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Maintaining Weight Loss: Early Evidence on Microbiome-Derived Supplementation

Dr. Maeusli:

Welcome to *NutritionEdge* on ReachMD. I'm Dr. Mimi Maeusli.

Dr. Blevins:

And I'm Dr. Hallie Blevins. Mimi, it's so good to get back together and chat about some interesting science.

Dr. Maeusli:

Yeah, Hallie, I'm so excited to do this with you again.

Dr. Blevins:

Today we'll be diving into a paper published in *Nature Medicine* in May 2026 that looked at how dietary supplementation with a pasteurized bacterial strain, *Akkermansia muciniphila*, also called *A. muciniphila* or Muc^T, could help people maintain weight loss after dieting.

Dr. Maeusli:

I think that we can start off our conversation today by framing why this research matters. To start, people can lose weight to help achieve their health goals, but sometimes, maintaining that weight loss can be challenging for some people. What gut microbial research has started to uncover is that the issue of keeping that weight off can sometimes go beyond an individual's willpower to maintain those healthy habits.

And so I'd say that the broader goal of this study was to look at whether there may be any underlying biological mechanisms that can impact this weight regain, especially as it relates to the gut barrier in taking supplements derived from bacteria. The study focused on a bacteria called *Akkermansia muciniphila*. It's a well-studied species in the context of the gut microbiome, but what sets it apart is the clinical evidence supporting its relevance in the gut barrier biology and metabolic health. I'd say there's a decent amount of pre- and postbiotic research, but a lot of it has yet to take that next step beyond correlation-based microbiome associations. But the scientists behind this study, along with many other scientists who've studied *Akkermansia*, have built a strong case for *Akkermansia muciniphila*.

I'll also add that *Akkermansia muciniphila* is present in more than 90 percent of healthy adults. It lives in the mucus layer coating the intestinal epithelium, and it actually feeds on the mucus proteins, which helps stimulate that healthy, protective mucus layer in the gut.

This specific study was looking at the bacterial strain of *Akkermansia muciniphila* called Muc^T. But what's interesting is that they've actually done some mouse studies on this Muc^T strain, and so the dietary supplementation with Muc^T prevented diet-induced obesity and helped regulate metabolic health and gut barrier function.

Dr. Blevins:

That's what I found when I was looking a little more into this too. There's a lot of other studies on Muc^T. And while there are also other candidates for the microbiome for obesity, they're mostly preclinical, and they face a lot of challenges in terms of shelf life and commercialization. And Muc^T is on the frontlines, for obesity at least. In fact, pasteurized *A. muciniphila* Muc^T is pretty regulatorily advanced. It was the first next-generation bacterium to receive full regulatory approval anywhere. The European Food Safety Authority evaluated it as a novel food starting in 2019 and then issued a positive safety opinion in 2021, followed by a formal EU authorization in 2022.

Now, in the US, there are only two FDA drug approvals for microbiome therapeutics, and neither one of them is for obesity or weight

management, but Muc^T is sold as a dietary supplement. And when I was looking into these other two FDA-approved microbiome therapeutics in the US, I saw it was the live strains, and it had me questioning, why are we using the pasteurized version of Muc^T? And the reason for that really comes down to the shelf stability and the therapeutic predictability. In terms of the shelf stability, *A. muciniphila* really comes down to one protein. Prior research identified Amuc_1100, a protein that sits on the outer membrane of *A. muciniphila*. And in preclinical models of obesity and diabetes, Amuc_1100 alone—the purified protein alone—produced a lot of the benefits that we see with the pasteurized *A. muciniphila*.

So researchers think a lot of the therapeutic benefits of *A. muciniphila* come from this one surface protein. And in these studies, they also found that this protein is really resilient, especially to high temperatures for pasteurization. *A. muciniphila* is also an anaerobic bacterium because it's produced in the gut. Because it's anaerobic, it also makes commercialization challenging. You can't expose it to air, pH, things like that. So the live bacteria itself are just difficult.

At the end of the day, pasteurization makes more sense for *A. muciniphila*, which is fantastic. In terms of therapeutic predictability, having it pasteurized also avoids any potential impact on bacterial colonization or microbial communities that could occur with live strains. If you take a live strain and it does impact your microbial environment, it could influence the therapeutic response and things like that.

Dr. Maeusli:

I'd add one thing. In terms of the operational advantage that you mentioned, we might think that purifying the protein at scale might work, but I think that could potentially be expensive. I think, Hallie, based on your experience, you probably know a bit more than I do about that.

Dr. Blevins:

Yeah, it probably would be more expensive to use the purified protein in terms of manufacturing and probably to the consumer. Although I looked at the study they cited on purified Amuc_1100, and they were able to administer the protein orally to mice by gavage in solution.

Dr. Maeusli:

And that was really interesting because oral delivery is pretty challenging for biotherapeutic proteins because of the harsh GI environment and stomach. But the study showed that Amuc_1100 remained biologically active or effective after oral administration, although they didn't actually investigate the pharmacology and pharmaceuticals behind that.

And also, in terms of the process for manufacturing, if you think about the bioreactors, at these large scales, they can pasteurize directly in that same fermenter, and so there's a lot lower risk of contamination. So yeah, I thought that was a pretty clever and advantageous use of the pasteurized Muc^T.

Dr. Blevins:

I agree.

Dr. Maeusli:

One last thing before we get into today's study I also thought was interesting—I think it was the same investigators, but I'm not entirely sure—but there was a small three-month randomized controlled trial for people who were overweight and had metabolic syndrome that showed that this pasteurized specific Muc^T supplementation was safe and decreased fasting insulin and total cholesterol. And they also saw that the data trended towards an effect on weight loss, and so I think this was the study that effectively led to the longer study that we're about to talk about today. Hallie, do you mind going over the study design?

Dr. Blevins:

Yeah, I can do that. So this was a double-blind, randomized, placebo-controlled trial, so checking off quite a few good boxes there. It enrolled adults aged between 20 and 70—a pretty good range—who were overweight or had obesity. They were enrolled and went through an eight-week weight loss phase using a strict low-energy diet and meal replacements, and they were aiming for at least 8 percent body weight loss. 84 people who hit that 8 percent target were randomized one to one to Muc^T or placebo, and then they entered a 24-week weight maintenance phase where they followed an ad libitum healthy diet, which is just at your leisure. 80 participants completed the trial, and clinical assessments happened at week zero; week eight, which is the end of the weight loss period and the beginning of the weight maintenance period; and then at week 32, which is the end of the weight maintenance period. And they had additional weigh-ins throughout that.

In terms of the capsule design of Muc^T, the active capsule contained 30 billion heat-treated Muc^T cells, which is crazy to think that you're just eating 30 billion cells. That just is mind-blowing. But those cells were pasteurized at 70 degrees Celsius for 30 minutes, and the total

capsule weighed 400 milligrams. The placebo was made by the same manufacturer and matched in appearance, texture, color, and weight because, remember, this is double-blinded, except it used maltodextrin instead of the Muc^T bacterial cells.

Dr. Maeusli:

Yeah. I wasn't sure if you had maybe questioned this, but when I was reading the paper, I was like, "Why weren't the placebo and active capsules matched gram for gram?" And that confused me a little bit for a second, but then I was trying to think about it, and they probably had to account for the capsule fill properties, so density, texture, compressibility, and all that. And if you think about it, I think the additional filler for the placebo group was maltodextrin. And so relative to normal carbohydrate intake, that small amount of maltodextrin probably was going to have a negligible effect. But it was something that I thought of as, "Hmm, why didn't they just put 198 milligrams of maltodextrin and then match it gram for gram?"

For example, for Muc^T, we had 198 milligrams of the cellular pasteurized biomass. And so for the placebo capsule, I would have thought that they would add 198 milligrams of maltodextrin filler as like a one-for-one in terms of the gram weight. However, they didn't do that, and I think that's probably because of the densities and those fill properties that I mentioned that maybe weren't reported in the paper.

Dr. Blevins:

I think it does come down to that. I think at the end, both capsules weighed 400 milligrams, so weight for weight, it did weigh about the same. But I don't have a complete answer for that. I'm not sure.

Dr. Maeusli:

No, I just thought it was an interesting thing.

Dr. Blevins:

I guess if you have another friend in the trial and they're like, "My pill weighs significantly lighter than your pill," they could make some deductions there. No longer double blind.

Dr. Maeusli:

I think you did a great job summarizing the study design and the capsule design. So let's talk about what their primary outcome was. Their primary outcome was looking at the change in body weight after the 24-week maintenance period. So they were on this eight-week diet, and then at eight weeks, they did the 24 weeks of maintenance. And essentially, they were asking, did Muc^T reduce weight regain during that 24 weeks? And in short, the answer was yes.

So the Muc^T group regained less weight than the placebo recipients in the maintenance phase. And actually, the average weight regain was 1.2 kilograms for the Muc^T group, whereas the placebo group regained 3.2 kilograms on average. And to corroborate some of those numbers, the Muc^T group also had a 3.1-kilogram greater net weight loss from baseline to the end of the maintenance phase compared to the placebo group. And then in speaking in relative terms, the percentage of weight that they regained relative to the initial eight-week diet was about 14 percent in the Muc^T group, whereas it was almost 33 percent in the placebo group.

So I know that was a lot of numbers that I'm throwing out there, but basically what that means in terms of the percentage weight is the placebo participants regained roughly a third of what they'd lost, whereas the Muc^T participants regained under a sixth of the weight loss.

One last thing I just want to add about that is that about 40 percent of the participants in the Muc^T group continued losing weight during the maintenance phase. And this was in the context where calories weren't restricted and those diets were varied, as it was ad libitum, compared with only about 5 percent in the placebo group. So I thought that was pretty interesting to see and pretty powerful information.

Dr. Blevins:

Yeah. You said regaining one third of their weight back in placebo versus one sixth, so that's almost half, right?

Dr. Maeusli:

Yeah. Pretty crazy that it's just the pasteurized capsule that can do that for, what is it? Five, five and a half months?

Dr. Blevins:

Yeah. Pretty neat.

So the primary outcomes were really good. The whole point of the secondary outcomes, I would say, was to figure out why the primary outcomes were happening and figure out the mechanism behind Muc^T and what was improving the weight maintenance in that group.

So I'm going to start with body composition. Fat mass, lean mass, and waist and hip circumferences did have a trend in decreasing, and there was less regain in fat mass and visceral fat in the Muc^T group, but none of them were significant. So the trend was there, but it did not reach statistical significance. There was also no difference in lipids, inflammation, or other cardiometabolic parameters. Liver, renal, and thyroid function, no difference.

Now, when we get to insulin sensitivity and glucose metabolism, this was kind of a mixed bag of results. HOMA-IR, which stands for Homeostatic Model Assessment of Insulin Resistance, is basically a calculation that estimates how well your body responds to insulin using your fasting blood sugar and your fasting insulin levels. So the HOMA-IR and fasting plasma glucose levels trended towards improvement, but they were not significant. Fasting insulin and hepatic insulin resistance index were also not significant. But—and a huge “but”—the Matsuda Index, which is a measure of whole body insulin sensitivity, was significant with the Muc^T group retaining sensitivity better than the placebo group. And then on top of that, they did a sensitivity analysis, which removed an outlier—a person who had extreme fasting plasma insulin—and the sensitivity analysis showed that fasting insulin was significant as well as HOMA-IR and the Matsuda Index. So I think, depending on which metric you're looking at, it could be interpreted different ways. But I think overall insulin definitely played a role here, whether big or small.

Dr. Maeusli:

I'm just going to try to unpack what I was reading, and maybe you can chime in. I was reading it a little bit differently. So the Matsuda Index before adjusting for weight regain was, I think, significant. But after they adjusted for weight, they kind of lost that effect. And so essentially, if both groups had regained the same amount of weight, the question would be, would the Muc^T recipients still show a difference in insulin sensitivity? And I think what they actually found was no once they adjusted for the weight regain, but I could be wrong. But I think, in a sense, it's like we see some sort of activity in the insulin response driven by the body weight changes, but it's not necessarily an independent response of the weight. Does that make sense? So insulin sensitivity would be like a downstream effect of Muc^T's impact on weight.

I think either way you raise a good point, and the way the paper positioned itself, there is a lot of foundational research showing that there might be an effect on insulin sensitivity, and they weren't able to show that in this case based on the weight regain. But that doesn't mean that it's not important in the sense that losing that weight does still have an impact on the insulin sensitivity. But whether that's an independent effect or not was the question, and it doesn't seem to be so, but that might be different if they do a larger scale study or if they don't do the variable diets, for example.

Dr. Blevins:

Yeah. I would agree with that. I think this was probably a little small and it was probably a little short; this whole study was. So I think insulin sensitivity maybe does play a role, but it's not *the* role. You know what I mean?

Dr. Maeusli:

Yeah, exactly.

Dr. Blevins:

And then speaking of what did play the role or most likely played the role, so things that did show an effect, we'll start with fecal energy loss, which is the amount of unabsorbed calories and energy from food that leaves the body instead of being digested and used. Basically, what this found was that patients receiving Muc^T had an increase in fecal energy content compared to placebo, but it was not statistically significant between the two groups. However, within the Muc^T group, there was a negative correlation between changes in fecal energy content and changes in body weight, and that correlation was not present in the placebo group. So basically, in the Muc^T group, higher fecal energy content was associated with reduced weight regain. So that would suggest that the increased energy loss via feces might be part of one of the ways Muc^T improves that weight maintenance.

In the Muc^T group, the other thing they did was a subcutaneous adipose tissue transcriptomic study, which I'm going to call SCAT for obvious reasons. Basically, they took a piece of tissue subcutaneously, and they sent it for RNA sequencing. They did that during the weight maintenance phase. And what they found was patients taking the Muc^T had robust transcriptional remodeling with 3,101 differentially expressed genes compared to the 853 in placebo. You can definitely see transcriptionally things are underway in the Muc^T group.

Within the Muc^T group, genes tied to mitochondrial function, calcium handling, and energy expenditure were turned up while immune and inflammatory signaling genes were turned down. More specifically, in the immune and inflammatory signaling, this included genes in the innate immune signaling pathways, and those were related to adipose tissue macrophages.

Now, this actually goes back to something that the authors talked about in the introduction, which was another RNA-Seq study that was done in humans and mice that showed that adipose tissue kind of retains an obesity memory. It remembers the inflammation and things that happen during obesity. So even after weight loss, there's persistent macrophage infiltration and inflammation that's going on in the adipose tissue. And so what this RNA sequencing study and the SCAT experiment showed was that Muc^T is likely decreasing these immune signaling pathways related to these adipose tissue macrophages. So they think that Muc^T may block or suppress that immune and inflammatory signaling coming from that obesity memory, which I thought was very interesting.

Other metabolic pathways that were upregulated were things like the electron transport chain and citric acid cycle, which is great. And all of that points towards more metabolically active and less inflamed fat tissue during the regain in the weight maintenance period. On the other hand, in the placebo group, lipid metabolism, adipogenesis, and immune activation players were upregulated. And then they also did a histology study, but they didn't see any differences in adipocyte diameter, size, area, or anything like that between the Muc^T and the placebo groups.

Dr. Maeusli:

For those just joining us, you're listening to *NutritionEdge* on ReachMD.

I'm Dr. Mimi Maeusli.

Dr. Blevins:

And I'm Dr. Hallie Blevins.

Dr. Maeusli:

Hallie, I think you did a great job of summarizing the fecal energy loss data and the transcriptomics data. Next, what I wanted to do is take a minute to talk about their assessment of the gut microbiome. So this is where I'm just going to unleash the nerd.

Dr. Blevins:

Let it out.

Dr. Maeusli:

I'm a little bit of a microbe nerd. I love the little bacteria. They're great.

So in terms of the first question about the gut microbial community, the authors were asking, essentially, did the orally administered non-viable, so the pasteurized Muc^T, impact or restructure the gut microbiome? And they did this by using 16S rRNA sequencing, which is a common way to identify or barcode the microbes that are present by amplifying the 16S rRNA gene sequence. And so that's a sequence that's present in all bacteria but contains a variable region specific to the bacteria, kind of like just what I had mentioned before. It's a barcode, and it's pretty much good to the genus level and sometimes down to the species as well.

But one thing that's important to remember in our conversation today is that this can't discern whether the bacteria are live or dead. So once they did this sequencing and then the bioinformatic magic, they were looking at alpha and beta diversity. And so alpha diversity is the diversity within a sample, so how many different types of bacteria are present in that sample? And what are the relative abundances in one participant's stool at each collection time point? And then the beta diversity is more of the diversity between the samples, and so it's, how is the overall bacterial community over time changing potentially? And did it shift differently between the Muc^T group and then the placebo group?

And what they ultimately found was that there were no major changes in the alpha and beta diversity, which is actually an expected result because it's pasteurized Muc^T, so this is actually a good thing. It probably shouldn't colonize the gut, and it's unlikely to restructure the microbial community. So I just wanted to call that out because this is an expected result, or at least one that we would have hoped for.

Dr. Blevins:

A positive negative result.

Dr. Maeusli:

Exactly. And you know what? In science, when you can have one of those, you take it.

Dr. Blevins:

We like it.

Dr. Maeusli:

Exactly. And then one thing I wanted to call out is that the beta diversity during the weight loss phase, so not the weight maintenance

phase that we're talking about today, actually did show some modest shifts between the groups. But ultimately, there was no significant change in the weight maintenance phase, which is where we focused today.

And they also took a quick look at fecal and plasma microbial metabolites, so they're looking at short chain fatty acids, branched chain fatty acids, and changes over time in the stool. And these are fermentation byproducts of gut bacteria, and essentially, they didn't see any changes there either, meaning that the bacterial metabolism or activity isn't changing, really, between the groups. So ultimately, the data supports the idea that Muc^T is acting directly on the host biology as opposed to the microbial ecology itself, which is an interesting finding for these investigators.

The last part that I wanted to talk about that also has to do with the gut microbial ecology is the exploratory analysis that they did with the baseline abundance of *Akkermansia muciniphila*. So this was where they wanted to see whether the baseline abundance of *Akkermansia muciniphila*—so this is the native *Akkermansia* in the gut, not the Muc^T—could predict who responds to the pasteurized Muc^T supplementation. And so the participants were stratified into low versus high baseline *Akkermansia muciniphila* by measuring how much of its DNA was present in the participant's stool at eight weeks. So this is the point at which they had finished the weight loss diet and the start of the weight maintenance phase.

And what they found was that within the Muc^T group, participants with low baseline *Akkermansia muciniphila* abundance experienced less weight regain, and then there was a greater total weight loss from baseline, better insulin sensitivity, and higher fecal energy content. But none of these abundance-based differences were seen in the placebo group. So that was interesting.

And so this post-hoc analysis suggests that participants with low baseline or endogenous *Akkermansia muciniphila* may have the most room for improvement. But what I thought was interesting is that then you'd expect the placebo participants with high baseline *Akkermansia muciniphila* to show less weight regain than the placebo participants who started with low baseline *Akkermansia*.

Dr. Blevins:

Yeah. I clocked that too.

Dr. Maeusli:

Okay. So I was thinking about that as well, and that wasn't the case, right? I think what they were trying to say here, and I think they did this well with how they explained it, but their hypothesis is pointing more towards *Akkermansia muciniphila* abundance serving as more of an indication of their response to this treatment with pasteurized Muc^T as opposed to the overall protective benefit of endogenous *Akkermansia muciniphila* in the gut. Does that make sense?

Dr. Blevins:

Yeah, I can accept that at surface level, but I just need more answers. It piques my curiosity because I have the hypothesis here too, which is, like you said, people with lower endogenous concentrations of *A. muciniphila* have more to gain from taking the supplementation, and that the people who already have high levels of *A. muciniphila* are already benefiting from that high concentration. But if that were true, then you would see a better benefit in the placebo group of people with higher concentrations of *A. muciniphila*, and you don't. I think that's a big question for me: what is the supplement giving that the endogenous version isn't? If that's even a thing. I have no idea.

And then the other thing I noticed was a more subtle take-home message that more is not necessarily better. So people with high levels of *A. muciniphila* didn't benefit more from the supplementation. So it's almost like there's a ceiling of benefit. More is not better; it's just more.

Dr. Maeusli:

Yeah, I get you.

Dr. Blevins:

So yeah. I don't know. I definitely have that in my notes as an unanswered question of, why is the high concentration of *A. muciniphila* placebo people not benefiting better than the low, or not benefiting more than the low? I don't know. That could be an interesting question moving forward.

Dr. Maeusli:

This was under the exploratory section of the paper, so I'm sure that they have similar questions, and I think more to show certain signals. And yeah, I'm sure they're going to look into it in the future. But I definitely think it raised the little Spidey sense in both of us, like, "Hmm, what's going on there?" I'm sure the experts have that as well, where they're like, "We're not sure, but we want to report it because we think there might be something there." And I get that too.

Dr. Blevins:

I also wonder how expensive these tests are and if this could be used as a screening tool for people who have bariatric surgery or something like that to see who would benefit from it. Because we see so often that you don't want to take something if you know it's not going to work for you, so just get ahead of it and see if you would even benefit from that.

Dr. Maeusli:

Yeah. I think that's what they were thinking about in terms of the people who are on GLP-1s as well, or any weight loss diet.

Dr. Blevins:

Very interesting. So moving on to safety, the safety profile looked pretty good. Compliance was over 98 percent for both groups, and adverse events during the maintenance phase were pretty balanced, with about 16 in each group. And there were two serious adverse events, both in the Muc^T group, but neither of them was deemed related to the supplement. And GI symptoms like diarrhea, abdominal pain, reflux, and indigestion didn't differ between groups during that time either. So overall, pretty good.

Dr. Maeusli:

Yeah, I love to see it. So I think we can start to wrap up here. So let's put everything we've learned together and summarize it for our listeners.

First of all, really exciting early evidence supporting microbial supplementation for weight loss maintenance, specifically with pasteurized Muc^T. The pasteurized Muc^T significantly reduced weight regain after successful weight loss, with that progressive effect building across the 24-week maintenance window. And the strongest mechanistic signals that we saw were from the adipose tissue transcriptomics and the associations with the fecal energy loss.

Another interesting finding we saw was that the baseline *Akkermansia muciniphila* abundance may identify individuals who are most likely to benefit from this supplementation, with the caveat that this is still a hypothesis and that was exploratory.

But ultimately, clinically, all this matters because so much of obesity management focuses on the initial weight loss and whether that be through diet or GLP-1s, but this helps shift the focus a little bit to, how do we maintain that weight loss? How do we maintain the healthy targets for these people who have healthy weight goals?

Lastly, I think one thing that I wanted to add is, honestly, I really appreciated that these scientists were careful about level setting and not overstating the conclusions, which I think can oftentimes be a pitfall in the world of the gut microbiome and the world of the wellness, postbiotics, and prebiotics. I think they did a really good job of positioning the pasteurized Muc^T as a well-tolerated tool for maintaining weight loss as opposed to a broad cure-all for maintaining weight loss.

Dr. Blevins:

I would agree with that. They did a really good job of stating the facts, the data, and what could be happening without saying, black and white, "This is the best thing since sliced bread," which we see sometimes.

There are definitely some unanswered questions. One of the things that I would like to see is the use of other pasteurized strains to compare it to and to see what else happens. I would also really like to see a study looking at a modified version of Muc^T where Amuc_1100, which is the protein that we talked about earlier, is knocked out to see or to just to verify that is one of the key players in the therapeutic output of Muc^T. So I think that would be really interesting. I would also like to see a longer maintenance period. People want to maintain weight loss for long periods of time, so a year would be great.

And as a reader, I definitely still have questions about the baseline abundance of *A. muciniphila*, as we talked about before, and why we don't see that benefit in people who naturally have high concentrations of *A. muciniphila*. Some questions are unanswered, but overall, I think they frame Muc^T as a promising strategy for weight maintenance.

Dr. Maeusli:

Hallie, this was so fun, and I always love doing this with you. Just getting to read about the science, dissect it, and debate it is always so fun. Thank you so much.

Dr. Blevins:

Yeah, agreed. Let's nerd out again soon sometime.

Dr. Maeusli:

Will do.

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