#383 Hotcakes: Loop Diuretics for CHF, Time Restricted Eating, Breaks from Sitting, Early FMT for C. diff

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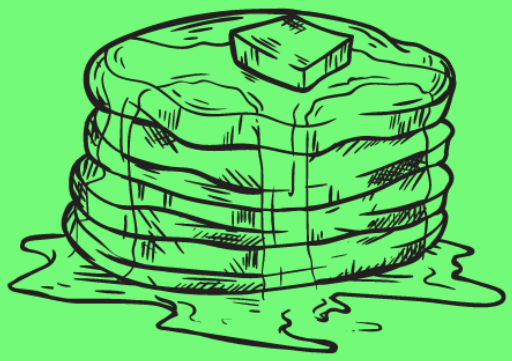

#383 HOTCAKES

Loop Diuretics for CHF

Time Restricted Feeding

Breaks from Sitting

Early Fecal Transplant for Cdiff

Matt: Hey, Paul, did you ever hear that England doesn't have a kidney bank?

Paul: No, I did not hear that, Matt.

Matt: But, Paul, you'll be glad to know it does have a Liverpool.

Paul: Great.

Matt: No, nothing.

[laughter]

Paul: Listeners. You'll find out when that's relevant soon enough, it is not.

[Disclaimer]

[Curbsiders theme]

Matt: Welcome back to the Curbsiders, I'm Dr. Matthew Watto, here with my great friend, Dr. Paul Nelson Williams and on tonight's show it's hotcakes. We're going to be going through a whole bunch of articles and you'll help us figure out whether or not they're practice changing, but we'll certainly give you our take before we introduce our two wonderful co-hosts for this. Paul, will you remind people what is it that we do on the Curbsiders?

Paul: Sure. Normally we're always *the* Internal Medicine podcast, but typically we use expert interviews to bring you clinical pearls and practice-changing knowledge. In that, you just beautifully outlined the hotcakes format. So, we're going to go through some potentially practice-changing articles and try to pick them apart, but not with any kind of nihilism, but with a hopeful, yet critical eye, aided by our two co-hosts, which I'm just going to go ahead and say the names, guys. Say the names. Matt?

Matt: Yep, we need to.

Paul: I'm not sure people are dying of your suspense, so we're joined by Drs. Nora Taranto and Rahul Ganatra. Thank you, guys.

Nora: Hello.

Matt: It now makes even less sense now that people can watch on video and see who's with us because it's not like we're hiding them.

[laughter]

Matt: But I did want to remind people that this and most episodes are available for CME for all health professionals through VCU Health at *curbsiders.vcuhealth.org*. We are going to get to our first article here. Rahul, you want to start us off?

Rahul: So, for my contribution to this week's Hotcakes, I'm going to be talking about the TRANSFORM-HF study. This was the study by Mentz and colleagues, and it appeared in a January 2023 issue of JAMA. So, the research question that these authors were asking was,

among patients hospitalized with acute heart failure, does torsemide reduce all-cause mortality compared with furosemide by at least 20% within 12 months?

So, you might be asking, why is this study important? Well, it turns out there is laboratory, pharmacologic, and clinical evidence to support the hypothesis that torsemide might work better than furosemide. Torsemide starts to block the aldosterone receptor leading to RAS inhibition, reduction in myocardial fibrosis. Torsemide also has better oral bioavailability and a longer half-life than furosemide. There's at least one RCT out there that found that torsemide was associated with lower readmissions for heart failure at one year compared with furosemide.

TRANSFORM-HF is the long-awaited RCT intended to settle this question once and for all. So, how is this study carried out? Well, this was a randomized open-label pragmatic comparative effectiveness trial. It was done at 60 hospitals in the United States from 2018 to 2022. 2800 patients hospitalized with CHF were randomized to torsemide or furosemide at discharge, and the dose was determined by their treating clinicians and they just followed up with their regular cardiologists in line with the pragmatic trial design. The primary outcome in this study was time to death from any cause. So, who were these patients? Well, the mean age was 65. A third of the patients were women. One in three were black. Patients had both chronic decompensated heart failure and acute de novo heart failure, meaning new diagnoses. They included patients with reduced and preserved ejection fractions.

What did the authors find? Well, the topline findings were that there was no difference in all-cause mortality in this study. About 26% of patients in both groups died over a median follow-up of 17 months. You can see this really unequivocally in figure two. The results were consistent across subgroups. Now that I've put the basics out there, I'll stop and ask does anybody have any questions or observations they want to share about how the trial was carried out?

Matt: I just first want to ask Paul about, Paul, TRANSFORM-HF, how do you rate the trial name?

Paul: Solid. I mean, the cardiologists are always ahead of the curve with these. This is a nice one. So well, done team.

Matt: Yeah. Nora, I think I cut you off there, but I just had to ask Paul about the trial name. You know, he's a big trial head.

Paul: Who died a little bit inside? Yeah.

Nora: Now I always spend like, one to two minutes trying to figure out where the letters come from in these names. I did the same for this one today.

Matt: Yeah, I like that they did this trial because this is one of those things where I think we've talked about on the show before. Torsemide seems to have a much more predictable bioavailability, higher, it's like 80% to 100% oral bioavailability versus LASIX is like 10% to 100%, at least according to some 30-year-old study. I was excited to see this one done. Also, I haven't read it yet because I just noticed that this was done. But the great Dr. Kittleson, wrote an editorial about this, so certainly I would have to check that out after this. But Rahul, what do you want to point out about this study because I'd love to know eventually your conclusion, but any limitations or anything you wanted to shine a light on?

Rahul: I mean, like you, Matt, I was also in the team torsemide camp thinking that based on all the reasons we've discussed, torsemide, I was expecting, was going to have benefits that extended beyond the period of acute hospitalization. Tony Breu actually put together a really outstanding Twitter thread on this question summarizing a lot of the data and we'll link to it in the show notes. But this was a negative study and publication of negative studies is really important so that we can decide if we think that a question is settled and can move on or not.

And a question that often gets raised when you're talking about negative studies is, "Could this have been underpowered? Could this have been a false-negative finding?" In my opinion, this study does not look like that. The way that an underpowered negative trial looks is when there is a difference in the point estimate, but the confidence interval just barely misses statistical significance.

This was not the case. It was 26.1% versus 26.2% of patients who reached the primary outcome of All-Cause Mortality in each group. Really, it seems like they're drawn from the same population, no difference there. Could there be subgroups in whom torsemide does have benefits? That's something that's possible and is impossible to really detect with a pragmatic trial. That's one of the sacrifices we make. But this is, I think, kind of how we could expect this to look if were to roll these results out to the general population despite all the mechanistic reasons and hypotheses for why torsemide might be better. This, to me, is pretty compelling evidence that for the general population at large there's probably not a big difference.

Paul: I was going to ask about the primary endpoint. I thought the choice of mortality's endpoint was an interesting one. Obviously, it's important even if you're talking about like knee pain.

Matt: Swing it through the [crosstalk]

[laughter]

Paul: Yeah, well you know, I've said it before, nothing affects quality of life like death. I mean, it's just from a heart failure standpoint, I feel like there're a million possible targets. Can you comment on why this one was chosen rather than hospital readmissions, which I know is a hot topic, or I don't know, symptom management or a million other things? Why death?

Rahul: This is something you are not used to seeing for cardiology and in particular heart failure trials, right? We're used to seeing these composite outcomes that contain lots of badness that is patient-centered. The choice of all-cause mortality has some pros and some cons. One benefit of studying all-cause mortality is that there is really no adjudication required. Either somebody is dead or they are not dead. [Paul laughs] And it doesn't matter the cause. To determine vital status in this study, they use something called the National Death Index, which can be considered as very sensitive and specific for knowing if someone is dead.

[laughter]

Matt: We've definitely talked about a study that used that before. I can't remember which one, but we have.

Rahul: This did make me wonder if reporting delays might be a source of bias, but I couldn't really find anything to elucidate that, so that's a benefit. A downside of studying all-cause mortality is that this is the cream of the crop of impact of a treatment on an outcome. And it can be difficult to show an impact on all-cause mortality particularly for something where the

exposure and the outcome are separated in time by a large amount, where there're opportunities for other things to sort of occur that influence mortality. It's a great outcome, particularly for an open-label study. It removes any concern about the effect of the lack of blinding on an outcome, requires no adjudication, and it's easy to determine, but it can be hard to show an effect.

Matt: I think we're probably going to have to wrap up on this one because we have a big show tonight. So, Rahul, what are your take homes for this? If you dare give a Hotcake rating, please, because at the very least we know the Hotcake rating will annoy Paul.

Rahul: And I would not pass up that opportunity. This was a really well-done study in my mind. It informs a really common clinical decision that we make in the inpatient setting. I interpret these findings as kind of giving me a license to use whichever loop diuretic the patient and I decide on. And I think this was well done. This is important evidence. I give this 4/5 hotcakes.

Matt: Paul, next up. The floor is yours.

Paul: The paper I bring to the group is from Zhao et al. from the Journal of the American Heart Association, this year this month. Eating, sleep intervals, and weight change is what they looked at. The article itself is the association of eating and sleeping intervals with weight change over time, the daily 24 cohort. The question that the authors are asking is "Does time-restricted eating or other eating patterns lead to weight loss or changes in weight in general." I picked this article. I still feel ill-prepared to counsel patients largely about how to eat and what to eat. I know that we've talked about time restricted or intermittent fasting before and there's wild enthusiasm. More recently, last year, there's an article that showed no real benefit or just cognitive restrictions, so, I feel like we still need some more data to kind of come up with good things to tell our patients as to what to do. Because as you know, I just want the answer, I don’t need nuance.

[laughter]

Matt: [crosstalk] tell me what to do. [laughs]

Paul: It's an interesting study it's a multi-site prospective cohort study. It's three big health systems Johns Hopkins, Geisinger, and UPMC and basically what they did is they recruited patients through the electronic health record. You had to have some electronic communication capacity, which I think is actually important. Patients were over the age of 18 and they had to have at least some height and weight measurement in the HR within two years before enrollment. They were recruited through the patient portal or through email. I don't know about you all, but we can talk about this, but if you've ever gotten messages from your patient portal unless you're expecting a result, there's zero chance I'm paying attention to that.

[laughs]

Paul: When patients, if they agreed to go through and they went through the consent process and they filled out the questionnaire properly, didn't screen you that up, then they were enrolled and they logged their meals and how much they ate in terms of whether it was a small meal, a medium meal or large meal, how often they ate and what their sleep looked like on an app that was exclusive for the study that was designed by the authors, all put together. Then they looked at the associations between what the patients recorded and changes in weight with their primary interest being and does the time-restricted eating impact weight loss or not. I will say the thing

that we were hoping to see maybe was that this time-restricted eating would actually cause weight loss, but time from first meal to last meal, how many interval lapsed between your first meal of the day and the your last meal a day that was not associated at all with weight change.

If you had more frequent smaller meals that actually did seem to be associated with weight loss, and if you ate more frequent larger meals, you gain weight. The suggestions that the authors are saying is that this is a suggestion that maybe total calories are still probably an important driver of at least weight gain, which to my money- [crosstalk]

Matt: Make sense.

Paul: -is probably a reasonable conclusion.

Matt: Paul, you mentioned you made the joke about if you're getting messages from the EHR, I mean, they had to send 70,000 plus messages and then they recruited 1000 and then they ended up only getting about half of those people to actually use the Daily-24 app to be enrolled in the study. This is selecting very specific type of person that's answering that kind of message. I guess that's a major limitation.

Paul: This was the thing that I thought most about. I think this was a good study and I think it certainly has information. In terms of the patient that would actually go through with this, it's someone who has technological literacy, who invested in this kind of thing, and who has the time to do it. I also think the fact that the food intake was self-reported is interesting because people tend to underestimate the number of calories they eat that's been studied. The other thing that I thought was this weird half-form thought I had that I'd like to hear what you guys think about is that it's also been shown that people who track their meals also do better with weight loss as well. I wonder if more frequent meals are not a marker of diligence rather than some other fancy metabolic thing.

I don't have evidence to back that up, but I feel like there's a lot of potential for bias and confounding here, even though I don't know how they would have done things much differently. I think this selects for a specific type of patient. I think there're lots of chances to misrepresent, not intentionally how you eat and what you've been eating.

Nora: Yeah. I was also kind of interested in the prior to enrollment data compared to the prospective data and the kind of intentionality that they tried to assess among patients and folks who were enrolled. Because the goal, at least as I could understand it in recruiting individuals was not to recruit people who wanted to lose weight, it was just to assess this. But I do kind of wonder whether there's some component of the observation from the study that actually affected activity and we don't really know exactly how it reflects activity in the real world.

Rahul: Yeah. Paul, you mentioned two of the biggest sources of problems in observational studies, which is bias and confounding. I think that's like the best thing to be on the lookout for in a paper like this. There's one additional problem that these authors highlight that was, I think, a fascinating example of this issue, something called reverse causality, which we've talked about on Hotcakes before. This is another way that the relationship between the exposure and the outcome can be distorted.

The authors bring up the possibility maybe people who lost weight are people who had underlying unmeasured illnesses that made them feel unwell and that's why they ate less. You can imagine, like, cachectic diseases making people feel unwell, their appetite goes down. In a

retrospective study or a study with retrospective elements, that can be really hard to tease out. Good things to be on the lookout for.

Matt: Yeah. I think this was like the people on team time-restricted eating were hoping that the shorter time from your first food to the last meal of the day was helping with weight loss, which we didn't see here. For years I've had people say "Eat small frequent meals, like, that's a good way to lose weight," and I never knew if that was really a thing or not. I don't think we can draw super firm conclusions from this, but I think that as of right now, you don't have super compelling evidence to tell people either way. Just maybe avoid, like Paul said, really large meals that will make your overall calories be more for the day.

Nora: I did find it interesting that the time to first meal from wake up seemed to be somehow related to less weight increase. I don't know whether you guys had any thoughts about that. You hear it kind of anecdotally that eating earlier in the day is better for energy metabolism, but I'm not sure whether that's actually database at all.

Paul: Well, I saw a different study that showed people who skip breakfast actually tend to lose more weight.

Nora: Right.

Paul: I feel like the more studies we do, [Nora laughs] the less we know. So, keep them up, I guess.

[laughter]

Rahul: It does make you wonder if maybe the mechanism of any putative benefit in time-restricted eating is people just end up eating fewer calories. That is compatible with the findings of this study. So, yeah, I agree. I think it's not really clear.

Nora: Yep.

Matt: All right, well, Paul, I think it's time for your take-home points and your Hotcakes rating from this.

Paul: Yeah, my take on points is I'm glad that people are adding to this body of knowledge. It's because it's something we're going to be talking about endlessly. I don't think this is super helpful in terms of guiding the discussion with patients, but more data is always better or usually better at least. I'll give it, I think I'm going to go say two and a half Hotcakes spaced out over the course of the day, so eating in six small meals.

[laughter]

Rahul: As a homerun, that's good.

Matt: All right, next up, I'm going to be presenting a paper by Andrea Duran et al. This is a group out of the Columbia University Medical Center in New York and this was published ahead of print in December 2022. They were trying to answer the question, what is the optimal frequency and duration for sedentary breaks to improve blood glucose that was a primary outcome and blood pressure that was a secondary outcome during an eight-hour sedentary period. You hear this sitting is the new smoking has been said over the past few years. And I

actually looked it up. There's a paper from 2018 which we could link to for the show notes, but it's hilarious. They're like, actually, that's not correct. [Paul laughs] While sitting is not great, the hazard ratio for mortality or whatever statistic they're looking at is like way less. Smoking is definitely worse than sitting.

[laughter]

Matt: But still, I do still think this is an important study and there are some associations with sitting and mortality and increased blood pressure and being sedentary. So, it is worth looking at. So, this is where they randomized. It was only 11 healthy adults. They were actually trying to randomize more than that, but COVID happened so they stopped enrollment. These were adults over 45 years old and they had to be sedentary for about 8 hours a day on average. They couldn't have any underlying conditions and they shouldn't be exercising too much, no more than three days a week. They brought them into a lab and they gave them a standardized breakfast and lunch. They experimented with walking breaks on a treadmill every half hour or every hour and they varied the length of the break.

They're trying to find the minimal effective dose of light physical activity to improve blood sugar and blood pressure. I thought it was a pretty cool study and this got a lot of play in the news. The topline results were like taking short breaks from sitting can drastically lower your blood sugar and can lower your blood pressure. So, that was the topline result. So, questions, comments, concerns? Maybe, Rahul, we can start with you here.

Rahul: Yeah, Matt, I think the thoughts that you shared before we recorded about this paper are really sophisticated, so I want to get out of your way and let you do that. I will just say though this paper is full of gems of lines. There's a line where they describe walking and they say walking was selected as the activity modality because compared with other aerobic activities, it is popular, familiar, convenient, and free. I hope somebody describes interacting with me like that someday because that's just a home run.

[laughter]

Matt: What about you Paul, anything, any questions or comments?

Paul: More questions? We talked a little about this, but I would just like to hear you say who are these 11 people. I'm just trying to think [Matt laughs] because it seems like they were pretty healthy based on what I'm reading, but they also didn't exercise and then also were often sedentary. It's like this weird unicorn person who's maybe not, again I apologize if you're one of these 11 people part of the study, to make it to 45 without being intentional about being healthy and then not having any major health problems, which actually were excluded in my understanding from the study, I guess I would like to hear about this population.

Matt: Well, a fair amount of them had prediabetes I think. Two of them are on blood pressure medication, so it wasn't like they were totally devoid, but they didn't have any major end-organ disease. High blood pressure, I consider, I thought that would have been exclusion criteria but when I was reading through, some of the patients did have high blood pressure. What's interesting about this is they looked at both periods of 1 minute of walking it was just on a treadmill at 2 miles per hour or 5 minutes of walking. They did 1 minute every 30 or 5 minutes every 30 or 1 minute every 60, or 5 minutes every 60 minutes of sitting. They found that for lowering blood sugar it looks like if you walk 5 minutes for every 30 minutes you're sitting, that seems to really lower blood sugar. My reading of this was like the difference between a totally

sedentary person and somebody walking 5 minutes out of every 30, there was like almost a 33-point difference in blood sugar at the peak after a meal.

They were given these standardized meals and they had continuous glucose monitors they were checking every 15 minutes. So, it did really blunt the peak. They also had lower nadir of blood sugar as well compared to the people who were sedentary. It did seem like it was regulating it. The blood sugar effects were really just seen with the 5-minute walking group out of every 30 minutes, but not the 5 minutes walking every 60 minutes. So, it's pretty frequent breaks. I'm not sure how realistic that is for the average office worker, but the blood pressure even just walking 1 minute out of every 30 or 1 minute out of every 60 on average, there was like a three to five-point drop in blood pressure just for taking those brief breaks.

I think all this stuff about the blood sugar and blood pressure has been shown in other studies. They were just trying to find like a minimum effective dose for this and something that was practical. I do think more research should be done on this. I just think this was such a small and controlled study in a specific group of patients that I just wonder would the effects be a lot bigger if you had a sicker group, like people who had dysregulated blood sugar, would it plummet even more and would the blood pressure drop even more? I definitely think this is worth looking into because like Rahul said it's free and it's a familiar activity. [laughs]

Paul: And goshdarnit, it's fun. [Matt laughs]

Nora: I also wonder how it would compare or add on to the baseline exercise recommendations that we give to patients in general, not that everyone is doing that. I kind of wonder whether, given that they completely restricted patients from actually exercising during the five days, kind of how that would change the results.

Matt: Yeah, because we talked on the last hotcakes about the 150 minutes, whether you do it in one or two days, or if you do it space it out over three or more days, you still reap those mortality benefits from that. I think this is very interesting and it makes for really sexy headlines, but this is why it's important to always look it up because I think this is a great hypothesis-generating study in my opinion, but not necessarily one that we can all just automatically tell everyone to start taking 5-minute breaks out of every 30. Although, I don't think that would hurt people and it'd probably get them more goes closer to their activity goal.

Rahul: It sounds pretty good actually. Can I say one more thing? I shouldn't have squandered my time joking around, because I did have one thing I actually wanted to say. This study had a red flag for me. This was a positive trial, meaning an association was shown between one of their exposures and the outcome. When I go to look up the protocol, I actually can't find the study protocol registered anywhere. That's really the only tool you have to kind of evaluate whether the primary outcome was changed or if there are any deviations from what they plan to do that could bias towards a positive finding. Something to look for in the appraisal of positive studies that was missing in this case.

Matt: I'm going to give this 3.5 Hotcakes rating, and that's for the reason that I stated. I don't think this is ready to change the way I'm counseling patients, although I do think it's probably great to take breaks from sitting. Even though sitting is not as bad as smoking, I still think patients should just try to make an effort to just, in general, move your body, be more active.

Nora: [unintelligible [00:26:10] we've been on here for like, 45 minutes.

Rahul: I think we need to walk around.

[laughter]

Nora: We are doing this on a treadmill.

Matt: I have one of those little mini bikes under my desk. I've just been pedaling the whole time.

Nora: Pedaling away. [laughs]

Matt: All right, Nora, let's get to your study. Time to talk about one of our favorite topics on the show, poo.

Nora: It's so true, you can't escape it. It's one of our favorite, favorite things. This is a really interesting study that came out in December of 2022 in Lancet Gastroenterology & Hepatology by Baunwall et al. This is the result of the EarlyFMT trial. It looked to address the question, does that early use of fecal transplant during first or second episode of C. diff infection improve the rate of symptom resolution compared to the standard of care, which is treatment with vancomycin alone? Importantly, this was looking at the addition of fecal transplant to vancomycin. The trial was a randomized, double-blind, placebo-controlled trial. It enrolled 42 patients ultimately. These were patients who were diagnosed with either a first or second episode of C. diff infection that's with greater than three watery stools per day and then a positive C. diff PCR. Patients were randomized either to fecal transplant after treatment with vancomycin for a standard of care for at least 10 days or just vancomycin alone with a placebo capsule.

The fecal transplant was given twice as was the placebo on day one and day three through seven for the second dose. Patients were followed for either eight weeks or until C. diff recurrence if it happened earlier. The primary outcome was the resolution of C. diff-associated diarrhea eight weeks after the study treatment.

The results topline were actually quite interesting. The trial was actually stopped early after the interim analysis of 42 of the intended 84 patients because there was a significantly lower rate of resolution of C. diff infections in the placebo group than the transplant group.

To put specific numbers to that, there was a 90% resolution achieved with transplant. That's in 19 of 21 patients with fecal transplant compared to 33% or seven of 21 in the placebo arm. I'm curious what questions you all had in reading this trial and what your initial thoughts were.

Matt: I have to ask my standard first question. Paul, this was called the early FMT trial. [Nora laughs] What do you give A for effort or? [laughs]

Paul: I kind of like it. It says what it is. I don't know. There's nothing wrong with that. There's no shame in that.

Matt: Okay, they didn't really cram in an acronym.

Nora: It was a trial that was done in Denmark, so I don't know whether they were just going for clarity here.

Paul: So, universality, right? It may not have translated well.

Nora: Exactly, exactly.

Paul: This might actually be [unintelligible [00:29:31] the show.

Nora: I don't know what it was in Danish.

[laughter]

Matt: All right, any of our Danish listeners, please let us know.

[laughter]

Paul: I think we have some.

Matt: I'm sure we do. Yeah. I'm being serious. Please let us know if there was a catchy title to this one. Paul, any comments about this one?

Paul: Nothing earth-shattering. Be curious to hear what the rest of you all think. But this all makes sense to me. It should have worked out and it looks like it didn't work out. I think just mechanistically, this kind of met what my expectations are going to be, so I couldn't find a whole lot to complain about, I'll be honest.

Matt: As I said to you beforehand, I mean, years ago on the show, we did a C. diff episode and our guest said, I think stool transplants in the future will be given after the course of antibiotics to repopulate the flora. You're treating dysbiosis with antibiotics. That's the old way. Now, this new way is like you treat the bacteria and then you try to repopulate with healthy flora again. So, it does make sense mechanistically, they were looking to enroll 84 patients here and they stopped it early after they had only enrolled half the patients because it was working so well. The 90% efficacy that's pretty much what we've seen with patients who are getting it for a third recurrence. Like the more traditional threshold for prescribing.

Rahul: I'll just add, this for me was very reminiscent of that paper in 2013 in the New England Journal. Not by the same authors, but that was kind of the first paper to gain widespread attention among a general audience establishing the efficacy of FMT for multiple recurrences of C. diff. And that was also stopped early. We talked a lot, when that paper came out, about what are the consequences of stopping studies early? I actually don't think that that's a huge concern for me in this study. They captured the biologically relevant time frame for the recurrence of C. diff which CDC defines as the first eight weeks.

One thing that is a little troubling to me is that the lack of resolution in the vanc group was a lot-- The vanc group did a lot worse than I think vancomycin-treated patients typically do. CDC says that one in six people often are at risk for experiencing recurrence after their first infection. I think only 33% of patients had resolution of diarrhea after vancomycin alone in the placebo group. I'm not quite sure what was up with that.

Nora: I do wonder I know the inclusion criteria and exclusion criteria were a little bit more welcoming than other trials prior, in that they included immunocompromised patients, patients who lived in nursing homes. I do wonder whether some of that has to do with some kind of overall frailty and higher risk recurrence just in the population generally.

Rahul: Mm, that's great, though.

Matt: Yeah. I think Nora, do you want to get to take-home points? Is there anything else you wanted to say about this one?

Nora: I think that this data is exciting to me and quite promising in terms of changing the standard of care for first and second-line C. diff infection. The issue that we had talked a little bit about before that I think remains to be worked out, is a standardization of these products and accessibility of these products. I think in the paper they quoted something like "Only 10% of patients who were eligible for third-line fecal transplant treatment actually went on to receive it." I think there's a gap between the data and the eligible populations and actually being able to get it. But we do now have an FDA-approved fecal transplant drug as of December 2022.

Matt: Yeah, I think we're going to start seeing this once the logistics are worked out. I imagine this and maybe there will be more trials, but I think we're going to start seeing it earlier. People go to these earlier than we have seen in the past, and maybe they'll find a minimal effective dose. I think they were giving at least 25 capsules here, like, was the median or something like that? So, I think it'll be interesting. Nora, you mentioned just for further reading for the audience, they should read the methods section about how they prepared the capsules, it was riveting.

Nora: That was the exact word I was going to use. It was indeed riveting. On that note, in terms of the specific number of capsules, I would give this trial, for Hotcakes I would probably say, like, four capsules.

Matt: Four capsules, okay.

Nora: Yeah.

[laughter]

Matt: To round things out here, Paul and I both talked about nutrition, fitness, weight loss-type things, and this popped up on my radar. It was a 60-minute segment that pretty much ran, in my opinion, like an ad for semaglutide, which is a medication that I do prescribe often and I think has a great place, it's great to have now chronic medications that we're using to treat obesity. But the way that this 60 minutes' episode was edited, it just seemed more like it was an ad for the medication than actually, they didn't talk anything about going upstream and trying to prevent obesity, and they didn't acknowledge at all that America is just like this toxic food environment where people are you know really the right choice is almost never the easy choice when you're trying to choose what you're going to eat and it's not clear what people should be eating.

I think school lunches, having four kids in elementary school are a total nightmare, there's sugar in every meal, and trying to prevent people from gaining weight should be a lot more of an effort than there is and there're all sorts of malevolent forces at very high levels, people are pawns in this as were saying before. But I do think that the other part of the 60 minutes' episode that I didn't love was it kind of came off the way it was edited, as if patients there's no agency, that we have no hope that we're all just going to become obese. And I don't think that's true. I think we really need to, as physicians, try to advocate when we can try to get our patients moving, eating the right things, and trying wherever we can, voting to get this situation improved.

I'm not sure if anyone else has any comments on this, but semaglutide and these drugs are just blowing up right now and I feel like we need them because things are so bad that we have so many people that just like that's the only way they can be helped right now. Hopefully, we could prevent people from getting to that point.

Paul: You're talking to a primary care doctor that speaks to my soul like education and prevention. We think so much about preventing things like cancer or disease and I think also part of our job is just to maintain and preserve health as well. I think doing that early and making sure that education is part of the process is important. Like, we talked about, off air, I'll say the phrase again, I think we're fighting a capitalist hellscape that reinforces a lot of this stuff. You do the best that you can, but I think you're right that education has to start early and we have to give people the tools to actually preserve their health.

Matt: Nora, I just wanted to ask. I mean you're the editor of the digest, will Ozempic face be covered in the digest?

[laughter]

Nora: I have a feeling it'll be coming up in the next few issues. It's a hot topic right now.

[laughter]

Nora: It is a very interesting phenomenon that I think we'll see more and more and that obviously has had a lot of coverage in the news, kind of broadly speaking, not just in the medical space.

Matt: Yeah. There was a New York Times article a couple weeks back probably by the time this airs that just talking about people's face becoming so gaunt that they have just skin hanging off it and it looks like they're aging super-fast because I think semaglutide has fallen into the hands of a lot of people who maybe don't need to lose so much weight. The enthusiasm has kind of run wild. Yeah. Look it up, everybody, Ozempic face.

[laughter]

[music]

Matt: Any final comments before we get to the outro? I think we've done a great job tonight. Rahul, thank you for guiding us through all these articles.

Rahul: No, anytime. I didn't really do anything. You all are guiding yourselves.

Paul: This has been another episode of the Curbsiders bringing you a little knowledge food for your brain hole.

Rahul: Yummy.

Nora: Yummy.

Paul: All right, nice. [laughs] Get your show notes at *thecurbsiders.com* and sign up for our mailing list to get our weekly show notes in your inbox. Plus, twice each month you'll get our

Curbsiders Digest recapping the latest practice-changing articles, guidelines, and news in internal medicine.

Matt: We're committed to high-value practice changing knowledge and we want your feedback, so please subscribe, rate, and review the show. You could follow us on YouTube, Spotify, or Apple Podcasts. You can also email us at *askcurbsiders@gmail.com*. A reminder that this and most episodes are available for free CME through VCU Health at *curbsiders.vcuhealth.org*. I wanted to thank Paul, Rahul, and Nora for helping to write and produce this episode. Our technical production is done by the team at Pod Paste. Elizabeth Proto and Jen Watto run our social media and Stuart Brigham composed our theme music. With all that, until next time, I've been Dr. Matthew Frank Watto.

Rahul: I've been Dr. Rahul Ganatra.

Nora: I've been Dr. Nora Taranto.

[laughter]

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

[Transcript provided by SpeechDocs Podcast Transcription]