Dr. Kendal Williams: Welcome, everyone, to the Penn Primary Care podcast. I'm your host, Dr. Kendal Williams.

In this podcast, we seek to bring sort of practical advice to practicing primary providers across the Penn system and in the broader world. This is the second part of a two-part podcast series we're doing on lipid management. In that first podcast, we did, I think, a broad overview with Dr. Dan Soffer of lipid management and some of the major topics. And in this podcast, we wanted to delve into some of the more specific questions that we all face managing patients with lipid disorders and who are at risk for atherosclerotic disease, which is really just basically all of us.

So, I want to welcome back, Dr. Dan Soffer. He's a practicing general internist, is a Penn lifer as we said. He also has extra training in preventive cardiology and lipidology at Penn. He sees patients at both Radnor as well as Perlman in the city in those roles. Thanks, Dan, for coming back..

Dr. Daniel Soffer: Thanks for having me back, Kendal.

Dr. Kendal Williams: So we were not able to be joined by Dr. Greg Troutman, who unfortunately his clinical schedule shifted that he needed to be in the CCU this evening, but someone we had invited on the first podcast and could not make it has now been able to make it, and that's Dr. Doug Jacoby. Dr. Jacoby is the Chief of Cardiology at Pennsylvania Hospital and the Medical Director of the Penn Medicine Center for Preventive Cardiology and Lipid Management. He is also the Director of Clinical Informatics for the Cardiovascular Medicine Service Line and a former colleague of mine at Presbyterian Hospital. Doug, thanks for being here.

Dr. Doug Jacoby: Kendal, thanks so much for having me. I'm looking forward to this.

Dr. Kendal Williams: So it's just me and two lipid experts, two of the best at Penn. So, I did request some folks to send me questions that we could discuss in this and we'll be going through that. But I wanted to start out with a little bit of just a broad overview of where we were last time.

We talked about how atherosclerosis is really a natural process. I think of it as biological corrosion of our pipes and it leads to blockage of vessels and manifests itself as stroke and MI and other things. It's the single leading cause of death in the country, 25% of all deaths. We know that it is mostly, if not entirely, you know, more than 70% to 80% driven by age, smoking, diabetes, hypertension and elevated cholesterol. Together, those risk factors explain, as I said, most of what we see.

Atherosclerosis is a cumulative process that occurs over time. And we want to intervene on that process before it leads to lasting effects. So we talked in the last podcast about how the atherosclerotic disease risk calculator allows us to use risk factors to predict who is vulnerable and needs treatment.

And we also talked about calcium scoring. And Dr. Soffer made the point that we're actually not just talking about that as a risk factor, but we're actually detecting actual atherosclerosis. So, it's really a measure of prevalent disease in the patient. So let's sort of leave my overview comments at that.

But Dan, I wanted to circle back to something that you said at the end of our last podcast, and we're going to get into what I'll just say as don't, can, should, must. But I think for those who listened to the podcast, they were probably struck by how enthusiastic you were for statins, high-dose statins as well.

And I wanted to take a little bit more time and just go through this idea of don't, can't, should, must. So the idea is that there are certain people who should not be treated for whatever reason, but there's this much larger group that can be treated. Was that your point?

Dr. Daniel Soffer: I think that, you know, you made the comment about using the risk calculator to

determine the amount of risk and help determine intensity of therapy. It's really just a starting point for the conversation and that people often will ask me, "Can Mrs. Smith take a statin?" or "Can Mr. Jones be put on a statin?" And I always think that's a funny question because almost everybody can take a statin and that's not really the important clinical question.

The important clinical question is how strong is the evidence for using a statin at this time? Is it something that can wait? Are we treating short-term risk or are we treating long-term risk? But it's hardly ever about can. If it's “can” versus “cannot,” that “cannot” is the same as don't.

And that's such a tiny number of people who cannot take a statin where you should not use a statin. And the only people I consider people who absolutely should not be given a statin are people who have true neuromuscular disease where their neuromuscular specialist has said, "This person should not be taking any potentially neuromuscular toxic therapy." And the rest of us all fit into the box of who can.

The next step is who should take a statin. Well, those are the people who stand the most to gain from short-term treatment. And those are the people with high enough risk where they qualified based upon the national guidelines and where you would use language like it is reasonable to or it makes sense to treat in this case. And then the last group, of course, are the must take a statin where class I slam dunk indications, because they have characteristics that match those that were in the participants in the randomized placebo controlled trials where risk reduction was seen in this short-term trial.

So the can versus cannot, that's an easy distinction. The should versus must, that's where it gets a little more complicated. And that's where diving into the details of the guidelines can be very helpful.

Dr. Kendal Williams: So let's start with those guidelines, ones you directed me to that you felt, Dan, were the most important, were the ACC/AHA guidelines from 2018.

And, you know, I think one of the things I wanted to do in this is to actually go back through that and just be very clear about what the guidelines say, because in this podcast we're giving practical advice, but we should also, as you had pointed out, just have a baseline of who must get it or who should get it.

So, those guidelines say that anybody with prevalent atherosclerotic disease and has manifested, you know, symptoms or signs of that, and they've had enough acute coronary syndrome or stroke, they have signs of peripheral artery disease, those patients must get a statin and a high-intensity statin. Patients who have an LDL greater than 190 as their native cholesterol should be placed on a high intensity statin with the goal to get it down the LDL below a hundred and consider other options if that fails with a high intensity statin to do that. Anybody who is a diabetic and over the age of 40 years old should be placed on a statin and then there does seem to be some distinction between moderate and high intensity.

Let me just stop there for a minute, because I think those are sort of the low hanging fruit in a sense, but let you both comment on those two areas.

Dr. Daniel Soffer: Sure. I'll start and then I'll yield to Doug, but the basic distinction is terminology of secondary prevention and primary prevention and that, for secondary prevention, unless you have a contraindication to taking a statin, all secondary prevention patients should be offered statins if their LDL cholesterol level is greater than 70 milligrams per deciliter. And additional LDL cholesterol-lowering therapy might even be indicated even after they're on a statin in secondary prevention.

In primary prevention, there's different risk categories based upon certain characteristics where the risk for cardiovascular disease is high enough that regardless of what else is going on, they should be

offered statins. And so, you point out the categories, the adults over the age of 20 years old with an LDL cholesterol greater than or equal to 190 milligrams per deciliter, where we think of them as having inherited cholesterol syndrome, that the adult diabetics between the ages of 40 and 75 where their risk for cardiovascular disease is so significant that even if they don't have other classic features for cardiovascular disease, they should be offered statins.

And then the last category are those adults between the ages of 40 and 75 years old, where you would calculate their risk to start a conversation about whether or not statin therapy is indicated. And that's where you get into learning the distinction between who's at low risk, borderline risk, intermediate risk or high risk. And that's where I think people who aren't thinking in these terms all the time start getting bogged down by details. And oftentimes, it leads to no prescription rather than a nuanced prescription.

The last category, which is those people over the age of 75 years old, where it's reasonable to have a conversation about cardiovascular risk, and it's still reasonable to think about how to manage their care, but where the evidence for using statin therapy is less strong. And so that's sort of another category to think about in terms of cardiovascular risk in primary prevention.

Dr. Kendal Williams: So let's now turn to the patients where we're trying to assess risk.

So the guidelines say that if you're between the ages of 40 and 75, and you have a risk that's greater than 7.5% in the next 10 years, then you should be considered for a statin or should be recommended to be on a statin. Is that right?

Dr. Daniel Soffer: Right. That's considered a class I indication for statin therapy, if you're at intermediate risk with ten-year risk of between 7.5% and 20%.

Dr. Kendal Williams: And if you're lower than that, but potentially still at risk, now here's the thing we didn't get to last time. I don't know if we got it clearly, Dan and Doug, is who gets the calcium study, right? So let's say you're 8%, I mean, that patient should be on a statin. It's in the 5% to 7.5% that you're doing calcium studies?

Dr. Doug Jacoby: So the use of calcium studies for coronary artery calcium score is helpful to improve your risk assessment. And if you think about it, primary prevention is all about trying to get the best crystal ball that you can to predict the future. That's the struggle.

So I would order a coronary artery calcium score whenever you're uncertain, whether or not your patients should be treated with LDL-lowering therapy, especially statins. And if you look at the guidelines, they find it most useful in the category of 5% to 7.5% and 7.5% to less than 20%, because in those categories, basically the borderline risk and the intermediate risk, those are the categories where a positive score is reasonably prevalent and would tell you the patient should definitely be treated. But a zero score is also reasonably prevalent, which would reassure you that maybe the patient didn't have to be treated over the next 5% to 10 years. So that's where it's most powerful in essentially moving your prediction modeling.

But on occasion, we use it for people whose score is less than 5%. And on occasion, we use it for people who are over 20%. The calcium score is still valid then. It just tends not to be as helpful.

Dr. Kendal Williams: And Doug, when you get this study back, you're a primary care internist, you order this study, you get it back, it gives you this calcium score, and it also gives you a percentile risk, you know, adjusted for the rest of the population. What do you look at to determine? And what numbers are benchmarks for you?

Dr. Doug Jacoby: Kendal, you need to look at everything. It really fits in the whole context of the patient.

So for starters, a zero score is almost always very reassuring. It means the likelihood the person has a cardiovascular event in the next decade is exquisitely low, but not all zero scores are created equal. So a zero score in a person who has diabetes or is smoking as an example, is not as helpful as a zero score in someone who's not diabetic and not smoking. In other words, you still need to put it in the context of the other risk factors.

On the other hand, a positive score clearly means the person is building up plaque. Once the score is positive, I have to think about the age a little more because a positive score in a very young patient means something very different than a slightly positive score in a much older patient. And that's where knowing their percentile of risk matters. So what I would say is zero scores are always reassuring.

Most of the time, if you have a non-zero score, you should be treating the patient with a statin. And definitely, any time you're over the 75th percentile of risk, you should be treating them with at least a statin.

Dr. Kendal Williams: That's very helpful. I have a question, it's a pathophysiological question. How long does it take an atherosclerotic plaque to calcify such that you would see it on there? I mean, where is that in the process?

Dr. Doug Jacoby: So you're building up plaque basically your entire life, right? By the time you're a teenager, you start getting sort of little bits of non-calcified lipid building up in the vessels. And that's actually why cardiology is so perfect for long-term prevention, right? You have the world's number one killer, where we could probably eliminate 80% of the risk by modifying the risk factors. But calcification does come later on. So I think most relevant from the way I would think about it as a clinician is after four or five years, close to 25% of people that had a zero calcium score will convert to having a positive calcium score. And so if you have a zero score and you're using that as a reason not to treat someone or using it as a reason to treat someone, but not treat them very aggressively, then it's reasonable to do a surveillance repeat of that calcium score after four or five years, because that's the right timeline to think there's a chance the result you'll get has changed.

Dr. Daniel Soffer: I would add that if you want to get a sense of how long it takes for a plaque to calcify, we generally use 40 years old in men and 50 years old in women as the time where close to 75% of the population still has a calcium score of zero, but about 25% of the population is starting to have calcified plaque on average. And so those are the rough ages that we think of using a coronary calcium score as a risk estimating tool.

You can use calcium scoring in younger patients, but you really have to set the table properly and make sure they understand that the reason you're doing it is to find calcified plaque and that a calcium score in a young person who may have very high risk and other indications to treat their risk should not use a calcium score of zero to determine whether or not to treat their risk with statins or other types of therapies.

Dr. Doug Jacoby: Yeah, I completely agree with Dan. And that's why the younger the patient is, the more we ask ourselves, "Do we need imaging that's going to look for non-calcified plaque?" So that could be done in select cases with a cardiac CTA. So we're getting through angiography or, more commonly, it could be done with carotid IMT, which gives you ultrasound technology to look for a plaque and thickness in the carotids.

But the key take home message is a zero calcium score in a very young person is not helpful in reassuring you about their long-term risk.

Dr. Daniel Soffer: It's important to remember also that the calcified bits are not a target of therapy.

And it's something that every clinician who orders coronary calcium has been asked by their patients, "How do I make my calcium score go down? Once it's there, is it stuck there?" And you have to really talk to your patient about what it is that calcium represents. It's an estimate of the burden of atherosclerosis and gives you a sense of the duration and the pace that atherosclerosis is developing. And that in and of itself, the coronary calcium is not what you're targeting. You're targeting atherosclerosis in general.

And the way we do that is all the different therapies that we have to reduce cardiovascular events. And we talked about that before, healthy lifestyle, blood pressure control, LDL cholesterol lowering and anti-platelet therapy.

That's right. The calcium score really represents the tip of the iceberg. So it tells you some things there, but we're really concerned more about decreasing the overall total atherosclerotic burden. And in fact, the non-calcified portions of the plaque are probably even the higher risk portions that gets stabilized with LDL-lowering therapy like statins.

Dr. Kendal Williams: So let's just jump to statins now because this is our primary tool in reducing risk factors other than reducing blood pressure and managing diabetes and getting people off smoking and so forth, but beyond that, it's all about statin therapy.

So statins lower the risk of MI or stroke by, I think I saw 30%. They not only reduce the LDL, so they inhibit the process of continued atherosclerosis. But I was always taught that they also stabilize your existing plaque. So it is less risky to you.

Is that the current understanding of what statins are doing for us?

Dr. Doug Jacoby: I think that is the current understanding, but I want to actually rephrase your opening question where you said it's all about statins and I actually don't think it's all about statins. I think statins might be the foundation of what we're doing here. But by all means, I'd encourage everyone to look beyond statins.

I think it's really about achieving LDL-lowering and clearly getting people on moderate intensity or high intensity statins is step one in the initial goal. But in my mind, more important is actually getting those LDL below the threshold numbers, getting it to very aggressive goals and that's where you continue to get outcome benefit.

So it is perfectly reasonable and appropriate to be adding the non-statin agents onto that regimen. Definitely in secondary prevention for people that have had revascularizations or events, it's extremely frequent to need non-statin agents at this point to get to the optimal amount of risk reduction. And even in primary prevention, when we find high risk people in primary prevention, especially people that have a lot of subclinical atherosclerosis when we get the coronary calcium score. Those patients were frequently using non-statin agents in primary prevention as well at this point.

So I think that message that I would give to people is, yes, please start with statins, please encourage statins, but please don't stop with statins. Really look at what you've achieved in terms of LDL reductions and make sure you've gotten the person as aggressively lowered as appropriate for their level of risk.

Dr. Kendal Williams: And so Doug, let's just review that right now, the goals, your targets. Let's start with secondary prevention. You want to get the LDL less than 70?

Dr. Doug Jacoby: At an absolute minimum. So I would say almost everyone that had cardiovascular events, we should be getting their LDL below 70. The guidelines are written so that there's a threshold of 70 and it's considered optional to add non-statins agents to get below that number. I would say, even though it's optional in the guidelines, you should almost always opt in. You can reduce someone's risk by another 50% when you get them from that 70 cutoff to below 50 and even below 40. So the benefit goes all the way down with a very aggressive LDL lowering.

Dr. Kendal Williams: If patients have a calcium score that is high, let's say 75th percentile or above, then they have atherosclerotic disease, right? So you don't have to wait for an event to define them as sort of a secondary prevention event. What is your target in those patients?

Dr. Doug Jacoby: That target depends on their comorbidities and their age. I'm going to be much more aggressive with a 42-year-old that has a very high calcium score than someone who's in their 70s and happened to have a higher calcium score. But as a ballpark generalization, I would treat that as secondary prevention. I agree with your point. So I am very frequently adding non-statin agents in this sort of subclinical atherosclerosis category to get LDLs definitely below 70, preferably below 55 and getting to even lower than that.

If you look at the subclinical data, when you get LDLs below 50, the majority of patients actually gently regress atherosclerosis. So I would say that if you've diagnosed subclinical disease, most patients would rather have their plaque stabilized and possibly regress as opposed to progress. And if you leave their LDLs above 70, most people gently progress over time.

So I think when you have discussions with patients and you explain when they talk about the calcium score and they say, "I don't want it to get worse," the answer is, "If you don't want the amount of plaque burden you have to get worse, you should be trying to get your LDL below 50."

Dr. Daniel Soffer: I want to add a practical point here, which is somewhat based upon the semantics of what we're discussing. So instead of thinking about this in terms of targeting an LDL cholesterol, the language that the guideline authors felt was most appropriate, I really actually think is really elegant and useful in the clinic, that our goal is to prevent cardiovascular events and reduce atherosclerosis burden.

We target LDL cholesterol and non-HDL cholesterol with our therapies. And our threshold for introducing therapy is based upon the absolute LDL cholesterol. So in our secondary prevention patients, our threshold for adding more to the statins is an LDL cholesterol greater than 70 milligrams per deciliter.

Now, there's some real life constraints to what will happen. So if your LDL cholesterol is 71 and you add ezetimibe to the statin, you'll get about an 18% LDL cholesterol reduction. And you may lower your LDL cholesterol to a point where even if you wanted it to be 30 based upon what Doug just told us, we may not have another reasonable option to get us there. So we may think it's interesting and useful to target an LDL cholesterol of 30, but oftentimes in the clinic that's just not possible. And so using the nomenclature of the guideline, we have a threshold for adding additional therapy.

And in this case for secondary prevention, you're talking about a threshold of an LDL cholesterol greater than 70 milligrams per deciliter to either intensify your statin or add a non-statin to what you're doing along with the lifestyle modifications that you're counseling patients on at every visit.

Dr. Doug Jacoby: And I think to go back to Kendal's point that I'm very comfortable considering patients that have significant sub-clinical atherosclerosis to that same threshold for adding therapy of 70, that you're talking about, Dan.

So someone that has a high calcium score or even a low calcium score, but at a very young age, that triggers the same thought process in my mind, as someone who's had a prior event.

Dr. Daniel Soffer: And, you know, the National Lipid Association's statement on coronary calcium scoring actually has specific calcium scores that equate to the same cardiovascular risk as a point of comparison. I think we talked about this in the last podcast that calcium score greater than or equal to 100 at any age should equate to a good rationale to initiate statin therapy at any age, and that calcium scores greater than 300 and especially greater than a thousand equate to very high levels of risk to a point where you should be intensifying therapy and not settling even for greater than 50% LDL cholesterol reduction, but using that 70 milligram per deciliter threshold as a rationale to intensify your regimen.

Dr. Doug Jacoby: I know we're keeping to the ACC and AHA guidelines, which is really the right set of guidelines for our country, but just to call it out, there are European guidelines and other guidelines out there that still have the semantic of goals and they have extreme risk categories. And those extreme risk categories have LDL goals of less than 40. Just making the point that we do know LDLs all the way down to 30 are in fact better. And so it's a reasonable to keep in the back of your mind attempts to achieve that in your highest risk patients.

Dr. Daniel Soffer: Kendal, just so you know that Doug and I are like an old married couple that keep having the same discussion over and over again. And that, you know, he's very comfortable with goal LDL cholesterols, and I keep going back to using the terminology of thresholds because I think it's the most practical way to deal with patients in the clinic. And so I'm willing to keep having that with my daytime wife, Doug, and make sure that we all keep using the right nomenclature.

Dr. Kendal Williams: Well, I think, you know, the thing that we have to do as primary care physicians is convince our patients of the same things that you guys are convinced of. So I'm going to be a little bit of a devil's advocate for a moment. And I'm doing this as a foil. I very strongly believe in statins and aggressive statin therapy. But is there a risk? Is there a danger outside of cardiovascular issues of lowering your LDL too much? There are concerns about cognitive issues, for instance. Is there anything to that?

Dr. Daniel Soffer: No. I don't think so. I think there's pause for concern for hemorrhagic stroke. I think that has been the only sort of consistent even very low risk event that can occur at very low levels of LDL cholesterol. The physiology is not well understood for that. And the prevalence of that kind of event is so low and in such a low risk, but it's higher than the baseline risk for hemorrhagic stroke.

In terms of LDL cholesterol-lowering, while there are case reports and individual anecdotes of neurocognitive effects from LDL cholesterol-lowering, that side effect is not seen in any randomized placebo controlled trial. It didn't even show up in meta-analyses. And when specifically evaluated in a subpopulation from the Fourier study with evolocumab in patients with stable cardiovascular disease, where they looked at nearly 2000 patients achieving LDL cholesterol levels in the 20s and 30s with their PCSK9 monoclonal antibody versus controls, there was no difference in neurocognitive testing and that body of evidence is very strong.

The FDA thought there was enough anecdotal reporting and post-marketing surveillance from statin therapy that it warranted mentioning a possibility for neurocognitive effects. But it really amounts to idiosyncratic reactions and in a population that's highly prone to neurocognitive changes, people with cardiovascular disease and an older population. But I don't have any significant concerns about

neurocognitive effects from LDL cholesterol-lowering.

I want to point out that apo B, which is the main structural protein found in LDL, is not found in the central nervous system. LDL particles do not deliver cholesterol or any other product to the central nervous system. They don't get into the CNS. And so the brain can make its own cholesterol and it does, but is it possible that statins have some impact on brain function that goes beyond LDL cholesterol-lowering? That is possible, but it's not from LDL cholesterol-lowering.

Dr. Doug Jacoby: So I completely agree with what Dan just said. And I just want to answer it in a slightly different way, which is when I think about medications, I always ask myself, is there a safety concern here? Is there a risk? And as it relates to statins and neurocognitive issues, there is not a safety concern here. There's not a risk and patients are orders of magnitude safer on it than not on it, including protecting their brain from vascular dementia and from stroke and other areas. So from a safety perspective, patients that are worried about their brain should go on statins.

Now, that's different in my mind for me possible non-dangerous side effect. Are there patients that might feel as though their cognition isn't as sharp on a statin? Yes. I actually do believe that a plausible rare side effect that we don't understand, but it can happen. And if it does happen, when you stop the statin, that goes away the same way other statin side effects like myalgias go away. So no one should avoid trying a statin for fear of having a rare non-dangerous reversible side effect. If they want to protect themselves, they should take a statin. In the unlikely event they have a side effect, they can stop it. They'll go back to themselves and we'll try a different course of action to lower their risk.

Dr. Kendal Williams: So in the last podcast, Dan told us he starts everybody with high dose statins and uses. Crestor (rosuvastatin) is the primary agent and starts at a high dose.

So I want to ask you two questions. The first is that your practice as well? And two, are there any safety concerns about statin that you have outside of neurocognitive issues?

Dr. Doug Jacoby: So I almost exclusively start with the high potency statins, which are atorvastatin and rosuvastatin.

I typically start them at their lower doses and tell the patients straight up my plan is to increase gradually and uptitrate over time. I think they're safe enough that I've no objection to the strategy of just starting at a higher dose, but stylistically, I find my patients prefer starting low and going slow. Either way, I think we all agree you start a high potency and with the goal of ramping up.

But I will tell you, low dose rosuvastatin and even 5 milligrams statistically drops LDLs close to 40%. So you get an awful lot of risk reduction, even with that starting point.

In terms of, do I have any safety concerns? I don't have any safety concerns barring the couple exceptions of rare conditions. So when people have underlying muscle conditions, I will sometimes avoid statins. But once again, that's a rare population with pre-existing diagnoses there. And of course, barring women that are pregnant, pretty much almost everyone is safer on a statin than not on a statin.

The only time I've ever seen anyone have any semblance of harm on a statin within 15 years specializing adjusting cholesterol management has been when I thought people misused and missed a warning signs on statins. And in particular, those would be people that were on statins, had another drug started such as an antibiotic that interacted with statin, and had evidence of sort of myositis and rhabdo and muscle aches and were told by their doctors to keep taking it for weeks until it eventually caught up to them.

But as long as people are aware of drug interactions and if they have severe muscle aches start, they hold their statin, I've never seen any evidence of harm and would strongly encourage people once again that they're just safer on statin therapy.

Dr. Kendal Williams: So let's talk about the non-statin agents to get to some of those aggressive goals. There's that idea, which, you know, all of us could potentially prescribe. I think PCSK9 inhibitors are not something that most primary care physicians are comfortable with, but let's just talk about them and some of the pragmatic aspects of prescribing them and what you're trying to achieve.

Doug, maybe I'll start with you.

Dr. Doug Jacoby: So Kendal, my biggest message for everyone is that the non-statin agents, ezetimibe and the PCSK9 inhibitors are safe. They have proven benefit. And I think they're way underutilized in lowering people's risk. Acetamide decreases LDLs by 15 to 20% and has zero safety concerns. The two PCSK9 inhibitors out there, alirocumab and evolocumab decrease LDL levels by more than 50% also have no safety concerns and are extremely well tolerated.

So from my perspective, the algorithm goes, figure out what your threshold to add medication is. And then if you're going to add medication, it's reasonable to start with ezetimibe, because that is cheaper and more available.

And if you still don't get your LDL low enough, then it is reasonable to think about adding a PCSK9 inhibitor in people that either have FH, familial hypercholesterolemia, or have atherosclerotic disease. And in those categories, I think PCSK9 inhibitors are safe enough that primary care physicians could order them.

But I agree it is somewhat of a specialty medicine. So it is also reasonable to refer patients like that to sort of preventive cardiology and lipidologists to really assist in finessing the regimen and getting these expensive medications approved.

Dr. Kendal Williams: Dan, is there anything you'd like to add to that?

Dr. Daniel Soffer: Well, that was brilliant. I think you summed it up really nicely, Doug.

A reminder that the rationale for having statins as the foundation is based upon LDL cholesterol-lowering in large meta-analyses documenting all the benefits in the RCTs for the benefits of statins. And ezetimibe and PCSK9 inhibitors are now in that same body of work with evidence of risk reduction and should be thought of along the same lines.

And the main reason that should keep you from prescribing a PCSK9 monoclonal antibody right now is really the cost to the patient. And Penn Pharmacy has a fantastic program that really enables all of the doctors within the health system to be able to put in prescriptions for where they see fit at any of the Penn pharmacies and the Penn pharmacists will help them get their medicine if they qualify and if they need it.

And so it's a lot easier for us to use those medicines now that we have the assistance of the pharmacist and in the process.

Dr. Kendal Williams: So let's use the last minute here to just highlight the preventive cardiology work you all do and how people might get patients to you. I know, Dan, you're at Radnor, you're down at Perelman. Doug, you're also I think at Pennsylvania Hospital now, but maybe you could just tell us where the sites are. And there's not just the two of you, right?

Dr. Daniel Soffer: That's correct. We're part of a team of several physicians, nurse practitioners, nurses, a dietician, pharmacists and really a whole program designed to assess, evaluate and lower people's future cardiovascular risk.

We have sites at Radnor, at PCAM, at Pennsylvania Hospital and also at the VA.

And we're really happy to see patients anytime we can be of service. It can be patients with lipid disorders, but it can also be patients where people want help assessing their risk or where people know the risk is high, but want help optimizing that risk and lowering it aggressively.

So we're happy to get involved in any of those areas.

Dr. Kendal Williams: Well, thank you both for coming on the podcast. It's really excellent. I actually think there's some more stuff that we could get through. And I'll leave it that if folks do have questions for a future podcast, we can certainly bring Dr. Soffer and Dr. Jacoby back to talk a little bit more with us. So please email me if you have additional questions.

So thank you so much for joining the Penn Primary Care podcast. We look forward to seeing you at the next program. Take care.

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