Paul: A priest, a minister, and a rabbit walk into deliver blood. The priest says I'm a type A, the minister says I'm a type B, the rabbit says I think I'm a typo.

[laughter]

Matt: All right, Paul, this is all. Okay.

Paul: It says typo. And then, also it's not a rabbit. Yeah.

Matt: I like it.

[Disclaimer]

[Curbsiders theme music]

Matt: Welcome back to the Curbsiders. I'm, Dr. Matthew Frank Watto, here with my great friend, Dr. Paul Nelson Williams. Paul, how you doing today?

Paul: I just told a pun, Matt, I don't feel good. I feel kind of sick actually.

Matt: Yeah, this is weird. Is this *The Twilight Zone*?

Paul: Yeah. This might be a *Jacob's Ladder Scenario*.

[laughter]

Matt: On today's episode, we are going to discuss antiplatelet, anticoagulation, really secondary and primary prevention of cardiovascular disease or Primary-and-a-Half Prevention as we'll get to our guest Dr. Don Lloyd-Jones, who I'll tell you more about in a minute. But Paul, first, would you tell people what is it that we do on the show? And maybe throw in "Where are we as we're doing this?"

Paul: Oh, sure. That's a good idea, Matt. So, we are *the* Internal Medicine Podcast. We use expert interviews to bring you clinical paroles and practice-changing knowledge. This time, we got our expert at ACP. We are at ACPs Annual National Conference. In any case-- [crosstalk]

Matt: Internal Medicine Meeting 2025.

Paul: Hashtag. We are in San Diego, which is how we managed to corral Dr. Lloyd-Jones in to talk to us. I'm sure he'd have been happy to in any circumstance, but we're grateful to have the chance of this meeting to do so. So, before I ramble on too much further, Matt, why don't I let you tell us about our guest a little bit about what we talked about?

Matt: Sure. So, our guest is Dr. Don Lloyd-Jones. He attended Swarthmore College for

his BA majoring in history, Columbia University College of Physicians and Surgeons for his MD, Harvard School of Public Health for a Masters of Science of Epidemiology. He was a chief resident and cardiology fellow at Massachusetts General Hospital and junior faculty at Harvard Medical School. In 2004, he moved to Northwestern, and in 2009, he became the chair of the Department of Preventive Medicine. From 2012 to 2020, he was a Senior Associate Dean for Clinical and Translational Research and the director of the NUCATS Institute in 2021 to 2022. He served as the president of the American Heart Association and absolutely just a great guy, really enjoyed speaking with him. So, without further ado actually, with one further ado, Paul.

Paul: [laughs] Just the one.

Matt: A reminder that this episode and most episodes are available for CME for all health professionals through VCU Health at *curbsiders.vcuhealth.org*. And please check the show notes for any disclosures because I don't have them in front of me right now.

Well, Don, we've been chatting for a while. We're going to bring the audience in with us on this, and thank you so much for joining us. First question we want to hear from you is tell us a hobby or interest that you have outside of medicine.

Don: Thank you so much. It's great to be here with you. Important topic today, talking about antiplatelet and antithrombotic therapies.

Matt: Yes.

Don: But for me, even more important is I am a huge national park enthusiast, and the more I can hike or just be in national parks, the happier I am.

Matt: Oh, fantastic.

Paul: So, tell me your favorite, because this has been something on my list of things to do. Like, I just saw the Grand Canyon for the first time in the past three years.

Don: Shame on you.

Paul: Listen, I know, but now that I have, like, doctor money, I'm able to do so. I guess now that I'm flush with money and rich, where should I visit the country? What were your favorite?

Don: You're not just a poor country doctor.

Paul: Yes, yes, right. Okay. Still simple, but now I'm very, very wealthy, obviously, from the podcast.

Don: [laughs] What recommendations?

Paul: Yeah, your top one or top three, even.

Don: Yosemite, of course, right. You just can't get away from it. My family has a long history there. My dad actually worked in Yosemite for two summers during college and he was the guy who made the Firefall. I don't know if you know about the Firefall.

Matt: No.

Don: But it was a legendary thing back in the 50s and 60s in Yosemite, and they would push embers over the cliff, and they would reignite as they fell. And it was this beautiful thing. But of course--[crosstalk]

Matt: I am googling that later.

Paul: [laughs]

Don: Not necessarily safe.

Matt: Yeah, right.

Don: And so they don't do that anymore. So anyway, he made sure we went there about every three to five years and I've just continued that tradition with our family. And it can't get enough of it.

Paul: Excellent.

Matt: That's an excellent recommendation.

Don: So many good hikes there and so many good things to see.

Matt: How many run-ins have you had with bears in your national park enthusiasm. That's one of the things that I worry about.

Don: Mm-hmm. So, certainly have run into bears. I'm 6.8, I can make myself big, and the bears have not bothered me.

Matt: Okay, that's good.

Don: And it's interesting we were in Alaska in some national parks last summer, and they spent a lot of time warning you about the bears. But the truth is, when it comes down to it, they say if it's a bear, get big, make noise, and they'll go away. It's the moose you have to be afraid of.

Matt: Oh, yeah, I heard that.

Don: Bear? Hold your ground and you get big. Moose run like hell, apparently because

the moose is actually more dangerous. Who knew?

Matt: Wow. Yeah.

Paul: I feel like I saw a video of someone who covered themselves in moose urine to go hunting or something and then just got stampeded repeatedly. It was hard to watch, but also great at the same time.

Matt: I think that bear spray is just pepper spray, and I think that would probably work on a moose too right in just blinding them? Yeah.

Don: I assume so?

Paul: Medical advice.

Matt: Medical advice. [Paul laughs]

Don: Narrow therapeutic window, apparently, on moose urine.

Matt: Yeah.

Paul: Evidently, yes. I intend to not find out.

Don: [laughs]

Matt: All right, Paul, before we get to a case, anything you wanted to ask?

Paul: Let's ask any meaningful advice or feedback that you received either during your career or training or that you like to give?

Don: Yeah, maybe the best advice I ever got, because busy clinician, I do some research, I do some teaching, things like that. Somebody took me aside and said, "If you really want to do something and they've asked you to do it, but it's just not the wrong time, say no and, which is to say, say no now and you know what things will be better in a year, please, please recontact me, because I would love to consider this again," and it's never failed. If it was something I really wanted to do, they called back, and oftentimes that year later was better, and sometimes it wasn't, and I said it again, but it really works. So, that's a good way to say no but still, get to do things that you really enjoy doing.

Matt: Yeah. Well, thank you so much for saying yes to this, because I'm excited.

Paul: I don’t want to say why?

Don: Why, I was tempted? [Paul laughs]

Matt: I'm very, very excited to talk to you about this topic, which it's a vexing topic, Paul, you agree? Like, in primary care, we see a lot of people coming in and out of the hospital, in and out of cardiac events, and knowing what to continue, what not to continue. So, hopefully, we can shed some light on that today.

Paul: This is one of the topics in the resident clinic where resident will ask, "Well, how long should we do this for?" And I'll be like, "This is one of those things you should look up and get back to me." I mean, "I know, but I just want to find out if you know?"

[laughter]

Paul: And then I frankly look it up in the background. Yeah, it's a scary topic, so I'm glad to have your expertise.

Matt: Yeah. I hope it's okay to say, you said your wife is a primary care doctor, so she keeps you honest about this stuff around the house. So, I feel like you'll probably be exceptionally good at explaining this to us right because you're used to these conversations.

Don: I'm very used to these conversations. She asks me so many good questions and I do the same thing. "Love, you know what, sweetie? I got to go do this thing, but I'll be right back." And no, she's an amazing doc and definitely keeps me honest. And as we like to say, she is underwhelmed and unimpressed by my credentials.

Matt: Oh, there you go.

Don: So definitely keeps me on the straight and narrow.

Matt: All right, well, Paul, let's give him a case from Kashlak to start us off.

Paul: Jack is an 84-year-old gentleman with a history of CAD, type 2 diabetes, atrial fibrillation, currently on apixaban, hypertension, CKD 3, DJD of the knees and hips, uses a walker, who has been admitted for an NSTEMI. He had a drug-eluting stent placed in the mid LAD, his LV function is preserved, certainly he needs some sort of antiplatelet therapy, maybe even dual antiplatelet therapy. But he's already on the apixaban and already we're stymied and terrified that we're going to cause some sort of terrifying bleed, but we also don't want them to have instant thrombosis. We need your help to tell us what to do with all these medications. I think even before we get into how you might approach this patient, if you could just even define it for us. We're going to use the terms double and triple therapy a lot here and since there're lots of medications at play, I would love to hear exactly what your definitions are, just so that we're all on the same page to start.

Don: Sure, yeah, we do talk about triple therapy, double therapy, and monotherapy, and that's really the step down we're going to talk about for this particular patient, because, as you said, he has atrial fibrillation, he's on direct oral anticoagulant medication. Now,

he's come in and required a stent for an acute coronary syndrome event. He requires dual antiplatelet therapy for at least a little while to make sure that we get that stent off to a good start, we don't want the risk of stent thrombosis. And acute stent thrombosis in the near term after stent deployment will not be adequately treated by the direct oral anticoagulant alone. You want to keep going on that or what else would you like to talk about? I'm sorry, so triple therapy--[crosstalk]

Matt: Yeah. So dual antiplatelet therapy or DAPT as a lot of people abbreviated notes, that's, like, two antiplatelets, so aspirin, clopidogrel.

Don: Correct.

Matt: But this dual therapy versus triple therapy that Paul's talking about. What's triple therapy?

Don: Yeah. Thank you for getting me back on track. You, just like my wife.

[laughter]

Don: So, triple therapy is an oral anticoagulant, so that's antithrombotic and dual antiplatelet therapy, aspirin plus P2Y12 inhibitor like clopidogrel, ticagrelor, prasugrel. So that's triple therapy. The step down comes to double therapy. And this may actually throw people a little bit. That is the oral anticoagulant for the AFib and P2Y12 inhibitor. So, we drop aspirin first-

Matt: Right.

Don: -in these cases. A little bit unexpected maybe for some people because of some more recent data. Monotherapy in the long run for this patient is just going to be the oral anticoagulant. The apixaban or the rivaroxaban without aspirin or the P2Y12 inhibitor because once we're certainly 12 months beyond his acute event, the oral anticoagulant alone is enough to protect that stent. So, this patient will never be without something. But because of the AFib, the oral anticoagulant can serve as monotherapy for all of their conditions in the long run.

Matt: So, the idea is as you get far enough out from this-- this is a coronary event we presented, the patient had an NSTEMI. So, we're going to have him on a P2Y12 and an oral anticoagulant for some duration of time, maybe a year or so. And then at some point, we might say, "Okay, now this thing's re-epithelialized. Is that what you're thinking?

Don: Basically right, re-endothelialized, exactly, yeah, yeah.

Matt: Endothelialized? Sorry.

Don: So, let me play it out for you. For this patient, the sort of default approach would

be in the hospital triple therapy. He gets his oral anticoagulant for that chronic atrial fibrillation. We put the stent in and immediately he's on aspirin and the P2Y12 inhibitor. The default will be we're going to keep him on all three of those for a month.

Matt: Okay.

Don: Then stop the aspirin, keep him on the oral anticoagulant and the P2Y12 inhibitor because it's an acute coronary syndrome, probably out to 6 months, but as much as 12.

Matt: Yeah.

Don: And then after 12 months, just the oral anticoagulant.

Matt: Okay.

Don: So, that's the default. Now within that we like to think about. "Well, okay." Some of our patients are at higher ischemic risk that they could have a recurrent ischemic event. So, if that's the case, we're actually going to keep that dual antiplatelet therapy for the month and then could go out as long as three months for that patient just to make sure that a stent placed in an active lesion, we've got that really well re-endothelialized.

Matt: Right.

Don: And then the dual therapy up to 12 months and then monotherapy after 12.

Matt: Yeah. And so, this has to be a patient that the bleeding risk is acceptable and they have a really high risk of ischemia?

Don: Correct. Yes.

Matt: Okay.

Don: But if this was a stable lesion, I'm not so worried. They don't have a lot of other plaque, but I'm more worried about the bleeding risk. And we can talk about how to quantify that bleeding risk, but if I'm more worried about the bleeding risk, I'm going to get them off the aspirin within a week. So, dual therapy then only to three months and then switch over to monotherapy as soon as we can.

Matt: Oh wow. Okay.

Don: Yeah.

Paul: Yeah. I would like to hear about this calculus because I'm looking at Jack as a reminder, who looks like an extraordinarily high risk of ischemic stuff like he's a patient with diabetes, he has known CAD, and then this new recent event, the atrial fibrillation, but also designed by the cruel Matt Watto as someone who is likely to have some sort

of not likely, but could potentially have a bad outcome. He's old, has potential for falls, he has CKD 3. So, all these things increase the risk for, like, GI bleeding or intracranial bleeding. So, how are you sizing this patient up in terms of-- because it sounds like it's just a matter of sort of moving the various styles in terms of duration-

Don: That's, right.

Paul: -more than what you're using. So, I'd love to know how you think about this and actually quantify these kinds of risks.

Don: Yeah. We're committed to some triple therapy because he's got the fresh stent and the atrial fibrillation. We're going to get the aspirin off more quickly if we think he's high bleeding risk and then just be on the dual therapy of the oral anticoagulant P2Y12 and get to monotherapy more quickly if we're worried about the bleed risk. How do we quantify that bleed risk?

Just as we have the CHA2DS2-VASc score for thinking about who we want to treat for anticoagulation, for stroke, prophylaxis. We have the HAS-BLED score, another 9-point score, pretty easy to remember. H is hypertension, a is abnormal kidney or liver function. Get one point for each of those.

Matt: Okay.

Don: S, is for a history of stroke, so that's the HAS, B is history of bleeding. L is labile INRs if they've been on Coumadin previously, E is elderly, more than 65 and D is drug or alcohol use that would affect either because of drug interaction or alcohol use that could affect their liver function.

Matt: Okay.

Don: So, HAS-BLED 9-point score.

Matt: Yeah.

Don: If it's three or more, and I want to say this carefully, that is not a contraindication to anticoagulation. What it means is we should fix what we can fix about their bleeding risk and then monitor them much more carefully.

Matt: Okay.

Don: But it's not a contraindication to that oral anticoagulant for their AFib.

Matt: Yeah.

Don: And I think, I get it. We always worry, "This guy could really bleed?" But he could also have that massive AFib-related embolic stroke and live.

Matt: Yeah.

Don: And he will not, thank you.

Matt: Yes. So, this patient has definitely age, high blood pressure, and CKD-

Don: He's got a score of 3, exactly.

Matt: -3. And we didn't-

Don: Yeah, so hypertension.

Matt: - give any substance use. So, I think we're at 3 for this.

Don: I think he's appropriately on the oral anticoagulant, but we might want to think about a PPI. We might want to make sure that his environment is safe and he's not at risk for mechanical falls. Do everything we can to avoid those things and then keep him on the oral anticoagulant as long as is reasonable if he's continuing to be walkie talkie.

Matt: It sounds like you're probably going to be working with a cardiologist to do this calculus. I'm not sure if you think that's the best route or if primary care doctors should feel comfortable pulling the trigger. I mean, certainly, if it's like a year out and they're further out, but in that first 12 months, it sounds like that's the higher risk time where maybe you want some more input.

Don: I think that's right. I think it's really important to talk to the person who does the revascularization and say, "Okay, this lesion, was this a really high-risk lesion where we're going to want to treat that longer and make sure that stent really gets off to a good start." Or it's a pretty routine lesion and we don't have to worry about continuing all of this as long. And then bring your knowledge of the bleeding risk to this. But I would definitely talk to the person who did the revascularization say, "Do you feel like this is high ischemia risk in the next 12 months or routine low." In which case, you might get them off earlier. Yeah.

Matt: So, yeah. The ischemia risk would depend on the anatomy. What was that hardware put in, if that's the right terminology?

Don: The acuity of the presentation. If it was a stable chronic angina and the stent was put in for that's a different scenario. Don't need to treat as long as if it was an acute coronary syndrome-driven revascularization.

Matt: I have questions about with the newer, more potent P2Y12s, the ticagrelor, the prasugrel versus clopidogrel.

Don: Yeah.

Matt: How do you think about those in your head? I don't see as much prasugrel, Paul, I know we were talking about that. I saw some scary, like older age and some scarier things with that. It seems like maybe that's not used as much, but how should we think of those? How should we differentiate as primary care docs?

Don: Yeah, I think from the primary care perspective, the reason why we like ticagrelor in particular, but sometimes prasugrel is faster onset of action. So that's what we like to use in the acute setting fresh stent going in or in because we're just going to get more efficacy more quickly. The studies over the intermediate term do show that compared with clopidogrel, ticagrelor, and prasugrel, both associated with marginally lower recurrent ischemic events.

Prasugrel, a little bit more bleeding, ticagrelor a little bit less bleeding than clopidogrel. I think that's why you're not seeing as much prasugrel in part. But the truth is, once you're really out from the acute event three months or longer if the patient has that funny side effect to ticagrelor, I don't know if you've seen this, but some patients have this funny dyspnea reaction.

Matt: Yeah, I was reading about that, and also bradyarrhythmias reported too?

Don: Can be. That's right.

Paul: There was just a Tony Breu tweetorial, by the way, on ticagrelor and dyspnea.

Don: Yeah.

Matt: Interesting.

Don: Yeah, and so think of it as a possibility.

Matt: Yeah.

Don: But if they're having that or if there are cost issues, very reasonable to switch them over, even at a month, but certainly by three months to clopidogrel for their chronic therapy. That will be their P2Y12. And you can't just switch day to day. You do have to do a 300-mg load 12 hours after their ticagrelor dose and then just go once a day on the clopidogrel-

Matt: Oh, wow.

Don: 75 mg.

Matt: I feel like a lot of people would not think to do that.

Don: Yeah. But you do have to do a load.

Matt: That's scary. Paul.

[laughter]

Matt: Usually if I've ever done clopidogrel loading, it's usually been in the hospital.

Don: Yeah, most of the time of course you would get away with it, but you don't want to be the time that doesn't get away with it.

Matt: Yeah.

Paul: I like this early on. This is, again, something else where I'd be talking to a cardiologist, like, hey, I'm thinking about doing this thing, is there anything, because I'm also just a nervous person in general, and we're just like everyone's blessing for everything? So, I think that's something I'd probably checking about.

Matt: Yeah.

Don: Not wrong.

Matt: The other thing about this that's been just around and we can throw this question out if it's a bad one, but clopidogrel, there's genetic variability that affects how active it is for a given patient and then there're some drug interactions with omeprazole and things like that. What do you make of that? Do you think that is that important for us to consider?

Don: I think there was some enthusiasm for doing platelet function studies or genetic testing early on when these were identified. At least in our practice, we don't routinely look for that. We will still use clopidogrel. If a patient has a recurrent event, a stent thrombosis that was unanticipated or unexpected, then we'll make sure that whatever we put them on next, which won't be clopidogrel-

Matt: Yes.

Don: -is actually limiting their platelets or we'll do the genetic testing to understand what to do going forward.

Matt: Okay.

Don: But we're not doing that routinely on the front end unless there's a recurrent event that is unexpected.

Matt: Yeah. Because I've started to see some people test this, I guess at some time, some way you're testing P2Y12 activity. Is that sort of the idea?

Don: Right. Exactly. Essentially that's right.

Matt: Yeah. So, stay tuned for that audience. It's not super mainstream yet or maybe we don't know exactly how to interpret the testing and that timing and all that, imagine that has to be sorted out a bit.

Don: I think that's right.

Matt: Okay.

Don: It's available, but I don't think we should be making routine clinical decisions on it or measuring it routinely.

Matt: And I like that you mentioned the cost with the ticagrelor, because I have had that come up for a couple of patients and it was a couple of months. The first refill they got through, usually the hospitals discharge them with 30 to 90 days and so that maybe even the social worker helped get it covered. But then when it's time for that refill, it's been a problem-

Don: Yeah, it can be a shock.

Matt: -and knowing you might be able to switch them over at that time, that's good to know.

Don: Yeah. Quite reasonable.

Matt: Yeah. All right, Paul, let's move on with the case here.

Paul: Before we do, you had brought up PPI, which I think is a great question to ask. I mean, when would you consider that? Is that an automatic with triple therapy specifically, or when do you pull the trigger on prescribing a PPI if they're not already one, which seems like a miracle at this point?

Don: [laughs] Certainly low threshold for anybody with bleeding history, mono, dual or triple therapy. I think it reasonable to consider this for sure if they've got a GI bleeding history.

Matt: Okay.

Don: I guess I would say in the absence of a GI bleeding history, the short-term risk is pretty low, especially if you're going to get them off the aspirin. Because sure, P2Y12 blocks platelet activity, oral anticoagulants block thrombotic cascade. But aspirin is the problem because it actually directly irritates the stomach lining also in addition to blocking platelet activity. Now that we're sort of de-escalating the aspirin first, I worry a little bit less about it, I have to say, at least in terms of GI bleeding.

Matt: Oh, okay.

Don: Right.

Matt: Okay.

Don: And so, we're thinking about for sure, especially if there's a bleeding history, but if we're going to get the aspirin off soon, I'm a little bit less worried about that.

Paul: Fair.

Matt: So, Jack, this first patient here, so this was just to remind the audience we're going to close this case out. So, he had AFib, he was already on apixaban, then he had the NSTEMI. So, we briefly had him on triple therapy. Let's say it was the first month because we thought his bleeding risk was acceptable. And then we had him on a P2Y12 clopidogrel plus apixaban.

Don: Six or 12 months depending on how things are going on, but beyond 12 months, just the oral anticoagulant.

Matt: Just the oral anticoagulant. Okay. Now let's switch it up a little bit Paul, you want to throw a curveball here?

Paul: Sure, yeah. I'm not sure how much of a curveball it will be, but yeah, so we're going to change the case a little bit and have someone who develops the need for anticoagulation who already has CAD. So, it's still our friend Jack, but in this case, he has our chronic stable CAD. He's on aspirin for moderate coronary atherosclerosis, seen on CT imaging, good that everyone has because they walk through the door, type 2 diabetes, high blood pressure, CKD, DJD of the knees, and hips. He uses a walker. He's admitted with new atrial fibrillation. We calculate his CHA2DS2-VASc score and it comes to 4 and we decide to start apixaban to prevent stroke. So again, a little bit sort of maybe less urgency to it though I guess there're arguments made that we probably wait too long to start patients on DOACs in any case. But that's a talk for a different day. Our first question for you is, should we be continuing aspirin for our friend Jack that we've now started apixaban on for this new atrial fibrillation?

Don: Yeah, great question. Forgetting the atrial fibrillation for a moment, he has an indication for essentially lifelong aspirin therapy. You'll start to see maybe that turned into lifelong P2Y12 therapy as we gather more evidence perhaps. But let's say he's going to be on antiplatelet for that CAD for life unless something else intervenes. So, now he's got atrial fibrillation. He's still got that HAS-BLED score of 3. So, we're a little bit worried about him. But we're even more worried because of the CHA2DS2-VASc of 4. He is above that net benefit threshold. He should be on an oral anticoagulant. 2 or higher in men, 3 or higher in women on the CHA2DS2-VASc clear indication for an oral anticoagulant. So, he fits that.

And so, I would get that started as soon as possible. Probably acutely in the hospital, he's on heparin, but get him switched over to the oral and he gets discharged. There's no clear guidance on this, but what I would do is I would keep him on both for about a month and if things are going well with the oral anticoagulant, I would stop his aspirin at that point because again, we don't need both. The oral anticoagulant will take care of his CAD in addition to his atrial fibrillation.

Matt: Is the overlap just in case he doesn't fill the new med like the new oral anticoagulant or he doesn't like it and decides to stop taking,-

Don: Yes.

Matt: -now he's on nothing.

Don: Or he has some hematuria-

Matt: Okay.

Don: -let's say and we're going to have to now figure that out and it's going to be a negotiation with us and the urologist about while are we going to keep him on aspirin, we're going to keep him on this other thing, probably going to stop the DOACs at that point, honestly, and try to keep him on a little bit of aspirin while you figure out his hematuria? So, I like to give him a little bit of time to see if we're going to have some acute bleeding problem.

Matt: Oh. Okay.

Don: And then if not? Great, I'm going to stop the aspirin and just press on with the DOAC.

Matt: Yeah, and you mentioned, you kind of teased it a little bit there that it sounds like is the thinking now because these P2Y12 inhibitors are more potent than aspirin or they're I guess slightly more effective at secondary prevention that that might be going forward be what we're using?

Don: I think we're headed in that direction and for exactly the reasons you said.

Matt: I'm trying to think, have there been landmark studies that have shown that or is there something ongoing where we're expecting that? I'm just trying to remember. Cardiology, it's like a firehose of information.

Don: Yeah. Most of it comes from post-stent patients, there are five trials now looking at stopping the aspirin instead of the P2Y12 and then continuing the P2Y12. That's mostly not in patients with AFib, but some of that we do see in patients with AFib as well, so we understand how to manage it. But P2Y12s, again, give us benefit over aspirin in terms of reducing ischemic events, and in general they're better than aspirin in terms of

bleeding as well. So, it's a win, win and I think that's why we're going to see probably also more trials looking at long-term therapy because we only really have this out to about 12 months at this point.

Matt: Yeah. And as the cost comes down, I guess eventually with ticagrelor and clopidogrel is already generic-

Don: Right.

Matt: -so it's more feasible.

Don: I think that's right. So, seems to be where we're headed. But I think you can confidently say within that first 12 months after an acute coronary syndrome event or stenting for stable ischemic heart disease, just get them right to the P2Y12 at 3, 6, or 12 months without the aspirin and you're going to be fine.

Matt: Okay. Yeah. The next case will go into that a little bit. I wanted to throw one slight other variation to this. So, coronary artery bypass grafting, CABG as we abbreviate it. If he had an underlying CABG, not just chronic stable CAD, if he had had prior CABG, does that change the calculus? Because my understanding was with CABG, it's lifelong aspirin as well. Is it different if they need an OAC?

Don: It doesn't seem to be. You're right. If they've had a CABG, lifelong aspirin has been the recommendation to now, and personally, this is not a guideline and it's not really well covered by the adaptable trial, let's say comparing different doses of aspirin. But just knowing about saphenous vein grafts. I prefer 325 of aspirin for patients with saphenous vein grafts. If it's not all arterial conduit to 81, just because we see what happens as veins degenerate, the flow gets sluggish, and those platelets get clumpy.

Matt: Yeah.

Don: So, a little bit of a buffer there. If there's not bleeding risk, 325 is reasonable. But to answer your question, I think that pretty clear evidence that the DOAC is going to cover the bypass graft conduits as well as the aspirin, and so reasonable to stop the aspirin for those patients as well.

Matt: Okay. Yeah. So, they're not going to be on 325, like a higher dose.

Don: Right.

Matt: Yeah.

Don: That would not be good, I agree. Yeah.

Matt: Okay. Yeah, I did see that. Because it said 100 to 325 of aspirin is like the secondary prevention after-

Don: CABG.

Matt: -coronary bypass. And I had not realized that. So, yeah, that's one of those nuances that I thought 81 of aspirin was what everyone was just getting these days.

Don: Yeah. You know how sausage is made. You know how guidelines are made. They're the same. I mean guidelines are sausage making. You're dealt the evidence that the trials were designed to give you.

Matt: Right.

Don: It's not necessarily what you and I would do to design the trial to answer our most important clinical question, it's what industry or history gives us. And so, a lot of those earlier trials didn't test 81 mg for CABG because they were pretty early. These are trials back in the 70s and 80s. So, they weren't really testing low-dose aspirin at that point. That's why we don't have as much confidence to say it's great to use 81 MG. It might be just fine, but that's why the recommendation says what it says.

Matt: And I guess the final variation of this case, which comes up, of course, sometimes too, is if this person, let's say, more than a year ago had had a PCI for, like, an NSTEMI, as some coronary event or I don't even know if it matters if it's at least that far out, why they have the stent? But if they have a stent and they're on aspirin for that, how does that change your calculus?

Don: And they have a new AFib now?

Matt: New AFib, yeah.

Don: If they have that stent, they are on lifelong antiplatelet therapy, either aspirin or P2Y12. Now they have this new indication for an antithrombotic and an anticoagulant. And so, again, same thing, I would start the oral anticoagulant, make sure that's going to go well, and then you can stop the antiplatelet therapy.

Matt: Okay. Yeah.

Don: Yeah. Especially for those chronic patients.

Matt: And I gave you that caveat. Yeah, it's a chronic one. So, if it had been, like, a month ago they had a stent and now they have new-onset AFib, I feel like that would be more of a tricky situation or they'd be on dual therapy at least for some time.

Don: For sure.

Matt: Okay. All right, Paul, any questions or do you want to go on to the next?

Paul: We're doing great.

Matt: All right.

Paul: I'm loving the de-escalation talk by the way. This feels like to have a blessing to start peeling off medications at some point feels really nice.

Matt: It's good.

Don: Well, credit to the trialists who thought this might work, thought there was equipoise. I agreed that there was equipoise and went and did the work and showed us that this was not only safe but better for the patient.

Paul: Right.

Matt: Yeah. So, you tease those five trials, so the next case is going to sort of get into where those, I think, came from?

Paul: We're going to talk about Estelle, who is a 64-year-old female. She has type 2 diabetes, obesity, CKD 3A, high blood pressure, recently admitted with a STEMI. She's seeing us in our primary care office for hospital follow-up. She has been discharged on aspirin and ticagrelor and wants to know how long she needs ticagrelor because of easy bruising and also, it's just costing her a fortune at this point, not surprisingly. We recall recent trials of short-duration dual antiplatelet therapy followed by P2Y12 monotherapy. So, what can we tell Estelle how we're going to maybe manage things over the next 12 months?

Don: Yeah. So again, I think important to have a conversation with the person who did her revascularization acutely for that STEMI that she had just recently. We understand the burden of other diseases. How difficult was this particular lesion? Do we feel like the stent got well deployed? Just some technical mechanical issues to help us understand just how aggressive we're going to be with the antiplatelet therapy here. But she's concerned about cost and she's concerned about bruising.

If you think those are rate limiting, then reasonable to stop the aspirin and just continue with the P2Y12 as early as three months. But I'd personally try to get her to six months if it's at all possible because that's stent into a very fresh active lesion and I want to give that stent time to really get re-endothelialized. So, three months would be the earliest, six months better, 12 months even better. But I think as I say, three months would be the very earliest. Now, as we talked about earlier, we could get her switched over to clopidogrel and that would help at least address some of the cost issues.

Matt: Yeah. So, if she's seeing us at three months out or if it was one month, do you think that would be too early?

Don: No, I don't think so. You could do it at a month.

Matt: Yeah. Within that first three months, maybe we switch over to a lower cost P2Y12 inhibitor. Prasugrel in a woman, she's 64, I was reading that in patients over 75 you have to be really careful. Is that being used as much? Are we getting too into the weeds thinking about that sort of thing?

Don: I think you will see that we're using much more of the ticagrelor and the clopidogrel than we are using prasugrel. There is a benefit in terms of marginal of prasugrel in comparison with clopidogrel in terms of fewer ischemic events, but a little bit more bleeding at least in one of those trials. And so, a little bit more careful, I think, with prasugrel. And that's probably why you don't see as much of it around.

Matt: Yeah. And prasugrel, ticagrelor are both more potent P2Y12 inhibitors compared with clopidogrel?

Don: Yeah. More rapid onset, more potent.

Matt: Yeah.

Don: That's correct.

Matt: All right.

Paul: The bruising, I'm glad that you included that in this case. What do you do with that information? I feel like it does come up from time to time, but I don't know that I often would adjust therapy just sort of based on the patient's report of that. Do you have a specific way that you think about a patient who says, I'm having more bruising with these medications?

Don: Because we're often using these in older patients and we know with thinning of the dermis and even minor trauma, they're going to bruise anyway, sometimes it helps to remind them, "Well, remember you were bruising before this happened."

Matt: Right.

Don: But I think I would hesitate to limit good therapy for cosmetic reasons.

Matt: Yeah.

Don: But if it's, you know, really causing painful hematomas, if it's limiting function in their arm or, you know, just happening so often that, you know, it truly is becoming a quality-of-life issue, I think that's reasonable. So, I would have a conversation with them about potentially stopping this as early as three months, but I would really try to get her to three months if at all possible.

Paul: Got you.

Don: Yeah.

Paul: Helpful. Thank you.

Matt: And it sounds like if cost wasn't an issue, this is a patient we gave you, she had a STEMI, so she had a major coronary event. She does not have an indication for anticoagulation. She's just on the dual antiplatelet therapy. And when she gets out to that 12 months from her event, if she's okay, the clopidogrel may be the first choice now, but we could also do aspirin. It's sort of either is an okay answer at this point.

Don: Yes in 12 months either/or is fine. And I think if cost is not an issue, wouldn't that be nice?-- But if costs were not an issue, there is some benefit to ticagrelor compared with clopidogrel during those first 12 months. And the number needed to treat is about 50. We do other things where the number needed to treat is 50.

Matt: Yeah, of course.

Paul: Right.

Don: That is a straight up comparison of ticagrelor with clopidogrel. Treat 50 patients with ticagrelor instead of clopidogrel, you will prevent one ischemic event. But cost is an issue. So put that maybe in the back of your calculus.

Matt: I haven't seen patients on a really long-term ticagrelor, but beyond that one-year point, you could just choose whatever P2Y12-

Don: Or aspirin.

Matt: -0r aspirin. Okay. Yeah. So, this is becoming more clear now, Paul, I think?

Don: I hope so.

Matt: I'm sort of.

Don: Clear as mud, right?

Matt: Yeah. No, it is. And I think, Paul and I lament about this very often on the show, the fact that "I just want a simple yes, no."

Paul: [laughs] That's right.

Matt: Now, tell me what to do. And maybe-- [crosstalk]

Paul: It's an algorithm with no branch points, just a series of straight lines all the way down would be the dream.

Matt: Yes. Eventually, probably AI is going to tell us what to do for all these things, but I think we're not there yet.

Don: And then write a beautiful-

Matt: We still have the job, yeah.

Paul: [laughs]

Don: -discourse about it. Yes.

Matt: Yeah, we still have a job for now, Paul. So, we have to learn this stuff. I think that squares this case. So, we get her out to a year and she's okay. We decide we were going to do clopidogrel beyond a year as monotherapy for her. But let's talk about primary prevention, Paul, because I thought this was dead, but maybe not. So, let's get into a case.

Paul: No, I love it. So, we're going to talk about Regina, who is a 65-year-old woman who does not use tobacco. She has uncontrolled high blood pressure. She has type 2 diabetes that is not well controlled with an A1c of 9.4%. She has pure hypercholesterolemia but reports statin intolerance with myalgias and aches and pains and so just went out to take one. She's seeing you in the office for a follow-up of her high blood pressure. Her blood pressure in the clinic consistently is 165/92. She is without a whole lot of symptoms to worry. She doesn't have chest pain, she doesn't have shortness of breath, she doesn't have dyspnea on exertion, there is no edema and all that stuff.

You calculate her 10-year ASCVD risk, it is 25.3%, which seems high. She has a CAC score that was done three years ago of 114. And we remember that in 2018, we had three large well-done trials that were all negative for aspirin for primary prevention. But still, we don't feel great about Regina because she seems like someone who's just an ischemic event waiting to happen. How do you think about this patient? Are there exceptions of the aspirin verboten for patients for primary prevention? How are we thinking about these things these days?

Don: Yeah, so it's a wonderful question and I think this is right where the boundary condition is in a patient like Regina. So, remember why we used to recommend aspirin pretty routinely for primary prevention was those early trials in 80s, 90s, early aughts where there was a benefit to aspirin compared to placebo for patients who were at risk for cardiovascular disease and that exceeded the bleeding risk.

Matt: Yeah.

Don: We were preventing more heart attacks and strokes than we're causing bleeds. And that's why the recommendations routinely in the guidelines for primary prevention

were that we would recommend low-dose aspirin for primary prevention as long as there was not high bleeding risk and favoring patients at, let's say, a 10% or more tenure risk for cardiovascular events. And I think people were pretty comfortable with that. 2018 completely turned all of that on its head. So, three trials came out really within a month of each other. And just briefly if we have time, kind of review those. Yeah. So, one trial in patients 70 years of age and older, primary prevention, low-dose aspirin versus placebo, stopped early for futility and a concern that there was actually an increase in all-cause mortality driven by for the first time ever, never before seen an increase in cancer mortality.

Matt: Yeah, that was-- that didn't make--

Paul: It's just weird.

Don: Really weird. Never seen before since in all these aspirin trials we've done, nobody's ever reported that particular find.

Matt: And we were thinking it reduced colon cancer risk.

Paul: Colorectal cancer, yeah.

Don: Exactly. So, a play of chance, something funky, hard to know. But certainly, a good enough reason to stop that trial.

Matt: Yeah.

Don: Right. So, 70-year-older, maybe we should be rethinking recommendations about aspirin for primary prevention. Same issue of the journal was the study of patients with diabetes 40 years of age and older.

Matt: Right.

Don: And again, low-dose aspirin versus placebo, stopped early for futility, again, because the absolute risk difference, the benefit for ischemic events was less by 1.1%, but major bleeding increased by 0.9%. So, essentially awash.

Matt: Yeah.

Don: And I think it's fair to put those things on the same playing field. Major bleeding is a major event, just as a stroke or a heart attack is a major event. So, it was really awash. And so, that made us rethink recommendations for patients with diabetes. The last one, really, maybe the most interesting one was patients sort of middle-aged and older at elevated risks. They calculated their risk score, specifically targeted people with 10% to 20% 10-year risk of coronary disease, and said we're going to put these patients on aspirin and stopped early for futility. Now, there was very little bit of benefit, but the same bleeding risk, and they could have gone forever and it really wasn't going to

achieve statistical significance. And what was really fascinating about that was the event rates in that trial were far lower than they thought they were going to be, probably because 65% on antihypertensive therapy, 43% on statin therapy.

Matt: Yeah.

Don: There's really no room for the aspirin now to make a difference, right. Aspirin is really that safety net medication. If a plaque gets rolling, it's going to prevent the platelets from clumping.

Matt: Yes.

Don: But if we don't let that plaque get rolling in the first place, because we're treating the LDL, we're treating the blood pressure, we may not ever get to the point where we need the aspirin. And so, that's the thinking about why the change in the 90s, terrible job treating hypertension. We weren't treating people with statins for primary prevention. Now we are and aspirin just has less room to make a difference.

Matt: Yes. We have a lot better blood pressure meds. Audience, we talked about this one of our recent shows. We're still like, not getting-

Don: But we have work to do-

Matt: -where we want to go? We have a lot of work to do.

Don: -especially, after the pandemic and all those patients who got disconnected from their usual sources of care.

Matt: And then the bar has been lowered a little bit, what's considered controlled for, so it's tough.

Don: We could talk about 130/80 for a long time. I'm a fan, but I understand it's not easier.

Matt: Okay, so you coined this term may be Primary-and-a-Half Prevention. Can you talk what you mean by that?

Don: Yeah, we've used this phrase in my clinic for a long time with my fellows and I. So, Regina does not have secondary prevention needs. She does not have clinically manifested coronary disease or symptoms therefrom. She technically requires primary prevention therefore, because she's got risk factors. But she has the disease, you told me she has a coronary calcium score of 114. Right.

Matt: Yes.

Don: She has the disease. So, while it's not clinically manifest, I would call her Primary-

and-a-Half Prevention, and I'm going to be more aggressive with her than I would be with somebody who has a coronary calcium score of 0 for sure or if I saw some other manifestation of plaque somewhere else in her body, it's Primary-and-a-Half Prevention. And so, I'm definitely going to be more aggressive. Now, why do I care about that? Well, getting back to Regina, let me first say, I think our job today is to control her acute risk of having an event. She's not a smoker, so we don't have to worry about that. But that would be a great thing to get her to stop immediately. But the most important risk factor for her today is her blood pressure, because if we can control that, she doesn't have a trigger for a stroke, she doesn't have a trigger or not as much of one for an acute coronary syndrome event.

So, I would put all my effort today into getting that blood pressure under control and try to get her back in frequently, let's spend the next month getting her under control. Then I would start to think about her LDL and whether I want to put her on aspirin. Those are definitely secondary for me, but blood pressure is one by far for her.

Matt: Blood pressure number one?

Don: Yeah.

Matt: Yeah. In your slides and I don't know if this came from, Cainzos, what is it? Cainzos-Achirica circulation 2020? You had these graphs based on the CAC score of 0, number needed to treat is very high compared to the number needed to harm. And then once you get to that CAC score, it looked like greater than 100 for both men and women. It looks like it starts to make sense.

Don: So again, thinking about this net benefit on the absolute risk scales, are we more likely to prevent an event than to cause bleeding?

Matt: Right.

Don: So, does Regina need aspirin? So, allcomers, she has diabetes. She's in the range where we said futility, allcomers, default would be to say no. But we know a little bit more about Regina. She has this coronary calcium score of 114, putting her in my Primary-and-a-Half bin, and what she said is right. So, Miguel Cainzos-Achirica, beautiful paper using the MESA study where we went back and looked and said, "Okay, is there a threshold of coronary calcium where the net benefit appears for aspirin compared to the bleeding risk?" So, number needed to treat is better than number you need to harm. And the breakpoint was at 100 for the coronary calcium score. So that patient has enough burden of disease where you are more likely to prevent an event with aspirin than you are to cause a major bleed.

Matt: Yeah.

Don: So, for me, that's pretty meaningful because, again, it's the disease. It's not just risk. She has the disease and I think that's the real difference later.

Matt: And this was over a five-year period that you were looking at the number needed to treat, number needed to harm in this one.

Don: Correct.

Matt: Okay.

Don: So, what we're really doing is we're applying the projected benefit of aspirin and the projected bleed risk on these participants in MESA to say where's the breakeven point for the coronary calcium score?

Paul: Yeah. I have to think we're not going to be so absolute about this at some point in the future because I feel like that primary prevention is so nebulous in circumstances like this. Like, for instance, if you add tobacco use to this patient, they probably have I don't know if this is a term like subclinical CAD. It has to be there. So, I feel there's going to be some ways we're going to be a little bit more sophisticated about teasing out who may benefit even if they haven't had an ischemic event that declares itself yet. But I think sounds like we're not quite there yet other than CAC scoring, it sounds like.

Don: Yeah, I think that's right. We hopefully we'll get there. But you bring up important-- like a patient who's a heavy smoker, if their 10-year risk is 10% and they're a heavy smoker, I'm thinking hard about aspirin in that patient. As long as they don't have a huge bleed risk, I'm thinking pretty hard about it because that's the patient, as you said, probably got disease, I could go look. But that heavy smoking, all those risk factors that she has, she's going to have the disease and she's the person. Not everybody will benefit. That's why the default answer is don't do it. But there are people within that who will benefit and she's much more likely to be one of those people.

Paul: Right.

Matt: Assuming we're good primary care doctors, we have America's primary care doctor here. He would be trying to get-

Don: It's you.

Paul: Yes, yes.

Don: Who knew?

Matt: -her to stop smoking and control the blood pressure.

Paul: She's [unintelligible 00:48:34] really making it--[crosstalk]

Matt: Probably already on a cholesterol-lowering medication.

Don: Well, but she was statin intolerant and we can talk about that, too.

Matt: Yeah, if statin intolerant, yeah. so, we made it hard there. But the aspirin would be-- if you had to choose between statin and aspirin for patients for primary prevention, is statin still the tool of choice, like for most patients?

Don: For the intermediate to long term? Yes.

Matt: Yeah, okay.

Don: Because again, that's going to delipidate the plaque. It's going to passivate the plaque, going to make it much more stable. So, we're much less likely to need the aspirin. Short-term aspirin, long-term, get that LDL as low as possible.

Matt: Yeah. Okay. I'm sure we could iterate on this all day, but I know you've had a long day and we got to so much.

Paul: [unintelligible 00:49:19] consult at this point.

Matt: Yeah, this was really helpful. Definitely learned a lot. I want to get some take-home points and I want to ask you about this number eight on your coat there.

Don: Okay.

Matt: So first, if there's any major, like one or two take-home points that you really want our primary care listeners to remember from what we talked about today, or I guess our hospitalists too because they're going to be discharging people they need to know.

Don: So, I guess, I would say, think about the patient, are they secondary prevention or primary prevention? Secondary prevention, they need the therapy, it is indicated. And so, we're really making decisions about the amount of therapy and the duration of that therapy. And again, you said this well, I think the fact that we can now deescalate, deprescribe at relatively predictable intervals and know that it's safe to do that, I think that's hugely liberating.

And again, I would encourage primary care docs to talk to the operator who put that stent in or talk to the stroke neurologist to make sure we're doing the right thing. Based on what they see the clinical risk being. I think that's really actually quite powerful.

In primary prevention, the margin of decision-making is a little bit tighter. The benefit to risk is closer and so, I think use the tools of these risk scores so that you can really line up the decision-making on the right axis and say, "I really am more likely to prevent an event here than to cause a bleed." It's not going to be perfect. These are probabilities. We will have patients who will bleed. It doesn't mean you made the wrong decision. Try to do your best. Use the math to help you. And that's what those risk scores can do.

Matt: All right, so now for plugs, tell us about this number eight. You told us briefly about it, but I want to hear more about this.

Don: I had the privilege of working closely with the American Heart Association and was actually the Heart Association President last year. And one of the things that we've really been pushing over the last decade is the construct of cardiovascular health. We've all been working hard to reduce cardiovascular disease deaths. And we've seen dramatic improvements since the 1970s, 70% reductions in cardiovascular disease death rates.

Matt: Yeah.

Don: We don't celebrate that enough. That is pretty [crosstalk]

Paul: That's impressive.

Matt: That is. I did not know that number. That is impressive.

Don: And as we've been talking about today, we've been getting better at treating risk factors not good enough, but better. In 2010, the Heart Association said, let's actually start to think about promoting cardiovascular health, not just preventing disease and death. And so, they added this sort of new layer. They asked a group of us to define cardiovascular health. Like, easy to say. What is health? Health is more than just the absence of disease. And so, we created a quantifiable metric of cardiovascular health, which at the time was called Life Simple 7, and included a healthy diet, physical activity, not smoking, healthy weight, healthy blood pressure, healthy blood glucose, healthy blood cholesterol. And we gave thresholds for what was optimal and then what was less optimal. And you could create a cardiovascular health score if you will.

Matt: Oh, yeah. Okay.

Don: And it allowed people to focus on, what can I change today to improve my health? And not just think about preventing something that's going to happen 30 years from now.

Matt: I'm impressed you rattled off that list.

Don: Well, I've lived with it for 13 years.

Matt: Yeah. I'm impressed.

Don: So anyway, scientists did what they do. They dug in on it. They showed us that the cardiovascular health score is really tied to many, many favorable health outcomes over your lifespan. Less cancer, of course, less cardiovascular disease, yes, but less cancer, less chronic kidney disease, less atrial fibrillation, longer lifespan, longer health span. So, you avoid comorbidities as you age just by having a higher cardiovascular health score at younger ages.

So, we updated the construct a year ago. It's now instead of Life Simple 7, it's Life's Essential 8. We revamped the scoring, but we added a new metric, which is sleep duration, because we now have a lot of good evidence about the importance of sleep for heart health, right. It affects all those other things that I mentioned. Maybe not cholesterol, but for sure, your weight, your dietary choices, your ability to do physical activity, affects your blood pressure, affects your blood sugar, all those other things. And it independently actually can predict cardiovascular risk.

So, sleep duration optimal is 7 to 9 hours per night. And that gives you Life's Essential 8. And I think it's a great way for clinicians to help patients focus on, "Let's pick that one thing you want to work on. And we know we'll be improving your health." And we can actually-- if you go on the website Life's Essential 8.

Matt: Yeah.

Don: You can actually calculate your Life's Essential 8 score, 0 to 100. And as you improve and change, your cardiovascular health score will improve and change with you.

Matt: I love it. I love it. Yeah. I feel like this is a great thing for primary care, too, because this is--

Paul: For sure.

Matt: -basically, what we talk to patients about. And it's nice to have a website to point them to, like, "Here's the stuff you want to focus on."

Don: And it might seem overwhelming.

Matt: Right?

Don: Here are eight things. No, pick one. Work on that to make it better after you sort of do your score, you can get sort of red light, yellow light, green light for the different metrics, how you're doing, and click through on anything you want to work on, and you get the great American Heart Association content on how to make this better. And I think it can be a really useful tool for patients.

Paul: There's a score. It's gamified a little bit. I feel like you're more invested rather than you should just do better, which is not a helpful thing to be telling patients. But to have numbers that you can actually sort of improve on your own by making changes, it seems like it's a little bit more meaningful.

Don: And I think that's right. And I think that the goal here is not to get everybody to 100. That's not realistic, but "better is better."

Paul: Right.

Don: And they can actually see their numbers change as they improve things.

Matt: And audience, we'll be calculating Paul's score, posting it on Twitter.

Paul: Let's not do that. If sleep part matters? I'm in a lot of trouble.

[laughs]

Matt: All right, well, thank you so much. This has been fantastic.

Don: It's been a real pleasure. Thank you.

Paul: This has been another episode of The Curbsiders, bringing you away little knowledge food for your brain hole.

Matt: Yummy.

Paul: One of these days will be more definitive. It'll be yummy. It'll feel still gross? Still hungry. For more? Join our Patreon and get all of our episodes ad free plus twice-monthly bonus episodes at *patreon.com/curbsiders*. You can find our show notes at *thecurbsiders.com*, and you can sign up for our mailing list while you're there to get our weekly show notes in your inbox, which includes our Curbsiders Digest that recaps the latest practice-changing articles, guidelines, and news in Internal Medicine.

Matt: We're committed to high-value practice-changing knowledge, and to do that, we need your feedback, so please subscribe, rate, and review the show on YouTube, Spotify, or Apple Podcasts. You can also email us at *askcurbsiders@gmail.com*. A reminder that this and most episodes are available CME through VCU Health at *curbsiders.vcuhealth.org*. I wanted to give a special thanks to our whole Curbsiders team who makes it happen behind the scenes. Our technical production is done by the team at Pod Paste, Elizabeth Proto runs our social media, Chris “The Chiu Man" Chiu runs our discord, and Stuart Brigham composed our theme music. With all that, Paul, until next time, I've been Dr. Matthew Frank Watto.

Paul: And that would be Matthew Frank Watto, who is also the writer and producer for this episode, but he's too modest to name that himself while reading those things. And as always, I remain Dr. Paul Nelson Williams. Thank you and goodbye.

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