dan?

Dr. Soffer: Yeah. Almost like I use statins, Kendal. If you walk past me, I'm interested in getting a calcium score, because while I think all of data and variables are interesting. They don't tell me whether or not somebody has atherosclerosis. They may suggest a particular lifetime risk for an event, but they don't tell me whether or not somebody has significant atherosclerosis. Whereas coronary artery calcium scoring does. Know, I could see 20 years ago, sort of not feeling whether or not coronary calcium scoring was a useful test. It was still in its adolescence in terms of development. We were still using electron beam CAT scanning 20 years ago, which is a now defunct technology that no one uses anymore.

But some of the original data from the EBCT and now data with contemporary scanners is no longer just a consideration or no longer, just a possible way to assess risk, it should be really incorporated into, I think, routine general health care. It really has no role in managing the care of people with established cardiovascular disease.

Cause what you're trying to answer with it is roughly what is the burden of atherosclerosis that someone

has? And how developed is it over a time period. And so, what it looks for is calcified atherosclerosis, and it's a tool to quantify how much calcified atherosclerosis is. And just in case you don't know where the number comes from, what they do is they do these fast cat scan, a multidose cat scan, and the slices are, if I remember correctly, about five millimeters apart from each other and multiple slices through the heart. Each of them white bits and crusty bits are encircled by the tech and prompted by the program. And the program can measure the area of each of the crusty bits they see. And then also classify how crusty that little bit is on a scale of one through four in Hounsfield units. So you have the area of the calcified portion multiplied by a whiteness quotient and you get a score.

And then all of those bits are added together and that's the Agatston coronary artery calcium score. And if you use that score and you look at large populations in multiple different populations and multiple ethnicities, you can see that there's a roughly log linear relationship between the coronary calcium score and cardiovascular event rates. And this is not a test that should be considered sort of an extraneous biomarker for cardiovascular risk. It is the biomarker of cardiovascular risk because it shows atherosclerosis. And when you look at the utility of biomarkers, even, APO B or LPA or HS CRP, or some of the other biomarkers that you may have considered as a tool to help determine whether or not you should be treating somebody; the coronary calcium score changes the curve considerably. It really stands apart from every other biomarker in a way that it really should not be considered a biomarker.

It really is a true way to observe whether or not somebody has the disease that you want to treat.

Host: So for everything else Dan, you're just looking at risk factors, but here, this is actually looking to see inside the pipes. You know, how much atherosclerosis is there in a way that the best way that we can do at this time.

Dr. Soffer: Yeah. Yeah, it really is. Now there are some limitations, right? So it's looking for calcified atherosclerosis. So, younger patients may have significant atherosclerosis, but it hasn't had time to calcify yet. And so there's a high positive predictive value when you do a calcium score in a younger patient. For example, if you saw a 30-year-old who came in because he said my father had a heart attack and died at 32 and I wanted to know what to do. Even before I heard anything else about that patient, I'd already have my prescription pad out and be prescribing medicine to reduce his risk. But I would consider doing a calcium score in that very young patient, as long as he knew that a zero calcium score would not change my thought process about whether to treat him. And so the rationale for doing it in an unusual case like that, which is the kind of case that we see all the time in preventive cardiology, but a case like that, the reason to do it is so I can have it another way to estimate his atherosclerosis burden, because so far we've really just talked about whether to treat our patients.

But there's also a variation in the intensity of treatment. So it's not just statin. It's maybe high intensity statin, plus other LDL cholesterol lowering therapies, plus other therapies, perhaps anti-platelet therapies. And some of the other medicines we use for reducing atherosclerotic risk.

But first and foremost it's get on a statin.

Dr. Troutman: In your mind when you're kind of interpreting these results and having these conversations with patients, do you interpret someone kind of quote, positive coronary artery calcium score as a primary prevention or secondary prevention patient in your mind?

Dr. Soffer: You know, that's an active area of conversation in, across the country right now.

So, there's clearly a difference between a 24-year-old slender vegan marathon runner with you know, four living grandparents and two parents without any cardiovascular disease and no diabetes versus a 64-year-old hypertensive diabetic with hyperlipidemia, who's never had a cardiovascular event yet. They're both considered primary prevention. Right. So, I think that to think about primary prevention as everyone who's never had a heart attack or a stroke, or doesn't have some other clinical ASCVD is problematic because it's such a broad heterogeneous population. And so subclinical atherosclerosis is definitely a subtype of primary prevention where you've identified people who just haven't had cardiovascular events yet.

It's not quite the same as secondary prevention because someone who's had a cardiovascular event may have other features that promote not just atherosclerosis, but may promote destabilization of atherosclerosis.

And if your patient has never had an event, maybe they don't have some of those other features or maybe it just haven't happened yet. And you just, you don't know simply on the basis of atherosclerosis, but if your calcium score is greater than a hundred, your risk is high enough to support the use of higher intensity preventive strategies. If your score is greater than 300, your risk for cardiovascular disease is the same as people with established cardiovascular disease. And if your score is greater than a thousand, you're in the very high risk category, the same risk that we saw in the patient populations that were in the Fourier and Odyssey outcomes studies, two major RCTs for a PCSK 9 monoclonal antibodies in people already taking high-intensity statin. You can use the calcium score to stratify risk and guide intensity of therapy in that respect.

Host: So Dan, would you say that and I know the guidelines and we could go over them for moderate intensity, but for high-intensity, but just sort of philosophically, what I hear you saying is if you have identifiable atherosclerotic disease, it's in your, you can see the calcium score, it's there; that we really should be talking about high intensity statins at that stage?

Dr. Soffer: So, I'll just tell you my personal approach is. I tend to use rosuvastatin 20 milligrams on pretty much everyone I start on a statin, so there's no downside to driving someone's LDL cholesterol to lower levels than you might even think are beneficial for them in the short term.

And rosuvastatin is well tolerated, 20 milligrams has a psychological advantage of not sounding as high as 80. And so if that's part of your decision-making and conversation, I think there's some value to that. You get a high-intensity result and the better you lower someone's LDL cholesterol, the better their outcomes are going to be.

Now that's where you start the conversation. That's where I start the conversation. I'm willing to negotiate downward if it's really important to the patient to take a lower dose or a different statin. And it's not written in stone, but that's really where I start the conversation in anyone I'm bothering to put on a medication. I don't really see much advantage to using lower doses as your starting point for anybody.

However, the evidence from clinical trials supports using moderate intensity statin in those lower risk patients where you wanted to start. And it gives you the option to have that as your starting conversation, based upon randomized placebo controlled clinical trial. So I'm all for evidence-based medicine, don't get me wrong.

And I'm all for using the guideline as your guide for determining where you need to be as your starting point. But I'm also practical and I take care of patients in different environments and it's easier to just

have a one size fits all approach, which is, you know, if you have risks for cardiovascular disease, you should be on a statin. And if I'm going to start you on a statin, I generally would use the rosuvastatin 20 as your starting point.

Host: So let's talk about the side effects. Cause that's obviously often what people are worried about and I tell them, listen, I say there's no serious side effects with this thing. And, you know, I'm obviously hedging a little bit because there is some muscle necrosis that we've seen rarely and so forth, but, in general, this is a reversible side effect. It's really not a side effect even right, it's an effect of the drug right? Because you're inhibiting the HMG, COA, reductase and HIP enzyme, and it's present in muscle. And that has an effect, right? So, let's talk about statins and what you see in terms of side effects.

Dr. Soffer: Yeah, well, the side effect profile in randomized placebo controlled trials is fantastic, right? The side effect profile that we're seeing in the RCTs that led to the guideline production and all of the best evidence would suggest that statins are not much worse than taking a placebo. Except all of us know from talking to our patients, from talking to our friends and colleagues, from going to cocktail parties and just reading the newspapers that statins are the worst thing that anyone could ever possibly do. Right. That's the impression you get from talking to people.

Host: It's right up there with COVID vaccine.

Dr. Soffer: Right up there with COVID vaccines and there's a major disconnect between the actual outcomes in RCTs and the perception and the observation of our patients. There's a lot of reasons I think that are for that. And it's very complicated, but if you go into the conversation, let's say you're on board with yes, I know that statins reduce cardiovascular event rate. I see a patient here who would benefit from cardiovascular risk reduction. I want to give them everything possible I can, that will reduce their chances because I worry about that patient, but I've heard these things about statins and they worry me.

If you change your own personal mindset and you phrase it as there's a very low risk of side effects, these drugs have been around since 1987. There are seven different ones that the side effect profile is easy, the side effects are reversible with few exceptions that rhabdomyolysis you were talking about. And if you don't feel good on it, you're going to tell me about that at your follow-up visit and we can make adjustments and modifications, and we've got all these different tricks to help you feel better on it.

But I will assure you that I'm not worried about you taking this drug. It's a very safe drug. The only reason we do follow up blood tests is to make sure that we've achieved a good enough result. And that's the main reason for doing it. The other blood tests that we do at that time, are because you're also overweight and your blood sugar is a little high.

So we have to monitor these things and you have fatty liver. So we have to monitor your liver enzymes and your kidney function because you have diabetes. So we're doing these other tests anyhow, and it's going to inform what we do, but they're not really meant to monitor for toxicity. They're there to just to monitor your patient's care and make sure they're getting the care they need for excellent preventive care for a long-term. The rhabdomyolysis to your point is truly a rare event. And it's striking when you see it. I have to admit I've caused it more than once in my career. And you know, it, those give you pause for concern and you just have to really be careful about who you're going to be using high-intensity statin with and make sure that they're the right patient.

And so, you know, I've told you all the reasons why I do use high intensity statin with pretty much everybody. And the few exceptions are the frail, elderly, chronic kidney disease patients. Especially if they're hypothyroid and very sedentary. And polypharmacy will also contribute to risk of rhabdomyolysis and in those patients you know, it does make sense to use lower doses and to be more cautious about how

you prescribe every medicine, not just statins, but every medicine.

Host: I think one of the challenges of primary care is distinguishing sort of the aches and pains that humans normally get in life, that I certainly get from, it's really an issue that needs to be worked up or that in the case of statins, what's real true myalgias. You know, I tell patients that it should be a distinctive feeling, right? It's not just aches and pains. But I'm curious what you tell them.

Dr. Soffer: Well you know your patients are always right. So, no matter what they say, they're always right. And you have to show compassion whenever you're talking to them. And while there's a very strong body of evidence for their safety, and there's a strong body of evidence for the nocebo effect from statins, they're still right when they say this statin is causing me side effects.

And so, anything that you can do to ease them, make them feel comfortable with what you're doing. If it means a one month statin holiday, a rechallenge with the same dose or a lower dose, or a three time a week dosing or twice a week dosing, whatever it takes to help keep them on this very important therapy if they're high risk, I think is worthwhile.

Host: So we only have a few minutes left. There are some areas we want to address that we'll probably have to bring you back, Dan. So you know, for the primary care audience, are there any thoughts that you have to sort of close this out?

Dr. Troutman: Yeah, I think this has been a great conversation and Dr. Soffer has been a great mentor and it's been great to be able to spend time with you in the clinic and also hear you kind of talk through this case in this podcast format.

So I think something that's been really notable for me is seeing kind of how easy it is with the ASCVD risk score to get the data you need to have this result kind of both for us and for patients and something that kind of strikes me in the primary care setting, is this something that we should be discussing just on this patient case where it's a second visit for this opinion, statin or no statin, or is this something that we can kind of tie into other visits for patients who are coming in for kind of non ASCVD risk reduction complaints and kind of the push for if this is the bare minimum we should be doing to best serve our patients, finding ways to ensure that we're kind of bringing this up with as many patients as possible, as frequently as possible?

Host: Yeah, I agree. Dan, what are the things that you want to tell the primary care audience?

Dr. Soffer: Those were great comments, Greg. Thank you.

When I'm in my preventive cardiology office and I'm seeing patients; this is all we talk about and we spend a lot of time and we answer all the questions one by one, and we can really give people the comfort to go ahead with the treatment they need and intensifying their therapy as need.

In my primary care office, I know all of the demands on the time. There's way too much to do in any one office visit but this is such an important part of the care for your adult patients, that every adult patient deserves the opportunity to spend a focused time to talking about their cardiovascular risk, especially their atherosclerotic cardiovascular risk.

And you can feel free to offer statin therapy to anybody who comes in who's an adult and who doesn't have a reason to not take it. But you shouldn't twist their arm if they are at low risk. I like to think of it as

don't, can, should or must. Right. So there are certain people where they absolutely can't take statins and we didn't go through who those are, but it's a short list. The can is everybody. Pretty much everybody can take statins. We prescribe them for kids as young as seven years old, if they have an inherited cholesterol syndrome. The should are the people in the borderline groups where their risk is calculated to be a little bit lower, but they have risk enhancing factors perhaps in you're on the fence yourself about whether they can or should. And, you know, you're thinking about should they be on it?

Well, let's think about all the different things and that's where that calcium score can be extremely helpful or some of the other biomarkers. The must are the people who qualify based upon the guidelines that, you know, the 2018 ACCAHA multi society guidelines and to qualify that's evidence-based. Those are randomized placebo controlled trials and meta-analyses of the same that inform those decisions.

And so if you're withholding statins for people who qualify based upon the guidelines, then you're not practicing evidence-based medicine. Now, it's the starting point of the conversation. A patient may decline. That's fine, but these are people who should be taking and must be taking those drugs. And you can even raise it to another bar if they have other high risk features and you calculate their risk to be very high, or they have established cardiovascular disease, especially poly vascular disease. These are people who need intensification of their therapy beyond just the statin.

Host: Great Dan you know, this has sort of an overview if you will, of this topic. And I think there are going to be additional questions that people are going to have. If anybody has questions, please email me. I'm in the system, kendal.williams@pennmedicine.upenn.edu, and we'll plan to have Dan and Greg back.

And we'll have additional discussion on those questions specifically. So with that, I want to thank Greg and Dan for joining. It was wonderful having you both and to the audience out there, please just join us again for the next Penn Primary Care Podcast.