00:00:01:13 - 00:00:37:33

Michelle Chamberlain

Greetings for those joining from around the globe. My name is Michelle Chamberlain, and I have the privilege of being the Vice President of Advancement at the Salk Institute. We're exceptionally proud to present today's program as part of Science Can't Wait, a three-part webinar series created in partnership with the Del Mar Foundation. This collaboration brings together a community that values curiosity, connection, and impact and reflects our shared belief that the scientific challenges we face today cannot wait.

00:00:37:38 - 00:01:09:52

Michelle Chamberlain

Through this series, we're opening a window into Salk research, addressing some of today's most urgent challenges and issues, from how daily habits shape long term health to how plants can adapt to a changing world, and how the immune system can be harnessed to fight cancer. We're deeply grateful to the Del Mar Foundation for helping make access possible, and for standing with us and advocating for this essential discovery.

00:01:09:57 - 00:01:42:07

Michelle Chamberlain

Thanks to the Del Mar Foundation's generous one to one challenge match, any gifts made during this webinar series will be matched instantly, doubling your impact to our incredible scientific research. It's an extraordinary opportunity to accelerate foundational research that will improve our lives here and in our community around the world. I'd like to start by introducing you a bit to the Salk Institute.

00:01:42:12 - 00:02:11:31

Michelle Chamberlain

Many of you may know, but the Salk Institute was founded in the 1960 by Jonas Salk. We are an independent research institute that only focuses on science. This is all we do. I want to make sure, however, that I have the opportunity to share the type of science that is pursued at the Salk Institute, because it is very unique at the Salk Institute.

00:02:11:32 - 00:02:40:48

Michelle Chamberlain

We pursue what is known as basic science, or as we prefer to refer to it, foundational science. I like to think about the foundation of a house and how solid that needs to be to have a firm structure in that light. Our scientists are asking fundamental questions about biology and life itself, and as we find those answers, we publish them to the world for other scientists, industry, and the like to build upon, as you can see from these examples.

00:02:40:52 - 00:03:09:20

Michelle Chamberlain

Questions that were asked in the 1970s and the 1980s are responsible for pivotal areas of life and advancement that we rely on today. This is the research that is done at the Salk. We share our discoveries for the world to build on.

00:03:09:24 - 00:03:44:54

Michelle Chamberlain

How do we do this? Well, we like to emphasize that we do this through collaboration at the Salk Institute. We are connected through the questions we ask. We don't have departments or other silos that prevent information sharing. Instead, we take an interdisciplinary approach that looks at pivotal questions through an interdisciplinary lens and allows for discovery to be made in a faster, more comprehensive manner.

00:03:44:59 - 00:04:19:24

Michelle Chamberlain

Our scientists are empowered to ask the big, high-risk questions that have high impact on society. Today, we're asking some incredible questions, and I'd love for you to look at this list and take a moment and imagine a world if we knew the answer to what starts cancer, if we knew how we could direct plants to do what we need them to do in a world that is constantly changing, if we understood how the brain learns, remembers, and forgets.

00:04:19:29 - 00:04:52:58

Michelle Chamberlain

These are the questions of significance that Salk science is pursuing today. So I'm excited to give you a firsthand glimpse into what we're focused on in 2026, building on our very successful 2025 year of Alzheimer's disease, 2026 is going to be devoted to our year of brain health, which is the reason for this theme today during our webinar.

00:04:53:03 - 00:05:20:02

Michelle Chamberlain

We're going to be focused on what keeps our brains healthy and how can we keep them healthy through our lifetime. We aim to transform our understanding of brain health and lay the groundwork for new preventative strategies that we can all employ in our daily life. We're looking at this in a very comprehensive manner, from cardiovascular to exercise to healthy sleep.

00:05:20:06 - 00:05:51:48

Michelle Chamberlain

What are the elements that we can all deploy in our day-to-day life to ensure that we focus on healthspan, not necessarily lifespan, and keep our brains healthy and agile through our entire lifetimes? Today, to dive into this a bit deeper, I'm grateful to introduce you to Dr. Emily Manoogian. Dr. Manoogian works closely with Dr. Satchin Panda, who some of you may be familiar with his research.

00:05:51:52 - 00:06:22:24

Michelle Chamberlain

However, her awards and accolades are longer than I care to spend with you today. But suffice it to say, she's been awarded multiyear NIH grants. She's been recognized as an early career high achieving scientist and is an incredible asset to the Salk Institute. Dr. Manoogian will speak to us for about 20 minutes, and then we will open up time for Q&A, and I will guide you through what that process looks like when we arrive at it.

00:06:22:28 - 00:06:32:46

Michelle Chamberlain

For now, I'd love to introduce you. Dr. Manoogian, thank you for joining us.

00:06:32:51 - 00:06:35:55

Emily Manoogian

All right. Thank you so much for having me. Can you see the slides? Okay.

00:06:36:52 - 00:06:54:23

Emily Manoogian

Wonderful. Thank you everyone for joining us here today. I'm excited to talk to you about what I'm passionate about and what I'm working on a little bit every day. So let's jump right to it. So what are circadian rhythms? We're going to talk about what those are, what they're important for and how it all works.

00:06:54:31 - 00:07:20:07

Emily Manoogian

So you may or may not know your whole body is just filled with clocks. In fact, any cell in your body that has DNA, which is pretty much all of them, has a molecular clock that actually keeps time for approximately 24 hours. And this it's not just this one clock. It's this whole network which we'll talk about. But you, even at a whole-body level, are kind of a different person at different times of day.

00:07:20:12 - 00:07:42:04

Emily Manoogian

So in the middle of the night, you're in your deepest sleep. No surprise there. But just before you wake up, you actually have this burst of cortisol, which also leads to your sharpest rise in blood pressure. And this is to help you wake up. But again, this is kind of an anticipatory

system. So it helps you do what you're going to need to do in the later morning. Right around now actually we're probably at our highest alertness or cognitive ability.

00:07:42:04 - 00:08:00:24

Emily Manoogian

So hopefully this, hits quite well. In the later afternoon or early evening, we're actually at our greatest cardiovascular strength and ability. So if you want to beat someone in a race, it's better to do it in the late afternoon. You'll get your faster time there, although they might also. But still, if you're trying to beat your own time, do it in the afternoon.

00:08:00:28 - 00:08:20:34

Emily Manoogian

And then as you get into early evening, our blood pressure actually naturally rises. And then as we start to go towards bed, we actually get worse at metabolizing food. Our bodies want to relax a little bit more. And then that's how we get into our deeper sleep. So as I mentioned, this isn't just one thing.

00:08:20:35 - 00:08:42:01

Emily Manoogian

There's many ways that this works. And so the way I like to think about this system is to first realize your body is filled with these clocks and these networks. So internally within your body you have this timing system. And if you were put in a cave where you had no idea what time it was, you had no cues from the outside world, what time it was, you would still have an approximately 24-hour rhythm.

00:08:42:01 - 00:09:02:18

Emily Manoogian

And yes, scientists did do this to themselves in the 70s. But we don't do that anymore. But we know that this really is an internal system, and we don't just see this in humans. I'm

going to talk about humans for the rest of today. But you should know, this happens in all living organisms, from individual single cell bacteria to plants to animals.

00:09:02:18 - 00:09:20:30

Emily Manoogian

All living organisms have circadian rhythms because it's such a core part of how our bodies work. All right, so we're filled with these molecular clocks. And we have these networks to connect them so they can talk to each other. And these clocks lead to changes in all kinds of rhythmic outputs. And you can think about it at almost every level.

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Emily Manoogian

So from your behavior of when are you falling asleep? When are you getting tired? When are you waking up? When do you eat? When are you physically active? What's your cognitive ability? What's your mood? All of these things oscillate throughout a 24-hour day. Physiologically, I like to think about it as pretty much anything you could get tested at.

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Emily Manoogian

A doctor's office has a 24-hour rhythm, which is why it's a good idea to go to the doctor around the same time every time you get checkups, because your heart rate will change, your blood pressure will change, even your hormone levels can change. How you respond to a glucose test will change from the morning to the afternoon.

00:09:56:42 - 00:10:22:02

Emily Manoogian

Even how you're able to recover from a surgery changes if you have the surgery in the morning or an afternoon. And this goes beyond that. Even the individual cell function, when DNA is being translated, transcribed, when proteins are made, when different systems are

being regulated, all happens on a 24-hour system. And in fact, over 70% of all our genes are regulated by the circadian system.

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Emily Manoogian

Now, we don't live in an aperiodic environment. We live in a 24-hour world. And so the system is also built to take in signals from our environment. Or you can think of them as external inputs into the system. So things like light dietary intake. So foods, drinks, really anything you put in your body that it has to digest, an activity we know affect these clocks and they affect some clocks differently than others.

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Emily Manoogian

For instance, light is going to affect your behavioral rhythms a bit more so when you're sleeping and when you're awake, whereas dietary intake is actually going to affect all your metabolic clocks. So the clocks throughout your body that may not be central to behavioral timing but are key for how your liver works, how your stomach works, all those other types of things.

00:11:08:59 - 00:11:32:48

Emily Manoogian

And this doesn't only go in one way either. All these things be back on each other. You're going to get light when you're awake. So based on how light integrates with your rhythms and then changes your sleep output, that's going to affect when you actually end up getting the light the next day. So there's this very interconnected loop with our internal rhythms affecting our behavior, which then also gets incorporated with our external rhythms.

00:11:32:52 - 00:11:55:25

Emily Manoogian

And all these things work together to then create these nice circadian rhythms to keep everything in your body happening in the right place at the right time. And it's an amazing system because it's anticipatory. Our bodies actually do a lot of things that don't work to do at the same time, and so it kind of anticipates what your body's going to need to be able to do, and it prepares it for that.

00:11:55:30 - 00:12:17:44

Emily Manoogian

Another reason for that is think it's, you know, energetically very expensive to run a human body. And so to keep it efficient, you don't want to have everything prepared all the time. So again, having this anticipatory system allows you to prepare what you need when you need it and not overspend on things. Now the problem is, is as you can imagine, we do not live in this really beautiful I get to sleep whenever I want and wake up whenever I want system.

00:12:17:44 - 00:12:47:12

Emily Manoogian

A lot of modern society has really kind of attacked this in these natural rhythms, and that leads to circadian disruption. Now, one of the reasons that such a problem is because circadian disruption is linked to pretty much every chronic disease, from minor things like irritability or fatigue to more serious things that we think of like type two diabetes, cancer, obesity, affective disorders like depression, bipolar, anxiety.

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Emily Manoogian

All of these things are linked to disrupting the circadian system. You can kind of think of it as the circadian system is a really core part of how your body works. And when that part gets compromised, you are a weaker version of yourself. So anything you would be predisposed to, you have a much higher risk of getting.

00:13:07:13 - 00:13:23:15

Emily Manoogian

So one thing I want to talk to you about today, because a lot of my work focuses on shift work. So over 25% of the workforce does shift work. And even if you don't think of yourself as a shift worker, you've probably done something in your life that would qualify you as a shift worker.

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Emily Manoogian

At least a shift work schedule. For instance, if you've ever had a child and taken care of them in the first few months, you have lived a shift work lifestyle where you are having to wake up throughout the night, take care of someone else. You don't have a choice over your schedule and almost everyone has lived this at one point or another.

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Emily Manoogian

I know when I had my kids, that was an extremely challenging time. It is physically very difficult and part of that is is it messes with our circadian system. It's not surprising then, that we see many chronic diseases, increase rates of them in shift workers like cancer, diabetes, many cardiovascular diseases, affective disorders. In fact, the World Health Organization even considers shift work to be a carcinogen, meaning it increases rates for cancer.

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Emily Manoogian

It's not that surprising that firefighters who usually work either 12- or 24-hour shifts, and sometimes up to four days in a row, have elevated rates of cancer. That's partially due to smoke exposure. But what's interesting is their actual most common cause of death is heart events, meaning like heart attack or stroke. This is because it is not only an exposure thing.

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Emily Manoogian

This is also because of the shift work itself. And another important thing to remember is shift workers are almost always excluded from research. Now, I'm guilty of this myself. If I'm trying to test something in a very specific disease, I don't want to have some of my participants be shift workers, because it's such a big impact on the body that that could have confounding effects on the research, which is why multiple of our research programs now are specifically focused on only shift workers, because less than 0.0005% of clinical trials to test health interventions study shift workers.

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Emily Manoogian

They are frontline workers. They are protectors. They are at higher risk because of this, and they are frequently ignored. And so that's where a lot of our energy is going right now. So why is this shift work so damaging aside from, you know, just general circadian disruption? Obviously they have to wake up at night or be awake throughout the night.

00:15:22:09 - 00:15:43:28

Emily Manoogian

Different types of shift work have different types of challenges. But they're also eating at different times. And so we know that they're more likely to skip meals sometimes because they have a nap during the day or because they're on this really kind of switching around schedule. They frequently eat at night, mainly because they're awake at night and they might have been asleep during the day or just to help stay awake.

00:15:43:33 - 00:16:03:03

Emily Manoogian

Because of this, they also have very inconsistent eating times, and sometimes that can lead to increased caloric intake. Now there are also mixed report on foods. In fact, even in in some studies, shift workers are sometimes very healthy when they start. You can think of

firefighters, nurses, doctors you're thinking of are police officers. These are healthy individuals that are young.

00:16:03:03 - 00:16:22:06

Emily Manoogian

They're going into the field, they're working out, they're eating well. And they still may be reporting gaining weight even when they're maintaining that healthy lifestyle. So it's also not surprising to see that shift workers have these increased rates of obesity. So they have elevated weight gain even when they're more active than other people that are maybe sitting at desk jobs during the day.

00:16:22:06 - 00:16:48:38

Emily Manoogian

And like myself, a lot of the time, these people might be more active, but they're still gaining weight even if they're eating well. But we do know that because they're eating at night, we're seeing this association where the more food that you're eating at night actually leads to more cardio metabolic disorders. There was a really interesting study done, from Frank Shear's group at Harvard that got people to stay in the lab for a couple weeks, actually.

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Emily Manoogian

And they did lab simulated night shifts. So they would have them eat at different times of day and work at different times. And in one of the situations they had, the participants eat only during the day and fast during the shift work at night. And then in the other one, they had them eat during the night during their shift, and in both cases they would then do a glucose tolerance test the next morning.

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Emily Manoogian

A glucose tolerance test is when you drink these really quite disgusting often, but a really big bolus of sugar, like 50 or 75g of glucose, which is almost like a liter amount of, soda. But it's in a small amount. You drink that within five minutes and you see how your body is, how the glucose rises in your blood and how it comes down.

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Emily Manoogian

And that response is usually how type two diabetes is diagnosed. And it's really one of the best ways to understand how your body is able to regulate glucose. What was really interesting in this study was it wasn't even while they were eating, because we know if you eat at night, it'll go up higher and stay high longer.

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Emily Manoogian

But they also saw these really compromise shifts to a glucose challenge the next morning. So on the left you can see when they ate at night that orange bar compared to their baseline of before they did the night shifts, that the glucose went higher and stayed high much longer than it did when they didn't eat at night. And the insulin might explain that because the insulin is coming up later, it has a delayed, response, and it's staying high longer compared to the daytime eating group who fasted during that night shift did not see any kind of compromised response.

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Emily Manoogian

Now, this is important because elevated, that peak getting higher and staying high longer of the glucose and the delayed elevated insulin are both things that, if done chronically, will lead to, type two diabetes. And so we can very clearly see how these circadian disruptions are leading to glucose regulation problems. So how else does our diet interact with our circadian behavior.

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Emily Manoogian

So there was a study done, at Northwestern a little while ago that found when you put mice on a high fat diet, which is what is typically done to get them to gain weight so we can use them to test different treatments for diseases or understand diseases better. They don't only eat high fat food, they actually change when they start to eat their food across the day when they're normally sleeping.

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Emily Manoogian

And so there they actually change the rhythms of when they're eating, it almost looks like a night shift worker. And so, so Gene, in his group at the time, just before I joined the lab, had done this really cool study.

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Emily Manoogian

They asked a simple question. What if you just changed the time that the animals had access to food? So in one group, the mice were given 24-hour access to food. They could eat it whenever they wanted. You could think of it as just a free eating time. And it was on that high fat diet, so we knew they were going to eat during the day, in the night.

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Emily Manoogian

And the other group had that same high fat diet, but they could only access it during the night when they're normally awake. After about six months, we found that the mice that had access to the food whenever they wanted gained weight as expected, but the mice who ate the exact same amount of food, the same high fat diet, did not gain weight.

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Emily Manoogian

In fact, their body fat decreased dramatically compared to the other group. What was even more exciting was in the mice that gained weight. They developed fatty liver disease. As you'd expect, all those little white dots. There are little fat lipid or fat droplets that you're seeing in the liver. Whereas the mice that again ate that same high fat diet, the same amount of it had a healthy liver at the end of those six months, only because of the timing of when they ate.

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Emily Manoogian

Lab studies from our lab and many others have now shown that time restricted eating can have benefits throughout the body. No matter what you're looking at, you can see benefits in almost anything, from weight to your microbiome, to inflammation to cardiovascular health, to sleep, to even muscle function. This seems to be a core part of how your body works.

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Emily Manoogian

Now, what about humans? So unfortunately, we don't really know when humans eat. This is because the field really had not developed these questions. We always thought what you ate and how much you ate was important, but we really didn't think about when you ate. And if we did, we just thought like breakfast or lunch. But we really weren't thinking like how much variability, what exact time, how close is it to when you're sleeping?

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Emily Manoogian

In fact, many diets encourage people to eat very frequently and even late into the night, mainly to avoid binge eating. And so a first question for us was when do people eat? And so the lab developed a smartphone app called My Circadian clock, which is openly available

for anyone to use on iPhone or Android. It's a complete research app, meaning there's no commercial ties to it at all.

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Emily Manoogian

We're using this to collect data on a worldwide scale. And we also use it for more controlled clinical trials as well. So this has been super helpful because it gives us real time monitoring with participants. We have people take a quick picture and name it and then save it. That time stamps it. We can see when people are eating in real time within about 30s.

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Emily Manoogian

I can see your entry. And so we can see when participants are logging, we can capture about your food, your drinks, your medications, even when you're sleeping or exercising or other health factors that you want to answer. Or if we want to ask specific questionnaires, we're also able to send personal communications or educational information. And importantly, this is scalable.

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Emily Manoogian

So we can go on different levels. It doesn't only have to be people right around us. This is actually a worldwide application where we're collecting information from everywhere. And it can work remotely, obviously. And so this has been a really powerful tool that we've been using in our research. Now, luckily, if we ask people to take pictures of their food, they have.

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Emily Manoogian

So these are just a few examples of some of the photos that we've received. And what happens is we take these and we create what we call a feed or gram. And this is really just

so you have a 24-hour plot, say like midnight to midnight, and you link every you take them a little tick mark for everything that someone entered.

00:23:02:31 - 00:23:24:20

Emily Manoogian

Now, we don't want to just do this for one day because we actually have very variable eating times. And we know the variability in eating time. It's actually one of the problems most of the time. So we typically do this for a minimum of two weeks and sometimes up to a year in our in our research. Now this might be someone's, eating for one week, but we usually like to think about it a few different ways.

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Emily Manoogian

So one, you could collapse it into one line and say in that two weeks, this is when your body saw food, when it had to process it. And I think it's a little easier to think about it in a circle. So there's a 24-hour circle, not a 12-hour clock, it's a 24-hour clock. Or you can see food almost all the way around the clock.

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Emily Manoogian

But again, we don't just do this in one person. This was actually done in 156 people in San Diego. And you can see people are eating pretty much all around the clock. There's a down peak kind of around 3 or 4 in the morning. And when we first saw this, we thought, is there a data issue?

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Emily Manoogian

And we talked to some nutritionists. And the phrase that kept coming up was, if your eyes are open, your mouth is open. And the more people we talk to, that seems to be true. When

people are awake, they like to snack. And so if people are staying up late, they tend to have a snack or a drink or something.

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Emily Manoogian

And to note, these are caloric entries. These are not water. So that showed us that this may be really is a problem. And we really do need to do something, to help people, attack this issue. So what we found here was that over 50% of adults eat for over 15 hours or more. This means people are really not getting that proper fast.

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Emily Manoogian

So this led to time restricted eating. So in mice it was called time restricted feeding. When we moved to humans, people didn't like being told they fed. So we called it eating instead. But at the same concept, time restricted eating is unique from other types of like intermittent fasting in a few ways. One, it is embracing the circadian system, meaning that it's really it's only restricting calories by time.

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Emily Manoogian

It does not have any, explicit caloric restriction involved. So you're really just restricting your eating window to a consistent period of a 24-hour day, which results too, usually in a 14 or 18 hour fast. Water is always allowed. Medications are always allowed unsweetened tea or black coffee. All those things are okay. But it should stay the same and it should be customized to an individual.

00:25:26:58 - 00:25:50:17

Emily Manoogian

So you may have heard of some common time restricted eating windows like early try, which might be something like 6 a.m. to 2 p.m. or late try like noon to eight. Both of these

have some issues. So you sleep from 10:30 p.m. to 6:30 a.m. The 6 to 2 would be way too early for you to start before you even woke up, and the 12 to 8 would be far too late.

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Emily Manoogian

You'd have a long time after you woke up, and then you'd be eating. Probably too close to bed. So instead, what we do in all of our research where we test time restricted eating, is we create a personalized, time restricted eating window. So to do this, it's like four easy steps. First, identify when you sleep.

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Emily Manoogian

Eight hours you're at least attempting to try to sleep. So let's take 10:30 p.m. to 6:30 a.m., for example. Then we say, wait at least one hour after you wake up and at least three hours before you go to bed. And we can get into more details on this later. But this is to allow your body to prepare itself to digest food and to allow it to rest and process all the food you eat before you go to bed.

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Emily Manoogian

Next, identify any important family meals. If you have a family dinner at 6 p.m., I'm not going to tell you to not eat with your kids or your or your spouse or your friends. Have that meal. And then the fourth step is just to work back from that. If you're trying to hit an eight-hour window, that might look something like 1030 to 630, and you'd have four hours after you woke up and four hours before you went to bed.

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Emily Manoogian

Or what I think is usually sufficient is a ten hour. And that work might look like 8:30 a.m. to 6:30 p.m. I think it's really important to note that in these situations, we are never really

saying to skip meals or to starve yourself. A ten-hour eating window should not make you feel like you're starving. Although if you're eating over really long times, the first week might be a little weird, but your body adapts to this very easy.

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Emily Manoogian

The idea is to just allow your body to properly wake up and prepare to digest food, to eat food, and use it while you're awake, and then to allow your body to rest before you go to bed. So we've studied many different populations, as you could imagine, because the circadian system is such a core, part of how your body works, and also because it's linked to so many disorders, this could be a treatment for almost anyone.

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Emily Manoogian

And I think a core part of just a healthy lifestyle. But there's two that I'm going to talk to you about today. So the first is, a shift work study, and the second is metabolic syndrome. And obviously there's a lot more to talk about. But we have a limited time today. So I'm just going to touch on a couple high points.

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Emily Manoogian

And I wanted to note that we use a lot of different devices with participants. One of the ways we can get really cool data is not just when they eat, but what's actually going on in the body. We use the My Circadian clock app. We work with Dexcom, and we've been using continuous glucose monitors, which are able to measure glucose every 5 to 10 minutes for up to 10 to 14 days, depending on the monitor you're using completely passively, which is has given us huge insights into how the body digests and processed glucose, that we did not get from the single one time blood measures before.

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Emily Manoogian

We also use actigraph watches like this (https://condorinst.com/en/acttrust-two-actigraph/) that capture light, sleep temperature. We'll send scales or blood pressure cuffs home so we can capture those throughout, the studies as well. And when we do these things, we get these really cool graphs. So I can then say this person had this item, this is how their glucose responded in the middle here.

00:28:50:46 - 00:29:08:21

Emily Manoogian

And this is when they were awake and the light they were getting. And then we can get a full picture of how someone is living and moving and processing food. There are a couple studies I want to tell you about real quick. The first was our Healthy Hero study. This study completed just a couple of years ago.

00:29:08:21 - 00:29:31:46

Emily Manoogian

It was a collaboration between the San Diego Fire Department, our long term collaborators at UCSD, like Dr. Pam Taub there, who's a cardiologist there, and myself and Satchin, and this was really to address this question of how can we help kind of the heroes of our society. We know we can't make it so they don't have to work at night because we need them 24 hours a day.

00:29:31:51 - 00:29:58:27

Emily Manoogian

But maybe we could change when they eat, and maybe that would help them be healthier versions of themselves. So the first question was feasibility can firefighters do this? And this is very similar to the plots I showed you before where each little black dot is a food entry. These are just inlaid a little bit. So the inner circles you're seeing, baseline for both the standard of care group on the left here and a time restricted eating group here on the right, the outer circles.

00:29:58:32 - 00:30:21:06

Emily Manoogian

You're seeing what they did during intervention. So you can see the standard of care group stayed eating right around the same time. Whereas the time restricted eating group was able to achieve a ten hour eating window by delaying their breakfast and advancing their dinner. Again. We're not seeing meal skipping. We're seeing this consolidation of food into just a slightly smaller window and importantly, a consistent window.

00:30:21:11 - 00:30:42:10

Emily Manoogian

And this had big effects. So we were able to see that in a couple of the firefighters who did have prediabetes. We were able to see that at baseline. Their continuous glucose monitors, which you can see here in the yellow and baseline. I don't know if you can see my point or not, but you can see they have these elevated levels throughout the night.

00:30:42:10 - 00:30:57:56

Emily Manoogian

So you'd hope that it would be under 100 when you're fasting and that it would stay under 140 throughout the day as you're eating. And you can see on the one on the left, it's saying too high throughout the night. So even their fasting is elevated. And then when it does go high, it's going a little bit too high throughout the day.

00:30:58:01 - 00:31:18:22

Emily Manoogian

But by three months of time restricted eating just to those ten hours, you now see this blue line here where they're now at a very healthy around 80mg per deciliter at night, and they're staying in a healthy range throughout the day. The participant on the on the right, you're seeing the same type of data. But again, this person had a little bit higher levels at baseline.

00:31:18:33 - 00:31:41:57

Emily Manoogian

And then again had this really big improvement just from changing the timing of when they ate. It was also exciting to see that even though a majority of participants were healthy, we saw benefits in very low-density lipoprotein, which are these proteins that actually lead to causing plaques in your heart. This is because, they fill with triglycerides and they become really big.

00:31:41:57 - 00:32:02:20

Emily Manoogian

We actually saw those shrink even within healthy participants and in those that had elevated blood sugar levels. We saw those significantly decrease, as you probably saw. And the CGM slide I just showed you, we also saw decreases in diastolic blood pressure, which was really exciting because diastolic blood pressure is not treated with medication, only systolic blood pressure is.

00:32:02:34 - 00:32:27:48

Emily Manoogian

To see that go down was also very exciting. Now the next thing I want to tell you about is metabolic syndrome. This is in shift workers. This is just adults with metabolic syndrome. What is metabolic syndrome? It's a combination of having three of any of these five factors of elevated blood pressure triglycerides, a larger waistline, low good cholesterol or HDL cholesterol, and elevated blood sugar.

00:32:27:56 - 00:32:46:17

Emily Manoogian

And this is extremely common. About a third of all adults in the US have them. And by the time you get to the ages of 60 or 70, we're talking more like 60 or 70% of adults have these. Now, this dramatically increases the risk for cardiovascular disease and also has a 5-to-10-fold risk in developing type two diabetes.

00:32:46:22 - 00:33:21:12

Emily Manoogian

And this is unfortunately where a lot of Americans are. So we did a pilot study and then followed it up with a much larger randomized controlled trial that was published last year that showed that if we are able to do time restricted eating in these individuals for three or six months, that we're able to see a significant decrease in blood pressure and LDL cholesterol and waistline, and also in triglycerides and very importantly, in HbA1c, which is really the gold standard for how you're measuring blood sugar and how type two diabetes is diagnosed.

00:33:21:16 - 00:33:39:23

Emily Manoogian

And this is just another example of some of the data that we saw from a participant who had about a 14-hour eating window at baseline. And you see these orange really high glucose levels throughout the day over those two weeks, lots of variability. And after three months you can see that during the night, they're now at a healthy fasting level.

00:33:39:23 - 00:34:08:14

Emily Manoogian

And during the day they're staying in healthy levels throughout. Again, just by changing the timing of when they ate. We also have a collaboration with another doctor, Omar Mazari at UCSD, who's now testing to see if time restricted eating can even be used to help treat sleep apnea. And we're able to see that the time restricted eating participants actually increase their sleep duration, on average, by almost eight minutes a day, and the standard of care group was decreasing it by about 16 minutes a day.

00:34:08:29 - 00:34:30:46

Emily Manoogian

And so we're seeing that this may even be potentially a treatment for that. And that study is still ongoing. Now you might think, okay, how big of an effect is this? How does this compare to other things? Whenever you're talking about a prediabetic population, you're

not seeing these giant swings. So the current method for treating prediabetes is the diabetes prevention program.

00:34:30:46 - 00:34:50:28

Emily Manoogian

This is kind of the gold standard. It's a pretty involved program. It usually is at least six months long. You attend meetings, you have group meetings, you have exercise plans, you have dietary regimens. And this has been shown to decrease, the advancement to type two diabetes to really kind of stall that or prevent it completely significantly for at least two years.

00:34:50:33 - 00:35:17:12

Emily Manoogian

And the effect that they see an HbA1c reduction is 0.1%. And that's really saying we're stopping this advancement. We're going back a little bit. Now, if you think about metformin, which is one of the most common medications used, that actually only decreases A1c by 0.07, I believe it's less than 0.1%. And what we're seeing in our studies in the time restricted eating studies is in that same group, we're seeing a 0.1%, the same as the diabetes prevention program.

00:35:17:17 - 00:35:40:06

Emily Manoogian

The only thing that actually outperforms that is like a GLP-1, like an Ozempic or something like that, that is affecting your metabolism in a more severe way. The problem with that is a few fold. One, it can have a lot of side effects, so not everyone is able to take it. It's very expensive. It can cost, you know, for 100 million people that can be $1.2 trillion.

00:35:40:11 - 00:35:57:21

Emily Manoogian

And it also is not prescribed for prediabetes. This is something that is really prescribed for full blown type two diabetes. It is not always an option for people. So although it can be very powerful and should be another tool in our toolkit, trying to prevent the disease from developing in the first place is really an ideal goal.

00:35:57:32 - 00:36:22:45

Emily Manoogian

And we've also have some research now showing that combining theory with a GLP-1 can even enhance the effects even more so, the future of circadian biology is really multifaceted. We're understanding how we can do these kinds of simple lifestyle interventions that may be much more attainable than a caloric restriction or, severe intensive exercise, or combined with it to improve metabolism, your sleep, aging.

00:36:22:50 - 00:36:45:28

Emily Manoogian

Now even understanding how we're using a lot of data scientists to understand this big data, how it affects your brain, your cognitive abilities, your exercise, and leading to many different treatments. I'm also excited to tell you that right now we have an ongoing study called Chrono that we're using to compete in X Prize Healthspan.

00:36:45:33 - 00:37:18:46

Emily Manoogian

So X Prize Healthspan is a competition to try to decrease biological age by 10 to 20 years. We got to the semifinals last year and we'll be competing to get into the finals in just a couple of months. And we have some participants that are still in the study. They're about to finish where we did a multimodal lifestyle intervention to enhance circadian health at multiple levels, their nutrition and time restricted eating, timed exercise, timed sleep, and light exposure to try to make people the best versions of themselves and make them age healthier and happier.

00:37:18:51 - 00:37:44:50

Emily Manoogian

We also have other research going on right now. The study that I'm leading and I got an NIH grant for is called the shift study, where we're now working with nurses and nursing assistants who work 12 hour night shifts of 7 p.m. till 7 a.m., the ones who are taking care of us at our worst, again, trying time restricted eating and also a different version where we provide low glycemic snacks at night to see if there's other feasible ways to improve their health.

00:37:44:55 - 00:38:07:15

Emily Manoogian

And then we're doing a long term follow up on the metabolic syndrome study, where it's anyone who's 18 to 75, in the San Diego area who has metabolic syndrome. It's a year-long study to see how we can improve health. And we're trying to build more studies specifically for addressing aging, cognitive health, immune function, and physical ability.

00:38:07:20 - 00:38:30:56

Emily Manoogian

This year, just pending some funding. So with that, I would like to say thank you to the lab. This is not a one-person job by any means. It takes a village. And specifically our clinical team here, these are really the ones who make it happen. So with that, I'm excited to open this up for questions and, answer anything you'd like to know.

00:38:31:01 - 00:38:55:16

Michelle Chamberlain

Thank you so much, Emily. That was absolutely fascinating. Chock full of information. Really appreciate your time. We have so many questions. So I'm going to start going through them one at a time. If I don't get to your question, I apologize. For those who have not yet submitted a question, if you go to the bottom of your screen and scroll down about seven options over, you will see a question mark that says Q and A.

00:38:55:21 - 00:39:15:57

Michelle Chamberlain

If you click on that, a dialog box will open and allow you to submit a question. And as we address them, we will send them into the chat. So let's start, the first question that Emily is, what is a realistic restricted eating schedule for most people, eight, 10, 12 hours more?

00:39:16:02 - 00:39:31:58

Emily Manoogian

It's a great question. I think, you know, a lot of people think it has to be really severe. And there are all these different books, and there's a lot of like influencers that have come out with different things. When you get get below eight hours, you usually have some caloric restriction tight end, just because it's hard to eat as much within eight hours.

00:39:31:58 - 00:39:52:30

Emily Manoogian

And I think eight hours actually is quite challenging for some people. In all of our studies, we are doing somewhere between 8 and 10 and really based off of where you were to begin with. So I think ten hours is plenty sufficient and much more feasible if you're not able to get to ten, but you can stick to 12, keep a realistic 12 and stay consistent with your eating window.

00:39:52:30 - 00:40:10:12

Emily Manoogian

But I think ten is a great one to shoot for. And again, this could look like 9 a.m. to 7 p.m. it shouldn't be something so severe where you feel like you're starving yourself. It should be, a very reasonable eating time where you're really just eating when you're active and awake.

00:40:10:17 - 00:40:25:32

Michelle Chamberlain

Thank you. Next question is about the research. So one of our participants asked, how much do you think artificial light, dark cycles in animal facilities alter circadian regulation compared to in natural settings?

00:40:25:37 - 00:40:48:44

Emily Manoogian

I used to do animal work. When I was, doing my PhD and undergrad, having those artificial light dark cycles are extremely helpful because we control for that. So, that allows us to know the circadian phase of, and a rodent, and we can track that through a lot of different mechanisms.

00:40:48:49 - 00:41:04:47

Emily Manoogian

And so I actually find that is a really powerful tool because we can either control it or we can disrupt it. So most trials are actually using a light dark cycle as like a 12 on, 12 off. And this, this simulates like a summer day, which is usually kind of a good kind of standard to have.

00:41:05:02 - 00:41:33:15

Emily Manoogian

Where this does get complicated is sometimes, especially people outside of the circadian world may not be doing tests at the right time of day. And if you ignore the time of day that you challenge someone or take a sample, you can actually get mixed results. I think one of the bigger findings on this was in microbiome research. One of our former lab mates, who's now a professor and physician at UCSD, has done some beautiful work showing that if you sample the microbiome at different times of day, you'll get completely different responses.

00:41:33:19 - 00:41:53:37

Emily Manoogian

And so the whole microbiome field is somewhat confounded by this fact that a lot of times they don't report the time of day. So light dark conditions are actually very important. So we can understand what's going on there and control for that a little bit. And we can mimic them to be more or less realistic depending on the question you want to answer.

00:41:53:42 - 00:42:03:47

Michelle Chamberlain

Thank you. Final question on circadian rhythms. Someone points out the daylight savings time is coming up. How does that impact our circadian rhythm?

00:42:03:52 - 00:42:24:09

Emily Manoogian

Yeah, it messes it up. Daylight savings time is not great. Standard time, which is what we're currently on, has it. Moon is when the sun is kind of at its peak. That's really the ideal situation. When we switch to daylight savings time, it actually throws it an hour off. It means light's coming an hour too late now in San Diego.

00:42:24:09 - 00:42:40:33

Emily Manoogian

It doesn't hit us super hard, especially in the summer. But in March, when it's about to start, it means you're having to wake up when it's still a little bit dark outside. Kids might have this going to school at that time, that's a big problem. Our bodies aren't meant for that. Light is meant to be up, probably before we wake up.

00:42:40:38 - 00:42:57:12

Emily Manoogian

And to have it when we're there, it's very hard for our bodies to wake up without natural sunlight. And part of that is, is we're not very sensitive to light in the morning. And so you need this really bright light that is hard to get without real sun. And so it makes it very challenging.

00:42:57:23 - 00:43:23:08

Emily Manoogian

And you see the effects of that, you see increased car accidents, heart attacks, strokes, all in the week following that hour shift forward. And you do not see it in the hour shift back when we go back on to the right time. It's kind of a twofold problem. You have the problem of the shift itself. And then you have during the whole time we're in daylight savings time, we're a little bit off and it's sometimes adaptable and sometimes it isn't.

00:43:23:08 - 00:43:27:31

Emily Manoogian

And people have to wake up earlier. It hits them a lot harder.

00:43:27:36 - 00:43:29:06

Michelle Chamberlain

Not great news.

00:43:29:06 - 00:43:31:27

Emily Manoogian

No, we just need to get rid of it.

00:43:31:31 - 00:43:50:00

Michelle Chamberlain

All right. So now we have some questions about shift work. Because I think you definitely caught many people's attention with some of the negative health impacts of shift work. I'm going to ask two questions that are related. The first is to someone who always works a night shift, are they still considered a shift worker?

00:43:50:05 - 00:44:04:10

Michelle Chamberlain

And then the second part to that is, and if the answer to that is yes, how do we balance societal needs for 24 hour care in something like a hospital setting, with the disparate impact it's having on those workers?

00:44:04:15 - 00:44:24:13

Emily Manoogian

Those are great questions. So yes, anyone who's working at night or working, I believe the definition and there's different definitions. But if you're working for at least two or more hours between the hours of 10 p.m. and 5 a.m., then you count as a shift worker. And there's different kinds. There are these consistent shift workers that are always working nights.

00:44:24:18 - 00:44:43:33

Emily Manoogian

There are people who have rotating shifts. Honestly, if you can come up with a schedule, it probably exists. There's it's amazing how many different shift schedules there can be. And it goes by field and location. So many variables there. Some people can cope with it better than others. Part of that is, is each of us have a slightly different clock.

00:44:43:33 - 00:45:06:44

Emily Manoogian

Some of you know, you might think of yourself as like a morning person or a late person. That's because the actual period of your clock is a little bit different. And so people who are more morning people have a shorter period, or it's called your chronotype, actually. And people who are longer have a later period. And so some people that are late night are able to do night shifts better, or people who are early morning or do early shifts better.

00:45:06:46 - 00:45:30:09

Emily Manoogian

No one's really capable of working through the whole night, ideally, but some people can handle it better than others. Some people are also chronic shift workers. We do see differences in responses depending on how long you've been doing the shift. There's still usually a buildup of negative effects, but sometimes there's a little bit of reprieve if you've been doing it for long enough and found a suitable kind of situation, there.

00:45:30:14 - 00:45:48:54

Emily Manoogian

Really what we're trying to do with our research is find a way to answer your question, which is what can we do to help people with this? Because it is kind of a necessary evil. It's something that we need, but we know hurts them. And so we can't change when they get light because they're going to have to have a light on when you're responding to an emergency.

00:45:48:54 - 00:46:11:30

Emily Manoogian

We can't change the stress response. We can't change when it happens, but we can change when you eat. And so that is really what we're focused on right now, is trying to find ways to improve eating times. And then we want to expand that into other things using light exposure, using time to exercise. You know, really getting into the macronutrients of if you do need a snack, what could you have that would make it easier on your digestive system?

00:46:11:45 - 00:46:15:50

Emily Manoogian

So we can try to kind of decrease those negative effects over time.

00:46:15:55 - 00:46:29:41

Michelle Chamberlain

Thank you. And before I go into some questions about timing, one final question. Can the body fully recover from years of circadian disruption or some of these effects just long lasting?

00:46:29:45 - 00:46:51:06

Emily Manoogian

Yes and no. Just like anything, if you never worked out for your whole life, there's going to be some consequence of that, right? Like you're kind of probably building up a compromised system and it's working at a, at a lesser ability. Or you might be building up some damage over time, but switching in to having a better circadian lifestyle is always going to be beneficial.

00:46:51:16 - 00:47:08:52

Emily Manoogian

So it depends on what the effects are. It depends on what your health status is. It depends on a lot of other things going on in your life. For instance, if you're eating super healthy food and the right amount and you're exercising a lot, but you were eating at the wrong time, you're going to have a less effect than if you were also eating only fast foods and sugar foods.

00:47:08:52 - 00:47:27:56

Emily Manoogian

And we're never exercising. You know, there's kind of a it's not a one switch on or off. It's kind of a whole picture. So yeah, it's probably going to do damage over time, but you can definitely come back from that. And you can totally overcome that. I think, a lot of the research has been shown both in animal models and humans.

00:47:27:56 - 00:47:36:18

Emily Manoogian

We're usually starting with people that are at a compromised state, and we're seeing these really big improvements. So it's not too late, just get started today.

00:47:36:23 - 00:48:11:22

Michelle Chamberlain

Thank you. Thank you. So now switching to some of the timing and when your body is most appropriately ready for certain activities, questions about what time is best for exercise to not only reduce weight but to have a positive impact on other health factors and then in a separate but somewhat related question, we have someone that is asking if you have prediabetes or diabetes, is there truth to being in bed by a certain point, because the pancreas is restoring at a certain time in the evening?

00:48:11:27 - 00:48:30:21

Emily Manoogian

Great questions. Okay, so the timing of exercise I think is a budding field and a lot is coming out about that. For instance, a paper came out last year that I think a lot of people were surprised to see was that if you work out within about three hours of when you go to sleep, your sleep is compromised, and that's because it's really stimulatory to the system.

00:48:30:21 - 00:48:48:44

Emily Manoogian

It's telling your body it's time to be awake. But when to work out. So you're probably the least likely to get an injury because you have the fastest muscle response. You have a better heart rate, you have a better blood pressure, and you have more muscle strength. All in all, kind of like later afternoon. And that's somewhat relative.

00:48:48:44 - 00:49:18:19

Emily Manoogian

If you're a super early person, that might be a little early or if you're really late person might be a little later, but in kind of late afternoon. Some people think that if you work out when you've fasted, you're more likely to burn fat. Now, that may be true. However, there have been some studies and I think it's too early to say this fully, but there have been some examples of where people with prediabetes or type two diabetes, if they even go for a long walk before they eat something in the morning, it can actually spike their glucose higher.

00:49:18:24 - 00:49:42:52

Emily Manoogian

You actually see this in gestational diabetes. And this is because your muscles are your biggest regulator of glucose. And so when you start to walk and be active, it can over release glucose in individuals that aren't regulating it properly. You can get these really big spikes. So for some individuals, especially if you're more compromised, ideally get a continuous glucose monitor and test it yourself because it is dependent on individuals.

00:49:42:57 - 00:50:02:52

Emily Manoogian

But it's probably a good idea to have, lower carb breakfast, say, avocado, egg, something, that has a lot of protein or fiber, whole grains, not too big. And then maybe an hour or two after that, then go for your walk or even just following the meal. Go for a light walk. Go for a walk after a meal.

00:50:02:52 - 00:50:17:57

Emily Manoogian

It can be extremely helpful at any time of day. And this isn't a strenuous exercise. This is just really helping pull that glucose out of the blood by going for a simple, even ten minute walk can be super helpful. If it's really cold or you can't go outside for whatever reason, just walk around the house a little bit.

00:50:18:02 - 00:50:45:56

Emily Manoogian

But that straight sit down is is not ideal. As far as going to bed for diabetes? Yeah, to some extent there's been evidence to show that the variability. So like having really different times that you go to bed or different times that you eat or both have negative health associations. So finishing the time that you eat at the same time, at least three hours before you go to bed, and then getting to bed at the same time every day is a great way to help support your digestive health.

00:50:46:11 - 00:51:04:02

Emily Manoogian

So yes, the pancreas is working differently. Your gut lining can repair differently, your glucose can function much better. And that's really because, you know, there's so many different parts here. And I can't get into all the detail, but it's really a combination of like insulin and glucagon and all these different things and melatonin, and they're all regulating each other.

00:51:04:17 - 00:51:23:29

Emily Manoogian

And you want to make sure that during the night when your body is trying to rest, you're not stimulating it with food. That doesn't mean you have to go to sleep super early. That just means you need to stop eating at least three hours before bed. Try to dim the lights a bit, and then get to sleep at your regular time and try to keep that consistent to really kind of optimize your health.

00:51:25:12 - 00:51:45:55

Michelle Chamberlain

Excellent. Emily, one of our participants is asking if you or others are looking into how some of this information might impact women and men differently and how, for example, hormone cycles may create a difference in ideal timing or food intake needs.

00:51:46:00 - 00:52:07:12

Emily Manoogian

That is a wonderful question. So sex differences are real. And in any research that we do, humans or animals, we're always trying to look. Is there a sex difference? Now depending on the study and the number of participants, we may or may not be able to answer that question. Just statistically because we need more people. But we do see benefits in both.

00:52:07:17 - 00:52:26:58

Emily Manoogian

One of the more exciting things that we're getting into now is we're doing some intensive analysis on some of the blood samples that we've stored, doing multi-omics analysis, looking at transcriptome, proteomics, metabolomics. And there we're starting to see some clear sex differences in the mechanism of what's going on. The nice thing is we see benefits in both groups.

00:52:26:58 - 00:52:46:32

Emily Manoogian

But we think we're they're benefiting a little bit differently. For instance, it's more likely for women to not have weight loss, but actually have a bigger cardiometabolic effect, a bigger benefit. But in the absence of weight loss. So I think it is important to keep in mind that weight loss is just one of the things that may happen.

00:52:46:32 - 00:53:12:35

Emily Manoogian

It's not a weight loss intervention, it may happen. But we see this as kind of improving overall physiology. There are other groups, and I'm a consultant on one of them to help lead studies that are specifically targeting women who are, either pre, peri, or postmenopausal and trying to understand that menopause transition, because that has a huge effect on how our bodies digest food, how we store fats.

00:53:12:35 - 00:53:23:37

Emily Manoogian

We know that this is a big problem. And so looking at circadian interventions to help, with a menopause transition I think is also super important. And there are multiple groups looking at this now.

00:53:23:42 - 00:53:45:02

Michelle Chamberlain

Thank you. Emily. There was actually a question for me. So I'm going to take advantage of that, about how everything happening with the National Institutes of Health and federal funding is impacting the Salk Institute and research, such as what Emily went through with us today. So I just want to take a moment to say that there has been and will continue to be an impact.

00:53:45:02 - 00:54:24:13

Michelle Chamberlain

There is a tremendous amount of uncertainty surrounding federal funding and the work that an institution like the Salk Institute pursues has always been funded through a combination of federal support and private philanthropy. Approximately 50% of Salk's research dollars come from the federal government. And as more and more questions loom about not only what funding will be available, but what science will be prioritized, we have really relied more and more on private philanthropy and the power of those dollars.

00:54:24:18 - 00:54:49:13

Michelle Chamberlain

I think you all saw when Emily shared in her thank you slide, there was certainly some NIH money that was mentioned, but there were many, many private individuals, foundations and other sources of funds from the private sector that are making this research possible. And we have such incredible gratitude for those of you on this webinar who have helped us with that.

00:54:49:18 - 00:55:16:36

Michelle Chamberlain

So with that, I just want to remind everyone that philanthropy is essential to our work. It is, it is what allows us to support high risk, high reward science. And the incredible endeavors Emily has shared with you, so many findings. This is, you know, the result of her work over years, if not decades. And it is so essential that we're able to continue with this work.

00:55:16:36 - 00:55:50:17

Michelle Chamberlain

We can't just pause science. Hence the title of this series, Science Can't Wait. I want to thank all of our Discovery Society members and partners in research who have joined this incredible experience, and so much gratitude for the Del Mar Foundation in making this possible. I want to thank everyone who has joined us, and please consider putting a hold on your calendar for March 11th and May 13th when we will continue these discussions, albeit on very different topics.

00:55:50:30 - 00:56:10:42

Michelle Chamberlain

So science is fascinating and we have so much ground to cover. With that, I hope that this was a very good use of your time. I hope you got most of your questions answered. For those who I didn't get to your questions, I'm very sorry. The Q&A was incredibly active. And of course, massive thanks to Emily for joining us.

00:56:10:51 - 00:56:14:37

Michelle Chamberlain

We wish you a wonderful day and look forward to seeing you again soon.