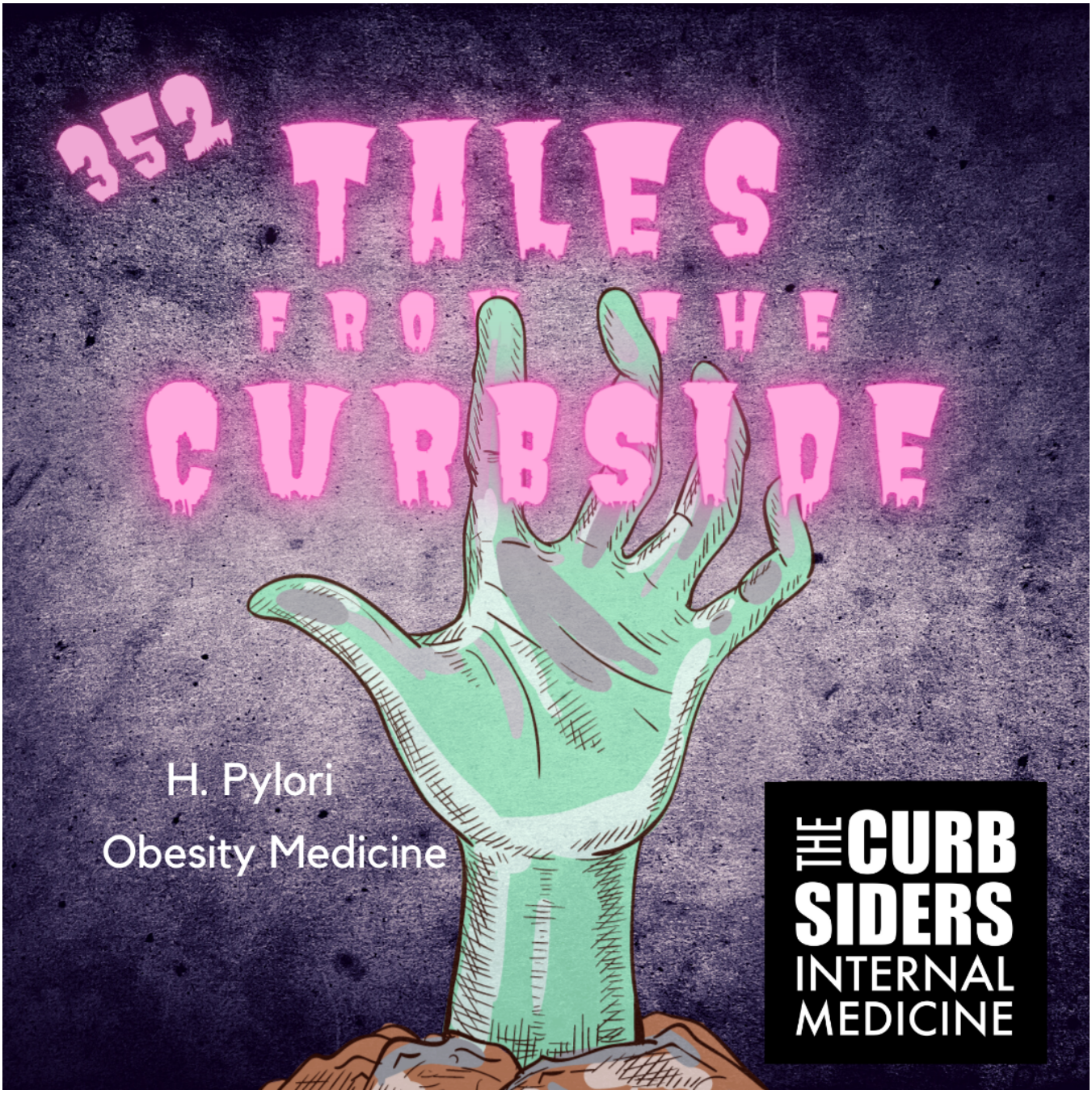
#352 H. pylori and Obesity Medicine FAQ: A rapid review (TFTC)



[The Curbsiders Podcast theme]

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

Paul: Matt? We're talking H. Pylori, we're talking obesity, I'm here with my great friend Matt Watto, what could be better? I'm doing fantastic.

Matt: Once again, Paul, it is a weeknight and we [Paul laughs] are recording a podcast. What more would I be wanting to do with my life?

Paul: When I was a seven-year-old child, my parents asked me what I want to do when I grew up. This was exactly what I described to them, to the letter. So, things are looking up, Williams

Matt: Tonight, we were going to recap two fantastic episodes that were very practice changing for me. We talked about H. Pylori, and again, we're going to talk about obesity medicines and frequently asked questions. And, Paul, before we get to that, can you remind the audience, who are we and what do we do?

Paul: Yeah, Matt, we are *the* Internal Medicine Podcast. Ordinarily, we use expert interviews to bring you clinical pearls and practice changing knowledge. This is our Peabody-award-winning-- someday, we're going to get sued for that probably. I should probably stop saying that. But the tales from the curbside, where we recap two episodes that are, in this case, very loosely related, but we sort of go through it and sort of highlight the pearls that we thought were especially useful or meaningful. In this case, we're talking about H. Pylori, with Dr. Saffouri and obesity medicine FAQs with Dr. Cody Stanford. So, a lot of high yield stuff in both of these episodes. I think, Matt, we're going to start with H. pylori.

Matt: Yeah, first I just want to remind the audience that for these shorter episodes, to give ourselves a break, these are not available for CME, but the two episodes we're talking about were individually available. So, if you go to *curbsiders.vcuhealth.org*, then you can claim your free CME credit through VCU Health. And now with that, episode 322, H. Pylori with George Saffouri. This was produced and with graphics by the great Beth Garbitelli. Now, Dr. Beth Garbitelli, Paul. So proud.

Paul: She did it. She did [Matt laughs] No surprises there.

Matt: All right, to start us off, Paul, I wanted to talk a little bit about the epidemiology of this because this is-- A lot of this was new to me. I thought H. pylori is like, "Oh, yeah, just throw some antibiotics at him for two weeks and you're done." Not that easy, but H. pylori mostly is a childhood illness. And in the US, it is here, not as prevalent as in some other places. But it's really a marker of like cramped living conditions and it tends to spread through families just because the way that it's spread, fecal/oral route. So, families get colonized with this, which makes sense. That's one of the points that we'll come up with later about screening. Why you might screen people who are first generation from a country where there's a high prevalence. And, Paul, I wanted to ask you the symptoms of H. pylori. We're going to talk about some maybe asymptomatic patients we might screen but what makes you think about H. pylori?

Paul: Yeah, well, I mean, before this episode or previously, we've talked before about this, I'd probably lumped together upper GI symptoms in this sort of amorphous process that hopefully responded to proton pump inhibitors. So, regardless of whether you had heartburn symptoms, or regurgitation, or postprandial fullness, or epigastric pain, I just kind of hoped that that would respond to the same medication. And Dr. Saffouri advocated for really doing your due diligence, separating those things out into GERD versus dyspepsia when appropriate. Because GERD, it's pretty reasonable to treat with a proton pump inhibitor. Empirically, see how you do with it and kind of reassess your therapy. Dyspepsia should prompt you to do your H. pylori testing. And dyspepsia, as a reminder, are things like this this

postprandial fullness or the epigastric pain that happens after meals. That is more dyspepsia than a GERD-type picture. So, those things should make you think H. pylori.

And then, otherwise, the symptoms tend to be relatively nonspecific, sort of GI stuff. You can have pain, you can feel kind of gassy. There can be bloating and belching. But symptoms along those lines should all kind of prompt H. pylori testing, and which we'll get into what the best tests are for those.

Matt: And one of the overlaps between GERD and H. pylori, when it comes to testing, if the person has bleeding or like unintentional weight loss, you're going to right to upper endoscopy for that. Just to make that point it seems obvious, but that is-- that's how it's going to be. And then, Paul, talking about endoscopy. For my patients under 60, I think I'm okay to just do either a urea breath test or an H. pylori stool antigen. Most of the papers I was reading said they're fairly comparable, so it's mostly just what-- I know one's slightly better than the other but in general, it's just whatever they're comfortable with locally at your lab, just use that test, they should both be okay. But what about patients over 60? How does that differ?

Paul: Yeah, over 60, you've earned yourself upper endoscopy, which is not to say that you're not doing H. pylori testing. It's just that H. pylori testing you're doing is going to be done via biopsy. And the reason for that line of demarcation is over the age of 60, statistically, these problems and symptoms are more likely to be caused by malignancy than under the age of 60. And so, probably direct visualization is-- a little bit more aggressive evaluation is probably warranted in your older patients. But in any case, regardless if you're having these symptoms, as you say, even in the absence of red flag symptoms, you're going to get yourself H. pylori testing just over the age of 60, that puts you high risk enough that you actually warrant an endoscopic evaluation as well.

Matt, before we sort of ship our patients say we're not getting endoscopic evaluation. Let's say they're under the age of 60, but you have some suspicion for H. pylori, or at least some reason to test, what kind of practical considerations are you thinking about? And what kind of housekeeping do you have to do before we can send your patient off for testing?

Matt: Well, let's deal with the easy one first. So, proton pump inhibitors, those should be held for at least a month. I think some of the guidelines say two weeks, but most of the people we've talked to, Paul, they're like, "I'd like to wait at least four," because you don't want to put someone through a test-- regardless whether it's collecting their own stool or having an endoscopy, you don't want to put them through a test and have a lower chance of finding what you're looking for. So, off of PPI and I would throw in antibiotics into that category as well, just don't have the patient on that. With H2 receptor antagonists, it's a little more complicated, because Dr. Saffouri he said he doesn't like the patient to take those because the literature has been a little mixed as to how much it does or doesn't lower your yields. So, it might affect your testing, and you might get a false negative. I don't know about you, Paul. What have you been telling patients?

Paul: Yeah, I kind of keep them in my back pocket if needed. Apparently, you can use acids or calcium carbonate prior to testing for symptoms. I think stopping a PPI when someone who's using it for symptom control, regardless of the underlying etiology, it's kind of a challenging proposition, depending on how severe your symptoms are. So, I will tell them to avoid them if possible. If you need something and the antacids are covering it, I then go ahead and do that. But that's my own personal practice, and certainly not with Dr. Safari recommended.

Matt: Yeah, I've taken the same route. Essentially, can they get by? Hopefully they can get the test. Especially if it's a stool test, hopefully they can just collect it within a week. And then, once they've sent the test, you can start them on PPI if you need to or certainly H2 receptor antagonists. But yeah, I do the same thing. Try to get by with the antacids. If I really need to, I'll put them on an H2 receptor

antagonist. For what it's worth, the New England Journal review by Dr. Crowe from 2019, she did mention she thinks it's okay to do H2 receptor antagonists but we'll leave it to you and your endoscopist if they're going for endoscopy, what they prefer.

But who to test? Because we talked about testing patients with dyspepsia. Of course, you're going to test people who have red flag symptoms. But here's how I would lump it together. Dyspepsia is one of the things, if someone has confirmed peptic ulcer disease, those patients should be tested for H. pylori. There are two types of cancers that can be associated as well. So, gastric cancer, anyone who has early gastric cancer, you should test for H. pylori, because you're going to treat it if you find it. And same thing with low-grade MALToma, Paul, because if you treat H. pylori in those patients, it might actually treat the MALToma.

Paul: Right.

Matt: For hematologic abnormalities, there's unexplained iron deficiency, think about H. pylori. And then, immune thrombocytopenia is one of the other ones that you can think about. And then, Paul, what do you think about some of these, I guess, maybe softer recommendations? Has this been practice changing for you?

Paul: No, no, is the short answers. The soft recommendations being like if someone is on long-term aspirin or NSAIDs, I will have a lower threshold to evaluate, but it's not going to be a leading indication for me to actually do it. And same goes for-- a family history of gastric cancer, I will think of it though that doesn't come up all that often. And then, the first-generation immigrants from high prevalence countries, again, it's something where I might have a lower threshold to test but I can't promise it's going to trigger me to sort of-- that's the first thing that I'm going to talk to this patient about. I'm not sure how that reflects your practice.

Matt: I take the same-- I worry that we would have so many patients for testing if it was NSAID or aspirin use. Hopefully, I don't have a lot of patients on long-term NSAIDs, but I do have patients who are intermittently taking them over the long term. So yeah, those ones, I'm not as absolute on but certainly the earlier ones we talked about, I am testing. And then, Paul, the management--

Paul: Actually, before we get to the manage-- I just wanted to say real quick because the listeners may have noticed that we did not mention serologic testing for H. pylori and that was--

Matt: Oh, [crosstalk].

Paul: I just want to be explicit about that. Dr. Saffouri says, as a gastroenterologist, he has never ordered them. And he made the point, if I remember correctly, that it's not the worst test in the world, but we have much better tests. So, why not use the good tests? So, it's not all that helpful a test. So, you'll notice when we're talking about testing for H. pylori, serologic testing is nowhere part of the conversation because it's not as helpful as the other tests that we have, namely-- obviously, biopsies but also the breath testing and the stool testing. So, I just want to make sure I mentioned that out loud because I feel like that's a question that comes up sometimes.

Matt: Yeah. And I know we got one message from a listener about this, and I think they were just practicing in a different region where maybe it is used but in at least the US practice guidelines, really just mentioned that it'll be hard to interpret an H. pylori IgG. You don't know if it's active infection and just like Paul was saying, the sensitivity, specificity wise, all that stuff, it's just not our best test. So, we just we just don't really have cause to use it. Every case, I'm sure you could think of a situation where it might be helpful, but for the most part, that's going to be few and far between.

So, Paul, the management of H. pylori, I mean, this is-- We haven't done it yet on this episode, Paul, so I've got to throw this to you. [Paul chuckles] All right, I'm going to say something which maybe it's wrong, Paul, you tell me. H. pylori, medications super well tolerated, highly effective, very low rate of treatment failure. How am I doing?

Paul: So, of course, obviously, all wrong. We were having this conversation, before in terms of-- it is just bananas to me that we have not yet come up with a single-pill regimen for 14 days that can manage H. pylori. That's just not anywhere close to what the actual practicality of treatment looks like. Having said that, Matt, what should we be reaching for? Is there a preferred regimen according to Dr. Saffouri?

Matt: Well, I wish there was a clear-cut winner. I could say the preferred regimen we don't want to use is the clarithromycin-based triple therapy because there's such high rates of clarithromycin resistance. the part of the problem with all these regimens, Paul, is it's like pill burden. They're taking these things for 10 days, give or take. And then, it's a lot of just GI side effects, nausea, vomiting, diarrhea, just upset stomach. So, they're hard regimens for patients to take.

Right now, if you're practicing in the West or in the US, Dr. Saffouri was telling us that he will often try a quadruple therapy, which is like bismuth, PPI, tetracycline, metronidazole. And then, he'll retest and if that doesn't work, then he's going to use a different regimen altogether. Often, levofloxacin would be either his second-line regimen if he didn't use it for the first round. But that's pretty much-- those are two of the regimens. There's like eight or nine different regimens, Paul. The main principles are, avoid the clarithromycin-based triple therapy as a first line unless you know the sensitivities, and then don't use the same regimen twice. But, Paul, does any of that differ from what you're doing or what you've seen done locally?

Paul: No, no, I think that's fairly consistent. And I think we avoid the fluoroquinolone-based therapy for a lot of reasons initially, I think, to keep it in our back pockets, but then also because we're just all terrified of medications that we used to hand out like candy 15 years ago. [Matt laughs]. I will say, we talked a little bit about how Dr. Saffouri manages intolerance to the regimens. So, it's just probably worth bringing up that you can do on Ondansetron for the nausea. He has, God bless him, tried the isopropyl alcohol aromatherapy with the patients [Matt laughs] and he says it works some of the time.

And then, he did make the point that if patients started having diarrhea, you will actually probably consider C. diff testing for C. diff negative, then loperamide. Because obviously, if you're throwing antibiotics at someone, they start having diarrhea, there's a couple of reasons it could be, but you don't want to miss C. diff and give loperamide and cause problems that way. So, there are things you can do to help patients manage the GI side effects but none of it's great, unfortunately.

Matt: Yeah, and just remember to retest the person. Wait about a month after they finish because again, you want a month after antibiotics and after proton pump inhibitor therapy. And then, you would retest. Now, Paul, at ACP, the Internal Medicine Meeting 2022, I was home with COVID, but you were there [Paul laughs] But fortunately, I was able to remotely see a talk by Dr. Brooks Cash, former Curbsiders guest on our IBS episode, like in the 20s, Paul. That was like 300 Plus episodes ago, but still, he's still great. And Dr. Cash was talking about the latest in H. pylori treatment. And it looks like this Rifabutin-containing therapy, which is rifabutin, omeprazole, and amoxicillin, there is an article by Graham I can link to in the show notes for this episode, talking about that as an emerging therapy that looks like it's going to help because we have such a resistance problem that we needed to come up with new things.

And, Paul, the other new therapy that everyone's excited about is this vonoprazan, this is a potassium-competitive acid blocker or a P-CAB and I'm just going to say P-CAB from now on, Paul, because it's hard to say.

Paul: That feels best, yeah.

Matt: But this P-CAB-containing therapy, those seem really promising. The P-CAB are almost like-- think of them as a newer, better form of proton pump inhibitor. They work on the same kind of hydrogen, sodium, potassium, ATPase. But they seem to be longer acting, they seem to be a little bit more just stable in the acidic environment of the stomach. So, there's a lot of things people are excited about with these. And I think we're going to start seeing these more often. They're already being used in the East. And they seemed in a big meta-analysis by [unintelligible 00:16:19] in 2021, Paul. The vonoprazan-containing therapy, and the reverse hybrid therapy seemed like two of the winners out of eight therapies that they studied. In the West, levofloxacin-containing therapies, we're still doing okay. But the clarithromycin, metronidazole, and fluoroquinolones worldwide all have this increasing resistance. Now, Paul, do you know what this reverse hybrid therapy is?

Paul: I was going to ask you to define it because it sounds so cool, and I feel like it's the type of thing that we want to be able to throw out there, but we should probably be able to back it up. So, what is reverse hybrid therapy?

Matt: Well, it's where you're going to give 14 days of treatment, Paul. The first seven days, they're getting just a PPI and amoxicillin and those two are going to continue for the full 14 days. But for the last 7 days of that 14-day period, you're giving clarithromycin and metronidazole. So probably, you're going to need to pull out your Ondansetron, and maybe your loperamide as we previously talked about.

Paul: [laughs] Sure. And your alcohol pads, yeah.

Matt: So, it's sort of like-- that's why I guess it's the reverse hybrid. So, it's not just a clever name, Paul, which I always like when it's not just a clever name.

Paul: [laughs] It's like the triple lindy.

Matt: Yeah, so that's some cool stuff. So, H. pylori, to recap, I think the big points are, just make sure to think about it in the groups that we talked about. Certainly, when people have dyspepsia, which Paul told us how to differentiate from just your classic GERD, heartburn symptoms. And then, make sure you retest people, because there's a lot of resistance out there. Paul, how do you want to transition to our second topic? I'll let you start us off here.

Paul: Well, I don't have your expertise to transition. All right, I'm going to try this. Matt, would you like to talk about obesity medicine now? [Matt laughs]

Matt: I thought you'd never ask Paul. [Paul laughs] This is 324, Obesity Medicine FAQ with Dr. Fatima Cody Stanford. This was of course produced with graphics by the great Isabel Valdez, PA. Just a fantastic person that works with us on our show, made a bunch of graphics for this one. So, check those out. And, Paul, tell me, now with obesity, we've done a great job as physicians using language that is respectful and not stigmatizing patients and treating this as a chronic ailment. Am I right, or am I wrong?

Paul: So, I see you're employing the classic Watto reversal, where in fact we as physicians have not historically done a great job in terms of discussing obesity as an illness. A lot of the times, I feel we sort of confer moral judgment along with it. We use language that is insensitive. We talk about it in a way that is-- describe it more as a failing than actually a disease process. And so, one of the things that we

were tasked with early on in the episode is actually describing it as we would any other disease. So, this is a patient with obesity, not this patient is obese. And then also, a point that I like that was made early on is that morbid obesity is not a thing. We should probably just throw that out of our vocabulary. We don't talk about other morbid disease states like morbid cancer or morbid hypertension. So, you can certainly have severe obesity, you can have class 3 obesity, but calling it morbid obesity just is unnecessary and not terribly scientific and maybe serves to just sort of broaden the stigma.

And I think-- why don't I let you talk? You have a specific approach when you're sort of talking to patients about weight loss and about their weight. How do you frame that conversation? How do you even start that conversation, Matt?

Matt: Yeah, I usually like to ask, "Is it okay if we talk about your weight?" And if they say yes, my next question is, "Can you tell me what's the heaviest weight you've ever been? How does that compare to where we are now?" Because sometimes patient in front of you is 300 pounds, and they'll be like, "I was 450 pounds." So, you should be congratulating that person. But you're sitting there thinking, "Okay, this person looks like they have weight to lose." Part of what that gets to is knowing where someone is in their weight loss journey. And also, just the fact that we are-- I've totally changed the way that I think about this, because I think patients come, they've often felt stigmatized. They've often tried a lot of things, and they've started to plateau, or they've gained weight despite doing it or they've done well for a while and then started to regain even if they kept up whatever good habits, lifestyle changes they've made. So, I like to tell patients, "Listen, this is a chronic disease. We have to treat it like that. And we may have to have you on medications. And in some cases, patients get surgery for this. And right now, those are the best tools that we have. The medications are getting better. And it's not your fault. Literally, your metabolism slows down. And your body makes you feel more, hungry when you start to lose weight, because there's a setpoint. And we are just trying to figure out how to overcome that with medications, but we're not there yet." I think patients feel relieved when they hear that.

Paul: Yeah, and we talked about this before recording too. I do think one of the biggest disservices that we've done to patients in terms at least of obesity management, is framing it as a simple math problem and just putting all the onus exactly on the patient just not trying hard enough. And if they just would have taken less calories in than what they required, they would have lost weight. It would just peel off because it's that easy, which is obviously not the case. And it is a far more complicated process than that and your metabolism is working against you in a lot of ways that we don't still fully understand. So, I just think that framework also has to be discarded pretty quickly.

Matt: And then, I know we've gotten some-- I think probably people that hadn't actually listened to our episodes, because I think we've always been very respectful the way that we've talked about this. But I do think that it's important to also point out to the patient that we're not going to pick a specific weight loss target. Like, you don't have to look a certain way to be metabolically healthy. You don't need to look like a Marvel superhero. We are trying to, number one, get you feeling better. And then, number two, we want your metabolic parameters to improve. So, Paul, what do you look at or what do you follow? Do you have the conversation in a similar way?

Paul: Yeah, I've started to, because I think it gets to what are we after here exactly. In anything, there's no utility in just treating an absolute number, how are we promoting health? And so, the concerns that we have with obesity are the comorbidities that tend to ride along with it. So, following their glycemic control, is there A1C getting better? We know that 10% weight loss confers a lot of blood pressure improvements. So, is their blood pressure improving the way that we would like? What's their lipid panel look like? Are we seeing their transaminases tendon down? So, reduced inflammation that you might see with metabolic associated fatty liver disease. Even things like symptoms of sleep apnea, have those improved? I think those are the outcomes that we should probably be focusing on, rather than actually trying to give a concrete number to get to because that's just fairly arbitrary. So, what does

healthy look like for this patient? And I think we have fairly objective metrics we can follow, that show improvements in health.

Matt: The closest I'll come to putting a number on anything is I will just say to the patient, "We know from studies that if you lose 5% weight, you may have some metabolic changes favorable. If you lose 10%, a better chance that some of your metabolic parameters will improve. That's all I can tell you, and we'll see how you're doing how you're feeling, and we can use the tools available to us to try to get you there, and to try to improve these metabolic parameters that you just talked about." And I guess, Paul, the one of the things about the-- you mentioned earlier, I just noticed, once she started telling us not to use this morbid obesity as a diagnosis code, if you actually look, the codes now say, like, Class 1, 2, or 3 obesity with or without complications or serious comorbidities. I think that's a good way to think about it, is like, are their comorbidities? Are they sick from this extra weight that's there? Because if they're not and they feel okay, then it's less clear how aggressive you need to be about that. And I think patients appreciate when you can talk to them that way about it.

Now, Paul, let's start to talk a little bit about treatment here. And tell me, Paul, we're doing a great job, right? Prescribing medications, it's a high percentage of patients, like 99% of patients are on what are the approved therapies?

Paul: [Laughs] Wow.

Matt: Am I right? How are my stats?

Paul: Yeah, no, I think that's true for almost any disease state. We're probably treating all of it 99% correctly. And obesity, the point that you're making here is that we are notoriously undertreating-- at least we are not using the tools that are available to us. So, I think the number thrown out there was less than 1% of patients who would qualify for medications for management of obesity, you're actually receiving those medications. And we have a ton of things at our disposal. We actually didn't even start with the GLP-1 agonists, which are medications that we think of commonly just because we use those with our patients with diabetes so frequently, but we have a lot, a lot of options. So, Matt, I'm going to ask you, what things have changed in terms of your own practice? What are you reaching for now that you've had this episode and gave it some critical thought to how you would like to use medications to manage obesity?

Matt: Yeah, and I want to-- I think some of the audience members, and not many, but we got some emails after this episode saying like, "You guys didn't even talk about GLP-1 agonist." Well, we did. I did listen back to it today. And we kind of brushed through it quickly. But we basically said we're going to talk about what's affordable to most patients, I know certain states, you can get GLP-1 agonists, if you're prescribed them for weight loss. In the place where I practice, Pennsylvania, I'm really only able to get GLP-1 agonists if the patient has type 2 diabetes. So, for my patients with obesity and type 2 diabetes, they're in luck. I can put them on the medications, and I can try to push the dose to get them doing better from that perspective.

But this conversation with Dr. Stanford was really about focusing on what is she doing if cost is an issue and she's not able to access these other medications? So, she talked about the FDA medications. There's couple of them. Phentermine, topiramate, bupropion, naltrexone. And then, there's like orlistat, which she said, "I don't use much of that, because most patients don't like oily underwear." So, enough said. We're not going to talk more about that on this episode. Paul, let's talk about-- she said she splits up the medicines, and she'll start one agent, titrate up. She may start a second agent. But she said, "Even if I had the combination pills available to me affordably, I probably wouldn't go right to them." She prefers to go one agent at a time. So, Paul, tell me about phentermine because I was always terrified of this drug.

Paul: Yeah, no, the same. And just to touch briefly on your earlier point, I think the other reason we didn't dwell on the GLP-1s is because that's a class of medications we already have comfort with. And I think having comfort with these medications is going to be key to prescribing them. So, I think that's probably one of the other reasons we sort of spent a little more time on some of the other classes.

But to your question, phentermine is one that has terrified me as well, historically. Because patients with obesity are more likely to have high blood pressure. It's a medication I'm always a bit reticent to start I worry about it causing hypertension or tachycardia or sort of other sort of cardiovascular concerns. But it turns out that those are not completely unfounded. But also, probably overblown, I guess, is the point that Dr. Cody Stanford made. So, in fact, bupropion, which we'll talk about, is probably more likely to actually negatively impact blood pressure than phentermine is.

So, Dr. Cody Stanford will start at the lowest dose and then increase every three months as needed. She goes low, and she starts slow. She does monitor blood pressure, obviously, and she'll have the patients check at home over multiple times throughout the day, just to get a sense of patterns and kind of make sure that she's not actually causing hypertension. But as she mentioned, it's not something that happens very often. So, she'll just starts at 50 mg per day, and then sort of increase it every three months as she gets to know the patients. And then, if she needs to, classically, we think of phentermine in combination with topiramate, but we talked about other reasons to start topiramate too, but she may add on topiramate after the fact and start at 25 mg, then titrate that up. And that's the medication she tends to start at bedtime, because there are classic cognitive effects that go along with it. So, lovingly referred to as Dopamax by some patients because of the somnolence, and confusion and brain fog that may come along with it.

Matt: Because I had asked her about some of, when does she think about getting a food psychologist involved, and she mentioned people that have issues with eating at nighttime, especially like binge eating and nighttime, topiramate seems to be a good one to try for them. And so, I have used it for that indication, actually, for patients before and I think topiramate is another one that maybe because it cross-purposes with migraines that internists at least-- I think some internists are more comfortable using that one. So, it's a good choice to try. You've just got to make sure the patient doesn't have history of kidney stones. That would be one of the contraindications.

But yeah, so phentermine and Topiramate. Start low, go slow. You can pick one or the other. You can layer them on over time. With phentermine, she did mention she goes about three months or so between dose changes. And then, you've just got to check with your state. I think Ohio and Florida, I believe, are the two states where you might not be able to prescribe long term. You might have to take a break. Go three months, take a break, go three months.

The next two, bupropion and naltrexone, Paul, you already mentioned that bupropion can elevate the blood pressure and the heart rate, maybe even more than phentermine does. But I think as internists, this is another medicine where we should be comfortable with this. We use this for smoking cessation, we use this for depression. So, I think this is a good choice. She says she starts at 150 mg of the sustained release twice a day. So, that's the 12-hour version. And the reason she's doing that is to more closely approximate what would be found in that combination pill that's FDA approved for obesity. And then, the max dose might be they're taken 300 mg in the morning and 150 mg in the evening. And of course, this is like expert opinion, this is in her experience, what she said has worked. And we go a little more in detail on it on the full episode.

Paul, any other comments on that? Before we talk about Naltrexone. I know you have some experience with Naltrexone prescribing for addiction medicine. But have you used it yet for obesity?

Paul: I have only-- because prior to hearing this episode, I had actually used the brand name combination medication with bupropion and naltrexone. I had heard anecdotally that it is good for patients who have that impulse eating that we described earlier. So, there are one or two patients that I've tried it for, that have had moderate success with. I think the evidence for it is not nearly as strong as for the other agents. So, I've used it rarely, but a couple of times, but usually as part of the combination pill, not separately. So, I look forward to having this sort of in my back pocket to use in a different kind of way now.

Matt: Yeah. So, naltrexone and the way she said she uses it, she has patients take like a quarter tab, and then they go up every week or so by a quarter tab until they're taking a half a tab twice a day. And that's the way she does it. It may be given in combination with bupropion. But if you try to prescribe the combination pills of phentermine-topiramate, or bupropion-naltrexone, you run into this cost issue. Most of these combination medications I just mentioned, the weight loss is somewhere on the line of like 6%. That's the average weight loss with them, compared to-- if you get the GLP-1 agonists like semaglutide and push the dose way up, it's like a 15% weight loss. And just more recently, terzepitide, which is this GIP/GLP-1 agonist, Paul, that just came out the week we're recording this anyway, and that one is like 20% weight loss?

Paul: 20% percent. Yeah.

Matt: Seems a lot, like more than half the patients? I mean, it's crazy. I think maybe it's because we're finally getting medications that more address the underlying metabolic changes. Maybe we're changing the setpoint again, I don't know. I think what remains to be seen is, do these patients, if they stop the medications, does the weight all come back? I think the answer is yes, at least some of its going to come back. But I mean, this is a chronic disease thing. So, we're not often stopping blood pressure meds to be like, "Oh, look at that. The blood pressure went back up." I think we have to probably think of this as the same way, Paul.

Paul: Yeah, I agree with all of them.

Matt: So, any last comments about this, Paul? I think we've done, as always, hero's work going through two really great episodes and I learned a lot going back through this again.

Paul: Yeah, as much as I hate hearing the sound of my own voice, I will say revealing for these is always hugely helpful. So, this kind of space learning is helpful for me and I hope it's also helpful for our listeners too.

Matt: One last word of caution for the audience, because I always forget this and I want to-- the meds we just talked about for obesity, all of them should not be used during pregnancy. So, if your patient is pregnant or plans to become pregnant, you should stop the medications and Dr. Sanford actually said the GLP-1 agonists, she stops them a couple of months, because they're so long acting, she tries to stop them two months before they plan to conceive. So, that'll be the last pearl we leave the audience with. And, Paul, will you take us to the outro?

Paul: My pleasure, Matt. This has been another episode of the Curbsiders to bring you a little knowledge food for your brain hole.

Matt: Yummy.

Paul: Great. Get your show notes at *thecurbsiders.com*. And while you're there, sign up for our mailing list to get our weekly show notes in your inbox. Plus, twice each month, you'll get our new Curbsiders digest recapping the latest practice-changing articles, guidelines, and news in internal medicine.

Matt: And we're committed to high-value, practice-changing knowledge. So, we want your feedback. Please subscribe, rate, and review the show on Apple Podcasts or on Spotify. I don't know what Spotify is, Paul. [Paul laughs] Or you can email us at *thecurbsiders@gmail.com*. A reminder that most episodes are available for free CME through VCU Health at *curbsiders.vcuhealth.org*. And a special thanks, Paul, to you for helping to write and produce this episode, and to the whole Curbsiders team. Our episodes are produced and edited by Pod Paste. Elizabeth Proto runs our social media. Stuart Brigham composed our theme music. And now, Paul, until next time, I've been Dr. Matthew Frank Watto.

Paul: And as always, I remain Dr. Paul Nelson Williams. Thank you and goodbye.

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