WEBVTT

00:00:00.000 --> 00:00:05.564 Regita, that was an amazing introduction and

00:00:05.564 --> 00:00:10.076 and again I've I've enjoyed working with you

00:00:10.080 --> 00:00:12.798 for so many years in such an incredible way.

00:00:12.800 --> 00:00:16.160 So let me just get this started and

00:00:16.160 --> 00:00:19.670 and we will, there we go. All right,

00:00:19.670 --> 00:00:21.920 hopefully everyone can see my slides.

00:00:21.920 --> 00:00:25.200 So I'll be speaking with you about anti

00:00:25.200 --> 00:00:27.478 obesity medications just as Regita said.

00:00:27.480 --> 00:00:29.776 And I decided that I would actually

00:00:29.776 --> 00:00:32.225 start with my thank you slide because

00:00:32.225 --> 00:00:34.313 often times this is the the,

00:00:34.320 --> 00:00:35.995 the final slide and there

00:00:35.995 --> 00:00:37.000 isn't sufficient time.

00:00:37.000 --> 00:00:40.506 And I wanted to highlight the fact

NOTE Confidence: 0.32191926

00:00:40.506 --> 00:00:43.397 that none of us get here alone.

NOTE Confidence: 0.32191926

00:00:43.400 --> 00:00:47.999 And I've been at Yale for over 17 years

NOTE Confidence: 0.32191926

00:00:48.000 --> 00:00:50.800 and my initial mentor was Bob Sherwin.

NOTE Confidence: 0.32191926

00:00:50.800 --> 00:00:53.596 And Bob introduced me to Rajita.

NOTE Confidence: 0.32191926

00:00:53.600 --> 00:00:56.688 And I can honestly say that I would

NOTE Confidence: 0.32191926

00:00:56.688 --> 00:00:59.645 not be here today and I would not be

NOTE Confidence: 0.32191926

00:00:59.645 --> 00:01:01.749 doing the work that I'm doing if it was

NOTE Confidence: 0.32191926

00:01:01.749 --> 00:01:03.984 not for her help and her support and

NOTE Confidence: 0.32191926

00:01:03.984 --> 00:01:06.320 her guidance every step along the way.

NOTE Confidence: 0.32191926

00:01:06.320 --> 00:01:10.497 And I can say this with true transparency.

NOTE Confidence: 0.32191926

00:01:10.497 --> 00:01:13.924 Rajita is the one who enabled me to

NOTE Confidence: 0.32191926

00:01:13.924 --> 00:01:16.021 see patients with obesity without

NOTE Confidence: 0.32191926

00:01:16.021 --> 00:01:18.547 any other weight related diseases in

NOTE Confidence: 0.32191926

00:01:18.547 --> 00:01:21.080 the Yale stress center years ago.

NOTE Confidence: 0.32191926

00:01:21.080 --> 00:01:24.899 And she inspired me to take chances and

NOTE Confidence: 0.32191926

00:01:24.899 --> 00:01:27.291 to do the work that I was interested

NOTE Confidence: 0.32191926

00:01:27.291 --> 00:01:29.677 in doing and supported me every,

NOTE Confidence: 0.32191926

00:01:29.680 --> 00:01:30.680 every step of the way.

NOTE Confidence: 0.32191926

00:01:30.680 --> 00:01:32.044 So I'm incredibly grateful.

NOTE Confidence: 0.32191926

00:01:32.044 --> 00:01:34.090 So thank you for that introduction

NOTE Confidence: 0.32191926

00:01:34.151 --> 00:01:36.127 and thank you for all of your help

NOTE Confidence: 0.32191926

00:01:36.127 --> 00:01:37.275 across the years now.

NOTE Confidence: 0.32191926

00:01:37.275 --> 00:01:37.590 Additionally,

NOTE Confidence: 0.32191926

00:01:37.590 --> 00:01:39.795 as I was putting the slide together,

NOTE Confidence: 0.32191926

00:01:39.800 --> 00:01:42.117 I also wanted to highlight all the

NOTE Confidence: 0.32191926

00:01:42.117 --> 00:01:44.948 work that I do with many of you

NOTE Confidence: 0.32191926

00:01:44.948 --> 00:01:46.356 here in this department.

NOTE Confidence: 0.32191926

00:01:46.360 --> 00:01:48.676 And so I started highlighting some

NOTE Confidence: 0.32191926

00:01:48.676 --> 00:01:51.066 of the funding sources and some of

NOTE Confidence: 0.32191926

00:01:51.066 --> 00:01:53.280 the P is that I share work with.

NOTE Confidence: 0.32191926

00:01:53.280 --> 00:01:55.704 And I decided to go to to the

NOTE Confidence: 0.32191926

00:01:55.704 --> 00:01:58.549 website just to see all the different

NOTE Confidence: 0.32191926

00:01:58.549 --> 00:02:00.714 individuals and faculty I've worked

NOTE Confidence: 0.32191926

00:02:00.788 --> 00:02:03.105 with over the years here at Yale.

NOTE Confidence: 0.32191926

00:02:03.105 --> 00:02:04.995 And two things came to light.

NOTE Confidence: 0.32191926

00:02:05.000 --> 00:02:07.436 One, your department is very large.

NOTE Confidence: 0.32191926

00:02:07.440 --> 00:02:08.090 And two,

NOTE Confidence: 0.32191926

00:02:08.090 --> 00:02:10.690 it's just amazing how many of you I've

NOTE Confidence: 0.32191926

00:02:10.768 --> 00:02:14.080 worked with, whether it's on a paper,

NOTE Confidence: 0.32191926

00:02:14.080 --> 00:02:15.120 a grant,

NOTE Confidence: 0.32191926

00:02:15.120 --> 00:02:18.560 whether it got funded or not on

NOTE Confidence: 0.32191926

00:02:18.560 --> 00:02:20.160 committees and various other things.

NOTE Confidence: 0.32191926

00:02:20.160 --> 00:02:21.160 So thank you so much.

NOTE Confidence: 0.32191926

00:02:21.160 --> 00:02:23.608 And I really do think it takes a village

NOTE Confidence: 0.32191926

00:02:23.608 --> 00:02:25.900 and I'm an endocrinologist and within

NOTE Confidence: 0.32191926

00:02:25.900 --> 00:02:28.600 psychiatry you have also been my village.

NOTE Confidence: 0.32191926

00:02:28.600 --> 00:02:30.184 So thank you.

NOTE Confidence: 0.32191926

00:02:30.184 --> 00:02:33.076 So now let's get on with our talk.

NOTE Confidence: 0.32191926

00:02:33.080 --> 00:02:34.814 So these are my disclosures and

NOTE Confidence: 0.32191926

00:02:34.814 --> 00:02:36.692 they are all related to the

NOTE Confidence: 0.32191926

00:02:36.692 --> 00:02:38.357 exciting field of obesity medicine.

NOTE Confidence: 0.32191926

00:02:38.360 --> 00:02:39.991 You should know that I do consult

NOTE Confidence: 0.32191926

00:02:39.991 --> 00:02:41.925 for many of the companies that make

NOTE Confidence: 0.32191926

00:02:41.925 --> 00:02:43.695 these medications and I will also

NOTE Confidence: 0.32191926

00:02:43.753 --> 00:02:45.853 be discussing some off label use of

NOTE Confidence: 0.32191926

00:02:45.853 --> 00:02:47.660 medications and that's important for

NOTE Confidence: 0.32191926

00:02:47.660 --> 00:02:51.840 you to know because this is a CME talk.

NOTE Confidence: 0.32191926

00:02:51.840 --> 00:02:54.480 So let's start with an astonishing

NOTE Confidence: 0.32191926

00:02:54.480 --> 00:02:57.056 and very sad fact.

NOTE Confidence: 0.32191926

00:02:57.056 --> 00:03:01.612 So currently there are over 760 million

NOTE Confidence: 0.32191926

00:03:01.612 --> 00:03:05.384 people living with obesity by 20-30.

NOTE Confidence: 0.32191926

00:03:05.384 --> 00:03:08.144 It's projected that globally the

NOTE Confidence: 0.32191926

00:03:08.144 --> 00:03:11.184 prevalence of obesity is expected to

NOTE Confidence: 0.32191926

00:03:11.184 --> 00:03:13.860 reach 1 billion in America by 20-30.

NOTE Confidence: 0.32191926

00:03:13.860 --> 00:03:15.930 More than half of us are

NOTE Confidence: 0.9675282

00:03:16.011 --> 00:03:18.159 anticipated to have obesity.

NOTE Confidence: 0.9675282

00:03:18.160 --> 00:03:22.000 So obesity really touches every one of us,

NOTE Confidence: 0.9675282

00:03:22.000 --> 00:03:25.800 whether it is ourselves or our loved ones,

NOTE Confidence: 0.9675282

00:03:25.800 --> 00:03:27.920 but no one is spared.

NOTE Confidence: 0.9675282

00:03:27.920 --> 00:03:29.996 So when we think about obesity,

NOTE Confidence: 0.9675282

00:03:30.000 --> 00:03:31.900 often times we think about

NOTE Confidence: 0.9675282

00:03:31.900 --> 00:03:33.800 the many sequelae of obesity,

NOTE Confidence: 0.9675282

00:03:33.800 --> 00:03:36.680 the 200 other obesity related diseases.

NOTE Confidence: 0.9675282

00:03:36.680 --> 00:03:39.508 And often times this focus is on

NOTE Confidence: 0.9675282

00:03:39.508 --> 00:03:41.985 metabolic health and functional health.

NOTE Confidence: 0.9675282

00:03:41.985 --> 00:03:45.870 But it's really important to remember that

NOTE Confidence: 0.9675282

00:03:45.959 --> 00:03:49.760 obesity is also Co occurring with depression,

NOTE Confidence: 0.9675282

00:03:49.760 --> 00:03:52.280 anxiety and many other

NOTE Confidence: 0.9675282

00:03:52.280 --> 00:03:55.600 aspects of mental health.

NOTE Confidence: 0.9675282

00:03:55.600 --> 00:03:56.377 But right now,

NOTE Confidence: 0.9675282

00:03:56.377 --> 00:03:58.190 we are in the midst of an

NOTE Confidence: 0.9675282

00:03:58.260 --> 00:04:00.076 incredible transformation and that

NOTE Confidence: 0.9675282

00:04:00.076 --> 00:04:02.800 transformation is brought on by the

NOTE Confidence: 0.9675282

00:04:02.868 --> 00:04:05.318 introduction of these new highly

NOTE Confidence: 0.9675282

00:04:05.318 --> 00:04:07.278 effective anti obesity medications,

NOTE Confidence: 0.9675282

00:04:07.280 --> 00:04:09.260 many of which you've probably

NOTE Confidence: 0.9675282

00:04:09.260 --> 00:04:11.240 heard about in the news.

NOTE Confidence: 0.9675282

00:04:11.240 --> 00:04:13.148 And to illustrate this and to

NOTE Confidence: 0.9675282

00:04:13.148 --> 00:04:15.439 really bring it back to the patient,

NOTE Confidence: 0.9675282

00:04:15.440 --> 00:04:17.316 because really that's why we're all here.

NOTE Confidence: 0.9675282

00:04:17.320 --> 00:04:18.436 It's for the patient.

NOTE Confidence: 0.9675282

00:04:18.436 --> 00:04:21.478 I'm going to show you 2 examples of patients,

NOTE Confidence: 0.9675282

00:04:21.480 --> 00:04:24.138 one who was taking medications which

NOTE Confidence: 0.9675282

00:04:24.138 --> 00:04:26.479 were previously used and older

NOTE Confidence: 0.9675282

00:04:26.479 --> 00:04:28.959 medications and they're still used,

NOTE Confidence: 0.9675282

00:04:28.960 --> 00:04:31.326 they are still FDA approved and we

NOTE Confidence: 0.9675282

00:04:31.326 --> 00:04:34.200 still use them and one with a newer

NOTE Confidence: 0.9675282

00:04:34.200 --> 00:04:36.480 medication in within a clinical trial.

NOTE Confidence: 0.9675282

00:04:36.480 --> 00:04:38.976 So the first patient was on these previous

NOTE Confidence: 0.9675282

00:04:38.976 --> 00:04:40.958 older medications and is still taking them.

NOTE Confidence: 0.9675282

00:04:40.960 --> 00:04:41.920 When I first saw her,

NOTE Confidence: 0.9675282

00:04:41.920 --> 00:04:44.360 she was 18 and her BMI was 57.

NOTE Confidence: 0.9675282

00:04:44.360 --> 00:04:46.292 She was considering bariatric surgery and

NOTE Confidence: 0.9675282

00:04:46.292 --> 00:04:48.878 wanted to see what her other options were.

NOTE Confidence: 0.9675282

00:04:48.880 --> 00:04:51.715 She had developed obesity at a young

NOTE Confidence: 0.9675282

00:04:51.715 --> 00:04:54.997 age and already had some of the obesity

NOTE Confidence: 0.9675282

00:04:54.997 --> 00:04:58.080 related diseases that we we know coexist.

NOTE Confidence: 0.9675282

00:04:58.080 --> 00:04:59.160 So this is her course.

NOTE Confidence: 0.9675282

00:04:59.160 --> 00:05:01.160 Over about four years,

NOTE Confidence: 0.9675282

00:05:01.160 --> 00:05:03.160 we started several medications,

NOTE Confidence: 0.9675282

00:05:03.160 --> 00:05:03.816 metformin,

NOTE Confidence: 0.9675282

00:05:03.816 --> 00:05:04.472 laraglatide,

NOTE Confidence: 0.9675282

00:05:04.472 --> 00:05:06.440 the combination naltrexone,

NOTE Confidence: 0.9675282

00:05:06.440 --> 00:05:06.832 bupropion.

NOTE Confidence: 0.9675282

00:05:06.832 --> 00:05:09.576 And over the course of that time

NOTE Confidence: 0.9675282

00:05:09.576 --> 00:05:12.080 period she lost about 140 pounds,

NOTE Confidence: 0.9675282

00:05:12.080 --> 00:05:15.504 which was about a 45% total body weight

NOTE Confidence: 0.9675282

00:05:15.504 --> 00:05:18.355 reduction over the years and her BMI

NOTE Confidence: 0.9675282

00:05:18.355 --> 00:05:21.113 decreased to 31 and her A1C normalized.

NOTE Confidence: 0.9675282

00:05:21.120 --> 00:05:23.000 So with these previous medications,

NOTE Confidence: 0.9675282

00:05:23.000 --> 00:05:24.840 it took about four agents,

NOTE Confidence: 0.9675282

00:05:24.840 --> 00:05:27.848 several years to reach that degree of weight

NOTE Confidence: 0.9675282

00:05:27.848 --> 00:05:30.360 reduction and improvement in her health.

NOTE Confidence: 0.9675282

00:05:30.360 --> 00:05:31.956 Now this is the second patient.

NOTE Confidence: 0.9675282

00:05:31.960 --> 00:05:33.112 When I saw her,

NOTE Confidence: 0.9675282

00:05:33.112 --> 00:05:34.552 she was 49 years old,

NOTE Confidence: 0.9675282

00:05:34.560 --> 00:05:35.952 her BMI was 34.

NOTE Confidence: 0.9675282

00:05:35.952 --> 00:05:38.799 And you can see her trajectory of weight

NOTE Confidence: 0.9675282

00:05:38.800 --> 00:05:41.473 over the years before she came to see me.

NOTE Confidence: 0.9675282

00:05:41.480 --> 00:05:43.314 And every time you see a dip,

NOTE Confidence: 0.9675282

00:05:43.320 --> 00:05:45.678 that is her employing her prefrontal

NOTE Confidence: 0.9675282

00:05:45.678 --> 00:05:47.620 cortex and doing everything that

NOTE Confidence: 0.9675282

00:05:47.620 --> 00:05:49.720 she can in terms of improving her,

NOTE Confidence: 0.9675282

00:05:49.720 --> 00:05:51.796 her healthy eating and her exercise.

NOTE Confidence: 0.9675282

00:05:51.800 --> 00:05:53.557 And she was very successful at that,

NOTE Confidence: 0.9675282

00:05:53.560 --> 00:05:56.080 but unfortunately always regained the weight.

NOTE Confidence: 0.9675282

00:05:56.080 --> 00:05:58.015 She had already developed some

NOTE Confidence: 0.9675282

00:05:58.015 --> 00:05:59.950 of the obesity related diseases

NOTE Confidence: 0.9675282

00:06:00.012 --> 00:06:01.757 that we spoke about earlier.

NOTE Confidence: 0.9675282

00:06:01.760 --> 00:06:03.848 So her BMI was 34 and we enrolled

NOTE Confidence: 0.9675282

00:06:03.848 --> 00:06:05.936 her in one of our clinical trials

NOTE Confidence: 0.9675282

00:06:05.936 --> 00:06:07.960 of one of these new agents.

NOTE Confidence: 0.9675282

00:06:07.960 --> 00:06:10.328 And what you can see is that over

NOTE Confidence: 0.9675282

00:06:10.328 --> 00:06:12.764 the course of a year she lost a

NOTE Confidence: 0.9675282

00:06:12.764 --> 00:06:14.704 significant amount of weight and

NOTE Confidence: 0.9675282

00:06:14.704 --> 00:06:17.239 her BMI decreased to about 20.

NOTE Confidence: 0.9675282

00:06:17.240 --> 00:06:19.984 She lost over 90 pounds with a total

NOTE Confidence: 0.9675282

00:06:19.984 --> 00:06:22.608 body weight reduction of about 45%.

NOTE Confidence: 0.9675282

00:06:22.608 --> 00:06:24.880 So next generation medication,

NOTE Confidence: 0.9675282

00:06:24.880 --> 00:06:27.148 one agent over a course of a

NOTE Confidence: 0.9675282

00:06:27.148 --> 00:06:28.120 year and about

NOTE Confidence: 0.86687434

00:06:28.120 --> 00:06:29.281 45% weight reduction.

NOTE Confidence: 0.86687434

00:06:29.281 --> 00:06:31.990 So again you can see that this

NOTE Confidence: 0.86687434

00:06:32.074 --> 00:06:35.098 was possible before and it is now

NOTE Confidence: 0.86687434

00:06:35.098 --> 00:06:37.452 possible and potentially will be

NOTE Confidence: 0.86687434

00:06:37.452 --> 00:06:39.556 significantly easier to attain.

NOTE Confidence: 0.86687434

00:06:39.560 --> 00:06:41.846 But obesity remains vastly under treated

NOTE Confidence: 0.86687434

00:06:41.846 --> 00:06:44.658 and we're going to talk about some of

NOTE Confidence: 0.86687434

00:06:44.658 --> 00:06:46.999 the barriers of and why that may be.

NOTE Confidence: 0.86687434

00:06:47.000 --> 00:06:49.400 So let's look at these numbers.

NOTE Confidence: 0.86687434

00:06:49.400 --> 00:06:54.100 So there's about about 45 or 46% of

NOTE Confidence: 0.86687434

00:06:54.100 --> 00:06:56.562 adults in the United States or almost

NOTE Confidence: 0.86687434

00:06:56.562 --> 00:06:59.100 half that meet the recommendations for

NOTE Confidence: 0.86687434

00:06:59.100 --> 00:07:01.960 treatment with anti obesity pharmacotherapy.

NOTE Confidence: 0.86687434

00:07:01.960 --> 00:07:04.088 So that's ABMI of greater than 30

NOTE Confidence: 0.86687434

00:07:04.088 --> 00:07:06.436 or greater than 27 with a weight

NOTE Confidence: 0.86687434

00:07:06.436 --> 00:07:07.120 related disease.

NOTE Confidence: 0.86687434

00:07:07.120 --> 00:07:08.380 So it's about half.

NOTE Confidence: 0.86687434

00:07:08.380 --> 00:07:10.893 So now let's see how many individuals

NOTE Confidence: 0.86687434

00:07:10.893 --> 00:07:13.628 in the United States receive

12

NOTE Confidence: 0.86687434

00:07:13.628 --> 00:07:15.269 appropriate pharmacotherapy for

NOTE Confidence: 0.86687434

00:07:15.269 --> 00:07:21.680 their obesity treatment and it is 2%.

NOTE Confidence: 0.86687434

00:07:21.680 --> 00:07:23.680 And so when I initially saw this statistic,

NOTE Confidence: 0.86687434

00:07:23.680 --> 00:07:25.520 I thought, Oh my goodness, 2%,

NOTE Confidence: 0.86687434

00:07:25.520 --> 00:07:28.920 is it OK to treat 2% of patients

NOTE Confidence: 0.86687434

00:07:28.920 --> 00:07:31.892 with diabetes or 2% of patients

NOTE Confidence: 0.86687434

00:07:31.892 --> 00:07:34.191 with hypertension or 2% of

NOTE Confidence: 0.86687434

00:07:34.191 --> 00:07:35.244 patients with depression?

NOTE Confidence: 0.86687434

00:07:35.244 --> 00:07:36.999 And I thought to myself,

NOTE Confidence: 0.86687434

00:07:37.000 --> 00:07:38.280 for any other disease,

NOTE Confidence: 0.86687434

00:07:38.280 --> 00:07:40.538 we would not treat 2% of patients.

NOTE Confidence: 0.86687434

00:07:40.538 --> 00:07:42.512 And yet that's what we're doing

NOTE Confidence: 0.86687434

00:07:42.512 --> 00:07:44.599 with our patients with obesity.

NOTE Confidence: 0.86687434

00:07:44.600 --> 00:07:46.220 And for bariatric surgery,

NOTE Confidence: 0.86687434

00:07:46.220 --> 00:07:47.435 it's even less,

NOTE Confidence: 0.86687434

00:07:47.440 --> 00:07:49.925 It's less than 1% of individuals who

NOTE Confidence: 0.86687434

00:07:49.925 --> 00:07:51.865 qualify for bariatric surgery who

NOTE Confidence: 0.86687434

00:07:51.865 --> 00:07:53.880 receive surgery for their obesity.

NOTE Confidence: 0.86687434

00:07:53.880 --> 00:07:55.248 Now as a comparison,

NOTE Confidence: 0.86687434

00:07:55.248 --> 00:07:57.300 here's type 2 diabetes and we're

NOTE Confidence: 0.86687434

00:07:57.374 --> 00:07:59.939 treating about 86% of individuals

NOTE Confidence: 0.86687434

00:07:59.939 --> 00:08:01.598 with appropriate pharmacotherapy.

NOTE Confidence: 0.86687434

00:08:01.600 --> 00:08:04.096 So we're not perfect, but we're

NOTE Confidence: 0.86687434

00:08:04.096 --> 00:08:06.639 certainly better than the abysmal 2%.

NOTE Confidence: 0.86687434

00:08:06.640 --> 00:08:08.740 So we have medications,

NOTE Confidence: 0.86687434

00:08:08.740 --> 00:08:10.315 we have surgery,

NOTE Confidence: 0.86687434

00:08:10.320 --> 00:08:11.796 We have lifestyle interventions.

NOTE Confidence: 0.86687434

00:08:11.796 --> 00:08:14.010 What are some of the barriers

NOTE Confidence: 0.86687434

00:08:14.071 --> 00:08:15.556 that can be causing this?

NOTE Confidence: 0.86687434

00:08:15.560 --> 00:08:16.920 And to illustrate this,

NOTE Confidence: 0.86687434

00:08:16.920 --> 00:08:19.520 I'm going to talk about a patient

NOTE Confidence: 0.86687434

00:08:19.520 --> 00:08:21.424 at the beginning here and then come

NOTE Confidence: 0.86687434

00:08:21.424 --> 00:08:23.838 back to him through the course of the

NOTE Confidence: 0.86687434

00:08:23.838 --> 00:08:25.840 discussion and end with how he did.

NOTE Confidence: 0.86687434

00:08:25.840 --> 00:08:27.982 And this patient when I saw him

NOTE Confidence: 0.86687434

00:08:27.982 --> 00:08:30.555 was 59 and actually I saw this

NOTE Confidence: 0.86687434

00:08:30.555 --> 00:08:32.919 patient at the Yale Stress Center.

NOTE Confidence: 0.86687434

00:08:32.920 --> 00:08:35.580 He had come to the Yale Stress

NOTE Confidence: 0.86687434

00:08:35.580 --> 00:08:37.639 Center specifically for his anxiety,

NOTE Confidence: 0.86687434

00:08:37.640 --> 00:08:39.920 which he did not actually report to me.

NOTE Confidence: 0.86687434

00:08:39.920 --> 00:08:41.285 What he did tell me about was

NOTE Confidence: 0.86687434

00:08:41.285 --> 00:08:42.360 his Type 2 diabetes,

NOTE Confidence: 0.86687434

00:08:42.360 --> 00:08:45.360 his hypertension and his hyperlipidemia.

NOTE Confidence: 0.86687434

00:08:45.360 --> 00:08:47.997 And what he asked me is basically he said,

NOTE Confidence: 0.86687434

00:08:48.000 --> 00:08:49.920 Doc, I'm a walking time bomb.

NOTE Confidence: 0.86687434

00:08:49.920 --> 00:08:50.946 It's only a matter of time

NOTE Confidence: 0.86687434

15

00:08:50.946 --> 00:08:52.199 before I have a heart attack.

NOTE Confidence: 0.86687434

00:08:52.200 --> 00:08:54.756 Can you help me? I need to lose weight.

NOTE Confidence: 0.86687434

00:08:54.760 --> 00:08:57.502 He was very anxious and did

NOTE Confidence: 0.86687434

00:08:57.502 --> 00:08:59.942 not want surgery and again was

NOTE Confidence: 0.86687434

00:08:59.942 --> 00:09:01.358 interested in other options.

NOTE Confidence: 0.86687434

00:09:01.360 --> 00:09:02.444 His history was similar

NOTE Confidence: 0.86687434

00:09:02.444 --> 00:09:03.799 to many of our patients,

NOTE Confidence: 0.86687434

00:09:03.800 --> 00:09:05.599 He had gained weight slowly over time.

NOTE Confidence: 0.86687434

00:09:05.600 --> 00:09:07.640 He had tried everything and

NOTE Confidence: 0.86687434

00:09:07.640 --> 00:09:09.680 every time he was successful.

NOTE Confidence: 0.86687434

00:09:09.680 --> 00:09:10.350 In fact,

NOTE Confidence: 0.86687434

00:09:10.350 --> 00:09:12.360 with meal replacement he lost £60.00.

NOTE Confidence: 0.86687434

00:09:12.360 --> 00:09:13.878 But the issue was he always

NOTE Confidence: 0.86687434

00:09:13.878 --> 00:09:15.432 regained the weight as is the

NOTE Confidence: 0.86687434

00:09:15.432 --> 00:09:16.878 case with many of our patients.

NOTE Confidence: 0.86687434

00:09:16.880 --> 00:09:17.627 As I said,

NOTE Confidence: 0.86687434

00:09:17.627 --> 00:09:19.121 he reported to me that he

NOTE Confidence: 0.86687434

00:09:19.121 --> 00:09:20.560 already had type 2 diabetes,

NOTE Confidence: 0.86687434

00:09:20.560 --> 00:09:21.125 Hypertension,

NOTE Confidence: 0.86687434

00:09:21.125 --> 00:09:23.950 hyperlipidemia was taking a bunch

NOTE Confidence: 0.86687434

00:09:23.950 --> 00:09:26.920 of medications and his A1C was 8.5,

NOTE Confidence: 0.86687434

00:09:26.920 --> 00:09:30.480 so his his diabetes was not well controlled.

NOTE Confidence: 0.86687434

00:09:30.480 --> 00:09:31.508 So I noticed OK,

NOTE Confidence: 0.86687434

00:09:31.508 --> 00:09:33.800 he was taking two medicines for his diabetes,

NOTE Confidence: 0.8700528

00:09:33.800 --> 00:09:35.840 2 medicines for his blood pressure,

NOTE Confidence: 0.8700528

00:09:35.840 --> 00:09:38.200 a statin for his hyperlipidemia.

NOTE Confidence: 0.8700528

00:09:38.200 --> 00:09:39.600 And I thought to myself,

NOTE Confidence: 0.8700528

00:09:39.600 --> 00:09:42.000 when we care for this patient with obesity,

NOTE Confidence: 0.8700528

00:09:42.000 --> 00:09:44.166 why are all these other diseases

NOTE Confidence: 0.8700528

00:09:44.166 --> 00:09:46.200 being addressed but not obesity,

NOTE Confidence: 0.8700528

00:09:46.200 --> 00:09:48.372 not the disease that is likely

NOTE Confidence: 0.8700528

00:09:48.372 --> 00:09:50.846 causing if not at least contributing

NOTE Confidence: 0.8700528

00:09:50.846 --> 00:09:53.678 to all of these other diseases.

NOTE Confidence: 0.8700528

00:09:53.680 --> 00:09:54.958 And so the question was well,

NOTE Confidence: 0.8700528

00:09:54.960 --> 00:09:58.075 do we have medications to treat obesity.

NOTE Confidence: 0.8700528

00:09:58.080 --> 00:09:59.543 And as I showed you with the

NOTE Confidence: 0.8700528

00:09:59.543 --> 00:10:01.197 example of the first patient we do,

NOTE Confidence: 0.8700528

00:10:01.200 --> 00:10:03.025 there are several FDA approved

NOTE Confidence: 0.8700528

00:10:03.025 --> 00:10:04.120 anti obesity medications.

NOTE Confidence: 0.8700528

00:10:04.120 --> 00:10:06.200 There's also another one

NOTE Confidence: 0.8700528

00:10:06.200 --> 00:10:08.280 specifically for monogenic obesity.

NOTE Confidence: 0.8700528

00:10:08.280 --> 00:10:08.639 Additionally,

NOTE Confidence: 0.8700528

00:10:08.639 --> 00:10:10.793 we have many medications that we

NOTE Confidence: 0.8700528

00:10:10.793 --> 00:10:13.360 can use and these are off label use

NOTE Confidence: 0.8700528

00:10:13.360 --> 00:10:15.232 and some of these are components

NOTE Confidence: 0.8700528

00:10:15.232 --> 00:10:17.002 of the FDA approved medications

NOTE Confidence: 0.8700528

00:10:17.002 --> 00:10:18.850 because oftentimes these FDA

18

NOTE Confidence: 0.8700528

00:10:18.850 --> 00:10:20.698 approved medications are not

NOTE Confidence: 0.8700528

00:10:20.698 --> 00:10:22.840 covered by our patient's insurance.

NOTE Confidence: 0.8700528

00:10:22.840 --> 00:10:24.800 If the patient has type 2 diabetes,

NOTE Confidence: 0.8700528

00:10:24.800 --> 00:10:27.327 we may even have additional options and

NOTE Confidence: 0.8700528

00:10:27.327 --> 00:10:29.039 they're highlighted here in purple.

NOTE Confidence: 0.8700528

00:10:29.040 --> 00:10:31.448 And many of these medications also lead

NOTE Confidence: 0.8700528

00:10:31.448 --> 00:10:33.311 to weight reduction and we're going

NOTE Confidence: 0.8700528

00:10:33.311 --> 00:10:35.520 to focus in on some of these today.

NOTE Confidence: 0.8700528

00:10:35.520 --> 00:10:35.850 Again,

NOTE Confidence: 0.8700528

00:10:35.850 --> 00:10:37.500 the indication for using these

NOTE Confidence: 0.8700528

00:10:37.500 --> 00:10:39.758 medications is ABMI of greater than 30,

NOTE Confidence: 0.8700528

00:10:39.760 --> 00:10:42.464 greater than or equal to 30 or greater

NOTE Confidence: 0.8700528

00:10:42.464 --> 00:10:44.712 than equal to 27 with a weight related

NOTE Confidence: 0.8700528

00:10:44.712 --> 00:10:46.440 disease such as type 2 diabetes,

NOTE Confidence: 0.8700528

00:10:46.440 --> 00:10:48.405 hypertension or hyperlipidemia.

NOTE Confidence: 0.8700528

00:10:48.405 --> 00:10:51.680 Now we have these medications,

NOTE Confidence: 0.8700528

00:10:51.680 --> 00:10:53.836 we've had them for quite some time.

NOTE Confidence: 0.8700528

00:10:53.840 --> 00:10:55.387 And so the question is you know

NOTE Confidence: 0.8700528

00:10:55.387 --> 00:10:56.992 what are some of the challenges

NOTE Confidence: 0.8700528

00:10:56.992 --> 00:10:58.467 and barriers to treating our

NOTE Confidence: 0.8700528

00:10:58.467 --> 00:10:59.999 patients with these medications?

NOTE Confidence: 0.8700528

00:11:00.000 --> 00:11:00.328 Well,

NOTE Confidence: 0.8700528

00:11:00.328 --> 00:11:02.296 there's the perception that obesity is

NOTE Confidence: 0.8700528

00:11:02.296 --> 00:11:04.747 not a disease and I'm going to focus

NOTE Confidence: 0.8700528

00:11:04.747 --> 00:11:06.560 in on this specific barrier today.

NOTE Confidence: 0.8700528

00:11:06.560 --> 00:11:08.270 I think it's actually the most

NOTE Confidence: 0.8700528

00:11:08.270 --> 00:11:10.398 important one and I also think there

NOTE Confidence: 0.8700528

00:11:10.398 --> 00:11:12.681 are so many parallels in terms of

NOTE Confidence: 0.8700528

00:11:12.681 --> 00:11:15.110 obesity not being viewed as a disease

NOTE Confidence: 0.8700528

00:11:15.181 --> 00:11:17.636 for so long and and mental health

NOTE Confidence: 0.8700528

00:11:17.636 --> 00:11:19.731 issues like depression not being

NOTE Confidence: 0.8700528

00:11:19.731 --> 00:11:22.078 viewed as a disease and now it is.

NOTE Confidence: 0.8700528

00:11:22.080 --> 00:11:24.600 And what can we learn from the way

NOTE Confidence: 0.8700528

00:11:24.600 --> 00:11:26.280 that all of you manage this and

NOTE Confidence: 0.8700528

00:11:26.339 --> 00:11:28.359 brought forward mental health issues?

NOTE Confidence: 0.8700528

00:11:28.360 --> 00:11:30.944 What can we learn in the obesity space

NOTE Confidence: 0.8700528

00:11:30.944 --> 00:11:33.414 to really bring forward that obesity is

NOTE Confidence: 0.8700528

00:11:33.414 --> 00:11:36.519 a disease and needs to be treated as such?

NOTE Confidence: 0.8700528

00:11:36.520 --> 00:11:37.830 There's also the fear of

NOTE Confidence: 0.8700528

00:11:37.830 --> 00:11:38.878 causing dangerous side effects.

NOTE Confidence: 0.8700528

00:11:38.880 --> 00:11:40.410 We'll talk about this the perception

NOTE Confidence: 0.8700528

00:11:40.410 --> 00:11:42.079 that the medicines are not effective,

NOTE Confidence: 0.8700528

00:11:42.080 --> 00:11:44.000 which is rapidly changing.

NOTE Confidence: 0.8700528

00:11:44.000 --> 00:11:46.880 There's cost to consider and scalability

NOTE Confidence: 0.8700528

00:11:46.880 --> 00:11:49.244 and these are really huge barriers

NOTE Confidence: 0.8700528

00:11:49.244 --> 00:11:52.680 that we are facing now since so many

NOTE Confidence: 0.8700528

00:11:52.680 --> 00:11:55.472 patients have obesity and the cost issue.

NOTE Confidence: 0.8700528

00:11:55.472 --> 00:11:57.755 The question here is why is there

NOTE Confidence: 0.8700528

00:11:57.755 --> 00:12:00.324 this tenfold increase in cost in the

NOTE Confidence: 0.8700528

00:12:00.324 --> 00:12:02.962 United States where many of these new

NOTE Confidence: 0.8700528

00:12:02.962 --> 00:12:05.213 medications are are available at a

NOTE Confidence: 0.8700528

00:12:05.213 --> 00:12:08.517 fraction of the cost at in other countries?

NOTE Confidence: 0.8700528

00:12:08.520 --> 00:12:08.791 OK.

NOTE Confidence: 0.8700528

00:12:08.791 --> 00:12:10.688 So let's focus in on this first

NOTE Confidence: 0.8700528

00:12:10.688 --> 00:12:12.678 barrier and spend some time on this.

NOTE Confidence: 0.8700528

00:12:12.680 --> 00:12:14.591 So why is it important to understand

NOTE Confidence: 0.8700528

00:12:14.591 --> 00:12:16.175 that obesity is a disease and

NOTE Confidence: 0.8700528

00:12:16.175 --> 00:12:17.827 how does it affect the way that

NOTE Confidence: 0.8700528

00:12:17.885 --> 00:12:19.197 we use these medications?

NOTE Confidence: 0.8700528

00:12:19.200 --> 00:12:19.742 And again,

NOTE Confidence: 0.8700528

00:12:19.742 --> 00:12:21.910 I think this comes back to the fact

NOTE Confidence: 0.8700528

00:12:21.974 --> 00:12:23.506 really understanding the biology

NOTE Confidence: 0.8700528

00:12:23.506 --> 00:12:25.804 of obesity and what we're really

NOTE Confidence: 0.5375271

00:12:25.869 --> 00:12:28.228 trying to to obtain with treatment.

NOTE Confidence: 0.5375271

00:12:28.228 --> 00:12:30.513 So back to our patient,

NOTE Confidence: 0.5375271

00:12:30.520 --> 00:12:31.760 what did he teach me?

NOTE Confidence: 0.5375271

00:12:31.760 --> 00:12:33.930 Well, he taught me that he was

NOTE Confidence: 0.5375271

00:12:33.930 --> 00:12:35.501 highly motivated and he tried

NOTE Confidence: 0.5375271

00:12:35.501 --> 00:12:37.503 every method under the sun that he

NOTE Confidence: 0.5375271

00:12:37.503 --> 00:12:39.558 had access to caloric reduction,

NOTE Confidence: 0.5375271

00:12:39.560 --> 00:12:41.560 meal replacement, Mediterranean diet,

NOTE Confidence: 0.5375271

00:12:41.560 --> 00:12:44.560 improving the quality of his food.

NOTE Confidence: 0.5375271

00:12:44.560 --> 00:12:46.800 And yet he always regained the weight.

NOTE Confidence: 0.5375271

00:12:46.800 --> 00:12:48.438 And so the question with him was

NOTE Confidence: 0.5375271

00:12:48.438 --> 00:12:50.513 why is it so difficult to lose

NOTE Confidence: 0.5375271

00:12:50.513 --> 00:12:52.153 weight and maintain weight loss?

NOTE Confidence: 0.5375271

00:12:52.160 --> 00:12:54.512 Well, it turns out that our body

NOTE Confidence: 0.5375271

23

00:12:54.512 --> 00:12:56.780 has this beautiful system that it

00:12:56.780 --> 00:12:58.760 it's evolved over over centuries.

00:12:58.760 --> 00:13:00.785 And basically there are hormones

00:13:00.785 --> 00:13:03.340 which are signals which tell our

00:13:03.340 --> 00:13:05.196 brain about energy homeostasis.

00:13:05.200 --> 00:13:07.314 And it turns out that our bodies

00:13:07.314 --> 00:13:09.589 and our brain have this concerted

00:13:09.589 --> 00:13:11.317 interest in carrying fuel,

00:13:11.320 --> 00:13:13.679 and it carries that fuel as fat.

00:13:13.680 --> 00:13:15.020 And so our body,

00:13:15.020 --> 00:13:16.360 and specifically our brain,

00:13:16.360 --> 00:13:19.160 defends a certain amount of fat mass.

00:13:19.160 --> 00:13:21.064 We don't want to starve if there's

00:13:21.064 --> 00:13:21.880 no food available.

00:13:21.880 --> 00:13:24.247 We also don't want to carry so much fat

00:13:24.247 --> 00:13:26.898 or so much energy that we can't carry

NOTE Confidence: 0.5375271

00:13:26.898 --> 00:13:28.960 out the activities of daily living.

NOTE Confidence: 0.5375271

00:13:28.960 --> 00:13:30.272 Now, one might ask,

NOTE Confidence: 0.5375271

00:13:30.272 --> 00:13:30.600 well,

NOTE Confidence: 0.5375271

00:13:30.600 --> 00:13:32.424 if our if our body and our brain

NOTE Confidence: 0.5375271

00:13:32.424 --> 00:13:34.058 has this beautiful system where

NOTE Confidence: 0.5375271

00:13:34.058 --> 00:13:35.923 we're going to carry exactly

NOTE Confidence: 0.5375271

00:13:35.923 --> 00:13:37.559 the appropriate amount of fuel,

NOTE Confidence: 0.5375271

00:13:37.560 --> 00:13:40.878 then why are so many people

NOTE Confidence: 0.5375271

00:13:40.880 --> 00:13:41.750 developing obesity?

NOTE Confidence: 0.5375271

00:13:41.750 --> 00:13:44.360 Well, it turns out our environment,

NOTE Confidence: 0.5375271

00:13:44.360 --> 00:13:47.240 which is filled with highly palatable,

NOTE Confidence: 0.5375271

00:13:47.240 --> 00:13:48.239 highly processed foods,

NOTE Confidence: 0.5375271

00:13:48.239 --> 00:13:50.280 lack of sleep, increased stress,

NOTE Confidence: 0.5375271

00:13:50.280 --> 00:13:52.360 lack of physical activity,

NOTE Confidence: 0.5375271

00:13:52.360 --> 00:13:56.124 all of these things impact how our

NOTE Confidence: 0.5375271

00:13:56.124 --> 00:13:59.218 brain and how our body decides to

NOTE Confidence: 0.5375271

00:13:59.218 --> 00:14:01.710 defend that that fat mass at that point

NOTE Confidence: 0.5375271

00:14:01.710 --> 00:14:03.918 and how much fat it wants to carry.

NOTE Confidence: 0.5375271

00:14:03.920 --> 00:14:06.734 And so this actually brought me to

NOTE Confidence: 0.5375271

00:14:06.734 --> 00:14:09.866 some of the earlier work that I started

NOTE Confidence: 0.5375271

00:14:09.866 --> 00:14:11.438 to do during my doctoral thesis.

NOTE Confidence: 0.5375271

00:14:11.440 --> 00:14:12.366 And Dr.

NOTE Confidence: 0.5375271

00:14:12.366 --> 00:14:15.607 Sinha was my primary mentor with Doctor

NOTE Confidence: 0.5375271

00:14:15.607 --> 00:14:18.524 Bob Sherwin for my doctoral thesis.

NOTE Confidence: 0.5375271

00:14:18.524 --> 00:14:21.110 And this started a range of

NOTE Confidence: 0.5375271

00:14:21.200 --> 00:14:23.400 work over over many years,

NOTE Confidence: 0.5375271

00:14:23.400 --> 00:14:25.320 kind of leading us to address

NOTE Confidence: 0.5375271

00:14:25.320 --> 00:14:26.600 some of these questions.

NOTE Confidence: 0.5375271

00:14:26.600 --> 00:14:30.829 So looking at how food cues may impact us,

NOTE Confidence: 0.5375271

00:14:30.829 --> 00:14:31.178 well,

NOTE Confidence: 0.5375271

00:14:31.178 --> 00:14:33.621 of course there are neural responses that

NOTE Confidence: 0.5375271

00:14:33.621 --> 00:14:36.236 occur that then result in eating behavior.

NOTE Confidence: 0.5375271

00:14:36.240 --> 00:14:37.916 So biology informs behavior.

NOTE Confidence: 0.5375271

00:14:37.916 --> 00:14:40.430 There are hormones that impact these

NOTE Confidence: 0.5375271

00:14:40.503 --> 00:14:42.858 neural responses and these hormones

NOTE Confidence: 0.5375271

00:14:42.858 --> 00:14:45.213 and metabolic factors are potentially

NOTE Confidence: 0.5375271

00:14:45.284 --> 00:14:47.480 changed in the setting of obesity,

NOTE Confidence: 0.5375271

00:14:47.480 --> 00:14:50.040 for example by insulin resistance.

NOTE Confidence: 0.5375271

00:14:50.040 --> 00:14:52.425 Now when we think about how this may then

NOTE Confidence: 0.5375271

00:14:52.425 --> 00:14:54.557 alter all of these downstream effects,

NOTE Confidence: 0.5375271

00:14:54.560 --> 00:14:55.792 so the neural responses,

NOTE Confidence: 0.5375271

00:14:55.792 --> 00:14:56.716 the eating behavior,

NOTE Confidence: 0.5375271

00:14:56.720 --> 00:14:58.834 this can all result in weight gain.

NOTE Confidence: 0.5375271

00:14:58.840 --> 00:15:01.050 And where anti obesity medications

NOTE Confidence: 0.5375271

00:15:01.050 --> 00:15:03.788 can intervene is in the brain

NOTE Confidence: 0.5375271

00:15:03.788 --> 00:15:05.981 specifically as well as changing

NOTE Confidence: 0.5375271

00:15:05.981 --> 00:15:08.086 these different things that that

NOTE Confidence: 0.5375271

00:15:08.086 --> 00:15:10.142 are perturbations of obesity that

NOTE Confidence: 0.5375271

00:15:10.142 --> 00:15:11.996 can then result in weight loss.

NOTE Confidence: 0.5375271

00:15:12.000 --> 00:15:14.096 And we're going to focus in and talk

NOTE Confidence: 0.5375271

00:15:14.096 --> 00:15:16.158 about how this may all be happening.

NOTE Confidence: 0.5375271

00:15:16.160 --> 00:15:17.770 Now, how do we study this and

NOTE Confidence: 0.5375271

00:15:17.770 --> 00:15:19.678 how did we start to study this?

NOTE Confidence: 0.5375271

00:15:19.680 --> 00:15:20.144 Well,

NOTE Confidence: 0.5375271

00:15:20.144 --> 00:15:22.000 we conducted studies in

NOTE Confidence: 0.5375271

00:15:22.000 --> 00:15:23.464 both adolescents and adults.

NOTE Confidence: 0.5375271

00:15:23.464 --> 00:15:26.320 We used F MRI to look at this,

NOTE Confidence: 0.5375271

00:15:26.320 --> 00:15:28.318 and we used a food snack

NOTE Confidence: 0.5375271

00:15:28.318 --> 00:15:29.650 test developed at the

NOTE Confidence: 0.86156386

00:15:29.732 --> 00:15:32.482 Yale Stress Center by Doctor Sinha to

NOTE Confidence: 0.86156386

00:15:32.482 --> 00:15:34.738 look at some of the changes that may

NOTE Confidence: 0.86156386

00:15:34.738 --> 00:15:36.839 occur in terms of eating behavior.

NOTE Confidence: 0.86156386

00:15:36.840 --> 00:15:38.352 And then of course,

NOTE Confidence: 0.86156386

00:15:38.352 --> 00:15:40.242 we assess hormones and metabolic

NOTE Confidence: 0.86156386

00:15:40.242 --> 00:15:42.520 factors as we're doing these studies.

NOTE Confidence: 0.86156386

00:15:42.520 --> 00:15:44.960 And so as an endocrinologist,

NOTE Confidence: 0.86156386

00:15:44.960 --> 00:15:46.226 I may have thought and maybe

NOTE Confidence: 0.86156386

00:15:46.226 --> 00:15:47.640 I did in the beginning,

NOTE Confidence: 0.86156386

00:15:47.640 --> 00:15:50.412 that everything that was important in

NOTE Confidence: 0.86156386

00:15:50.412 --> 00:15:52.956 terms of eating began and ended in

NOTE Confidence: 0.86156386

00:15:52.956 --> 00:15:54.690 the hypothalamus because it is the

NOTE Confidence: 0.86156386

00:15:54.750 --> 00:15:56.878 hunger and satiety center of the brain.

NOTE Confidence: 0.86156386

00:15:56.880 --> 00:15:59.182 But little did I know at the time that

NOTE Confidence: 0.86156386

00:15:59.182 --> 00:16:00.736 there were so many other regions of

NOTE Confidence: 0.86156386

00:16:00.736 --> 00:16:02.519 the brain that are so critical to this,

NOTE Confidence: 0.86156386

00:16:02.520 --> 00:16:03.690 so striatal regions,

NOTE Confidence: 0.86156386

00:16:03.690 --> 00:16:05.640 limbic regions and cortical regions.

NOTE Confidence: 0.86156386

00:16:05.640 --> 00:16:07.796 And of course speaking with this audience,

NOTE Confidence: 0.86156386

00:16:07.800 --> 00:16:10.800 you know all of this so much better than I.

NOTE Confidence: 0.86156386

00:16:10.800 --> 00:16:12.718 So when we were doing these studies,

NOTE Confidence: 0.86156386

00:16:12.720 --> 00:16:14.520 we were giving patients different

NOTE Confidence: 0.86156386

00:16:14.520 --> 00:16:15.600 types of cues.

NOTE Confidence: 0.86156386

00:16:15.600 --> 00:16:16.950 So food stories,

NOTE Confidence: 0.86156386

00:16:16.950 --> 00:16:19.200 food pictures and even ingestion,

NOTE Confidence: 0.86156386

00:16:19.200 --> 00:16:20.800 ingestion of macro nutrients

NOTE Confidence: 0.86156386

00:16:20.800 --> 00:16:22.800 such as glucose and fructose.

NOTE Confidence: 0.86156386

00:16:22.800 --> 00:16:25.314 We would expose participants to these

NOTE Confidence: 0.86156386

00:16:25.314 --> 00:16:28.040 various cues and then conduct MRI

NOTE Confidence: 0.86156386

00:16:28.040 --> 00:16:30.920 studies to to ascertain their response.

NOTE Confidence: 0.86156386

00:16:30.920 --> 00:16:32.672 So I'm just going to highlight

NOTE Confidence: 0.86156386

00:16:32.672 --> 00:16:34.320 a few studies that we did.

NOTE Confidence: 0.86156386

00:16:34.320 --> 00:16:36.544 And so if we wanted to look at

NOTE Confidence: 0.86156386

00:16:36.544 --> 00:16:38.125 neural responses to visual food

00:16:38.125 --> 00:16:40.045 cues in adolescence with obesity to

00:16:40.045 --> 00:16:42.029 see if they responded differently

00:16:42.029 --> 00:16:44.034 than adolescents who were lean.

00:16:44.040 --> 00:16:46.595 So we exposed them to food pictures,

00:16:46.600 --> 00:16:49.024 conducted scans and assessed

00:16:49.024 --> 00:16:50.236 hormonal responses.

00:16:50.240 --> 00:16:52.280 And so in this first study

00:16:52.280 --> 00:16:53.360 that I'm sharing with you,

00:16:53.360 --> 00:16:55.960 we looked at the the difference in

00:16:55.960 --> 00:16:58.360 terms of BOLD signal activation in

00:16:58.360 --> 00:17:01.360 terms of the response to high calorie

00:17:01.360 --> 00:17:03.703 foods versus non non food pictures.

00:17:03.703 --> 00:17:06.090 And this is in individuals with obesity

00:17:06.155 --> 00:17:08.040 versus individuals who are lean.

00:17:08.040 --> 00:17:10.231 And what we found was that adolescents

00:17:10.231 --> 00:17:12.023 with obesity had increased activation

NOTE Confidence: 0.86156386

00:17:12.023 --> 00:17:14.013 and reward motivation regions in

NOTE Confidence: 0.86156386

00:17:14.013 --> 00:17:16.519 response to high calorie food pictures.

NOTE Confidence: 0.86156386

00:17:16.520 --> 00:17:18.636 And specifically these adolescents

NOTE Confidence: 0.86156386

00:17:18.636 --> 00:17:20.752 demonstrated increased activation in

NOTE Confidence: 0.86156386

00:17:20.752 --> 00:17:22.816 striatal limbic regions including

NOTE Confidence: 0.86156386

00:17:22.816 --> 00:17:25.160 the amygdala, hypothalamus, caudate,

NOTE Confidence: 0.86156386

00:17:25.160 --> 00:17:27.960 putamen, thalamus and insula.

NOTE Confidence: 0.86156386

00:17:27.960 --> 00:17:28.255 Now,

NOTE Confidence: 0.86156386

00:17:28.255 --> 00:17:30.320 we also wanted to see whether there

NOTE Confidence: 0.86156386

00:17:30.320 --> 00:17:32.135 were differences in neural responses

NOTE Confidence: 0.86156386

00:17:32.135 --> 00:17:34.080 to monosaccharides in these adolescents.

NOTE Confidence: 0.86156386

00:17:34.080 --> 00:17:36.838 Adolescents take in a lot of sugar.

NOTE Confidence: 0.86156386

00:17:36.840 --> 00:17:39.395 So what we did is we brought

NOTE Confidence: 0.86156386

00:17:39.395 --> 00:17:42.958 our adolescents in fasting,

NOTE Confidence: 0.86156386

00:17:42.960 --> 00:17:46.117 we we did a baseline F MRI,

NOTE Confidence: 0.86156386

00:17:46.120 --> 00:17:48.106 and then we basically gave them

NOTE Confidence: 0.86156386

00:17:48.106 --> 00:17:50.127 either glucose or fructose and then

NOTE Confidence: 0.86156386

00:17:50.127 --> 00:17:52.250 scanned them and then assessed various

NOTE Confidence: 0.86156386

00:17:52.250 --> 00:17:55.960 metabolic factors during the F MRI scan.

NOTE Confidence: 0.86156386

00:17:55.960 --> 00:17:58.576 And what we saw in this study was

NOTE Confidence: 0.86156386

00:17:58.576 --> 00:18:00.079 that adolescents with obesity

NOTE Confidence: 0.86156386

00:18:00.080 --> 00:18:02.150 in response to drinking glucose

NOTE Confidence: 0.86156386

00:18:02.150 --> 00:18:03.806 demonstrated decreased perfusion in

NOTE Confidence: 0.86156386

00:18:03.806 --> 00:18:05.800 decision making regions of the brain,

NOTE Confidence: 0.86156386

00:18:05.800 --> 00:18:07.840 so various regions like the

NOTE Confidence: 0.86156386

00:18:07.840 --> 00:18:09.880 prefrontal cortex and the ACC.

NOTE Confidence: 0.86156386

00:18:09.880 --> 00:18:12.420 And they demonstrated increased

NOTE Confidence: 0.86156386

00:18:12.420 --> 00:18:14.960 perfusion and reward motivation

NOTE Confidence: 0.86156386

00:18:14.960 --> 00:18:16.960 regions as you can see here.

NOTE Confidence: 0.86156386

00:18:16.960 --> 00:18:19.078 And you can see for comparison,

NOTE Confidence: 0.86156386

00:18:19.080 --> 00:18:21.490 lean adolescence and their response

NOTE Confidence: 0.86156386

00:18:21.490 --> 00:18:23.900 in the prefrontal cortex and

NOTE Confidence: 0.86156386

00:18:23.982 --> 00:18:26.317 the ACC was actually increased.

NOTE Confidence: 0.86156386

00:18:26.320 --> 00:18:28.560 Now we were also interested in looking at,

NOTE Confidence: 0.86156386

00:18:28.560 --> 00:18:28.813 well,

NOTE Confidence: 0.86156386

00:18:28.813 --> 00:18:30.331 what was the effect of leptin

NOTE Confidence: 0.86156386

00:18:30.331 --> 00:18:31.640 on these neural responses.

NOTE Confidence: 0.86156386

00:18:31.640 --> 00:18:34.608 So leptin is an adipokine or a hormone

NOTE Confidence: 0.86156386

00:18:34.608 --> 00:18:37.279 that's secreted proportionally to fat mass.

NOTE Confidence: 0.86156386

00:18:37.280 --> 00:18:38.760 So as we gain weight,

NOTE Confidence: 0.34135723

00:18:38.760 --> 00:18:40.956 most people increase their leptin levels.

NOTE Confidence: 0.34135723

00:18:40.960 --> 00:18:43.438 This isn't homogeneous across the population,

NOTE Confidence: 0.34135723

00:18:43.440 --> 00:18:45.768 but in general leptin is proportionally

NOTE Confidence: 0.34135723

00:18:45.768 --> 00:18:48.365 increased in terms of the amount of

NOTE Confidence: 0.34135723

00:18:48.365 --> 00:18:50.315 fat mass that somebody may have.

NOTE Confidence: 0.34135723

00:18:50.320 --> 00:18:52.496 And indeed this is what we found in

NOTE Confidence: 0.34135723

00:18:52.496 --> 00:18:54.560 our sample, that the individuals who

NOTE Confidence: 0.34135723

00:18:54.560 --> 00:18:56.840 had obesity had higher leptin levels.

NOTE Confidence: 0.34135723

00:18:56.840 --> 00:18:58.919 So what we did is conducted whole

NOTE Confidence: 0.34135723

00:18:58.919 --> 00:19:00.909 brain correlations with leptin and we

NOTE Confidence: 0.34135723

00:19:00.909 --> 00:19:02.654 found that higher endogenous leptin

NOTE Confidence: 0.34135723

00:19:02.654 --> 00:19:04.123 levels correlated with decreased

NOTE Confidence: 0.34135723

00:19:04.123 --> 00:19:05.918 perfusion in the prefrontal cortex

NOTE Confidence: 0.34135723

00:19:05.918 --> 00:19:07.560 in adolescence with obesity.

NOTE Confidence: 0.34135723

00:19:07.560 --> 00:19:10.824 And we thought that perhaps altered

NOTE Confidence: 0.34135723

00:19:10.824 --> 00:19:12.680 or dysfunctional leptin signaling

NOTE Confidence: 0.34135723

00:19:12.680 --> 00:19:15.000 there could be leptin resistance.

NOTE Confidence: 0.34135723

00:19:15.000 --> 00:19:17.530 This may contribute to lower

NOTE Confidence: 0.34135723

00:19:17.530 --> 00:19:19.554 prefrontal cortical responses in

NOTE Confidence: 0.34135723

00:19:19.554 --> 00:19:21.039 adolescence with obesity.

NOTE Confidence: 0.34135723

00:19:21.040 --> 00:19:24.490 And actually this this was congruent

NOTE Confidence: 0.34135723

00:19:24.490 --> 00:19:27.368 with studies conducted by Sadaf Farooqi,

NOTE Confidence: 0.34135723

00:19:27.368 --> 00:19:30.515 where she actually gave leptin back to

NOTE Confidence: 0.34135723

00:19:30.515 --> 00:19:32.915 individuals who have leptin deficiency,

NOTE Confidence: 0.34135723

00:19:32.920 --> 00:19:35.765 and she demonstrated that those

NOTE Confidence: 0.34135723

00:19:35.765 --> 00:19:38.041 individuals then had increased

NOTE Confidence: 0.34135723

00:19:38.041 --> 00:19:40.639 activation in the prefrontal cortex.

NOTE Confidence: 0.34135723

00:19:40.640 --> 00:19:42.397 OK, so the of course with these

NOTE Confidence: 0.34135723

00:19:42.397 --> 00:19:43.719 studies that I've shown you,

NOTE Confidence: 0.34135723

00:19:43.720 --> 00:19:46.840 there are many questions yet to be addressed.

NOTE Confidence: 0.34135723

00:19:46.840 --> 00:19:48.196 What is the cause and effect?

NOTE Confidence: 0.34135723

00:19:48.200 --> 00:19:49.320 So what happened first,

NOTE Confidence: 0.34135723

00:19:49.320 --> 00:19:51.000 the brain changes or the obesity,

NOTE Confidence: 0.34135723

00:19:51.000 --> 00:19:52.332 What's the timing?

NOTE Confidence: 0.34135723

00:19:52.332 --> 00:19:55.440 Does it happen during adolescence in utero?

NOTE Confidence: 0.34135723

00:19:55.440 --> 00:19:58.114 When does obesity really set in and

NOTE Confidence: 0.34135723

00:19:58.114 --> 00:19:59.518 what is the impact on behavior?

NOTE Confidence: 0.34135723

00:19:59.520 --> 00:20:00.632 Do we really know?

NOTE Confidence: 0.34135723

00:20:00.632 --> 00:20:02.741 And and of course these are things

NOTE Confidence: 0.34135723

00:20:02.741 --> 00:20:05.366 that need to be looked at and

NOTE Confidence: 0.34135723

00:20:05.366 --> 00:20:06.116 especially reversibility.

NOTE Confidence: 0.34135723

00:20:06.120 --> 00:20:08.650 So when patients actually undergo

NOTE Confidence: 0.34135723

00:20:08.650 --> 00:20:10.674 treatment for their obesity,

NOTE Confidence: 0.34135723

00:20:10.680 --> 00:20:14.600 are these changes potentially reversible?

NOTE Confidence: 0.34135723

00:20:14.600 --> 00:20:15.600 So back to the question,

NOTE Confidence: 0.34135723

00:20:15.600 --> 00:20:17.350 why is it so difficult to lose

NOTE Confidence: 0.34135723

00:20:17.350 --> 00:20:18.760 weight and maintain weight loss?

NOTE Confidence: 0.34135723

00:20:18.760 --> 00:20:19.342 And again,

NOTE Confidence: 0.34135723

00:20:19.342 --> 00:20:21.088 let's talk about this defended fat

NOTE Confidence: 0.34135723

00:20:21.088 --> 00:20:23.124 mass set point and this is a model

NOTE Confidence: 0.34135723

00:20:23.124 --> 00:20:24.919 that I'm going to tell you about.

NOTE Confidence: 0.34135723

00:20:24.920 --> 00:20:26.774 We don't know the molecular basis

NOTE Confidence: 0.34135723

00:20:26.774 --> 00:20:28.935 for it yet until maybe perhaps one

NOTE Confidence: 0.34135723

00:20:28.935 --> 00:20:31.240 of you can help us figure it out.

NOTE Confidence: 0.34135723

00:20:31.240 --> 00:20:34.660 So let's talk about the asset point.

NOTE Confidence: 0.34135723

00:20:34.660 --> 00:20:36.760 So let's talk about a house.

NOTE Confidence: 0.34135723

00:20:36.760 --> 00:20:38.278 And the house has a thermostat,

NOTE Confidence: 0.34135723

00:20:38.280 --> 00:20:40.068 and let's say that the thermostat

NOTE Confidence: 0.34135723

00:20:40.068 --> 00:20:42.560 is set to 70 degrees Fahrenheit.

NOTE Confidence: 0.34135723

00:20:42.560 --> 00:20:44.394 What happens when it is hot outside?

NOTE Confidence: 0.34135723

00:20:44.400 --> 00:20:45.680 Well, when it's hot outside,

NOTE Confidence: 0.34135723

00:20:45.680 --> 00:20:48.354 that thermostat senses, oh, it's 80 degrees.

NOTE Confidence: 0.34135723

00:20:48.360 --> 00:20:49.998 Let's turn on the air conditioner.

NOTE Confidence: 0.34135723

00:20:50.000 --> 00:20:51.918 This is not conscious. This just happens.

NOTE Confidence: 0.34135723

00:20:51.920 --> 00:20:53.400 You don't walk over to the air conditioner,

NOTE Confidence: 0.34135723

00:20:53.400 --> 00:20:55.199 it just does it itself as long

NOTE Confidence: 0.34135723

00:20:55.199 --> 00:20:56.590 as it's functioning properly.

NOTE Confidence: 0.34135723

00:20:56.590 --> 00:20:59.635 The opposite happens when it's cold outside.

NOTE Confidence: 0.34135723

00:20:59.640 --> 00:21:00.624 The furnace turns on.

NOTE Confidence: 0.34135723

00:21:00.624 --> 00:21:02.440 And again, this isn't a conscious decision.

NOTE Confidence: 0.34135723

00:21:02.440 --> 00:21:03.436 It just happens.

NOTE Confidence: 0.34135723

00:21:03.436 --> 00:21:05.760 Now what happens if it's July or

NOTE Confidence: 0.34135723

00:21:05.830 --> 00:21:07.996 August and it is incredibly hot?

NOTE Confidence: 0.34135723

00:21:08.000 --> 00:21:08.332 Well,

NOTE Confidence: 0.34135723

00:21:08.332 --> 00:21:09.992 sometimes that defended or that

NOTE Confidence: 0.34135723

00:21:09.992 --> 00:21:11.919 temperature set point is pushed up.

NOTE Confidence: 0.34135723

00:21:11.920 --> 00:21:14.594 It's really hard to maintain 70 degrees.

NOTE Confidence: 0.34135723

00:21:14.600 --> 00:21:16.142 You might open the windows and

NOTE Confidence: 0.34135723

00:21:16.142 --> 00:21:16.913 try different things,

NOTE Confidence: 0.34135723

00:21:16.920 --> 00:21:19.152 but sometimes that temperature just needs

NOTE Confidence: 0.34135723

00:21:19.152 --> 00:21:22.478 to be turned up for the system not to fail.

NOTE Confidence: 0.34135723

00:21:22.480 --> 00:21:24.232 And it turns out our body

NOTE Confidence: 0.34135723

00:21:24.232 --> 00:21:26.120 does this with many functions.

NOTE Confidence: 0.34135723

00:21:26.120 --> 00:21:28.030 We call this homeostasis and

NOTE Confidence: 0.34135723

00:21:28.030 --> 00:21:30.400 it does this with fat mass.

NOTE Confidence: 0.34135723

00:21:30.400 --> 00:21:32.524 And now let's look at our body and let's

NOTE Confidence: 0.34135723

00:21:32.524 --> 00:21:34.475 see how it does this with fat mass.

NOTE Confidence: 0.929106

00:21:34.480 --> 00:21:36.755 So now our brain is the thermostat

NOTE Confidence: 0.929106

00:21:36.755 --> 00:21:39.199 and it defends a fat mass set point.

NOTE Confidence: 0.929106

00:21:39.200 --> 00:21:41.314 So what happens when we gain weight

NOTE Confidence: 0.929106

00:21:41.314 --> 00:21:43.197 or specifically when we gain fat mass?

NOTE Confidence: 0.929106

00:21:43.200 --> 00:21:45.636 Well, the signals to our brain via

NOTE Confidence: 0.929106

00:21:45.636 --> 00:21:47.915 various hormones that we have gained fat

NOTE Confidence: 0.929106

00:21:47.915 --> 00:21:50.727 mass and it should signal us to increase

NOTE Confidence: 0.929106

00:21:50.727 --> 00:21:52.715 thermogenesis and decrease appetite.

NOTE Confidence: 0.929106

00:21:52.720 --> 00:21:54.682 But what happens when we lose

NOTE Confidence: 0.929106

00:21:54.682 --> 00:21:56.400 weight or lose fat mass?

NOTE Confidence: 0.929106

00:21:56.400 --> 00:21:58.997 Well, this should signal us to increase

NOTE Confidence: 0.929106

00:21:58.997 --> 00:22:00.505 appetite and decrease thermogenesis

NOTE Confidence: 0.929106

00:22:00.505 --> 00:22:03.177 and this is what we think is the

NOTE Confidence: 0.929106

00:22:03.177 --> 00:22:05.275 defended fat mass or set point model.

NOTE Confidence: 0.929106

00:22:05.280 --> 00:22:08.022 But now what happens in our

NOTE Confidence: 0.929106

00:22:08.022 --> 00:22:09.393 current obesogenic environment,

NOTE Confidence: 0.929106

00:22:09.400 --> 00:22:12.088 this environment filled with highly processed

NOTE Confidence: 0.929106

00:22:12.088 --> 00:22:14.592 food that's available all the time,

NOTE Confidence: 0.929106

00:22:14.592 --> 00:22:16.440 increased stress, lack of sleep,

NOTE Confidence: 0.929106

00:22:16.440 --> 00:22:17.880 lack of physical activity.

NOTE Confidence: 0.929106

00:22:17.880 --> 00:22:19.959 Well, this defended fat mass set point

NOTE Confidence: 0.929106

00:22:19.959 --> 00:22:22.200 is pushed up on a population level.

NOTE Confidence: 0.929106

00:22:22.200 --> 00:22:25.518 We are responding to our environment.

NOTE Confidence: 0.929106

00:22:25.520 --> 00:22:27.319 And so when we think about obesity,

NOTE Confidence: 0.929106

00:22:27.320 --> 00:22:29.847 really what obesity is and what it

NOTE Confidence: 0.929106

00:22:29.847 --> 00:22:31.951 results from is an inappropriate

NOTE Confidence: 0.929106

00:22:31.951 --> 00:22:34.771 dysregulation or or setting of that

NOTE Confidence: 0.929106

00:22:34.771 --> 00:22:37.194 defended fat mass set point and

NOTE Confidence: 0.929106

00:22:37.194 --> 00:22:39.164 what obesity treatment then requires

NOTE Confidence: 0.929106

00:22:39.164 --> 00:22:41.601 is resetting or re regulation of

NOTE Confidence: 0.929106

00:22:41.601 --> 00:22:43.959 that defended fat mass set point.

NOTE Confidence: 0.929106

00:22:43.960 --> 00:22:45.952 And so why is all this important and

NOTE Confidence: 0.929106

00:22:45.952 --> 00:22:48.221 why am I talking about it in the

NOTE Confidence: 0.929106

00:22:48.221 --> 00:22:50.120 context of anti obesity medications?

NOTE Confidence: 0.929106

00:22:50.120 --> 00:22:51.920 That's because any treatment that

NOTE Confidence: 0.929106

00:22:51.920 --> 00:22:53.360 we use for obesity,

NOTE Confidence: 0.929106

00:22:53.360 --> 00:22:55.880 the goal should be re regulation

NOTE Confidence: 0.929106

00:22:55.880 --> 00:22:58.040 of this defended fat mass.

NOTE Confidence: 0.929106

00:22:58.040 --> 00:22:59.840 So when we think about anti

NOTE Confidence: 0.929106

00:22:59.840 --> 00:23:00.440 obesity medications,

NOTE Confidence: 0.929106

00:23:00.440 --> 00:23:01.950 the goal is to decrease

NOTE Confidence: 0.929106

00:23:01.950 --> 00:23:03.158 that defended fat mass.

NOTE Confidence: 0.929106

00:23:03.160 --> 00:23:05.484 So you have all of these different

NOTE Confidence: 0.929106

00:23:05.484 --> 00:23:07.352 things pushing up the defended

NOTE Confidence: 0.929106

00:23:07.352 --> 00:23:09.968 fat mass and in our obesogenic

NOTE Confidence: 0.929106

00:23:09.968 --> 00:23:12.463 environment and what we want is

NOTE Confidence: 0.929106

00:23:12.463 --> 00:23:14.388 anti obesity medications to bring

NOTE Confidence: 0.929106

00:23:14.388 --> 00:23:16.917 it back down to re regulate it.

NOTE Confidence: 0.929106

00:23:16.920 --> 00:23:20.084 Now the question is how can anti

NOTE Confidence: 0.929106

00:23:20.084 --> 00:23:22.079 obesity medications potentially do this?

NOTE Confidence: 0.929106

00:23:22.080 --> 00:23:24.089 How can they reset or re regulate

NOTE Confidence: 0.929106

00:23:24.089 --> 00:23:26.078 that defended fat mass at that point?

NOTE Confidence: 0.929106

00:23:26.080 --> 00:23:26.412 Well,

NOTE Confidence: 0.929106

00:23:26.412 --> 00:23:28.736 it turns out a majority of the

NOTE Confidence: 0.929106

00:23:28.736 --> 00:23:30.775 medications that we have work in the

NOTE Confidence: 0.929106

00:23:30.775 --> 00:23:32.590 brain and it's not surprising because

NOTE Confidence: 0.929106

00:23:32.590 --> 00:23:35.213 the brain is what we think sets or

NOTE Confidence: 0.929106

00:23:35.213 --> 00:23:37.278 regulates that defended fat mass.

NOTE Confidence: 0.929106

00:23:37.280 --> 00:23:38.912 Now the one medication that's not

NOTE Confidence: 0.929106

00:23:38.912 --> 00:23:41.183 on here that is FDA approved for

NOTE Confidence: 0.929106

00:23:41.183 --> 00:23:42.675 obesity treatment is Orlistat.

NOTE Confidence: 0.929106

00:23:42.680 --> 00:23:46.208 We don't think that Orlistat re

NOTE Confidence: 0.929106

00:23:46.208 --> 00:23:48.048 regulates that defended fat mass

NOTE Confidence: 0.929106

00:23:48.048 --> 00:23:49.152 at that point.

NOTE Confidence: 0.929106

00:23:49.160 --> 00:23:51.416 So let's talk about the brain

NOTE Confidence: 0.929106

00:23:51.416 --> 00:23:52.920 again a little bit.

NOTE Confidence: 0.929106

00:23:52.920 --> 00:23:55.482 So we talked about the brain and

NOTE Confidence: 0.929106

00:23:55.482 --> 00:23:58.021 there are different regions that work

NOTE Confidence: 0.929106

00:23:58.021 --> 00:24:00.380 together to control eating behavior.

NOTE Confidence: 0.929106

00:24:00.380 --> 00:24:02.280 So cognitive executive regions,

NOTE Confidence: 0.929106

00:24:02.280 --> 00:24:03.633 hedonic and homeostatic.

NOTE Confidence: 0.929106

00:24:03.633 --> 00:24:06.339 And again initially it was thought

NOTE Confidence: 0.929106

00:24:06.339 --> 00:24:08.268 that the hypothalamus controlled

NOTE Confidence: 0.929106

00:24:08.268 --> 00:24:11.180 most of this in terms of being the

NOTE Confidence: 0.929106

00:24:11.180 --> 00:24:13.160 hunger center and the satiety center.

NOTE Confidence: 0.929106

00:24:13.160 --> 00:24:16.912 And so initially when looking at how

NOTE Confidence: 0.929106

00:24:16.912 --> 00:24:20.368 GLP one receptor agonist may work,

NOTE Confidence: 0.929106

00:24:20.368 --> 00:24:24.680 the focus was initially on the hypothalamus.

NOTE Confidence: 0.929106

00:24:24.680 --> 00:24:27.160 And if we and again GLP one receptor

NOTE Confidence: 0.929106

00:24:27.160 --> 00:24:29.575 agonist just to level set their

NOTE Confidence: 0.929106

00:24:29.575 --> 00:24:30.874 medications like somaglitide,

NOTE Confidence: 0.929106

00:24:30.880 --> 00:24:31.243 tirzepatide,

NOTE Confidence: 0.929106

00:24:31.243 --> 00:24:33.058 the things that you've been

NOTE Confidence: 0.929106

00:24:33.058 --> 00:24:35.079 likely reading about in the news.

NOTE Confidence: 0.929106

00:24:35.080 --> 00:24:38.640 So the thought is that GLP one directly

NOTE Confidence: 0.929106

00:24:38.640 --> 00:24:42.271 activates pump C CART neurons in the

NOTE Confidence: 0.929106

00:24:42.271 --> 00:24:44.395 hypothalamus and indirectly inhibits

NOTE Confidence: 0.49373502

00:24:44.400 --> 00:24:47.034 NPYAGRP neurons and collectively this results

NOTE Confidence: 0.49373502

00:24:47.034 --> 00:24:49.599 in signaling that reduces food intake.

NOTE Confidence: 0.49373502

00:24:49.600 --> 00:24:51.680 Of course, we know now that the story

00:24:51.680 --> 00:24:54.051 is much more complex and there is

00:24:54.051 --> 00:24:55.841 research ongoing actually looking at

00:24:55.906 --> 00:24:57.805 how these medications may impact reward

00:24:57.805 --> 00:25:00.244 and motivation regions of the brain and

00:25:00.244 --> 00:25:02.200 I think this is incredibly interesting.

00:25:02.200 --> 00:25:04.210 We were also interested in looking

00:25:04.210 --> 00:25:06.263 at this and looking at some of

00:25:06.263 --> 00:25:08.799 the the animal studies.

00:25:08.800 --> 00:25:10.795 There has been evidence that for example,

00:25:10.800 --> 00:25:13.866 some maglitide does act in

00:25:13.866 --> 00:25:15.918 the hypothalamus as as well as

00:25:15.918 --> 00:25:18.117 various regions in the hind brain.

00:25:18.120 --> 00:25:20.120 For us, we had an early pilot study,

00:25:20.120 --> 00:25:23.466 it was funded by the ADA and this

00:25:23.466 --> 00:25:26.285 was conducted by a pediatric

NOTE Confidence: 0.49373502

00:25:26.285 --> 00:25:28.510 endocrinology fellow who's now an

NOTE Confidence: 0.49373502

00:25:28.510 --> 00:25:30.590 assistant professor as well as a a

NOTE Confidence: 0.49373502

00:25:30.590 --> 00:25:33.080 post grad who is now in medical school.

NOTE Confidence: 0.49373502

00:25:33.080 --> 00:25:35.720 And we did this work with Regita and

NOTE Confidence: 0.49373502

00:25:35.720 --> 00:25:38.633 Bob Sherwin where we gave individuals

NOTE Confidence: 0.49373502

00:25:38.633 --> 00:25:42.198 laraglatide for about 12 weeks

NOTE Confidence: 0.49373502

00:25:42.200 --> 00:25:43.680 and we assessed various things,

NOTE Confidence: 0.49373502

00:25:43.680 --> 00:25:45.740 metabolic function or response,

NOTE Confidence: 0.49373502

00:25:45.740 --> 00:25:47.800 neural response and behavior.

NOTE Confidence: 0.49373502

00:25:47.800 --> 00:25:50.038 And I'll just highlight very briefly

NOTE Confidence: 0.49373502

00:25:50.040 --> 00:25:52.574 some of the some of the findings

NOTE Confidence: 0.49373502

00:25:52.574 --> 00:25:55.070 from this pilot that then led to

NOTE Confidence: 0.49373502

00:25:55.070 --> 00:25:57.520 an RO one that we currently have.

NOTE Confidence: 0.49373502

00:25:57.520 --> 00:26:00.621 So what we looked at was brain

NOTE Confidence: 0.49373502

00:26:00.621 --> 00:26:03.517 response again using F MRI and we gave

NOTE Confidence: 0.49373502

00:26:03.520 --> 00:26:05.120 participants this time these were

NOTE Confidence: 0.49373502

00:26:05.120 --> 00:26:07.392 young adults, high fructose corn syrup.

NOTE Confidence: 0.49373502

00:26:07.392 --> 00:26:09.432 It was a small sample,

NOTE Confidence: 0.49373502

00:26:09.440 --> 00:26:11.304 but what we found and what we looked

NOTE Confidence: 0.49373502

00:26:11.304 --> 00:26:13.262 at was basically the neural response

NOTE Confidence: 0.49373502

00:26:13.262 --> 00:26:15.052 after three months of treatment

NOTE Confidence: 0.49373502

00:26:15.052 --> 00:26:16.120 with loraglitide.

NOTE Confidence: 0.49373502

00:26:16.120 --> 00:26:18.106 And so this is the difference

NOTE Confidence: 0.49373502

00:26:18.106 --> 00:26:19.826 between during treatment with

NOTE Confidence: 0.49373502

00:26:19.826 --> 00:26:21.674 loraglitide versus at baseline.

NOTE Confidence: 0.49373502

00:26:21.680 --> 00:26:23.138 And the the difference that we

NOTE Confidence: 0.49373502

00:26:23.138 --> 00:26:24.840 found was in the hypothalamus,

NOTE Confidence: 0.49373502

00:26:24.840 --> 00:26:26.970 which is an important relay center

NOTE Confidence: 0.49373502

00:26:26.970 --> 00:26:28.035 in the brain.

NOTE Confidence: 0.49373502

00:26:28.040 --> 00:26:28.289 Again,

NOTE Confidence: 0.49373502

00:26:28.289 --> 00:26:30.281 this was a small sample but at least

NOTE Confidence: 0.49373502

00:26:30.281 --> 00:26:32.847 it gave us a clue that there were some

NOTE Confidence: 0.49373502

00:26:32.847 --> 00:26:34.879 differences that were ongoing in the brain.

NOTE Confidence: 0.49373502

00:26:34.880 --> 00:26:36.998 We also adapted the food snack

NOTE Confidence: 0.49373502

00:26:36.998 --> 00:26:39.170 task which was developed by Regita

NOTE Confidence: 0.49373502

00:26:39.170 --> 00:26:41.592 and we adapted it because we were

NOTE Confidence: 0.49373502

00:26:41.592 --> 00:26:43.408 interested in looking at sweet

NOTE Confidence: 0.49373502

00:26:43.408 --> 00:26:45.153 taste preference at the time.

NOTE Confidence: 0.49373502

00:26:45.160 --> 00:26:46.845 There was some indication that

NOTE Confidence: 0.49373502

00:26:46.845 --> 00:26:48.193 potentially GLP one receptor

NOTE Confidence: 0.49373502

00:26:48.193 --> 00:26:49.823 agonist may impact this and that

NOTE Confidence: 0.49373502

00:26:49.823 --> 00:26:51.360 was based on some animal work.

NOTE Confidence: 0.49373502

00:26:51.360 --> 00:26:52.260 So we plate,

NOTE Confidence: 0.49373502

00:26:52.260 --> 00:26:54.360 we replaced some of the foods with

NOTE Confidence: 0.49373502

00:26:54.427 --> 00:26:56.595 you can see some 3 sweet foods and

NOTE Confidence: 0.49373502

00:26:56.600 --> 00:26:59.678 three foods that are carbohydrate and

NOTE Confidence: 0.49373502

00:26:59.678 --> 00:27:02.560 potentially containing fat but not sweet.

NOTE Confidence: 0.49373502

00:27:02.560 --> 00:27:04.685 We videotaped participants and they

NOTE Confidence: 0.49373502

00:27:04.685 --> 00:27:07.232 had the opportunity for 30 minutes

NOTE Confidence: 0.49373502

00:27:07.232 --> 00:27:09.675 and then we measured the food that

NOTE Confidence: 0.49373502

00:27:09.675 --> 00:27:11.956 they ate and how much they ate.

NOTE Confidence: 0.49373502

00:27:11.960 --> 00:27:15.288 And what you'll see on these graphs are

NOTE Confidence: 0.49373502

00:27:15.288 --> 00:27:17.758 lean individuals are depicted in blue.

NOTE Confidence: 0.49373502

00:27:17.760 --> 00:27:21.090 Yellow are participants with obesity

NOTE Confidence: 0.49373502

00:27:21.090 --> 00:27:23.754 before receiving any laraglatide,

NOTE Confidence: 0.49373502

00:27:23.760 --> 00:27:26.020 then orange are participants

NOTE Confidence: 0.49373502

00:27:26.020 --> 00:27:28.280 during treatment with laraglatide.

NOTE Confidence: 0.49373502

00:27:28.280 --> 00:27:30.114 And then the green is the change,

NOTE Confidence: 0.49373502

00:27:30.120 --> 00:27:32.375 the difference between pre and

NOTE Confidence: 0.49373502

00:27:32.375 --> 00:27:33.277 post treatment.

NOTE Confidence: 0.49373502

00:27:33.280 --> 00:27:35.668 So first, in terms of caloric consumption,

NOTE Confidence: 0.49373502

00:27:35.668 --> 00:27:38.384 what you can see is that individuals

NOTE Confidence: 0.49373502

00:27:38.384 --> 00:27:41.080 with obesity did eat more than

NOTE Confidence: 0.49373502

00:27:41.080 --> 00:27:43.000 lean individuals at baseline,

NOTE Confidence: 0.49373502

00:27:43.000 --> 00:27:44.728 which is not surprising.

NOTE Confidence: 0.49373502

00:27:44.728 --> 00:27:45.160 Again,

NOTE Confidence: 0.49373502

00:27:45.160 --> 00:27:46.960 they're trying to defend this

NOTE Confidence: 0.49373502

00:27:46.960 --> 00:27:49.191 higher defended fat mass and so

NOTE Confidence: 0.49373502

00:27:49.191 --> 00:27:50.655 they're consuming more calories

NOTE Confidence: 0.49373502

00:27:50.655 --> 00:27:52.485 to defend that amount of

NOTE Confidence: 0.9534879

00:27:52.552 --> 00:27:54.402 fat. Then during treatment they ate less

NOTE Confidence: 0.9534879

00:27:54.402 --> 00:27:56.919 and it was not statistically significant.

NOTE Confidence: 0.9534879

00:27:56.920 --> 00:27:58.565 Again, this may be because of power

NOTE Confidence: 0.9534879

00:27:58.565 --> 00:28:00.549 and this is a consistent theme that

NOTE Confidence: 0.9534879

00:28:00.549 --> 00:28:02.079 you'll see with these findings.

NOTE Confidence: 0.9534879

00:28:02.080 --> 00:28:04.016 And here you can just see the change

NOTE Confidence: 0.9534879

00:28:04.016 --> 00:28:05.800 in terms of how much people eat.

NOTE Confidence: 0.9534879

00:28:05.800 --> 00:28:07.396 Then we looked at the observed

NOTE Confidence: 0.9534879

00:28:07.396 --> 00:28:08.194 sweet food intake.

NOTE Confidence: 0.9534879

00:28:08.200 --> 00:28:10.516 That's what I was interested in.

NOTE Confidence: 0.9534879

00:28:10.520 --> 00:28:13.040 And again, you can see that individuals

NOTE Confidence: 0.9534879

00:28:13.040 --> 00:28:15.168 with obesity depicted here in yellow

NOTE Confidence: 0.9534879

00:28:15.168 --> 00:28:17.280 did consume more sweet foods than

NOTE Confidence: 0.9534879

00:28:17.343 --> 00:28:19.317 those who were lean at baseline.

NOTE Confidence: 0.9534879

00:28:19.320 --> 00:28:21.385 And then with treatment again we saw

NOTE Confidence: 0.9534879

00:28:21.385 --> 00:28:23.858 a trend for decreased and sweet food

NOTE Confidence: 0.9534879

00:28:23.858 --> 00:28:25.744 intake but but not statistically

NOTE Confidence: 0.9534879

00:28:25.744 --> 00:28:28.000 significant and you can see the

NOTE Confidence: 0.9534879

00:28:28.073 --> 00:28:30.318 difference here depicted in green.

NOTE Confidence: 0.9534879

00:28:30.320 --> 00:28:31.625 Now this LED,

NOTE Confidence: 0.9534879

00:28:31.625 --> 00:28:34.670 this was sufficient pilot data to lead

NOTE Confidence: 0.9534879

00:28:34.756 --> 00:28:37.325 to an RO one that I have the privilege

NOTE Confidence: 0.9534879

00:28:37.325 --> 00:28:41.031 of of conducting with Regita as as Co PIS.

NOTE Confidence: 0.9534879

00:28:41.031 --> 00:28:43.250 And here is some of our wonderful

NOTE Confidence: 0.9534879

00:28:43.325 --> 00:28:45.747 team who is actually doing all the

NOTE Confidence: 0.9534879

00:28:45.747 --> 00:28:48.386 work and some of our junior faculty

NOTE Confidence: 0.9534879

00:28:48.386 --> 00:28:50.678 who are now progressing on into

NOTE Confidence: 0.9534879

00:28:50.680 --> 00:28:52.436 further ladder track positions.

NOTE Confidence: 0.9534879

00:28:52.436 --> 00:28:55.545 And this RO one we're looking at

NOTE Confidence: 0.9534879

00:28:55.545 --> 00:28:58.317 Somagnetide and the effects of food cues,

NOTE Confidence: 0.9534879

00:28:58.320 --> 00:29:00.295 stress and motivation for highly

NOTE Confidence: 0.9534879

00:29:00.295 --> 00:29:01.875 palatable food and weight.

NOTE Confidence: 0.9534879

00:29:01.880 --> 00:29:04.208 And what we're doing is we're

NOTE Confidence: 0.9534879

00:29:04.208 --> 00:29:06.228 randomizing individuals with obesity to

NOTE Confidence: 0.9534879

00:29:06.228 --> 00:29:08.238 receive either placebo or Somagnetide.

NOTE Confidence: 0.9534879

00:29:08.240 --> 00:29:10.459 They received that for 12 weeks and

NOTE Confidence: 0.9534879

00:29:10.459 --> 00:29:12.758 then we actually also look at a one

NOTE Confidence: 0.9534879

00:29:12.758 --> 00:29:14.484 month follow up off the medication

NOTE Confidence: 0.9534879

00:29:14.484 --> 00:29:15.996 to see what happens.

NOTE Confidence: 0.9534879

00:29:16.000 --> 00:29:17.392 We're looking at weight,

NOTE Confidence: 0.9534879

00:29:17.392 --> 00:29:19.480 but we're actually what we're really

NOTE Confidence: 0.9534879

00:29:19.539 --> 00:29:21.134 interested in are the metabolic

NOTE Confidence: 0.9534879

00:29:21.134 --> 00:29:23.169 responses as well as how individuals

NOTE Confidence: 0.9534879

00:29:23.169 --> 00:29:25.049 may be consuming food differently

NOTE Confidence: 0.9534879

00:29:25.049 --> 00:29:27.045 and we're using this validated

NOTE Confidence: 0.9534879

00:29:27.045 --> 00:29:29.955 food snack test to assess this.

NOTE Confidence: 0.9534879

00:29:29.960 --> 00:29:32.354 And so we are in year four.

NOTE Confidence: 0.9534879

00:29:32.360 --> 00:29:35.660 So anticipate those results fairly

NOTE Confidence: 0.9534879

00:29:35.660 --> 00:29:38.184 soon and hopefully next time

NOTE Confidence: 0.9534879

00:29:38.184 --> 00:29:40.480 I I present to all of you,

NOTE Confidence: 0.9534879

00:29:40.480 --> 00:29:43.438 we'll have some data on that.

NOTE Confidence: 0.9534879

00:29:43.440 --> 00:29:44.120 Now additionally,

NOTE Confidence: 0.9534879

00:29:44.120 --> 00:29:46.500 let's focus in briefly again on the

NOTE Confidence: 0.9534879

00:29:46.500 --> 00:29:48.349 hedonic salience regions of the brain

NOTE Confidence: 0.9534879

00:29:48.349 --> 00:29:50.524 and I think there will be a lot

NOTE Confidence: 0.9534879

00:29:50.524 --> 00:29:51.994 more work with GLP ones specifically

NOTE Confidence: 0.9534879

00:29:51.994 --> 00:29:54.118 on these regions of the brain.

NOTE Confidence: 0.9534879

00:29:54.120 --> 00:29:56.316 But up till now, what has been looked at?

NOTE Confidence: 0.9534879

00:29:56.320 --> 00:29:57.514 Well, of course,

NOTE Confidence: 0.9534879

00:29:57.514 --> 00:29:59.504 dopaminergic pathways that are so

NOTE Confidence: 0.9534879

00:29:59.504 --> 00:30:01.656 important for reward and motivation

NOTE Confidence: 0.9534879

00:30:01.656 --> 00:30:03.796 as well as serotonergic pathways.

NOTE Confidence: 0.9534879

00:30:03.800 --> 00:30:06.170 Now there are medications that have

NOTE Confidence: 0.9534879

00:30:06.170 --> 00:30:07.750 targeted these different pathways

NOTE Confidence: 0.9534879

00:30:07.814 --> 00:30:08.558 in the brain.

NOTE Confidence: 0.9534879

00:30:08.560 --> 00:30:11.080 Lorcasterin is no longer on the market,

NOTE Confidence: 0.9534879

00:30:11.080 --> 00:30:13.920 but it targeted serotonergic pathways,

NOTE Confidence: 0.9534879

00:30:13.920 --> 00:30:14.439 bupropion,

NOTE Confidence: 0.9534879

00:30:14.439 --> 00:30:16.515 phentermine and then naltrexone

NOTE Confidence: 0.9534879

00:30:16.515 --> 00:30:18.591 and topiramate target different

NOTE Confidence: 0.9534879

00:30:18.591 --> 00:30:19.959 types of pathways.

NOTE Confidence: 0.9534879

00:30:19.960 --> 00:30:21.808 And it's just to say again that

NOTE Confidence: 0.9534879

00:30:21.808 --> 00:30:22.943 these medications target these

NOTE Confidence: 0.9534879

00:30:22.943 --> 00:30:24.398 different regions of the brain.

NOTE Confidence: 0.9534879

00:30:24.400 --> 00:30:26.370 And there are investigators like

NOTE Confidence: 0.9534879

00:30:26.370 --> 00:30:28.340 Carlos Grillo and Valentina Ivisage

NOTE Confidence: 0.9534879

00:30:28.403 --> 00:30:30.245 who have also had the privilege

NOTE Confidence: 0.9534879

00:30:30.245 --> 00:30:32.000 of working on various studies,

NOTE Confidence: 0.9534879

00:30:32.000 --> 00:30:33.878 both in terms of looking at

NOTE Confidence: 0.9534879

00:30:33.878 --> 00:30:35.572 naltrexone bupropion in the setting

NOTE Confidence: 0.9534879

00:30:35.572 --> 00:30:37.076 of binge eating disorder,

NOTE Confidence: 0.9534879

00:30:37.080 --> 00:30:40.846 as well As for loss of control

NOTE Confidence: 0.9534879

00:30:40.846 --> 00:30:43.320 eating following bariatric surgery.

NOTE Confidence: 0.9534879

00:30:43.320 --> 00:30:45.160 And now what about cognitive

NOTE Confidence: 0.9534879

00:30:45.160 --> 00:30:47.000 executive regions of the brain?

NOTE Confidence: 0.9534879

00:30:47.000 --> 00:30:48.071 For so long,

NOTE Confidence: 0.9534879

00:30:48.071 --> 00:30:50.570 it was thought that patients could control

NOTE Confidence: 0.9534879

00:30:50.643 --> 00:30:52.918 every morsel of food that they eat.

NOTE Confidence: 0.9534879

00:30:52.920 --> 00:30:54.438 For the rest of their lives,

NOTE Confidence: 0.83755195

00:30:54.440 --> 00:30:56.340 they could simply impart

NOTE Confidence: 0.83755195

00:30:56.340 --> 00:30:58.240 executive function and decision

NOTE Confidence: 0.83755195

00:30:58.240 --> 00:30:59.776 making to make these decisions.

NOTE Confidence: 0.83755195

00:30:59.776 --> 00:31:02.021 But of course we know as as we've

NOTE Confidence: 0.83755195

00:31:02.021 --> 00:31:03.839 just talked about that the striatum,

NOTE Confidence: 0.83755195

00:31:03.840 --> 00:31:04.546 the hypothalamus,

NOTE Confidence: 0.83755195

00:31:04.546 --> 00:31:07.017 all of these brain regions work in

NOTE Confidence: 0.83755195

00:31:07.017 --> 00:31:08.933 concert and biology is really pushing

NOTE Confidence: 0.83755195

00:31:08.933 --> 00:31:11.149 us and making it very difficult for

NOTE Confidence: 0.83755195

00:31:11.149 --> 00:31:13.438 us to make those types of decisions.

NOTE Confidence: 0.83755195

00:31:13.440 --> 00:31:15.547 It's almost as if we were asking

NOTE Confidence: 0.83755195

00:31:15.547 --> 00:31:17.929 our patients to hold their breath

NOTE Confidence: 0.83755195

00:31:17.929 --> 00:31:20.050 indefinitely in the same way we're

NOTE Confidence: 0.83755195

00:31:20.050 --> 00:31:22.116 asking them to to decide on every

NOTE Confidence: 0.83755195

00:31:22.116 --> 00:31:24.084 morsel food that they eat for the

NOTE Confidence: 0.83755195

00:31:24.084 --> 00:31:26.128 rest of their life when their biology

NOTE Confidence: 0.83755195

00:31:26.128 --> 00:31:28.112 is telling them that they are

NOTE Confidence: 0.83755195

00:31:28.112 --> 00:31:29.792 incredibly hungry or craving foods.

NOTE Confidence: 0.83755195

00:31:29.800 --> 00:31:30.586 And of course,

NOTE Confidence: 0.83755195

00:31:30.586 --> 00:31:31.372 there's many interventions

NOTE Confidence: 0.83755195

00:31:31.372 --> 00:31:32.880 that can be used for this,

NOTE Confidence: 0.83755195

00:31:32.880 --> 00:31:35.400 but it does make it very difficult.

NOTE Confidence: 0.83755195

00:31:35.400 --> 00:31:37.416 So all of these regions of

NOTE Confidence: 0.83755195

00:31:37.416 --> 00:31:38.760 the brain work together.

NOTE Confidence: 0.83755195

00:31:38.760 --> 00:31:42.090 They impact food intake as

NOTE Confidence: 0.83755195

00:31:42.090 --> 00:31:44.754 well as energy homeostasis.

NOTE Confidence: 0.83755195

00:31:44.760 --> 00:31:45.072 OK.

NOTE Confidence: 0.83755195

00:31:45.072 --> 00:31:46.944 So we've talked a lot about

NOTE Confidence: 0.83755195

00:31:46.944 --> 00:31:47.880 this first barrier,

NOTE Confidence: 0.83755195

00:31:47.880 --> 00:31:49.914 and that's what I really wanted to focus on,

NOTE Confidence: 0.83755195

00:31:49.920 --> 00:31:52.456 But let's touch on a couple of others

NOTE Confidence: 0.83755195

00:31:52.456 --> 00:31:54.678 and then return to our patient.

NOTE Confidence: 0.83755195

00:31:54.680 --> 00:31:57.333 So the next barrier is this fear

NOTE Confidence: 0.83755195

00:31:57.333 --> 00:31:59.479 of causing dangerous side effects.

NOTE Confidence: 0.83755195

00:31:59.480 --> 00:32:01.376 This has been something that's come

NOTE Confidence: 0.83755195

00:32:01.376 --> 00:32:03.484 about from the fact that these

NOTE Confidence: 0.83755195

00:32:03.484 --> 00:32:05.439 medications that were approved for

NOTE Confidence: 0.83755195

00:32:05.439 --> 00:32:07.880 obesity treatment have had a sordid history.

NOTE Confidence: 0.83755195

00:32:07.880 --> 00:32:10.876 And of course many of you I'm

NOTE Confidence: 0.83755195

00:32:10.876 --> 00:32:12.160 sure remember Romanaband,

NOTE Confidence: 0.83755195

00:32:12.160 --> 00:32:14.400 but if we look at the second

NOTE Confidence: 0.83755195

00:32:14.400 --> 00:32:16.168 generation medication, so for example,

NOTE Confidence: 0.83755195

00:32:16.168 --> 00:32:17.383 phentermine, topiramate, naltrexone,

NOTE Confidence: 0.83755195

00:32:17.383 --> 00:32:17.846 bupropion,

NOTE Confidence: 0.83755195

00:32:17.846 --> 00:32:20.161 the components of these medications

NOTE Confidence: 0.83755195

00:32:20.161 --> 00:32:22.503 have been used for different

NOTE Confidence: 0.83755195

00:32:22.503 --> 00:32:24.279 indications over many years.

NOTE Confidence: 0.83755195

00:32:24.280 --> 00:32:26.352 So it's not to say that they

NOTE Confidence: 0.83755195

00:32:26.352 --> 00:32:27.886 were specifically looked at for

NOTE Confidence: 0.83755195

00:32:27.886 --> 00:32:28.759 safety and obesity,

NOTE Confidence: 0.83755195

00:32:28.760 --> 00:32:30.979 but we at least have more information

NOTE Confidence: 0.83755195

00:32:30.979 --> 00:32:33.517 about them in different contexts now.

NOTE Confidence: 0.83755195

00:32:33.517 --> 00:32:34.708 Loraglitide and Somaglitide,

NOTE Confidence: 0.83755195

00:32:34.708 --> 00:32:37.090 which are both FDA approved for

NOTE Confidence: 0.83755195

00:32:37.160 --> 00:32:39.680 obesity treatment belong to a class

NOTE Confidence: 0.83755195

00:32:39.680 --> 00:32:41.160 of medications called Glucagon

NOTE Confidence: 0.83755195

00:32:41.160 --> 00:32:42.999 like peptide receptor agonist,

NOTE Confidence: 0.83755195

00:32:43.000 --> 00:32:44.806 and they've been used for the treatment

NOTE Confidence: 0.83755195

00:32:44.806 --> 00:32:47.319 of type 2 diabetes for nearly two decades.

NOTE Confidence: 0.83755195

00:32:47.320 --> 00:32:47.950 So again,

NOTE Confidence: 0.83755195

00:32:47.950 --> 00:32:50.155 we have more safety data on these

NOTE Confidence: 0.83755195

00:32:50.160 --> 00:32:50.507 medications.

NOTE Confidence: 0.83755195

00:32:50.507 --> 00:32:52.589 Now there are common side effects

NOTE Confidence: 0.83755195

00:32:52.589 --> 00:32:54.157 of these medications and we

NOTE Confidence: 0.83755195

00:32:54.157 --> 00:32:55.555 hear about this all the time.

NOTE Confidence: 0.83755195

00:32:55.560 --> 00:32:57.108 I don't think there's any medicine

NOTE Confidence: 0.83755195

00:32:57.108 --> 00:32:58.472 for any disease that doesn't

NOTE Confidence: 0.83755195

00:32:58.472 --> 00:32:59.596 have any side effects,

NOTE Confidence: 0.83755195

00:32:59.600 --> 00:33:02.342 but certainly these are important to

NOTE Confidence: 0.83755195

00:33:02.342 --> 00:33:04.800 consider as we counsel our patients.

NOTE Confidence: 0.83755195

00:33:04.800 --> 00:33:06.690 So most of them are gastrointestinal

NOTE Confidence: 0.83755195

00:33:06.690 --> 00:33:08.781 side effects, but for example,

NOTE Confidence: 0.83755195

00:33:08.781 --> 00:33:11.703 topiramate can have mental fogginess or

NOTE Confidence: 0.83755195

00:33:11.703 --> 00:33:14.320 paresthesias that we have to look out for.

NOTE Confidence: 0.83755195

00:33:14.320 --> 00:33:17.400 Naltrexone of course can lead to nausea.

NOTE Confidence: 0.83755195

00:33:17.400 --> 00:33:19.712 So there are other side effects that we

NOTE Confidence: 0.83755195

00:33:19.712 --> 00:33:22.515 have to counsel our patients about as well.

NOTE Confidence: 0.83755195

00:33:22.520 --> 00:33:24.880 Now just focusing in on the GI side

NOTE Confidence: 0.83755195

00:33:24.880 --> 00:33:27.039 effects because these come up quite a bit.

NOTE Confidence: 0.83755195

00:33:27.040 --> 00:33:28.558 Let's look at nausea and diarrhoea.

NOTE Confidence: 0.83755195

00:33:28.560 --> 00:33:30.696 These are the most commonly reported

NOTE Confidence: 0.83755195

00:33:30.696 --> 00:33:32.800 with the newer medications especially.

NOTE Confidence: 0.83755195

00:33:32.800 --> 00:33:35.560 So this is depicting the observation

NOTE Confidence: 0.83755195

00:33:35.560 --> 00:33:38.160 or the time during a trial.

NOTE Confidence: 0.83755195

00:33:38.160 --> 00:33:39.714 It was a trial which was appetite.

NOTE Confidence: 0.83755195

00:33:39.720 --> 00:33:41.239 And what you can see with nausea

NOTE Confidence: 0.83755195

00:33:41.239 --> 00:33:42.678 is that in the placebo group

NOTE Confidence: 0.83755195

00:33:42.678 --> 00:33:44.154 at the start of the trial,

NOTE Confidence: 0.83755195

00:33:44.160 --> 00:33:45.240 more participants reported

NOTE Confidence: 0.83755195

00:33:45.240 --> 00:33:47.760 nausea and it that was also the

NOTE Confidence: 0.3997720592

00:33:47.824 --> 00:33:49.499 case with the 10 milligram

NOTE Confidence: 0.3997720592

00:33:49.499 --> 00:33:51.174 dose of tirzepatide and the

NOTE Confidence: 0.3997720592

00:33:51.239 --> 00:33:53.039 incidence of this was higher.

NOTE Confidence: 0.3997720592

00:33:53.040 --> 00:33:55.704 But you can see that after the dose

NOTE Confidence: 0.3997720592

00:33:55.704 --> 00:33:57.400 escalation phase this decreased.

NOTE Confidence: 0.3997720592

00:33:57.400 --> 00:34:00.046 You can see the same trend for

NOTE Confidence: 0.3997720592

00:34:00.046 --> 00:34:02.544 diarrhea with both placebo as well

NOTE Confidence: 0.3997720592

00:34:02.544 --> 00:34:05.112 as with tirzepatide that over time

NOTE Confidence: 0.3997720592

00:34:05.120 --> 00:34:07.676 these side effects began to decrease.

NOTE Confidence: 0.3997720592

00:34:07.680 --> 00:34:09.672 And so we learned from these

NOTE Confidence: 0.3997720592

00:34:09.672 --> 00:34:11.000 trials that most gastro,

NOTE Confidence: 0.3997720592

00:34:11.000 --> 00:34:12.995 most of the side effects with these

NOTE Confidence: 0.3997720592

00:34:12.995 --> 00:34:14.760 newer medications are gastrointestinal,

NOTE Confidence: 0.3997720592

00:34:14.760 --> 00:34:17.352 they are transient and primarily occurred

NOTE Confidence: 0.3997720592

00:34:17.352 --> 00:34:20.200 during the dose escalation phase and are

NOTE Confidence: 0.3997720592

00:34:20.200 --> 00:34:22.312 mostly mild to moderate in severity.

NOTE Confidence: 0.3997720592

00:34:22.320 --> 00:34:24.000 Now overall for the medications,

NOTE Confidence: 0.3997720592

00:34:24.000 --> 00:34:26.919 what are some important things to discuss?

NOTE Confidence: 0.3997720592

00:34:26.920 --> 00:34:28.864 Well, first it's important to share

NOTE Confidence: 0.3997720592

00:34:28.864 --> 00:34:30.676 with our patients that there aren't

NOTE Confidence: 0.3997720592

00:34:30.676 --> 00:34:31.966 really medications for any disease

NOTE Confidence: 0.3997720592

00:34:31.966 --> 00:34:33.320 that don't have side effects.

NOTE Confidence: 0.3997720592

00:34:33.320 --> 00:34:35.588 So let's talk about the side effects

NOTE Confidence: 0.3997720592

00:34:35.588 --> 00:34:37.919 before the patient starts the medication,

NOTE Confidence: 0.3997720592

00:34:37.920 --> 00:34:39.516 so that they're aware and they know

NOTE Confidence: 0.3997720592

00:34:39.516 --> 00:34:41.737 what to look out for and they tell you

NOTE Confidence: 0.3997720592

00:34:41.737 --> 00:34:43.399 when they experience these side effects.

NOTE Confidence: 0.3997720592

00:34:43.400 --> 00:34:45.824 So some common themes that we can do

NOTE Confidence: 0.3997720592

00:34:45.824 --> 00:34:47.681 as providers to help our patients

NOTE Confidence: 0.3997720592

00:34:47.681 --> 00:34:49.907 is to always start with the lowest

NOTE Confidence: 0.3997720592

00:34:49.907 --> 00:34:52.205 starting dose of any medication to

NOTE Confidence: 0.3997720592

00:34:52.205 --> 00:34:54.182 monitor our patients for side effects

NOTE Confidence: 0.3997720592

00:34:54.182 --> 00:34:56.100 and invite them to share those side

NOTE Confidence: 0.3997720592

00:34:56.155 --> 00:34:58.226 effects with us when they have them or

NOTE Confidence: 0.3997720592

00:34:58.226 --> 00:35:00.034 if they have them and to up titrate

NOTE Confidence: 0.3997720592

00:35:00.034 --> 00:35:02.359 the dose only is tolerated by the patient.

NOTE Confidence: 0.3997720592

00:35:02.360 --> 00:35:03.800 So if a patient's having nausea,

NOTE Confidence: 0.3997720592

00:35:03.800 --> 00:35:06.565 we wouldn't go up until that nausea

NOTE Confidence: 0.3997720592

00:35:06.565 --> 00:35:08.100 dissipates because we don't want

NOTE Confidence: 0.3997720592

00:35:08.100 --> 00:35:09.240 them to have vomiting.

NOTE Confidence: 0.3997720592

00:35:09.240 --> 00:35:11.216 And to borrow a phrase that all of

NOTE Confidence: 0.3997720592

00:35:11.216 --> 00:35:13.508 you I'm sure are very familiar with

NOTE Confidence: 0.3997720592

00:35:13.508 --> 00:35:15.243 for for other treatments within

NOTE Confidence: 0.3997720592

00:35:15.306 --> 00:35:16.718 the mental health space,

NOTE Confidence: 0.3997720592

00:35:16.720 --> 00:35:19.168 our goal is to start low and go

NOTE Confidence: 0.3997720592

00:35:19.168 --> 00:35:21.237 slow and that is the theme.

NOTE Confidence: 0.3997720592

00:35:21.240 --> 00:35:24.078 And specifically with the newer medications

NOTE Confidence: 0.3997720592

00:35:24.080 --> 00:35:26.120 and the gastrointestinal side effects,

NOTE Confidence: 0.3997720592

00:35:26.120 --> 00:35:27.608 this slow dose escalation as I

NOTE Confidence: 0.3997720592

00:35:27.608 --> 00:35:29.258 showed you in the previous slide

NOTE Confidence: 0.3997720592

00:35:29.258 --> 00:35:31.076 that we learned from the trials,

NOTE Confidence: 0.3997720592

00:35:31.080 --> 00:35:33.330 Our patients can also implement

NOTE Confidence: 0.3997720592

00:35:33.330 --> 00:35:35.580 various mitigation strategies such as

NOTE Confidence: 0.3997720592

00:35:35.645 --> 00:35:37.714 eating smaller amounts at mealtimes,

NOTE Confidence: 0.3997720592

00:35:37.714 --> 00:35:39.616 stopping to eat when they're full

NOTE Confidence: 0.3997720592

00:35:39.616 --> 00:35:41.833 and noting which foods may exacerbate

NOTE Confidence: 0.3997720592

00:35:41.833 --> 00:35:42.597 their symptoms.

NOTE Confidence: 0.3997720592

00:35:42.600 --> 00:35:46.240 And most commonly these are high fat foods.

NOTE Confidence: 0.3997720592

00:35:46.240 --> 00:35:49.516 And again the goal is start low and go,

NOTE Confidence: 0.3997720592

00:35:49.520 --> 00:35:51.440 go slow and don't go up.

NOTE Confidence: 0.3997720592

00:35:51.440 --> 00:35:53.300 If your patient is having significant

NOTE Confidence: 0.3997720592

00:35:53.300 --> 00:35:53.920 side effects,

NOTE Confidence: 0.3997720592

00:35:53.920 --> 00:35:57.480 wait a few months and then go up on the dose.

NOTE Confidence: 0.3997720592

00:35:57.480 --> 00:35:59.565 Now there's another challenge which

NOTE Confidence: 0.3997720592

00:35:59.565 --> 00:36:02.151 is this perception that anti obesity

NOTE Confidence: 0.3997720592

00:36:02.151 --> 00:36:04.331 medications are not effective and

NOTE Confidence: 0.3997720592

00:36:04.331 --> 00:36:06.075 this is rapidly changing.

NOTE Confidence: 0.3997720592

00:36:06.080 --> 00:36:08.456 So previously we would say well

NOTE Confidence: 0.3997720592

00:36:08.456 --> 00:36:10.837 with one medication and you may

NOTE Confidence: 0.3997720592

00:36:10.837 --> 00:36:13.422 lose somewhere between 5 and 10% if

NOTE Confidence: 0.3997720592

00:36:13.422 --> 00:36:15.954 you are have a good response.

NOTE Confidence: 0.3997720592

00:36:15.960 --> 00:36:18.193 Now if we obviously if we combine

NOTE Confidence: 0.3997720592

00:36:18.193 --> 00:36:20.088 these medications as I showed you

NOTE Confidence: 0.3997720592

00:36:20.088 --> 00:36:21.828 with the first patient this could

NOTE Confidence: 0.3997720592

00:36:21.828 --> 00:36:24.064 be more but really Smeglitide was

NOTE Confidence: 0.3997720592

00:36:24.064 --> 00:36:25.896 the first medication that changed

NOTE Confidence: 0.3997720592

00:36:25.896 --> 00:36:27.984 this landscape and helped us to

NOTE Confidence: 0.3997720592

00:36:27.984 --> 00:36:30.239 leap from the past to the future.

NOTE Confidence: 0.3997720592

00:36:30.240 --> 00:36:32.389 And we are currently at this watershed

NOTE Confidence: 0.3997720592

00:36:32.389 --> 00:36:34.495 that's brought on by the recent

NOTE Confidence: 0.3997720592

00:36:34.495 --> 00:36:35.999 introduction of these medications.

NOTE Confidence: 0.3997720592

00:36:36.000 --> 00:36:38.364 So here are the medications that

NOTE Confidence: 0.3997720592

00:36:38.364 --> 00:36:39.940 that were that are

NOTE Confidence: 0.4603952

00:36:40.019 --> 00:36:42.446 currently FDA approved and here are

NOTE Confidence: 0.4603952

00:36:42.446 --> 00:36:44.140 some of the medications that are in

NOTE Confidence: 0.4603952

00:36:44.193 --> 00:36:46.008 development and leading the charge

NOTE Confidence: 0.4603952

00:36:46.008 --> 00:36:47.460 are nutrient stimulated hormone

NOTE Confidence: 0.4603952

00:36:47.460 --> 00:36:49.038 based therapies and I'll share a

NOTE Confidence: 0.4603952

00:36:49.038 --> 00:36:51.022 few of the new ones with you today.

NOTE Confidence: 0.4603952

00:36:51.022 --> 00:36:52.392 There's others that I don't

NOTE Confidence: 0.4603952

00:36:52.392 --> 00:36:53.520 have time to get to.

NOTE Confidence: 0.4603952

00:36:53.520 --> 00:36:55.745 So active and receptor inhibitors

68

NOTE Confidence: 0.4603952

00:36:55.745 --> 00:36:58.471 that actually can help maintain muscle

NOTE Confidence: 0.4603952

00:36:58.471 --> 00:37:00.636 mass while decreasing fat mass.

NOTE Confidence: 0.4603952

00:37:00.640 --> 00:37:02.824 There's also an MC4 agonist for

NOTE Confidence: 0.4603952

00:37:02.824 --> 00:37:05.191 monogenic obesity and there are many

NOTE Confidence: 0.4603952

00:37:05.191 --> 00:37:06.879 other mechanisms being explored.

NOTE Confidence: 0.4603952

00:37:06.880 --> 00:37:08.740 So let's focus in on nutrient

NOTE Confidence: 0.4603952

00:37:08.740 --> 00:37:10.764 stimulated hormones. What are these?

NOTE Confidence: 0.4603952

00:37:10.764 --> 00:37:13.771 Well, GLP One is the nutrient stimulated

NOTE Confidence: 0.4603952

00:37:13.771 --> 00:37:16.033 hormone that we're most familiar with,

NOTE Confidence: 0.4603952

00:37:16.040 --> 00:37:18.070 used for the treatment of type 2

NOTE Confidence: 0.4603952

00:37:18.070 --> 00:37:20.079 diabetes as a receptor agonist.

NOTE Confidence: 0.4603952

00:37:20.080 --> 00:37:21.598 But what are these in general?

NOTE Confidence: 0.4603952

00:37:21.600 --> 00:37:23.820 Well, these hormones are any hormone

NOTE Confidence: 0.4603952

00:37:23.820 --> 00:37:25.915 that is stimulated when we eat

NOTE Confidence: 0.4603952

00:37:25.915 --> 00:37:27.819 food and they signal to our brain

NOTE Confidence: 0.4603952

00:37:27.819 --> 00:37:30.337 and to various tissues in our body

NOTE Confidence: 0.4603952

00:37:30.337 --> 00:37:32.316 about energy homeostasis and that

NOTE Confidence: 0.4603952

00:37:32.316 --> 00:37:35.412 includes food intake as well as

NOTE Confidence: 0.4603952

00:37:35.412 --> 00:37:36.960 potentially energy expenditure.

NOTE Confidence: 0.4603952

00:37:36.960 --> 00:37:38.600 So starting with GLP one,

NOTE Confidence: 0.4603952

00:37:38.600 --> 00:37:40.406 we saw that there was weight reduction

NOTE Confidence: 0.4603952

00:37:40.406 --> 00:37:42.238 in our patients with type 2 diabetes.

NOTE Confidence: 0.4603952

00:37:42.240 --> 00:37:45.340 But now we know that pairing GLP

NOTE Confidence: 0.4603952

00:37:45.340 --> 00:37:47.190 one with other nutrients stimulated

NOTE Confidence: 0.4603952

00:37:47.190 --> 00:37:48.880 hormones such as Glucagon,

NOTE Confidence: 0.4603952

00:37:48.880 --> 00:37:51.414 Amylin or *** and dual agonist or

NOTE Confidence: 0.4603952

00:37:51.414 --> 00:37:53.412 triple agonist can actually increase

NOTE Confidence: 0.4603952

00:37:53.412 --> 00:37:56.338 the amount of weight reduction that can

NOTE Confidence: 0.4603952

00:37:56.338 --> 00:37:59.757 be attained as well as other health benefits.

NOTE Confidence: 0.4603952

00:37:59.760 --> 00:38:02.880 And so this slide I update almost daily.

NOTE Confidence: 0.4603952

00:38:02.880 --> 00:38:04.448 It is just a snapshot of some

NOTE Confidence: 0.4603952

00:38:04.448 --> 00:38:05.535 of the nutrient stimulated

NOTE Confidence: 0.4603952

00:38:05.535 --> 00:38:07.360 hormones that are in development.

NOTE Confidence: 0.4603952

00:38:07.360 --> 00:38:09.624 These are just the ones in phase two

NOTE Confidence: 0.4603952

00:38:09.624 --> 00:38:11.886 and three double this and that's how

NOTE Confidence: 0.4603952

00:38:11.886 --> 00:38:14.200 many are in development in phase one.

NOTE Confidence: 0.4603952

00:38:14.200 --> 00:38:16.965 And the ones that are outlined and

NOTE Confidence: 0.4603952

00:38:16.965 --> 00:38:19.226 that I just highlighted here are the

NOTE Confidence: 0.4603952

00:38:19.226 --> 00:38:21.527 ones in phase three and I'll share

NOTE Confidence: 0.4603952

00:38:21.527 --> 00:38:23.519 with you very briefly about these.

NOTE Confidence: 0.4603952

00:38:23.520 --> 00:38:25.536 So some maglitide was the first one

NOTE Confidence: 0.4603952

00:38:25.536 --> 00:38:28.349 that is a long acting GLP and receptor

NOTE Confidence: 0.4603952

00:38:28.349 --> 00:38:30.234 agonist that was FDA approved.

NOTE Confidence: 0.4603952

00:38:30.240 --> 00:38:32.334 It is once weekly and injectable

NOTE Confidence: 0.4603952

00:38:32.334 --> 00:38:34.231 and it demonstrated an average

NOTE Confidence: 0.4603952

00:38:34.231 --> 00:38:36.726 weight reduction of 16.9% at 68

NOTE Confidence: 0.4603952

00:38:36.726 --> 00:38:39.138 weeks and that's an average weight

NOTE Confidence: 0.4603952

00:38:39.138 --> 00:38:40.996 reduction of £34 in this trial.

NOTE Confidence: 0.4603952

00:38:40.996 --> 00:38:42.850 It was also demonstrated that there

NOTE Confidence: 0.4603952

00:38:42.915 --> 00:38:44.665 were improvements in cardio metabolic

NOTE Confidence: 0.4603952

00:38:44.665 --> 00:38:47.136 measures and one of the questions was

NOTE Confidence: 0.4603952

00:38:47.136 --> 00:38:49.460 well do does improvement in these lab

NOTE Confidence: 0.4603952

00:38:49.460 --> 00:38:51.560 values and these these risk factors,

NOTE Confidence: 0.4603952

00:38:51.560 --> 00:38:53.630 does it actually improve outcome And

NOTE Confidence: 0.4603952

00:38:53.630 --> 00:38:56.075 now we're at the cusp of knowing

NOTE Confidence: 0.4603952

00:38:56.075 --> 00:38:58.067 the answer to that the select

NOTE Confidence: 0.4603952

00:38:58.067 --> 00:39:00.338 trial which we were a site for here

NOTE Confidence: 0.4603952

00:39:00.338 --> 00:39:03.280 as well with the help of YCCI.

NOTE Confidence: 0.4603952

00:39:03.280 --> 00:39:07.692 This trial resulted in a 20% reduction

NOTE Confidence: 0.4603952

00:39:07.692 --> 00:39:09.876 in major cardiovascular events.

NOTE Confidence: 0.4603952

00:39:09.880 --> 00:39:12.250 So receiving some agletite as compared

NOTE Confidence: 0.4603952

00:39:12.250 --> 00:39:14.852 to placebo did improve and and

NOTE Confidence: 0.4603952

00:39:14.852 --> 00:39:17.117 decrease the the cardiovascular events

NOTE Confidence: 0.4603952

00:39:17.117 --> 00:39:19.799 that our patients are experiencing.

NOTE Confidence: 0.4603952

00:39:19.800 --> 00:39:22.460 Now these are just top line results

NOTE Confidence: 0.4603952

00:39:22.460 --> 00:39:24.875 and will be the results will be the

NOTE Confidence: 0.4603952

00:39:24.875 --> 00:39:26.794 full results will be presented at the

NOTE Confidence: 0.4603952

00:39:26.794 --> 00:39:28.279 American Heart Association next week.

NOTE Confidence: 0.4603952

00:39:28.280 --> 00:39:31.240 So stay tuned for that.

NOTE Confidence: 0.4603952

00:39:31.240 --> 00:39:33.880 Now Tirzepatide is the next molecule

NOTE Confidence: 0.4603952

00:39:33.880 --> 00:39:36.612 that that is farthest along in terms

NOTE Confidence: 0.4603952

00:39:36.612 --> 00:39:39.098 of phase three and coming next it

NOTE Confidence: 0.4603952

00:39:39.098 --> 00:39:41.084 is a GIPGL P1 receptor agonist.

NOTE Confidence: 0.4603952

00:39:41.084 --> 00:39:43.190 It is one molecule targeting both

NOTE Confidence: 0.7956563

00:39:43.251 --> 00:39:45.795 receptors and it is also a once weekly

NOTE Confidence: 0.7956563

00:39:45.795 --> 00:39:47.872 injectable and we were fortunate to conduct

NOTE Confidence: 0.7956563

00:39:47.872 --> 00:39:50.433 this trial and I was the lead author

NOTE Confidence: 0.7956563

73

00:39:50.433 --> 00:39:52.431 on this study that Regita mentioned.

NOTE Confidence: 0.7956563

00:39:52.440 --> 00:39:54.575 This treatment with tirzepatide with

NOTE Confidence: 0.7956563

00:39:54.575 --> 00:39:57.575 the highest dose resulted in an average

NOTE Confidence: 0.7956563

00:39:57.575 --> 00:40:00.505 weight reduction of 22.5% at 72 weeks and

NOTE Confidence: 0.7956563

00:40:00.505 --> 00:40:02.801 this translated to an average absolute

NOTE Confidence: 0.7956563

00:40:02.801 --> 00:40:06.520 weight reduction of £52 at that time point.

NOTE Confidence: 0.7956563

00:40:06.520 --> 00:40:08.120 Additionally, on this dose,

NOTE Confidence: 0.7956563

00:40:08.120 --> 00:40:10.280 nearly 40% of participants lost at

NOTE Confidence: 0.7956563

00:40:10.280 --> 00:40:12.320 least 1/4 of their body weight.

NOTE Confidence: 0.7956563

00:40:12.320 --> 00:40:14.553 So that's somebody starting the trial at

NOTE Confidence: 0.7956563

00:40:14.553 --> 00:40:17.614 a weight of 200 losing down to 150 pounds.

NOTE Confidence: 0.7956563

00:40:17.614 --> 00:40:19.949 Tirzepatide also resulted in improvements

NOTE Confidence: 0.7956563

00:40:19.949 --> 00:40:22.125 in cardio metabolic measures as

NOTE Confidence: 0.7956563

00:40:22.125 --> 00:40:24.237 we had seen with some agglutide.

NOTE Confidence: 0.7956563

00:40:24.240 --> 00:40:25.904 Now where is tirzepatide?

NOTE Confidence: 0.7956563

00:40:25.904 --> 00:40:28.400 Well the phase three trials are

NOTE Confidence: 0.7956563

00:40:28.477 --> 00:40:30.957 are moving forward and completing.

NOTE Confidence: 0.7956563

00:40:30.960 --> 00:40:32.857 There is an extension of the surmount

NOTE Confidence: 0.7956563

00:40:32.857 --> 00:40:33.399 one trial.

NOTE Confidence: 0.7956563

00:40:33.400 --> 00:40:34.196 Surmount 2,

NOTE Confidence: 0.7956563

00:40:34.196 --> 00:40:36.584 which was participants with diabetes also

NOTE Confidence: 0.7956563

00:40:36.584 --> 00:40:39.160 resulted in significant weight reduction

NOTE Confidence: 0.7956563

00:40:39.160 --> 00:40:42.275 as well as a hemoglobin A1C reduction.

NOTE Confidence: 0.7956563

00:40:42.280 --> 00:40:44.588 Tirzepatide after intensive lifestyle

NOTE Confidence: 0.7956563

00:40:44.588 --> 00:40:46.896 intervention also resulted in

NOTE Confidence: 0.7956563

00:40:46.896 --> 00:40:49.199 significant weight reduction as did

NOTE Confidence: 0.7956563

00:40:49.200 --> 00:40:51.440 longer duration of tirzepatide use,

NOTE Confidence: 0.7956563

00:40:51.440 --> 00:40:54.450 which resulted in 26% total body

NOTE Confidence: 0.7956563

00:40:54.450 --> 00:40:56.200 weight reduction at 88 weeks.

NOTE Confidence: 0.7956563

00:40:56.200 --> 00:40:58.384 There's also a cardiovascular

NOTE Confidence: 0.7956563

00:40:58.384 --> 00:41:00.650 outcomes trial looking at both

NOTE Confidence: 0.7956563

00:41:00.650 --> 00:41:02.600 heart and renal outcomes ongoing.

NOTE Confidence: 0.7956563

00:41:02.600 --> 00:41:04.350 And tirzepatide is currently under

NOTE Confidence: 0.7956563

00:41:04.350 --> 00:41:06.100 FDA review for chronic weight

NOTE Confidence: 0.7956563

00:41:06.155 --> 00:41:07.959 management and obesity treatment.

NOTE Confidence: 0.7956563

00:41:07.960 --> 00:41:09.500 It's already FDA approved for

NOTE Confidence: 0.7956563

00:41:09.500 --> 00:41:11.432 type 2 and the obesity indication

NOTE Confidence: 0.7956563

00:41:11.432 --> 00:41:13.072 we should know very soon,

NOTE Confidence: 0.7956563

00:41:13.080 --> 00:41:16.279 so stay tuned for that as well.

NOTE Confidence: 0.7956563

00:41:16.280 --> 00:41:18.562 Now the next one that is in

NOTE Confidence: 0.7956563

00:41:18.562 --> 00:41:20.519 the works is CAGRI SEMA.

NOTE Confidence: 0.7956563

00:41:20.520 --> 00:41:22.064 It is a combination.

NOTE Confidence: 0.7956563

00:41:22.064 --> 00:41:24.960 It's an Amylin analog with a GLP

NOTE Confidence: 0.7956563

00:41:24.960 --> 00:41:26.439 one receptor agonist.

NOTE Confidence: 0.7956563

00:41:26.440 --> 00:41:29.205 So this is 2 molecules both once

NOTE Confidence: 0.7956563

00:41:29.205 --> 00:41:31.120 weekly that are used in combination

NOTE Confidence: 0.7956563

00:41:31.120 --> 00:41:32.640 to see if there's synergistic

NOTE Confidence: 0.7956563

00:41:32.701 --> 00:41:34.117 effect on weight reduction.

NOTE Confidence: 0.7956563

00:41:34.120 --> 00:41:35.604 And what you can see in this

NOTE Confidence: 0.7956563

00:41:35.604 --> 00:41:37.304 trial is when you compare some

NOTE Confidence: 0.7956563

00:41:37.304 --> 00:41:38.994 maglitide to the combination of

NOTE Confidence: 0.7956563

00:41:38.994 --> 00:41:40.479 cagrillantide with some maglitide,

NOTE Confidence: 0.7956563

00:41:40.480 --> 00:41:42.475 you achieve greater weight reduction

NOTE Confidence: 0.7956563

00:41:42.475 --> 00:41:44.920 with the combination at 20 weeks.

NOTE Confidence: 0.7956563

00:41:44.920 --> 00:41:48.046 What you can see is a 17.1% reduction

NOTE Confidence: 0.7956563

00:41:48.046 --> 00:41:49.984 with this combination and you can

NOTE Confidence: 0.7956563

00:41:49.984 --> 00:41:52.805 see as depicted by the red arrow that

NOTE Confidence: 0.7956563

00:41:52.805 --> 00:41:54.680 participants were still losing weight.

NOTE Confidence: 0.7956563

00:41:54.680 --> 00:41:56.105 Now what happens when you

NOTE Confidence: 0.7956563

00:41:56.105 --> 00:41:56.960 stop the medication?

NOTE Confidence: 0.7956563

00:41:56.960 --> 00:41:58.640 Well, as any chronic disease,

NOTE Confidence: 0.7956563

00:41:58.640 --> 00:42:00.200 when you stop the medication,

NOTE Confidence: 0.7956563

00:42:00.200 --> 00:42:02.360 the weight is regained and that's

NOTE Confidence: 0.7956563

00:42:02.360 --> 00:42:04.784 because the defended fat mass set point

NOTE Confidence: 0.7956563

00:42:04.784 --> 00:42:07.440 goes back up and we're going to come

NOTE Confidence: 0.7956563

00:42:07.517 --> 00:42:10.478 back to that with our patient at the end.

NOTE Confidence: 0.7956563

00:42:10.480 --> 00:42:13.045 Now the next one or the next few that

NOTE Confidence: 0.7956563

00:42:13.045 --> 00:42:15.639 are in development are Glucagon GLP,

NOTE Confidence: 0.7956563

00:42:15.640 --> 00:42:17.344 one receptor agonist,

NOTE Confidence: 0.7956563

00:42:17.344 --> 00:42:21.026 cervutatide is the farthest along here in

NOTE Confidence: 0.7956563

00:42:21.026 --> 00:42:23.154 a phase two trial that was just presented.

NOTE Confidence: 0.7956563

00:42:23.160 --> 00:42:25.530 This resulted in an average weight

NOTE Confidence: 0.7956563

00:42:25.530 --> 00:42:27.924 reduction of 18.7% at 46 weeks.

NOTE Confidence: 0.7956563

00:42:27.924 --> 00:42:31.763 The next one after that is a triple

NOTE Confidence: 0.7956563

00:42:31.763 --> 00:42:34.439 hormone receptor agonist retatrutide

NOTE Confidence: 0.7956563

00:42:34.440 --> 00:42:36.906 and this is a combination of GIPGL

NOTE Confidence: 0.7956563

00:42:36.906 --> 00:42:39.236 P1 and Glucagon receptor agonism.

NOTE Confidence: 0.7956563

00:42:39.240 --> 00:42:42.948 And we also just published on this and

NOTE Confidence: 0.7956563

00:42:42.948 --> 00:42:45.360 I was the lead on this trial as well.

NOTE Confidence: 0.7956563

00:42:45.360 --> 00:42:46.668 And at 48 weeks,

NOTE Confidence: 0.7956563

00:42:46.668 --> 00:42:49.092 what we found in this phase two

NOTE Confidence: 0.7956563

00:42:49.092 --> 00:42:51.240 trial was placebo lost 2.1% of

NOTE Confidence: 0.7956563

00:42:51.240 --> 00:42:52.440 their total body weight,

NOTE Confidence: 0.7956563

00:42:52.440 --> 00:42:54.365 whereas with the highest dose

NOTE Confidence: 0.7956563

00:42:54.365 --> 00:42:56.290 of retatruitide on average the

NOTE Confidence: 0.31840372

00:42:56.356 --> 00:42:57.905 weight reduction was 24.2%.

NOTE Confidence: 0.31840372

00:42:57.905 --> 00:43:00.025 So nearly 1/4 of the body weight was

NOTE Confidence: 0.31840372

00:43:00.025 --> 00:43:02.176 lost at just eleven months and you

NOTE Confidence: 0.31840372

00:43:02.176 --> 00:43:04.047 can see that participants were still

NOTE Confidence: 0.31840372

00:43:04.047 --> 00:43:05.835 actively losing weight at the time

NOTE Confidence: 0.31840372

00:43:05.835 --> 00:43:08.296 that the study drug was discontinued.

NOTE Confidence: 0.31840372

00:43:08.296 --> 00:43:10.616 This translated to an absolute

NOTE Confidence: 0.31840372

00:43:10.616 --> 00:43:13.040 weight reduction of £58 during

NOTE Confidence: 0.31840372

00:43:13.040 --> 00:43:15.640 the course of this trial.

NOTE Confidence: 0.31840372

00:43:15.640 --> 00:43:16.210 Now additionally,

NOTE Confidence: 0.31840372

00:43:16.210 --> 00:43:17.920 when we think about weight reduction,

NOTE Confidence: 0.31840372

00:43:17.920 --> 00:43:20.440 we look at weight reduction targets 5%

NOTE Confidence: 0.31840372

00:43:20.440 --> 00:43:22.720 has traditionally been focused in on.

NOTE Confidence: 0.31840372

00:43:22.720 --> 00:43:25.042 This is something that can certainly

NOTE Confidence: 0.31840372

00:43:25.042 --> 00:43:27.400 be attained with lifestyle intervention

NOTE Confidence: 0.31840372

00:43:27.400 --> 00:43:29.997 as well as with the older generation

NOTE Confidence: 0.31840372

00:43:29.997 --> 00:43:32.555 of medications and the FDA uses it now

NOTE Confidence: 0.31840372

00:43:32.555 --> 00:43:35.040 with the two highest doses of retatrutide,

NOTE Confidence: 0.31840372

00:43:35.040 --> 00:43:37.416 we found that 100% of participants

NOTE Confidence: 0.31840372

00:43:37.416 --> 00:43:39.804 lost at least 5% of their body weight.

NOTE Confidence: 0.31840372

00:43:39.804 --> 00:43:41.758 I don't know if I'll ever be able to

NOTE Confidence: 0.31840372

00:43:41.758 --> 00:43:43.156 say this in a scientific presentation.

NOTE Confidence: 0.31840372

00:43:43.160 --> 00:43:45.120 Again, this was a phase two trial.

NOTE Confidence: 0.31840372

00:43:45.120 --> 00:43:47.031 So we'll have to wait the results

NOTE Confidence: 0.31840372

00:43:47.031 --> 00:43:48.983 of the phase three trial that we

NOTE Confidence: 0.31840372

00:43:48.983 --> 00:43:50.561 are now moving forward with.

NOTE Confidence: 0.31840372

00:43:50.561 --> 00:43:52.643 Now looking at higher body weight

NOTE Confidence: 0.31840372

00:43:52.643 --> 00:43:54.338 reduction targets, I'll just follow.

NOTE Confidence: 0.31840372

00:43:54.338 --> 00:43:56.680 I'll just focus in on the highest dose,

NOTE Confidence: 0.31840372

00:43:56.680 --> 00:43:57.764 the 12 milligram dose.

NOTE Confidence: 0.31840372

00:43:57.764 --> 00:44:00.114 We found that 9 out of 10 participants

NOTE Confidence: 0.31840372

00:44:00.114 --> 00:44:02.720 lost at least 10% of their body weight,

NOTE Confidence: 0.31840372

00:44:02.720 --> 00:44:05.248 nearly 2/3 lost more than 20% of their

NOTE Confidence: 0.31840372

00:44:05.248 --> 00:44:07.376 body weight and a quarter of participants

NOTE Confidence: 0.31840372

00:44:07.376 --> 00:44:09.878 lost at least 30% of their body weight.

NOTE Confidence: 0.31840372

00:44:09.880 --> 00:44:11.880 So really significant weight reductions.

NOTE Confidence: 0.31840372

00:44:11.880 --> 00:44:12.710 And again,

NOTE Confidence: 0.31840372

00:44:12.710 --> 00:44:15.486 this is just at 11 months now.

NOTE Confidence: 0.31840372

00:44:15.486 --> 00:44:17.202 I just want to highlight that

NOTE Confidence: 0.31840372

00:44:17.202 --> 00:44:18.680 with any obesity treatment,

NOTE Confidence: 0.31840372

00:44:18.680 --> 00:44:21.518 there is a variability in response.

NOTE Confidence: 0.31840372

00:44:21.520 --> 00:44:23.398 So these are different doses of

NOTE Confidence: 0.31840372

00:44:23.398 --> 00:44:25.372 retatrutite and what you can see

NOTE Confidence: 0.31840372

00:44:25.372 --> 00:44:27.022 is individual participants and how

NOTE Confidence: 0.31840372

00:44:27.022 --> 00:44:29.080 much weight they lost in the trial.

NOTE Confidence: 0.31840372

00:44:29.080 --> 00:44:31.048 And what you can see is that most

NOTE Confidence: 0.31840372

00:44:31.048 --> 00:44:32.360 participants lost a lot of weight,

NOTE Confidence: 0.31840372

00:44:32.360 --> 00:44:33.908 but there are differences in terms

NOTE Confidence: 0.31840372

00:44:33.908 --> 00:44:35.480 of how much weight they lost.

NOTE Confidence: 0.31840372

00:44:35.480 --> 00:44:37.112 And we don't have great predictors

NOTE Confidence: 0.31840372

00:44:37.112 --> 00:44:38.919 to know how people will respond.

NOTE Confidence: 0.31840372

00:44:38.920 --> 00:44:41.590 So there is great variability in

NOTE Confidence: 0.31840372

00:44:41.590 --> 00:44:44.812 terms of response and this is true

NOTE Confidence: 0.31840372

00:44:44.812 --> 00:44:47.077 with any treatment for obesity.

NOTE Confidence: 0.31840372

00:44:47.080 --> 00:44:49.054 Now all the medications I've talked about

NOTE Confidence: 0.31840372

00:44:49.054 --> 00:44:51.160 till now are once weekly injectable.

NOTE Confidence: 0.31840372

00:44:51.160 --> 00:44:53.086 What about oral GLP one receptor

NOTE Confidence: 0.31840372

00:44:53.086 --> 00:44:54.921 agonist or oral nutrient stimulated

NOTE Confidence: 0.31840372

00:44:54.921 --> 00:44:56.400 hormone based therapies.

NOTE Confidence: 0.31840372

00:44:56.400 --> 00:44:58.892 So there is an oral formulation of

NOTE Confidence: 0.31840372

00:44:58.892 --> 00:45:01.039 some maglitide and at higher doses

NOTE Confidence: 0.31840372

00:45:01.040 --> 00:45:02.756 that are not yet FDA approved.

NOTE Confidence: 0.31840372

00:45:02.760 --> 00:45:05.184 The trial demonstrated that the average

NOTE Confidence: 0.31840372

00:45:05.184 --> 00:45:07.756 weight reduction was 17.4% at 68 weeks,

NOTE Confidence: 0.31840372

00:45:07.756 --> 00:45:10.720 so on par with the weekly injectable.

NOTE Confidence: 0.31840372

00:45:10.720 --> 00:45:12.610 There's also small molecules that

NOTE Confidence: 0.31840372

00:45:12.610 --> 00:45:14.868 are under investigation that are GLP

NOTE Confidence: 0.31840372

00:45:14.868 --> 00:45:16.722 1 receptor agonist and the farthest

NOTE Confidence: 0.31840372

00:45:16.722 --> 00:45:18.793 one along here is orphorglipron and

NOTE Confidence: 0.31840372

00:45:18.793 --> 00:45:20.959 it resulted in an average weight

NOTE Confidence: 0.31840372

00:45:20.959 --> 00:45:22.805 reduction of 14 percent,

NOTE Confidence: 0.31840372

00:45:22.805 --> 00:45:25.280 14.7% at just 36 weeks.

NOTE Confidence: 0.31840372

00:45:25.280 --> 00:45:27.424 So we'll have to wait for the phase

NOTE Confidence: 0.31840372

00:45:27.424 --> 00:45:29.359 three trials of these agents as well.

NOTE Confidence: 0.31840372

00:45:29.360 --> 00:45:31.598 Now there's also a monthly formulation

NOTE Confidence: 0.31840372

00:45:31.598 --> 00:45:34.085 of a *** receptor antagonist and

NOTE Confidence: 0.31840372

00:45:34.085 --> 00:45:36.360 a GLP 1 receptor agonist.

NOTE Confidence: 0.31840372

00:45:36.360 --> 00:45:38.472 So if if taking something once

NOTE Confidence: 0.31840372

00:45:38.472 --> 00:45:40.360 a week is too much,

NOTE Confidence: 0.31840372

00:45:40.360 --> 00:45:42.970 there may potentially also be a

NOTE Confidence: 0.31840372

00:45:42.970 --> 00:45:45.160 once monthly formulation at some

NOTE Confidence: 0.31840372

00:45:45.160 --> 00:45:46.920 point in the future.

NOTE Confidence: 0.31840372

00:45:46.920 --> 00:45:48.756 So I hope I've shown you

NOTE Confidence: 0.31840372

00:45:48.756 --> 00:45:49.980 with these medications that

NOTE Confidence: 0.91629124

00:45:50.040 --> 00:45:51.150 substantial weight reduction

NOTE Confidence: 0.91629124

00:45:51.150 --> 00:45:53.370 is possible and we are filling

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NOTE Confidence: 0.91629124

00:45:53.370 --> 00:45:55.280 the treatment gap and beyond.

NOTE Confidence: 0.91629124

00:45:55.280 --> 00:45:57.872 So we have current pharmacotherapy and

NOTE Confidence: 0.91629124

00:45:57.872 --> 00:46:00.015 intensive lifestyle that could achieve

NOTE Confidence: 0.91629124

00:46:00.015 --> 00:46:02.479 this weight reduction of five to 10%.

NOTE Confidence: 0.91629124

00:46:02.480 --> 00:46:04.300 We have bariatric surgery that

NOTE Confidence: 0.91629124

00:46:04.300 --> 00:46:06.120 could achieve a lot more,

NOTE Confidence: 0.91629124

00:46:06.120 --> 00:46:07.758 but now we're filling the treatment gap.

NOTE Confidence: 0.91629124

00:46:07.760 --> 00:46:09.076 And I only had time to highlight

NOTE Confidence: 0.91629124

00:46:09.076 --> 00:46:10.200 a few of the agents,

NOTE Confidence: 0.91629124

00:46:10.200 --> 00:46:12.080 but there are so many more in development

NOTE Confidence: 0.91629124

00:46:12.080 --> 00:46:13.879 and so many different mechanisms.

NOTE Confidence: 0.91629124

00:46:13.880 --> 00:46:17.016 And all of these can be paired with

NOTE Confidence: 0.91629124

00:46:17.016 --> 00:46:18.588 other therapies using combination

NOTE Confidence: 0.91629124

00:46:18.588 --> 00:46:21.240 therapy to really help our our patients

NOTE Confidence: 0.91629124

00:46:21.240 --> 00:46:23.280 achieve the goals that they need.

NOTE Confidence: 0.91629124

00:46:23.280 --> 00:46:25.779 So I'm going to just highlight that

NOTE Confidence: 0.91629124

00:46:25.779 --> 00:46:28.755 all of this work we're going to try and

NOTE Confidence: 0.91629124

00:46:28.755 --> 00:46:31.279 continue at the Yale Obesity Research Center,

NOTE Confidence: 0.91629124

00:46:31.280 --> 00:46:33.485 which is a new center that I've

NOTE Confidence: 0.91629124

00:46:33.485 --> 00:46:35.760 been asked to create and direct.

NOTE Confidence: 0.91629124

00:46:35.760 --> 00:46:37.783 And the focus of the center is

NOTE Confidence: 0.91629124

00:46:37.783 --> 00:46:39.481 on the investigation of novel

NOTE Confidence: 0.91629124

00:46:39.481 --> 00:46:40.636 anti obesity medications.

NOTE Confidence: 0.91629124

00:46:40.640 --> 00:46:43.384 The focus is also on clinical obesity

NOTE Confidence: 0.91629124

00:46:43.384 --> 00:46:45.820 research where we're going to be looking

NOTE Confidence: 0.91629124

00:46:45.820 --> 00:46:49.000 at the clinical Physiology of obesity,

NOTE Confidence: 0.91629124

00:46:49.000 --> 00:46:50.208 conducting these clinical trials,

NOTE Confidence: 0.91629124

00:46:50.208 --> 00:46:52.840 many of which I've shown you and there we

NOTE Confidence: 0.91629124

00:46:52.840 --> 00:46:54.924 have many that are ongoing and starting up

NOTE Confidence: 0.91629124

00:46:54.924 --> 00:46:56.716 as well as looking at patient outcomes.

NOTE Confidence: 0.91629124

00:46:56.720 --> 00:46:58.960 And this will of course take collaboration.

NOTE Confidence: 0.91629124

00:46:58.960 --> 00:47:00.664 We want to mentor the next

NOTE Confidence: 0.91629124

00:47:00.664 --> 00:47:01.516 generation of physicians,

NOTE Confidence: 0.91629124

00:47:01.520 --> 00:47:03.800 scientists and investigators and we

NOTE Confidence: 0.91629124

00:47:03.800 --> 00:47:06.562 want to educate academic leaders and

NOTE Confidence: 0.91629124

00:47:06.562 --> 00:47:09.439 integrate all of this into clinical practice.

NOTE Confidence: 0.91629124

00:47:09.440 --> 00:47:12.136 Now I'm going to come back to our

NOTE Confidence: 0.91629124

00:47:12.136 --> 00:47:14.058 patient to kind of sum everything up

NOTE Confidence: 0.91629124

00:47:14.058 --> 00:47:16.146 and and and really highlight some of

NOTE Confidence: 0.91629124

00:47:16.146 --> 00:47:18.096 the points that we've talked about

NOTE Confidence: 0.91629124

00:47:18.096 --> 00:47:20.158 about treating obesity as a disease.

NOTE Confidence: 0.91629124

00:47:20.160 --> 00:47:20.716 And again,

NOTE Confidence: 0.91629124

00:47:20.716 --> 00:47:22.662 the highlight here is we treat these

NOTE Confidence: 0.91629124

00:47:22.662 --> 00:47:24.360 other diseases with medications.

NOTE Confidence: 0.91629124

00:47:24.360 --> 00:47:26.325 And let's ask ourselves three

NOTE Confidence: 0.91629124

00:47:26.325 --> 00:47:28.290 questions and then ask ourselves

NOTE Confidence: 0.91629124

00:47:28.354 --> 00:47:30.319 the same questions for obesity.

NOTE Confidence: 0.91629124

00:47:30.320 --> 00:47:31.902 So when we care for this patient

NOTE Confidence: 0.91629124

00:47:31.902 --> 00:47:32.354 with obesity,

NOTE Confidence: 0.91629124

00:47:32.360 --> 00:47:35.216 do we find it unusual that he requires

NOTE Confidence: 0.91629124

00:47:35.216 --> 00:47:37.040 several medications for his diabetes?

NOTE Confidence: 0.91629124

00:47:37.040 --> 00:47:39.420 Do we think that the anti hyperglycemic

NOTE Confidence: 0.91629124

00:47:39.420 --> 00:47:41.066 medications are not effective if

NOTE Confidence: 0.91629124

00:47:41.066 --> 00:47:43.040 his A1C is not less than seven?

NOTE Confidence: 0.91629124

00:47:43.040 --> 00:47:44.993 And now that his blood pressure is at goal,

NOTE Confidence: 0.91629124

00:47:45.000 --> 00:47:48.012 would we stop his anti hypertensive

NOTE Confidence: 0.91629124

00:47:48.012 --> 00:47:48.514 medications?

NOTE Confidence: 0.91629124

00:47:48.520 --> 00:47:51.463 And of course the answer to all of these

NOTE Confidence: 0.91629124

00:47:51.463 --> 00:47:53.520 questions is very easy for all of us.

NOTE Confidence: 0.91629124

00:47:53.520 --> 00:47:55.508 We would answer no to each one

NOTE Confidence: 0.91629124

00:47:55.508 --> 00:47:56.360 of these questions.

NOTE Confidence: 0.91629124

00:47:56.360 --> 00:47:58.430 And now let's ask ourselves these

NOTE Confidence: 0.91629124

00:47:58.430 --> 00:48:00.236 questions for obesity in the

NOTE Confidence: 0.91629124

00:48:00.236 --> 00:48:02.051 context of overcoming the barriers

NOTE Confidence: 0.91629124

00:48:02.051 --> 00:48:04.159 to treating obesity as a disease,

NOTE Confidence: 0.91629124

00:48:04.160 --> 00:48:05.996 as a disease that is heterogeneous,

NOTE Confidence: 0.91629124

00:48:06.000 --> 00:48:08.555 that is chronic and that is complex.

NOTE Confidence: 0.91629124

00:48:08.560 --> 00:48:09.538 So first heterogeneous.

NOTE Confidence: 0.91629124

00:48:09.538 --> 00:48:11.820 The question here is do we think

NOTE Confidence: 0.91629124

00:48:11.886 --> 00:48:13.666 that his anti hypoglycemic medication

NOTE Confidence: 0.91629124

00:48:13.666 --> 00:48:16.290 is not effective if his A1C is not

NOTE Confidence: 0.91629124

00:48:16.290 --> 00:48:17.076 less than seven?

NOTE Confidence: 0.91629124

00:48:17.080 --> 00:48:18.560 And the parallel question is,

NOTE Confidence: 0.91629124

00:48:18.560 --> 00:48:20.674 do we think that his anti obesity

NOTE Confidence: 0.91629124

00:48:20.674 --> 00:48:22.186 medication is not effective if

NOTE Confidence: 0.91629124

00:48:22.186 --> 00:48:24.076 his BMI is not less than 25?

NOTE Confidence: 0.91629124

00:48:24.080 --> 00:48:25.880 And of course BMI is not a great measure.

NOTE Confidence: 0.91629124

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00:48:25.880 --> 00:48:28.440 We're just using it as a surrogate here

NOTE Confidence: 0.91629124

00:48:28.440 --> 00:48:30.440 and of course the answer would be no.

NOTE Confidence: 0.91629124

00:48:30.440 --> 00:48:31.760 But let's look at this.

NOTE Confidence: 0.91629124

00:48:31.760 --> 00:48:33.800 So the average efficacy of

NOTE Confidence: 0.91629124

00:48:33.800 --> 00:48:35.840 medications to treat diabetes also

NOTE Confidence: 0.953123

00:48:35.907 --> 00:48:37.911 has variability just like

NOTE Confidence: 0.953123

00:48:37.911 --> 00:48:39.915 medications for obesity treatment.

NOTE Confidence: 0.953123

00:48:39.920 --> 00:48:42.440 And so because there's great variability

NOTE Confidence: 0.953123

00:48:42.440 --> 00:48:44.513 in response to any medication,

NOTE Confidence: 0.953123

00:48:44.513 --> 00:48:46.979 we may need to use different

NOTE Confidence: 0.953123

00:48:46.979 --> 00:48:48.940 medications and try and determine

NOTE Confidence: 0.953123

00:48:48.940 --> 00:48:51.154 what a patient will respond to.

NOTE Confidence: 0.953123

00:48:51.160 --> 00:48:53.554 So if we start a patient on any medication,

NOTE Confidence: 0.953123

00:48:53.560 --> 00:48:55.408 they may lose a little bit of weight

NOTE Confidence: 0.953123

00:48:55.408 --> 00:48:57.240 or they may lose a lot of weight,

NOTE Confidence: 0.953123

00:48:57.240 --> 00:48:59.256 but we can use this and incorporate

NOTE Confidence: 0.953123

00:48:59.256 --> 00:49:01.119 this into our treatment plans.

NOTE Confidence: 0.953123

00:49:01.120 --> 00:49:02.680 So as with the first patient,

NOTE Confidence: 0.953123

00:49:02.680 --> 00:49:05.116 you saw that I used several medications.

NOTE Confidence: 0.953123

00:49:05.120 --> 00:49:07.940 And if a patient loses 5% with one medicine,

NOTE Confidence: 0.953123

00:49:07.940 --> 00:49:08.840 10 with another,

NOTE Confidence: 0.953123

00:49:08.840 --> 00:49:09.977 five with another,

NOTE Confidence: 0.953123

00:49:09.977 --> 00:49:12.251 they may potentially have an added

NOTE Confidence: 0.953123

00:49:12.251 --> 00:49:14.338 benefit or total body weight reduction

NOTE Confidence: 0.953123

00:49:14.338 --> 00:49:16.545 of 20% or there may be synergy

NOTE Confidence: 0.953123

00:49:16.545 --> 00:49:18.418 with some of the medications and

NOTE Confidence: 0.953123

00:49:18.418 --> 00:49:20.588 they may lose more than 20% or the

NOTE Confidence: 0.953123

00:49:20.588 --> 00:49:22.058 medications may not be synergistic

NOTE Confidence: 0.953123

00:49:22.058 --> 00:49:24.039 and they may lose less than 20%.

NOTE Confidence: 0.953123

00:49:24.040 --> 00:49:26.560 But we don't know until we try.

NOTE Confidence: 0.953123

00:49:26.560 --> 00:49:28.478 The take home here is there's wide

NOTE Confidence: 0.953123

00:49:28.478 --> 00:49:29.969 variability in terms of responses

NOTE Confidence: 0.953123

00:49:29.969 --> 00:49:31.205 to these medications because

NOTE Confidence: 0.953123

00:49:31.205 --> 00:49:33.040 there's not one type of obesity,

NOTE Confidence: 0.953123

00:49:33.040 --> 00:49:34.678 there's many different types of obesity.

NOTE Confidence: 0.953123

00:49:34.680 --> 00:49:36.871 We just haven't had a way to

NOTE Confidence: 0.953123

00:49:36.871 --> 00:49:38.879 figure out what those are yet.

NOTE Confidence: 0.953123

00:49:38.880 --> 00:49:42.200 The next concept is that obesity is complex.

NOTE Confidence: 0.953123

00:49:42.200 --> 00:49:44.296 And the question here is do we find

NOTE Confidence: 0.953123

00:49:44.296 --> 00:49:46.624 it unusual that this the patient may

NOTE Confidence: 0.953123

00:49:46.624 --> 00:49:48.364 require several medications for his

NOTE Confidence: 0.953123

00:49:48.424 --> 00:49:50.475 obesity as he does for his diabetes.

NOTE Confidence: 0.953123

00:49:50.480 --> 00:49:52.840 And so if we look at a patient with diabetes,

NOTE Confidence: 0.953123

00:49:52.840 --> 00:49:55.000 we then they come in with

NOTE Confidence: 0.953123

00:49:55.000 --> 00:49:56.440 an elevated hemoglobin A1C.

NOTE Confidence: 0.953123

00:49:56.440 --> 00:49:59.156 We may start them on one medication,

NOTE Confidence: 0.953123

00:49:59.160 --> 00:50:01.758 then there are hemoglobin A1C decreases,

NOTE Confidence: 0.953123

00:50:01.760 --> 00:50:03.158 but it's not yet at goal.

NOTE Confidence: 0.953123

00:50:03.160 --> 00:50:05.140 So we started different medication and

NOTE Confidence: 0.953123

00:50:05.140 --> 00:50:06.802 perhaps the patient doesn't respond

NOTE Confidence: 0.953123

00:50:06.802 --> 00:50:08.518 or maybe they have side effects.

NOTE Confidence: 0.953123

00:50:08.520 --> 00:50:09.996 So we stop that medicine and

NOTE Confidence: 0.953123

00:50:09.996 --> 00:50:11.640 we start a third medication.

NOTE Confidence: 0.953123

00:50:11.640 --> 00:50:13.360 And now the patient's A1C

NOTE Confidence: 0.953123

00:50:13.360 --> 00:50:15.080 decreased and is at goal.

NOTE Confidence: 0.953123

00:50:15.080 --> 00:50:17.852 But what we've done here is we've tried 3

NOTE Confidence: 0.953123

00:50:17.852 --> 00:50:19.778 medications and continued to just in the

NOTE Confidence: 0.953123

00:50:19.778 --> 00:50:21.680 same way in a patient who has obesity,

NOTE Confidence: 0.953123

00:50:21.680 --> 00:50:23.320 we may try one medicine,

NOTE Confidence: 0.953123

00:50:23.320 --> 00:50:24.360 then a second medication.

NOTE Confidence: 0.953123

00:50:24.360 --> 00:50:25.660 If the patient has side

NOTE Confidence: 0.953123

00:50:25.660 --> 00:50:26.838 effects or doesn't respond,

NOTE Confidence: 0.953123

00:50:26.840 --> 00:50:29.342 we try 1/3 and we keep on going and

NOTE Confidence: 0.953123

00:50:29.342 --> 00:50:30.980 adding these medications sequentially

NOTE Confidence: 0.953123

00:50:30.980 --> 00:50:33.990 to see how the patient may respond

NOTE Confidence: 0.953123

00:50:34.064 --> 00:50:35.919 until they reach their goal.

NOTE Confidence: 0.953123

00:50:35.920 --> 00:50:38.300 So obesity is complex as so many

NOTE Confidence: 0.953123

00:50:38.300 --> 00:50:39.960 other complex chronic diseases.

NOTE Confidence: 0.953123

00:50:39.960 --> 00:50:43.278 So combination therapy is often needed.

NOTE Confidence: 0.953123

00:50:43.280 --> 00:50:45.560 Now what about chronicity of disease?

NOTE Confidence: 0.953123

00:50:45.560 --> 00:50:46.760 So the question here is,

NOTE Confidence: 0.953123

00:50:46.760 --> 00:50:49.352 when this patient's BMI or weight is at goal,

NOTE Confidence: 0.953123

00:50:49.360 --> 00:50:52.118 would we stop his anti obesity medication?

NOTE Confidence: 0.953123

00:50:52.120 --> 00:50:54.433 In the same way would we stop a medication

NOTE Confidence: 0.953123

00:50:54.433 --> 00:50:56.880 for a patient who has high blood pressure?

NOTE Confidence: 0.953123

00:50:56.880 --> 00:50:58.758 So here's our patient with hypertension.

NOTE Confidence: 0.953123

00:50:58.760 --> 00:51:01.476 We start a medication and what happens?

NOTE Confidence: 0.953123

00:51:01.480 --> 00:51:02.784 The blood pressure decreases.

NOTE Confidence: 0.953123

00:51:02.784 --> 00:51:04.088 But what happens when

NOTE Confidence: 0.953123

00:51:04.088 --> 00:51:05.680 we stop that medication?

NOTE Confidence: 0.953123

00:51:05.680 --> 00:51:05.946 Well,

NOTE Confidence: 0.953123

00:51:05.946 --> 00:51:07.276 when the medication is stopped,

NOTE Confidence: 0.953123

00:51:07.280 --> 00:51:09.045 the blood pressure increases and

NOTE Confidence: 0.953123

00:51:09.045 --> 00:51:11.276 we're not surprised we stop the

NOTE Confidence: 0.953123

00:51:11.276 --> 00:51:12.876 treatment for chronic disease.

NOTE Confidence: 0.953123

00:51:12.880 --> 00:51:15.076 And so when we have a patient with obesity,

NOTE Confidence: 0.953123

00:51:15.080 --> 00:51:17.750 when we started treatment and

NOTE Confidence: 0.953123

00:51:17.750 --> 00:51:19.886 the medication decreases that

NOTE Confidence: 0.953123

00:51:19.886 --> 00:51:21.918 patients defended fat mass.

NOTE Confidence: 0.33406872

00:51:21.920 --> 00:51:24.195 What happens when we stop that medication?

NOTE Confidence: 0.33406872

00:51:24.200 --> 00:51:26.223 Well, the defended fat mass goes back

NOTE Confidence: 0.33406872

00:51:26.223 --> 00:51:28.950 up and the weight is regained and this

NOTE Confidence: 0.33406872

00:51:28.950 --> 00:51:31.435 has now been shown in clinical trials.

NOTE Confidence: 0.33406872

00:51:31.440 --> 00:51:33.816 So in the step one extension with some

NOTE Confidence: 0.33406872

00:51:33.816 --> 00:51:36.472 Maglatide, what was done was after a

NOTE Confidence: 0.33406872

00:51:36.472 --> 00:51:39.000 year of some maglatide and you can see

NOTE Confidence: 0.33406872

00:51:39.000 --> 00:51:40.440 here depicted in the blue squares,

NOTE Confidence: 0.33406872

00:51:40.440 --> 00:51:41.960 participants lost weight when

NOTE Confidence: 0.33406872

00:51:41.960 --> 00:51:43.480 the medication was stopped.

NOTE Confidence: 0.33406872

00:51:43.480 --> 00:51:45.896 After a year, what happened is that patients

NOTE Confidence: 0.33406872

00:51:45.896 --> 00:51:48.157 began to regain the weight and again,

NOTE Confidence: 0.33406872

00:51:48.160 --> 00:51:49.820 we shouldn't be surprised because

NOTE Confidence: 0.33406872

00:51:49.820 --> 00:51:51.480 that defended fat mass set

NOTE Confidence: 0.33406872

00:51:51.538 --> 00:51:53.200 point continued to go back up.

NOTE Confidence: 0.33406872

00:51:53.200 --> 00:51:54.754 Now there is a difference here of

NOTE Confidence: 0.33406872

00:51:54.754 --> 00:51:56.480 about 5% and there's a question of,

NOTE Confidence: 0.33406872

00:51:56.480 --> 00:51:58.112 well, what if we had continued

NOTE Confidence: 0.33406872

00:51:58.112 --> 00:51:59.200 to follow these patients,

NOTE Confidence: 0.33406872

00:51:59.200 --> 00:52:01.685 would they have regained the weight or

NOTE Confidence: 0.33406872

00:52:01.685 --> 00:52:03.642 potentially would they have been able to

NOTE Confidence: 0.33406872

00:52:03.642 --> 00:52:05.680 maintain some of that weight reduction?

NOTE Confidence: 0.33406872

00:52:05.680 --> 00:52:08.008 There's also a question of did

NOTE Confidence: 0.33406872

00:52:08.008 --> 00:52:09.848 patients regain mostly fat rather

NOTE Confidence: 0.33406872

00:52:09.848 --> 00:52:11.000 than lean muscle mass?

NOTE Confidence: 0.33406872

00:52:11.000 --> 00:52:13.016 And we don't have the answers

NOTE Confidence: 0.33406872

00:52:13.016 --> 00:52:14.360 to those questions yet.

NOTE Confidence: 0.33406872

00:52:14.360 --> 00:52:16.432 What we do know is there's no cure

NOTE Confidence: 0.33406872

00:52:16.432 --> 00:52:18.764 for obesity yet, and so chronic,

NOTE Confidence: 0.33406872

00:52:18.764 --> 00:52:20.796 lifelong treatment is needed.

NOTE Confidence: 0.33406872

00:52:20.800 --> 00:52:23.159 OK, So what happened with our patient?

NOTE Confidence: 0.33406872

00:52:23.160 --> 00:52:25.038 So just to remind you again,

NOTE Confidence: 0.33406872

00:52:25.040 --> 00:52:26.504 he had tried all these different

NOTE Confidence: 0.33406872

00:52:26.504 --> 00:52:28.240 things over the course of his lifetime.

NOTE Confidence: 0.33406872

00:52:28.240 --> 00:52:29.598 And when we came to see me,

NOTE Confidence: 0.33406872

00:52:29.600 --> 00:52:33.155 his BMI was 47 and his A1C was 8.5.

NOTE Confidence: 0.33406872

00:52:33.160 --> 00:52:34.400 So what did we do?

NOTE Confidence: 0.33406872

00:52:34.400 --> 00:52:34.761 Well,

NOTE Confidence: 0.33406872

00:52:34.761 --> 00:52:36.927 we we started the lifestyle interventions

NOTE Confidence: 0.33406872

00:52:36.927 --> 00:52:39.676 that had worked for him so well in the past.

NOTE Confidence: 0.33406872

00:52:39.680 --> 00:52:41.560 We then added several medications.

NOTE Confidence: 0.33406872

00:52:41.560 --> 00:52:43.270 We added Laraglatide for his

NOTE Confidence: 0.33406872

00:52:43.270 --> 00:52:44.638 weight and his diabetes,

NOTE Confidence: 0.33406872

00:52:44.640 --> 00:52:46.999 an SGLT 2 inhibitor for his diabetes,

NOTE Confidence: 0.33406872

00:52:47.000 --> 00:52:49.400 which helped his weight plateau.

NOTE Confidence: 0.33406872

00:52:49.400 --> 00:52:51.840 Then we added a higher dose of Laraglatide.

NOTE Confidence: 0.33406872

00:52:51.840 --> 00:52:54.040 We then added naltrexone bupropion.

NOTE Confidence: 0.33406872

00:52:54.040 --> 00:52:54.360 Unfortunately,

NOTE Confidence: 0.33406872

00:52:54.360 --> 00:52:55.960 he did develop side effects.

NOTE Confidence: 0.33406872

00:52:55.960 --> 00:52:57.124 He developed Constipation.

NOTE Confidence: 0.33406872

00:52:57.124 --> 00:52:59.840 One of his providers recommended prune juice,

NOTE Confidence: 0.33406872

00:52:59.840 --> 00:53:02.450 which unfortunately did not resolve his

NOTE Confidence: 0.33406872

00:53:02.450 --> 00:53:04.720 Constipation and instead increased his A1C.

NOTE Confidence: 0.33406872

00:53:04.720 --> 00:53:06.870 He appropriately discontinued the naltrexone

NOTE Confidence: 0.33406872

00:53:06.870 --> 00:53:09.727 bupropion and instead at that point we

NOTE Confidence: 0.33406872

00:53:09.727 --> 00:53:11.647 had some agglutide available on the

NOTE Confidence: 0.33406872

00:53:11.647 --> 00:53:13.920 market and we were able to start that.

NOTE Confidence: 0.33406872

00:53:13.920 --> 00:53:15.584 And what you can see is during the

NOTE Confidence: 0.33406872

00:53:15.584 --> 00:53:17.000 course of these several years,

NOTE Confidence: 0.33406872

00:53:17.000 --> 00:53:19.328 he lost over 85 pounds with a total

NOTE Confidence: 0.33406872

00:53:19.328 --> 00:53:21.880 body weight reduction of 27% and

NOTE Confidence: 0.33406872

00:53:21.880 --> 00:53:24.200 he normalized his A1C.

NOTE Confidence: 0.33406872

00:53:24.200 --> 00:53:26.540 We continued three of his previous

NOTE Confidence: 0.33406872

00:53:26.540 --> 00:53:28.560 medications and discontinued three others.

NOTE Confidence: 0.33406872

00:53:28.560 --> 00:53:30.735 And overall he's feeling much

NOTE Confidence: 0.33406872

00:53:30.735 --> 00:53:32.475 healthier and much better.

NOTE Confidence: 0.33406872

00:53:32.480 --> 00:53:33.218 Now overall though,

NOTE Confidence: 0.33406872

00:53:33.218 --> 00:53:35.249 what we have to keep in mind is

NOTE Confidence: 0.33406872

00:53:35.249 --> 00:53:36.785 that the focus of obesity treatment

NOTE Confidence: 0.33406872

00:53:36.785 --> 00:53:38.480 is not just weight reduction,

NOTE Confidence: 0.33406872

00:53:38.480 --> 00:53:40.460 it is optimizing health where

NOTE Confidence: 0.33406872

00:53:40.460 --> 00:53:42.440 we're treating obesity and we're

NOTE Confidence: 0.33406872

00:53:42.507 --> 00:53:44.679 treating the patient at the focus.

NOTE Confidence: 0.33406872

00:53:44.680 --> 00:53:46.120 And I'm going to breeze through

NOTE Confidence: 0.33406872

00:53:46.120 --> 00:53:46.840 the next slide,

NOTE Confidence: 0.33406872

00:53:46.840 --> 00:53:48.196 but I actually think it's really,

NOTE Confidence: 0.33406872

00:53:48.200 --> 00:53:50.356 really important and this is that we

NOTE Confidence: 0.33406872

00:53:50.356 --> 00:53:52.516 need to support our patients through

NOTE Confidence: 0.33406872

00:53:52.516 --> 00:53:54.476 their weight and health journey.

NOTE Confidence: 0.33406872

00:53:54.480 --> 00:53:56.136 So we have our patient at the center

NOTE Confidence: 0.33406872

00:53:56.136 --> 00:53:58.156 here and there are many things to consider.

NOTE Confidence: 0.33406872

00:53:58.160 --> 00:53:58.478 One,

NOTE Confidence: 0.33406872

00:53:58.478 --> 00:54:00.704 we need to target the neuro metabolic

NOTE Confidence: 0.33406872

00:54:00.704 --> 00:54:02.581 Physiology of obesity that we talked

NOTE Confidence: 0.33406872

00:54:02.581 --> 00:54:05.039 about at the beginning of the talk today.

NOTE Confidence: 0.5442748

00:54:05.040 --> 00:54:06.882 We need to consider the heterogeneity

NOTE Confidence: 0.5442748

00:54:06.882 --> 00:54:08.777 of obesity and that not everybody

NOTE Confidence: 0.5442748

00:54:08.777 --> 00:54:10.595 will respond to the same thing.

NOTE Confidence: 0.5442748

00:54:10.600 --> 00:54:12.375 We need to consider factors

NOTE Confidence: 0.5442748

00:54:12.375 --> 00:54:13.440 in treatment selection,

NOTE Confidence: 0.5442748

00:54:13.440 --> 00:54:15.799 so whether that's the severity of obesity,

NOTE Confidence: 0.5442748

00:54:15.800 --> 00:54:17.272 other obesity condition related

NOTE Confidence: 0.5442748

00:54:17.272 --> 00:54:19.112 conditions a patient may have,

NOTE Confidence: 0.5442748

00:54:19.120 --> 00:54:21.505 their overall health including mental

NOTE Confidence: 0.5442748

00:54:21.505 --> 00:54:23.890 and metabolic health and various

NOTE Confidence: 0.5442748

00:54:23.962 --> 00:54:26.277 treatment targets we can consider.

NOTE Confidence: 0.5442748

00:54:26.280 --> 00:54:28.638 We need to individualize combination therapy,

NOTE Confidence: 0.5442748

101

00:54:28.640 --> 00:54:30.628 what's right for that patient who's sitting

NOTE Confidence: 0.5442748

00:54:30.628 --> 00:54:32.556 there in front of you in the office.

NOTE Confidence: 0.5442748

00:54:32.560 --> 00:54:34.558 We also need to optimize health.

NOTE Confidence: 0.5442748

00:54:34.560 --> 00:54:37.152 There's no medicine that helps us to make

NOTE Confidence: 0.5442748

00:54:37.152 --> 00:54:39.479 healthier food choices or to exercise more.

NOTE Confidence: 0.5442748

00:54:39.480 --> 00:54:41.118 When one of you develops that,

NOTE Confidence: 0.5442748

00:54:41.120 --> 00:54:42.532 please let me know.

NOTE Confidence: 0.5442748

00:54:42.532 --> 00:54:44.906 Until then, we really need to focus on how

NOTE Confidence: 0.5442748

00:54:44.906 --> 00:54:47.317 can we help our patients optimize health.

NOTE Confidence: 0.5442748

00:54:47.320 --> 00:54:49.648 Maximize nutritious food intake,

NOTE Confidence: 0.5442748

00:54:49.648 --> 00:54:51.394 prioritize protein intake,

NOTE Confidence: 0.5442748

00:54:51.400 --> 00:54:53.080 especially during the weight reduction

NOTE Confidence: 0.5442748

00:54:53.080 --> 00:54:54.760 phase when they're eating less,

NOTE Confidence: 0.5442748

00:54:54.760 --> 00:54:57.800 maximize physical activity, reduce stress,

NOTE Confidence: 0.5442748

00:54:57.800 --> 00:55:00.280 improve sleep quality and duration.

NOTE Confidence: 0.5442748

00:55:00.280 --> 00:55:01.930 We need to consider the rate

NOTE Confidence: 0.5442748

00:55:01.930 --> 00:55:02.755 of weight reduction,

NOTE Confidence: 0.5442748

00:55:02.760 --> 00:55:04.560 Make sure our patients aren't

NOTE Confidence: 0.5442748

00:55:04.560 --> 00:55:05.640 losing too quickly.

NOTE Confidence: 0.5442748

00:55:05.640 --> 00:55:06.848 Consider the quality of

NOTE Confidence: 0.5442748

00:55:06.848 --> 00:55:07.754 that weight reduction,

NOTE Confidence: 0.5442748

00:55:07.760 --> 00:55:10.358 so losing more fat than muscle.

NOTE Confidence: 0.5442748

00:55:10.360 --> 00:55:13.034 We also need to consider potential downsides,

NOTE Confidence: 0.5442748

00:55:13.040 --> 00:55:14.752 bone loss, vitamin deficiencies,

NOTE Confidence: 0.5442748

00:55:14.752 --> 00:55:16.036 muscle loss function,

NOTE Confidence: 0.5442748

00:55:16.040 --> 00:55:16.400 etcetera.

NOTE Confidence: 0.5442748

00:55:16.400 --> 00:55:18.200 We can achieve these degrees

NOTE Confidence: 0.5442748

00:55:18.200 --> 00:55:19.640 of weight loss now,

NOTE Confidence: 0.5442748

00:55:19.640 --> 00:55:21.296 but but all of these other

NOTE Confidence: 0.5442748

00:55:21.296 --> 00:55:23.160 things have to be considered.

NOTE Confidence: 0.5442748

00:55:23.160 --> 00:55:25.518 We also have to consider the bias and stigma,

NOTE Confidence: 0.5442748

00:55:25.520 --> 00:55:27.845 the psychosocial and the psychological

NOTE Confidence: 0.5442748

00:55:27.845 --> 00:55:29.240 implications of obesity.

NOTE Confidence: 0.5442748

00:55:29.240 --> 00:55:31.388 Treatment and access and

NOTE Confidence: 0.5442748

00:55:31.388 --> 00:55:32.999 affordability is key.

NOTE Confidence: 0.5442748

00:55:33.000 --> 00:55:36.038 Half of Americans are impacted by obesity,

NOTE Confidence: 0.5442748

00:55:36.040 --> 00:55:39.340 1/4 of the world population by the year 2035.

NOTE Confidence: 0.5442748

00:55:39.340 --> 00:55:41.040 So this is really important

NOTE Confidence: 0.5442748

00:55:41.040 --> 00:55:42.400 to consider as well.

NOTE Confidence: 0.5442748

00:55:42.400 --> 00:55:45.760 And I'll end with this patient quote.

NOTE Confidence: 0.5442748

00:55:45.760 --> 00:55:48.399 And I really believe that our patients

NOTE Confidence: 0.5442748

00:55:48.399 --> 00:55:50.878 and our participants teach us everything.

NOTE Confidence: 0.5442748

00:55:50.880 --> 00:55:52.920 They give us clues to everything.

NOTE Confidence: 0.5442748

00:55:52.920 --> 00:55:55.307 And this patient was one who was

NOTE Confidence: 0.5442748

00:55:55.307 --> 00:55:57.162 in the surmount 1 tirzepatide

NOTE Confidence: 0.5442748

00:55:57.162 --> 00:55:59.352 trial and she lost nearly £100.

NOTE Confidence: 0.5442748

00:55:59.352 --> 00:56:02.040 She lost over 90 pounds in the trial

NOTE Confidence: 0.5442748

00:56:02.040 --> 00:56:03.996 and she taught me about Physiology.

NOTE Confidence: 0.5442748

00:56:04.000 --> 00:56:05.512 And this is what she said to me

NOTE Confidence: 0.5442748

00:56:05.512 --> 00:56:06.838 during the course of the trial.

NOTE Confidence: 0.5442748

00:56:06.840 --> 00:56:08.716 And let me just set the stage

NOTE Confidence: 0.5442748

00:56:08.720 --> 00:56:10.244 before the trial.

NOTE Confidence: 0.5442748

00:56:10.244 --> 00:56:12.276 She ate healthy food,

NOTE Confidence: 0.5442748

00:56:12.280 --> 00:56:13.376 she exercised,

NOTE Confidence: 0.5442748

00:56:13.376 --> 00:56:16.936 she went to PTA meetings after the trial

NOTE Confidence: 0.5442748

00:56:16.936 --> 00:56:19.160 and during the trial she ate healthy food,

NOTE Confidence: 0.5442748

00:56:19.160 --> 00:56:19.844 she exercised,

NOTE Confidence: 0.5442748

00:56:19.844 --> 00:56:21.554 she went to PTA meetings,

NOTE Confidence: 0.5442748

00:56:21.560 --> 00:56:23.600 She did everything the same.

NOTE Confidence: 0.5442748

00:56:23.600 --> 00:56:26.439 The one thing that changed was that

NOTE Confidence: 0.5442748

00:56:26.439 --> 00:56:28.034 she received something during the

NOTE Confidence: 0.5442748

00:56:28.034 --> 00:56:30.439 trial and we think it was tirzepatide.

NOTE Confidence: 0.5442748

00:56:30.440 --> 00:56:32.664 And what she said to me is it's

NOTE Confidence: 0.5442748

00:56:32.664 --> 00:56:34.512 just as easy to lose weight as

NOTE Confidence: 0.5442748

00:56:34.512 --> 00:56:36.278 it ever was to gain weight.

NOTE Confidence: 0.5442748

00:56:36.280 --> 00:56:38.485 So all the things she had been

NOTE Confidence: 0.5442748

00:56:38.485 --> 00:56:40.713 trying for all those years now

NOTE Confidence: 0.5442748

00:56:40.713 --> 00:56:42.878 in the setting of tirzepatide,

NOTE Confidence: 0.5442748

00:56:42.880 --> 00:56:45.078 she was able to lose that weight.

NOTE Confidence: 0.5442748

00:56:45.080 --> 00:56:47.110 So thank you so much for your

NOTE Confidence: 0.5442748

00:56:47.110 --> 00:56:48.640 attention and the invitation to speak.

NOTE Confidence: 0.5442748

00:56:48.640 --> 00:56:49.054 And I'm,

NOTE Confidence: 0.5442748

00:56:49.054 --> 00:56:51.240 I would be very happy to take your questions.

NOTE Confidence: 0.5442748

00:56:51.240 --> 00:56:52.040 Thank you so much.