Q&A: How new blood testing could help doctors better treat obesity

MAY 3, 2021

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With more than 1 billion people worldwide living with obesity and predictions that 50% of American adults will have obesity by 2030, a physician-owned company is aiming to soon provide doctors with an easy-to-use tool to help diagnose and treat this global public health epidemic.

Phenomix Sciences was founded by National Institutes of Health (NIH)-funded obesity experts and Mayo Clinic physician-scientists Andres Acosta, MD, PhD, and Michael Camilleri, MD, in Rochester, Minnesota, in 2017. Health2047, the wholly-owned innovation subsidiary of the AMA created to overcome systemic dysfunction in the U.S. health care, recently launched the company.

Through a decade of research, Drs. Acosta and Camilleri identified four obesity phenotypes and treatments that work best to help patients fight obesity based on which phenotype or phenotypes they have. Work is well underway to make the company's MyPhenome™ test commercially available by the end of 2021. The test allows a physician to order a blood test that identifies the phenotype or phenotypes the patient has, giving the physician and patient a roadmap for how best to help the patient lose weight and keep it off.

Drs. Acosta and Camilleri led a team that co-wrote a recent study in the journal *Obesity* showing the prevalence of obesity phenotypes and their association with weight loss. In 450 patients, 27% had more than one phenotype and only 15% didn't show signs of any of the phenotypes. It found that this individualized treatment was associated with a 1.75-fold greater weight loss after a year. Dr. Acosta recently took time to speak with the AMA about his research and Phenomix Sciences.

AMA: Why you were interested in this research?

Dr. Acosta: On average, the adult with obesity is trying four to five diets per year. And unfortunately, most people lose some weight initially and then regain it all back, or they may not lose any weight. We keep thinking that one treatment is going to fit all people. But when we go to the real world,

unfortunately a new diet or new medication works great for a few and very bad for the majority.

So, how do we actually address this problem that the one-size-fits-all approach is not working? We decided to take a step back and actually study what we're calling obesity types or obesity phenotypes. We decided to look at the components of food intake and energy expenditure.

AMA: Your team has discovered four primary types of obesity, as explained at the Phenomix website. Tell our physician readers more about these phenotypes.

Dr. Acosta: The first one is patients who do not feel full. These are the patients who keep coming for seconds and thirds within a meal. They just don't have that sensation of fullness. We call that "Hungry Brain®" because the signal is supposed to come from our stomach to our brain, and the brain needs to say, "I feel full, stop." That signal is wrong in these individuals.

The second group of individuals is folks who eat, feel full, but then within an hour or two they feel hungry again. These patients have a problem with their gut. The gut needs to send signals to the brain and tell the brain, I want to stay feeling full because I need time to digest my meal. Unfortunately, these signals are not coming out of the gut to the brain. We call that "hungry gut."

Then there are the folks who are eating for their emotions. They have a good day, they want to eat something. They have a bad day, they want to eat something. And they look for food to cope with life. We call that "emotional hunger."

The last group is what brings most of my patients to the clinic. They are the ones who come in and say "Doc, I have a problem with my metabolism." This group should be burning more calories and they're not. They're just storing those calories. We call this the "slow burn" phenotype.

And your question may be, when we ask about phenotype, who cares what phenotype I have? It matters because we have multiple studies all the way from randomized placebo-controlled trials, observational studies, and now a trial that was developed in the clinic—real world evidence.

It matters because we can actually select the right therapy for these individuals and enhance the amount of weight loss and not only enhance it a little bit, but actually almost double the amount of weight that they're going to lose with these interventions. It identifies who is going to be successful with a tailored approach and walks away from this one-size-fits-all approach.

AMA: Can you give me an example of some of the different ways a physician would approach treatment once they know the phenotype?

Dr. Acosta: Based on our current studies, particularly the initial randomized placebo-controlled trials that we performed, we came up with a working hypothesis or a working algorithm that physicians can

use. I've been using it in my clinic to help us guide therapy. So, for example, patients with a hungry brain will have their unique, hungry-brain diet to help make them feel full for the purpose of getting to that sensation of fullness.

Then the FDA [Food and Drug Administration]-approved medication that will likely work the best for these patients, as we've shown in our studies, is phentermine-topiramate extended release. We have also FDA-approved devices, and I think most likely they will respond better to a vagal B block or an endoscopic sleeve gastroplasty. And the surgical approach that most likely will be successful in this is the laparoscopic sleeve.

For patients with emotional hunger, I think it's essential that these patients have a diet that is low on calories, and they really focus on trying not to seek food to cope with their emotions. It's when cognitive behavioral therapy and group therapies might be ideal. And then we have a medication that is FDA-approved for obesity, which is now naltrexone bupropion sustained-release, and this may likely be the best medication.

AMA: If I'm a practicing physician, how will Phenomix work?

Dr. Acosta: The hope is that within the next six months, Phenomix will have these tests commercially ready. You will be able to reach out to Phenomix Sciences and set up a way to order the test. My hope is that this will be as simple as doing a lipid panel. The physician orders the test, the physician gets the results, and then, together with the patient, there's a discussion about what is the best option for the patient, and what the patient wants to do.

AMA: How do you believe this will change the way obesity is understood and treated by physicians in practices across the country?

Dr. Acosta: It just is a game changer in the conversation with our patients, because I see all sorts of patients struggling with obesity—rural, urban, all ethnicities, all races—who feel they are failing. We keep telling them, "You need to be healthy. You need to lose weight." They try and they fail.

So, when suddenly you tell your patients, "Hey, hold on, I think your lack of success is because there is a problem in your brain that is not allowing you to feel full. Let me help you with a tailored diet, let me help you with a medication, let me help you with surgery," the conversation changes as to what the underlying problem is. We remove the stigma about obesity and we start talking obesity as a disease.

Also, we help physicians who are very busy, who need to address multiple problems during a clinical visit by giving them the tools to say, "Let's focus on this problem of obesity with this solution and with this follow-up," just as we do for every other disease.

My huge hope and wish is that these phenotype-guided approach will help insurance companies to say: We should cover obesity. We should take obesity seriously. We should cover reimbursement for obesity so physicians can address it.

AMA: What excites you the most about the technology and the ability to treat people on such an individualized level?

Dr. Acosta: It is how my patients are changing the conversation about this topic. It's not about—did I lose weight? Did I gain weight since the last appointment?

It's about my hungry brain, it's about my hungry gut, it's about my underlying pathophysiological problem. My patients are coming back and telling me, "This is working. Or, no, it's not working, and I'm still struggling. How can you help?"

I love this patient of mine who came in one day and told me, "For the first time in my life, I know what it is to feel full. You have changed my life."

AMA: How has Health2047's partnership helped Phenomix?

Dr. Acosta: We are academicians and physician-scientists in academic settings. We are doing all the discoveries and it takes sometimes more than a decade to translate to help patients. I was extremely excited when we started talking with Health2047 and learned how they're helping physician-scientist entrepreneurs like myself by bringing the resources needed to accelerate the translation of these technologies from a lab and academic setting to the real world, so patients and physicians can benefit from that.

I think that's what we have achieved and what we are achieving. Health2047 has brought a significant amount of resources to this technology, and to the company to develop the technology. I'm honored to have them as partners in this company and this endeavor.