WEBVTT

NOTE duration:"00:59:52"

NOTE recognizability:0.805

NOTE language:en-us

NOTE Confidence: 0.922118174285714

00:00:00.000 --> 00:00:02.380 I have the pleasure of introducing Dr.

NOTE Confidence: 0.922118174285714

00:00:02.380 --> 00:00:03.436 Danny Ecker today.

NOTE Confidence: 0.922118174285714

00:00:03.436 --> 00:00:05.196 Doctor Eckert received his Bachelor

NOTE Confidence: 0.922118174285714

00:00:05.196 --> 00:00:07.039 of Science degrees with honors,

NOTE Confidence: 0.922118174285714

00:00:07.040 --> 00:00:09.875 followed by his PhD in Sleep respiratory

NOTE Confidence: 0.922118174285714

00:00:09.875 --> 00:00:11.840 Physiology from Adelaide University.

NOTE Confidence: 0.922118174285714

00:00:11.840 --> 00:00:13.736 He's currently a Matthew Flinders professor

NOTE Confidence: 0.922118174285714

00:00:13.736 --> 00:00:15.796 and the director of Adelaide Institute

NOTE Confidence: 0.922118174285714

00:00:15.796 --> 00:00:18.016 for Sleep Health at Flinders University.

NOTE Confidence: 0.922118174285714

00:00:18.020 --> 00:00:20.036 He's also the principal research scientist

NOTE Confidence: 0.922118174285714

00:00:20.036 --> 00:00:22.326 and director of the Sleep Program

NOTE Confidence: 0.922118174285714

00:00:22.326 --> 00:00:24.098 at Neuroscience Research Australia.

NOTE Confidence: 0.922118174285714

00:00:24.100 --> 00:00:24.940 After his education,

NOTE Confidence: 0.922118174285714

00:00:24.940 --> 00:00:26.900 he worked briefly in the division of

NOTE Confidence: 0.922118174285714

00:00:26.950 --> 00:00:28.744 Sleep Medicine at Brigham and Women's

NOTE Confidence: 0.922118174285714

00:00:28.744 --> 00:00:30.340 Hospital in Harvard Med School.

NOTE Confidence: 0.922118174285714

00:00:30.340 --> 00:00:32.370 Before moving back to Australia,

NOTE Confidence: 0.922118174285714

00:00:32.370 --> 00:00:34.740 his research aims to improve understanding

NOTE Confidence: 0.922118174285714

00:00:34.740 --> 00:00:36.951 of obstructive sleep apnea and

NOTE Confidence: 0.922118174285714

00:00:36.951 --> 00:00:38.667 respiratory disease pathophysiology,

NOTE Confidence: 0.922118174285714

00:00:38.670 --> 00:00:40.526 identify novel therapeutic agents

NOTE Confidence: 0.922118174285714

00:00:40.526 --> 00:00:42.846 and develop new targeted therapies.

NOTE Confidence: 0.922118174285714

00:00:42.850 --> 00:00:45.482 His most well known for his work on

NOTE Confidence: 0.922118174285714

00:00:45.482 --> 00:00:46.934 respiratory endophenotype being leading

NOTE Confidence: 0.922118174285714

00:00:46.934 --> 00:00:49.154 to a new precision medicine therapeutics.

NOTE Confidence: 0.922118174285714

00:00:49.160 --> 00:00:51.820 Along with his research on the role

NOTE Confidence: 0.922118174285714

00:00:51.820 --> 00:00:53.878 of arousal mechanisms and hypnotics

NOTE Confidence: 0.922118174285714

00:00:53.878 --> 00:00:55.983 and sleep apnea pathogenesis treatment

NOTE Confidence: 0.922118174285714

00:00:55.983 --> 00:00:58.649 as well as OSA pharmacotherapy,

NOTE Confidence: 0.922118174285714

00:00:58.650 --> 00:01:00.410 he has received many awards.

NOTE Confidence: 0.922118174285714

00:01:00.410 --> 00:01:02.198 Is a recipient of several grants,

NOTE Confidence: 0.922118174285714

00:01:02.200 --> 00:01:04.558 including from the National Health and

NOTE Confidence: 0.922118174285714

00:01:04.558 --> 00:01:06.593 Medical Research Council of Australia

NOTE Confidence: 0.922118174285714

00:01:06.593 --> 00:01:09.386 and has authored over 100 and 8080

NOTE Confidence: 0.922118174285714

00:01:09.386 --> 00:01:11.500 publications including in JAMA Blue Journal,

NOTE Confidence: 0.922118174285714

00:01:11.500 --> 00:01:12.820 European Respiratory Journal.

NOTE Confidence: 0.922118174285714

00:01:12.820 --> 00:01:15.460 Doctor Eckert has also held leadership

NOTE Confidence: 0.922118174285714

00:01:15.460 --> 00:01:17.381 position in many national and

NOTE Confidence: 0.922118174285714

00:01:17.381 --> 00:01:18.797 international societies and has

NOTE Confidence: 0.922118174285714

00:01:18.797 --> 00:01:20.919 served in many editorial boards

NOTE Confidence: 0.922118174285714

00:01:20.919 --> 00:01:22.715 including Sleep Medicine Reviews.

NOTE Confidence: 0.922118174285714

00:01:22.720 --> 00:01:25.232 Thank you so much for being with us

NOTE Confidence: 0.922118174285714

00:01:25.232 --> 00:01:27.585 Doctor Eckert at 5:30 AM your Australian

NOTE Confidence: 0.922118174285714

00:01:27.585 --> 00:01:29.100 time and without further delay I

NOTE Confidence: 0.922118174285714

00:01:29.100 --> 00:01:30.910 would like to hand it over to you.

NOTE Confidence: 0.922118174285714

00:01:30.910 --> 00:01:33.395 To share your expertise on sleep apnea

NOTE Confidence: 0.922118174285714

00:01:33.395 --> 00:01:34.990 endives implications for precision

NOTE Confidence: 0.922118174285714

00:01:34.990 --> 00:01:36.938 Sleep Medicine, thank you again.

NOTE Confidence: 0.886675458

00:01:38.310 --> 00:01:40.206 Many, Many thanks for the kind

NOTE Confidence: 0.886675458

00:01:40.206 --> 00:01:41.881 words and introductions and and

NOTE Confidence: 0.886675458

00:01:41.881 --> 00:01:43.277 and good afternoon everyone.

NOTE Confidence: 0.886675458

00:01:43.280 --> 00:01:46.376 It's it's great to be here from afar.

NOTE Confidence: 0.886675458

00:01:46.380 --> 00:01:48.998 So to begin, as highlighted there are

NOTE Confidence: 0.886675458

00:01:48.998 --> 00:01:51.857 majority of my work funded by the NIH,

NOTE Confidence: 0.886675458

00:01:51.860 --> 00:01:53.824 NIH equivalent now NHMRC,

NOTE Confidence: 0.886675458

00:01:53.824 --> 00:01:57.468 but I do have various industry partnerships

NOTE Confidence: 0.886675458

00:01:57.468 --> 00:02:01.098 given the interest in developing new

NOTE Confidence: 0.886675458

00:02:01.098 --> 00:02:04.847 therapies for sleep apnea as listed here.

NOTE Confidence: 0.886675458

00:02:04.850 --> 00:02:06.812 I want to begin by acknowledging

NOTE Confidence: 0.886675458

00:02:06.812 --> 00:02:09.168 the land on which I I meet today.

NOTE Confidence: 0.886675458

00:02:09.170 --> 00:02:11.053 It's the land of the traditional owners

NOTE Confidence: 0.886675458

00:02:11.053 --> 00:02:13.037 or the custodians and the land of the

NOTE Confidence: 0.886675458

00:02:13.037 --> 00:02:14.550 Ghana people of the Adelaide planes,

NOTE Confidence: 0.886675458

00:02:14.550 --> 00:02:16.416 where learning and teaching has been

NOTE Confidence: 0.886675458

00:02:16.416 --> 00:02:18.323 taking place for 10s of thousands

NOTE Confidence: 0.886675458

00:02:18.323 --> 00:02:20.123 of years down here in Adelaide,

NOTE Confidence: 0.886675458

00:02:20.130 --> 00:02:20.448 Australia.

NOTE Confidence: 0.886675458

00:02:20.448 --> 00:02:23.310 But you can see with all these orange dots,

NOTE Confidence: 0.886675458

00:02:23.310 --> 00:02:25.578 we have a rather unique landscape and

NOTE Confidence: 0.886675458

00:02:25.578 --> 00:02:28.625 these are all the areas in which our

NOTE Confidence: 0.886675458

00:02:28.625 --> 00:02:30.229 university has campuses throughout

NOTE Confidence: 0.886675458

00:02:30.229 --> 00:02:32.229 these rather unique landscape.

NOTE Confidence: 0.82586313

00:02:34.610 --> 00:02:37.366 OK. So I guess the begin, you know,

NOTE Confidence: 0.82586313

00:02:37.366 --> 00:02:39.312 why do we need these new therapeutic

NOTE Confidence: 0.82586313

00:02:39.312 --> 00:02:40.430 approaches for sleep apnea?

NOTE Confidence: 0.82586313

00:02:40.430 --> 00:02:42.155 You know, perhaps I don't

NOTE Confidence: 0.82586313

00:02:42.155 --> 00:02:43.880 have to spend much time.

NOTE Confidence: 0.82586313

00:02:43.880 --> 00:02:46.470 But yeah, I think it's fair to

NOTE Confidence: 0.82586313

00:02:46.470 --> 00:02:49.128 say that the current ones are.

NOTE Confidence: 0.82586313

00:02:49.130 --> 00:02:51.450 In which the CPAP is,

NOTE Confidence: 0.82586313

00:02:51.450 --> 00:02:54.810 is typically delivered as as,

NOTE Confidence: 0.82586313

00:02:54.810 --> 00:02:57.486 as monotherapies is quite time consuming,

NOTE Confidence: 0.82586313

00:02:57.490 --> 00:02:59.614 costly and it's really

NOTE Confidence: 0.82586313

00:02:59.614 --> 00:03:01.738 failing too many patients.

NOTE Confidence: 0.82586313

00:03:01.740 --> 00:03:04.830 I won't go through all the

NOTE Confidence: 0.82586313

00:03:04.830 --> 00:03:06.890 various steps here as.

NOTE Confidence: 0.82586313

00:03:06.890 --> 00:03:08.540 Framework, I've just turned my video

NOTE Confidence: 0.82586313

00:03:08.540 --> 00:03:10.490 off because it's a little unstable,

NOTE Confidence: 0.82586313

00:03:10.490 --> 00:03:12.690 so I I hope, hope that that will

NOTE Confidence: 0.82586313

00:03:12.690 --> 00:03:14.847 make the audio a little clearer,

NOTE Confidence: 0.82586313

00:03:14.850 --> 00:03:18.105 but not obvious to say that first

NOTE Confidence: 0.82586313

00:03:18.105 --> 00:03:20.054 you have to suspect you have sleep

NOTE Confidence: 0.82586313

00:03:20.054 --> 00:03:21.366 apnea primary care referral,

NOTE Confidence: 0.82586313

00:03:21.370 --> 00:03:22.492 recognizing that there's

NOTE Confidence: 0.82586313

00:03:22.492 --> 00:03:23.988 different models of care.

NOTE Confidence: 0.82586313

00:03:23.990 --> 00:03:26.665 But also very true that

NOTE Confidence: 0.82586313

00:03:26.665 --> 00:03:28.270 it's quite convoluted.

NOTE Confidence: 0.82586313

00:03:28.270 --> 00:03:30.802 Every step along the way there's

NOTE Confidence: 0.82586313

00:03:30.802 --> 00:03:32.926 there's delays we're relying on

NOTE Confidence: 0.82586313

00:03:32.926 --> 00:03:35.086 on this technology for for our

NOTE Confidence: 0.82586313

00:03:35.086 --> 00:03:37.382 diagnosis often in a single night

NOTE Confidence: 0.82586313

00:03:37.382 --> 00:03:39.668 and it's and yet despite these

NOTE Confidence: 0.82586313

00:03:39.668 --> 00:03:41.750 different causes of sleep apnea as

NOTE Confidence: 0.82586313

00:03:41.750 --> 00:03:44.626 I'll talk about well over 90% of

NOTE Confidence: 0.82586313

00:03:44.626 --> 00:03:46.482 patients are initially prescribed

NOTE Confidence: 0.82586313

00:03:46.482 --> 00:03:48.810 CPAP half of whom will fail

NOTE Confidence: 0.82586313

00:03:48.810 --> 00:03:51.547 with our measures out to a year.

NOTE Confidence: 0.82586313

00:03:51.550 --> 00:03:54.368 And and this is despite our

NOTE Confidence: 0.82586313

00:03:54.368 --> 00:03:56.858 emerging evidence that you know

NOTE Confidence: 0.82586313

00:03:56.858 --> 00:03:58.850 things like oral appliances.

NOTE Confidence: 0.82586313

00:03:58.850 --> 00:04:01.314 And this is now you know this

NOTE Confidence: 0.82586313

00:04:01.314 --> 00:04:03.193 clinical trial conducted here in

NOTE Confidence: 0.82586313

00:04:03.193 --> 00:04:05.461 Australia over 10 years now showing

NOTE Confidence: 0.82586313

00:04:05.461 --> 00:04:07.214 similar health outcomes with

NOTE Confidence: 0.82586313

00:04:07.214 --> 00:04:09.699 oral appliance therapy to CPAP.

NOTE Confidence: 0.82586313

00:04:09.700 --> 00:04:12.676 More recently if we look at other therapies,

NOTE Confidence: 0.82586313

00:04:12.680 --> 00:04:15.824 this was a study led by Mika Antic

NOTE Confidence: 0.82586313

00:04:15.824 --> 00:04:18.828 and Doug McAvoy and our team showing

NOTE Confidence: 0.82586313

00:04:18.828 --> 00:04:21.156 you know the the the potential

NOTE Confidence: 0.82586313

00:04:21.156 --> 00:04:23.258 benefit for multi level surgery

NOTE Confidence: 0.82586313

00:04:23.258 --> 00:04:26.486 for many patients and yet you know

NOTE Confidence: 0.82586313

00:04:26.486 --> 00:04:28.906 this is again another development.

NOTE Confidence: 0.82586313

00:04:28.910 --> 00:04:31.460 In Australia, CPAP.

NOTE Confidence: 0.82586313

00:04:31.460 --> 00:04:33.980 Developed here in in Sydney,

NOTE Confidence: 0.82586313

00:04:33.980 --> 00:04:35.978 you know, many years ago now,

NOTE Confidence: 0.82586313

00:04:35.980 --> 00:04:37.480 but for many patients,

NOTE Confidence: 0.82586313

00:04:37.480 --> 00:04:39.355 despite the images like this,

NOTE Confidence: 0.82586313

00:04:39.360 --> 00:04:41.936 we can see all the sorts of the

NOTE Confidence: 0.82586313

00:04:41.936 --> 00:04:43.418 multiple sleep hygiene issues

NOTE Confidence: 0.82586313

00:04:43.418 --> 00:04:46.120 going on with this with blue light

NOTE Confidence: 0.82586313

00:04:46.199 --> 00:04:48.754 there and not sure you'd be having

NOTE Confidence: 0.82586313

00:04:48.754 --> 00:04:50.350 your CPAP machine on my.

NOTE Confidence: 0.82586313

00:04:50.350 --> 00:04:50.640 Nonetheless,

NOTE Confidence: 0.82586313

00:04:50.640 --> 00:04:52.090 for for many patients it

NOTE Confidence: 0.82586313

00:04:52.090 --> 00:04:53.250 feels more like this.

NOTE Confidence: 0.82586313

00:04:53.250 --> 00:04:56.218 So so whilst CPAP is a fantastic

NOTE Confidence: 0.82586313

00:04:56.218 --> 00:04:58.090 therapy and literally benefits

NOTE Confidence: 0.82586313

00:04:58.090 --> 00:05:01.186 millions of people around the planet,

NOTE Confidence: 0.82586313

00:05:01.190 --> 00:05:03.086 you know for many it's it's you know,

NOTE Confidence: 0.82586313

00:05:03.090 --> 00:05:06.146 they just cannot tolerate it or or are

NOTE Confidence: 0.82586313

00:05:06.146 --> 00:05:08.940 unwilling to do so or find it invasive.

NOTE Confidence: 0.82586313

00:05:08.940 --> 00:05:10.056 So as as I'll show you

NOTE Confidence: 0.82586313

00:05:10.056 --> 00:05:11.200 in the next few slides,

NOTE Confidence: 0.82586313

00:05:11.200 --> 00:05:13.126 you know sleep pattern is very

NOTE Confidence: 0.82586313

00:05:13.126 --> 00:05:14.410 much a heterogeneous disorder

NOTE Confidence: 0.82586313

00:05:14.466 --> 00:05:16.104 and as such the optimal therapy

NOTE Confidence: 0.82586313

00:05:16.104 --> 00:05:18.116 or therapies as the case may be

NOTE Confidence: 0.82586313

00:05:18.116 --> 00:05:19.272 likely varies between patients

NOTE Confidence: 0.82586313

00:05:19.272 --> 00:05:21.721 and this is where these precision

NOTE Confidence: 0.82586313

00:05:21.721 --> 00:05:24.356 medicine concept come into play.

NOTE Confidence: 0.82586313

00:05:24.360 --> 00:05:26.432 So really I'm just going to talk about

NOTE Confidence: 0.82586313

00:05:26.432 --> 00:05:27.907 three things in this presentation

NOTE Confidence: 0.82586313

00:05:27.907 --> 00:05:29.707 I'm going to briefly describe the

NOTE Confidence: 0.82586313

00:05:29.707 --> 00:05:31.037 four key pathophysiological traits

NOTE Confidence: 0.82586313

00:05:31.037 --> 00:05:33.312 or or and or types that contribute

NOTE Confidence: 0.82586313

00:05:33.320 --> 00:05:35.504 to OSA and highlight how that's

NOTE Confidence: 0.82586313

00:05:35.504 --> 00:05:36.960 the foundation for precision

NOTE Confidence: 0.82586313

00:05:37.026 --> 00:05:38.910 or personalized Sleep Medicine.

NOTE Confidence: 0.82586313

00:05:38.910 --> 00:05:41.190 I'll then talk about implications

NOTE Confidence: 0.82586313

00:05:41.190 --> 00:05:43.014 for targeted personalized therapy

NOTE Confidence: 0.82586313

00:05:43.014 --> 00:05:45.212 for this common respiratory chronic

NOTE Confidence: 0.82586313

00:05:45.212 --> 00:05:47.617 condition and then finally I'll

NOTE Confidence: 0.82586313

00:05:47.617 --> 00:05:49.060 I'll share some

NOTE Confidence: 0.882920391

00:05:49.139 --> 00:05:51.259 of the more recent highlights

NOTE Confidence: 0.882920391

00:05:51.259 --> 00:05:53.379 in terms of simplified tools.

NOTE Confidence: 0.882920391

00:05:53.380 --> 00:05:57.108 Steps into the clinic.

NOTE Confidence: 0.882920391

00:05:57.110 --> 00:05:59.572 So I guess just to begin we we

NOTE Confidence: 0.882920391

00:05:59.572 --> 00:06:01.539 know that well we now know that

NOTE Confidence: 0.882920391

00:06:01.539 --> 00:06:03.716 sleep apnea you know fundamentally

NOTE Confidence: 0.882920391

00:06:03.716 --> 00:06:05.544 this interaction between indeed

NOTE Confidence: 0.882920391

00:06:05.544 --> 00:06:08.459 the upper airway anatomy but also

NOTE Confidence: 0.882920391

00:06:08.459 --> 00:06:10.387 these non anatomical contributions.

NOTE Confidence: 0.882920391

00:06:10.390 --> 00:06:12.462 And so if we're just to take a

NOTE Confidence: 0.882920391

00:06:12.462 --> 00:06:14.248 static image of the upper airway,

NOTE Confidence: 0.882920391

00:06:14.250 --> 00:06:16.112 it really does not show the full

NOTE Confidence: 0.882920391

00:06:16.112 --> 00:06:17.869 picture of what's going on in this,

NOTE Confidence: 0.882920391

00:06:17.870 --> 00:06:20.587 in this very common disease here.

NOTE Confidence: 0.882920391

00:06:20.587 --> 00:06:22.643 If we look on the on the left,

NOTE Confidence: 0.882920391

00:06:22.650 --> 00:06:23.510 we would just say yes,

NOTE Confidence: 0.882920391

00:06:23.510 --> 00:06:25.449 this individual does not have sleep apnea,

NOTE Confidence: 0.882920391

00:06:25.450 --> 00:06:26.510 we'd look on the right.

NOTE Confidence: 0.882920391

00:06:26.510 --> 00:06:29.242 This crowded individual who is a base,

NOTE Confidence: 0.882920391

00:06:29.242 --> 00:06:31.048 we can say the adipose tissue

NOTE Confidence: 0.882920391

00:06:31.048 --> 00:06:32.856 throughout the genioglossus muscle and

NOTE Confidence: 0.882920391

00:06:32.856 --> 00:06:35.148 surrounding the upper airway would say

NOTE Confidence: 0.882920391

00:06:35.148 --> 00:06:37.559 yes this person does have sleep apnea,

NOTE Confidence: 0.882920391

00:06:37.560 --> 00:06:39.560 but actually you know ultimately

NOTE Confidence: 0.882920391

00:06:39.560 --> 00:06:41.160 it's this interaction between

NOTE Confidence: 0.882920391

00:06:41.160 --> 00:06:42.641 pharyngeal dilator muscles and

NOTE Confidence: 0.882920391

00:06:42.641 --> 00:06:44.681 the anatomy and these other non

NOTE Confidence: 0.882920391

00:06:44.681 --> 00:06:46.558 anatomical traits that I'll highlight.

NOTE Confidence: 0.882920391

00:06:46.560 --> 00:06:48.751 So this person again if we just

NOTE Confidence: 0.882920391

00:06:48.751 --> 00:06:50.740 look here narrow crowded airway,

NOTE Confidence: 0.882920391

00:06:50.740 --> 00:06:53.252 but actually because this

NOTE Confidence: 0.882920391

00:06:53.252 --> 00:06:55.194 individual despite being obese

NOTE Confidence: 0.882920391

00:06:55.194 --> 00:06:56.946 having an anatomically compromised.

NOTE Confidence: 0.882920391

00:06:56.950 --> 00:06:58.994 Either way is able to be protect

NOTE Confidence: 0.882920391

00:06:58.994 --> 00:07:00.229 themselves from sleep apnea

NOTE Confidence: 0.882920391

00:07:00.229 --> 00:07:01.744 because the muscles are working

NOTE Confidence: 0.882920391

00:07:01.744 --> 00:07:03.659 so well to protect that airway.

NOTE Confidence: 0.882920391

00:07:03.660 --> 00:07:03.951 Now,

NOTE Confidence: 0.882920391

00:07:03.951 --> 00:07:05.115 recognising that this is

NOTE Confidence: 0.882920391

00:07:05.115 --> 00:07:06.279 awake in this imaging,

NOTE Confidence: 0.882920391

00:07:06.280 --> 00:07:08.702 but we've also done studies to show

NOTE Confidence: 0.882920391

00:07:08.702 --> 00:07:10.410 that these individuals who are

NOTE Confidence: 0.882920391

00:07:10.410 --> 00:07:12.234 these who don't have sleep apnea

NOTE Confidence: 0.882920391

00:07:12.234 --> 00:07:14.098 have about three or four times.

NOTE Confidence: 0.882920391

00:07:14.100 --> 00:07:16.542 Get a muscle activation of the

NOTE Confidence: 0.882920391

00:07:16.542 --> 00:07:18.170 dilator muscles during sleep

NOTE Confidence: 0.882920391

00:07:18.247 --> 00:07:20.387 compared to their counterparts.

NOTE Confidence: 0.882920391

00:07:20.390 --> 00:07:22.469 Obviously this is not always the case.

NOTE Confidence: 0.882920391

00:07:22.470 --> 00:07:25.020 In some people they have this

NOTE Confidence: 0.882920391

00:07:25.020 --> 00:07:26.295 counterproductive motion where

NOTE Confidence: 0.882920391

00:07:26.295 --> 00:07:28.427 initially at the start of inspiration

NOTE Confidence: 0.882920391

00:07:28.427 --> 00:07:29.844 the tongue moves anteriorly,

NOTE Confidence: 0.882920391

00:07:29.844 --> 00:07:32.483 but here we can see the UVA

NOTE Confidence: 0.882920391

00:07:32.483 --> 00:07:34.351 falling back on the posterior

NOTE Confidence: 0.882920391

00:07:34.351 --> 00:07:36.350 wall and this individual's got

NOTE Confidence: 0.882920391

00:07:36.350 --> 00:07:38.210 moderately severe sleep apnea.

NOTE Confidence: 0.882920391

00:07:38.210 --> 00:07:41.330 And in other individuals,

NOTE Confidence: 0.882920391

00:07:41.330 --> 00:07:42.574 we've we've,

NOTE Confidence: 0.882920391

00:07:42.574 --> 00:07:46.306 we've got examples more like this

NOTE Confidence: 0.882920391

00:07:46.306 --> 00:07:49.503 where really there's no motion

NOTE Confidence: 0.882920391

00:07:49.503 --> 00:07:52.118 whatsoever of the dilator muscles,

NOTE Confidence: 0.882920391

00:07:52.118 --> 00:07:55.770 at least in terms of opening up that airway.

NOTE Confidence: 0.882920391

00:07:55.770 --> 00:07:59.490 And in, in those cases,

NOTE Confidence: 0.882920391

00:07:59.490 --> 00:08:01.778 this actual individual's got

NOTE Confidence: 0.882920391

00:08:01.778 --> 00:08:04.066 very severe sleep apnea.

NOTE Confidence: 0.882920391

00:08:04.070 --> 00:08:06.270 Yeah.

NOTE Confidence: 0.882920391

00:08:06.270 --> 00:08:07.956 So this is really our framework

NOTE Confidence: 0.882920391

00:08:07.956 --> 00:08:09.898 and how we think about it now.

NOTE Confidence: 0.882920391

00:08:09.900 --> 00:08:10.434 So yes,

NOTE Confidence: 0.882920391

00:08:10.434 --> 00:08:12.303 people will sleep and you've got some

NOTE Confidence: 0.882920391

00:08:12.303 --> 00:08:14.368 degree of sleep of anatomical compromise,

NOTE Confidence: 0.882920391

00:08:14.370 --> 00:08:15.882 but it varies dramatically

NOTE Confidence: 0.882920391

00:08:15.882 --> 00:08:18.150 between patients as I'll show you.

NOTE Confidence: 0.882920391

00:08:18.150 --> 00:08:20.208 And then of course there's that

NOTE Confidence: 0.882920391

00:08:20.208 --> 00:08:21.580 interaction between whether or

NOTE Confidence: 0.882920391

00:08:21.636 --> 00:08:23.262 not the muscles are able to

NOTE Confidence: 0.882920391

00:08:23.262 --> 00:08:24.789 keep that airway open or not.

NOTE Confidence: 0.882920391

00:08:24.790 --> 00:08:27.317 Other traits such as how easily they

NOTE Confidence: 0.882920391

00:08:27.317 --> 00:08:30.528 wake up to airway narrowing or this

NOTE Confidence: 0.882920391

00:08:30.528 --> 00:08:32.573 respiratory arousal threshold try and

NOTE Confidence: 0.882920391

00:08:32.573 --> 00:08:34.418 finally their control of breathing

NOTE Confidence: 0.882920391

00:08:34.418 --> 00:08:36.618 or or what we often refer to as.

NOTE Confidence: 0.882920391

00:08:36.620 --> 00:08:37.532 As Luke can.

NOTE Confidence: 0.882920391

00:08:37.532 --> 00:08:39.356 So let me just talk through

NOTE Confidence: 0.882920391

00:08:39.356 --> 00:08:41.390 the Physiology briefly here.

NOTE Confidence: 0.882920391

00:08:41.390 --> 00:08:43.022 That sort of lays out the

NOTE Confidence: 0.882920391

00:08:43.022 --> 00:08:44.410 foundation for what we've been

NOTE Confidence: 0.882920391

00:08:44.410 --> 00:08:46.125 doing and we and others in terms

NOTE Confidence: 0.882920391

00:08:46.125 --> 00:08:47.787 of these Ender typing concepts.

NOTE Confidence: 0.882920391

00:08:47.787 --> 00:08:49.732 So initially when we're trying

NOTE Confidence: 0.882920391

00:08:49.732 --> 00:08:51.380 to figure all this out,

NOTE Confidence: 0.882920391

00:08:51.380 --> 00:08:53.285 we inserted these fine wire

NOTE Confidence: 0.882920391

00:08:53.285 --> 00:08:55.190 electrodes just after a bit

NOTE Confidence: 0.882920391

00:08:55.264 --> 00:08:57.274 of lignocaine into the upper

NOTE Confidence: 0.882920391

00:08:57.274 --> 00:08:59.284 airway dilator muscles and in

NOTE Confidence: 0.724851055172414

00:08:59.356 --> 00:09:01.511 this case tensor palatini and

NOTE Confidence: 0.724851055172414

00:09:01.511 --> 00:09:03.235 genioglossus to get these,

NOTE Confidence: 0.724851055172414

00:09:03.240 --> 00:09:05.340 you know, very nice recordings of

NOTE Confidence: 0.724851055172414

00:09:05.340 --> 00:09:07.290 the upper airway dilator muscles.

NOTE Confidence: 0.724851055172414

00:09:07.290 --> 00:09:08.394 Uh, during sleep,

NOTE Confidence: 0.724851055172414

00:09:08.394 --> 00:09:10.234 there's an airway pressure sensor,

NOTE Confidence: 0.724851055172414

00:09:10.240 --> 00:09:11.900 uh just above the epiglottis,

NOTE Confidence: 0.724851055172414

00:09:11.900 --> 00:09:14.888 so we can measure respiratory effort,

NOTE Confidence: 0.724851055172414

00:09:14.890 --> 00:09:15.776 nasal mask,

NOTE Confidence: 0.724851055172414

00:09:15.776 --> 00:09:17.548 animatograph to measure accurately,

NOTE Confidence: 0.724851055172414

00:09:17.550 --> 00:09:19.998 measure airflow and then standard sleep

NOTE Confidence: 0.724851055172414

00:09:19.998 --> 00:09:22.310 staging and arousal scoring equipment.

NOTE Confidence: 0.724851055172414

00:09:22.310 --> 00:09:25.076 The participant breathes through a modified

NOTE Confidence: 0.724851055172414

00:09:25.076 --> 00:09:27.819 CPAP device that's goes to the room,

NOTE Confidence: 0.724851055172414

00:09:27.820 --> 00:09:29.500 the control room where we're sitting

NOTE Confidence: 0.724851055172414

00:09:29.500 --> 00:09:31.738 and then we we we manipulate the

NOTE Confidence: 0.724851055172414

00:09:31.738 --> 00:09:33.498 pressure throughout the night with

NOTE Confidence: 0.724851055172414

00:09:33.498 --> 00:09:35.359 this device and and I guess the.

NOTE Confidence: 0.771439227777778

00:09:37.390 --> 00:09:40.050 This device that enables us really to

NOTE Confidence: 0.771439227777778

00:09:40.050 --> 00:09:42.163 give anyone, even healthy individuals,

NOTE Confidence: 0.771439227777778

00:09:42.163 --> 00:09:44.418 sleep disorder breathing events and

NOTE Confidence: 0.771439227777778

00:09:44.418 --> 00:09:47.277 very controlled way where we can measure

NOTE Confidence: 0.771439227777778

00:09:47.277 --> 00:09:48.789 all these physiologic parameters.

NOTE Confidence: 0.771439227777778

00:09:48.790 --> 00:09:51.205 So here we've got the mask pressure.

NOTE Confidence: 0.771439227777778

00:09:51.210 --> 00:09:52.806 This is actually a healthy individual.

NOTE Confidence: 0.771439227777778

00:09:52.810 --> 00:09:54.210 We're starting them about four

NOTE Confidence: 0.771439227777778

00:09:54.210 --> 00:09:55.610 or five centimeters of water.

NOTE Confidence: 0.771439227777778

00:09:55.610 --> 00:09:57.182 We flick them switch on our

NOTE Confidence: 0.771439227777778

00:09:57.182 --> 00:09:58.849 PCRP machine and in this case,

NOTE Confidence: 0.771439227777778

00:09:58.850 --> 00:10:00.525 we've actually delivered about minus

NOTE Confidence: 0.771439227777778

00:10:00.525 --> 00:10:02.749 2 centimeters of water to the mask.

NOTE Confidence: 0.771439227777778

00:10:02.750 --> 00:10:04.969 So now here's their breathing effort as

NOTE Confidence: 0.771439227777778

00:10:04.969 --> 00:10:07.510 measured by that epiglottic pressure swings.

NOTE Confidence: 0.771439227777778

00:10:07.510 --> 00:10:09.176 We can see that they've had gone

NOTE Confidence: 0.771439227777778

00:10:09.176 --> 00:10:10.958 from very nice air flow to a

NOTE Confidence: 0.771439227777778

00:10:10.958 --> 00:10:12.223 mild hypopnea in this instance.

NOTE Confidence: 0.771439227777778

00:10:12.230 --> 00:10:14.967 And overtime they're building up some CO2.

NOTE Confidence: 0.771439227777778

00:10:14.970 --> 00:10:17.720 Every blood pressure or those

NOTE Confidence: 0.771439227777778

00:10:17.720 --> 00:10:19.920 negative airway pressure deflections

NOTE Confidence: 0.771439227777778

00:10:19.920 --> 00:10:22.864 are increasing as it does in a

NOTE Confidence: 0.771439227777778

00:10:22.864 --> 00:10:25.430 hypopnea and indeed an apnea event.

NOTE Confidence: 0.771439227777778

00:10:25.430 --> 00:10:27.644 And this allows us to sort of very carefully

NOTE Confidence: 0.771439227777778

00:10:27.644 --> 00:10:29.509 measure these traits that are interested.

NOTE Confidence: 0.771439227777778

00:10:29.510 --> 00:10:30.905 And obviously the most important

NOTE Confidence: 0.771439227777778

00:10:30.905 --> 00:10:33.142 thing that we want to figure out is

NOTE Confidence: 0.771439227777778

00:10:33.142 --> 00:10:34.983 how collapsible is that airway or how

NOTE Confidence: 0.771439227777778

00:10:35.041 --> 00:10:36.846 bad is their anatomical compromise.

NOTE Confidence: 0.771439227777778

00:10:36.850 --> 00:10:37.780 So we look at these.

NOTE Confidence: 0.771439227777778

00:10:37.780 --> 00:10:38.129 Yes,

NOTE Confidence: 0.771439227777778

00:10:38.129 --> 00:10:39.874 you breaths immediately following a

NOTE Confidence: 0.771439227777778

00:10:39.874 --> 00:10:42.199 pressure reduction and we can see and

NOTE Confidence: 0.771439227777778

00:10:42.199 --> 00:10:43.945 most people they don't generate much

NOTE Confidence: 0.771439227777778

00:10:43.945 --> 00:10:45.744 muscle activity in these first few

NOTE Confidence: 0.771439227777778

00:10:45.744 --> 00:10:48.211 breaths until we they start to build up

NOTE Confidence: 0.771439227777778

00:10:48.211 --> 00:10:50.570 some CO2 and and and negative pressure.

NOTE Confidence: 0.771439227777778

00:10:50.570 --> 00:10:53.738 So we really are mainly looking at that

NOTE Confidence: 0.771439227777778

00:10:53.738 --> 00:10:55.831 interaction with the passive anatomy

NOTE Confidence: 0.771439227777778

00:10:55.831 --> 00:10:58.581 in these first few breaths and what we

NOTE Confidence: 0.771439227777778

00:10:58.581 --> 00:11:00.003 see in these three different examples.

NOTE Confidence: 0.771439227777778

00:11:00.010 --> 00:11:02.062 So here we've just dropped the

NOTE Confidence: 0.771439227777778

00:11:02.062 --> 00:11:03.942 pressure level at varying different

NOTE Confidence: 0.771439227777778

00:11:03.942 --> 00:11:06.115 levels throughout the night in

NOTE Confidence: 0.771439227777778

00:11:06.115 --> 00:11:07.940 these individuals again and again.

NOTE Confidence: 0.771439227777778

00:11:07.940 --> 00:11:08.880 And here's an individual,

NOTE Confidence: 0.771439227777778

00:11:08.880 --> 00:11:10.290 some of that sort of mild

NOTE Confidence: 0.771439227777778

00:11:10.343 --> 00:11:11.359 anatomical compromise.

NOTE Confidence: 0.771439227777778

00:11:11.360 --> 00:11:13.704 So what we've plotted here is the peak

NOTE Confidence: 0.771439227777778

00:11:13.704 --> 00:11:15.214 inspiratory flow versus the pressure

NOTE Confidence: 0.771439227777778

00:11:15.214 --> 00:11:17.660 we've delivered in the mask on the X axis.

NOTE Confidence: 0.771439227777778

00:11:17.660 --> 00:11:19.376 And then we can construct these

NOTE Confidence: 0.771439227777778

00:11:19.376 --> 00:11:21.307 curves to figure out where the

NOTE Confidence: 0.771439227777778

00:11:21.307 --> 00:11:23.117 Airways closing for each individual.

NOTE Confidence: 0.771439227777778

00:11:23.120 --> 00:11:24.208 So for this individual,

NOTE Confidence: 0.771439227777778

00:11:24.208 --> 00:11:25.840 they actually require that minus 4

NOTE Confidence: 0.771439227777778

00:11:25.888 --> 00:11:28.000 centimeters of water to close off the airway.

NOTE Confidence: 0.771439227777778

00:11:28.000 --> 00:11:28.782 This individual,

NOTE Confidence: 0.771439227777778

00:11:28.782 --> 00:11:30.737 it's more like atmospheric pressure.

NOTE Confidence: 0.771439227777778

00:11:30.740 --> 00:11:32.895 And this individual was severe

NOTE Confidence: 0.771439227777778

00:11:32.895 --> 00:11:33.757 anatomical compromise.

NOTE Confidence: 0.771439227777778

00:11:33.760 --> 00:11:36.070 Their airway is actually collapsing

NOTE Confidence: 0.771439227777778

00:11:36.070 --> 00:11:38.380 at about 5 centimetres of.

NOTE Confidence: 0.771439227777778

00:11:38.380 --> 00:11:41.644 So severely anatomically

NOTE Confidence: 0.771439227777778

00:11:41.644 --> 00:11:43.820 compromised individual.

NOTE Confidence: 0.771439227777778

00:11:43.820 --> 00:11:46.444 OK so there's there's the range of an

NOTE Confidence: 0.771439227777778

00:11:46.444 --> 00:11:49.185 enemy issues we then look at you know

NOTE Confidence: 0.771439227777778

00:11:49.185 --> 00:11:51.339 can these muscles actually recruit and

NOTE Confidence: 0.771439227777778

00:11:51.339 --> 00:11:53.943 and and dilate the airway during sleep.

NOTE Confidence: 0.771439227777778

00:11:53.950 --> 00:11:55.546 It turns out that that that

NOTE Confidence: 0.771439227777778

00:11:55.546 --> 00:11:57.259 cannot be done in all cases.

NOTE Confidence: 0.771439227777778

00:11:57.260 --> 00:11:59.080 Many people with sleep apnea

NOTE Confidence: 0.771439227777778

00:11:59.080 --> 00:12:00.536 this mechanism isn't working.

NOTE Confidence: 0.771439227777778

00:12:00.540 --> 00:12:02.360 But here is more of an example

NOTE Confidence: 0.771439227777778

00:12:02.360 --> 00:12:04.300 of the first image that we saw,

NOTE Confidence: 0.771439227777778

00:12:04.300 --> 00:12:05.865 that dynamic image where that

NOTE Confidence: 0.771439227777778

00:12:05.865 --> 00:12:07.430 individual had a narrow crowded

NOTE Confidence: 0.771439227777778

00:12:07.490 --> 00:12:09.308 airway and yet they were protected

NOTE Confidence: 0.771439227777778

00:12:09.308 --> 00:12:11.330 from sleep apnea because they had

NOTE Confidence: 0.771439227777778

00:12:11.330 --> 00:12:12.838 fantastic dilator muscle responses.

NOTE Confidence: 0.771439227777778

00:12:12.840 --> 00:12:15.060 So. Here's an example of this

NOTE Confidence: 0.771439227777778

00:12:15.060 --> 00:12:16.170 person during sleep.

NOTE Confidence: 0.771439227777778

00:12:16.170 --> 00:12:17.600 We've narrowed off the airway.

NOTE Confidence: 0.771439227777778

00:12:17.600 --> 00:12:19.490 We can see here in the first few breaths

NOTE Confidence: 0.771439227777778

00:12:19.490 --> 00:12:21.429 the airway is almost completely closed.

NOTE Confidence: 0.771439227777778

00:12:21.430 --> 00:12:22.588 But look at what happens within.

NOTE Confidence: 0.771439227777778

00:12:22.590 --> 00:12:24.210 A few breaths are able to

NOTE Confidence: 0.771439227777778

00:12:24.210 --> 00:12:25.290 recruit the dilator muscles.

NOTE Confidence: 0.666904327142857

00:12:25.290 --> 00:12:26.970 This is tensor palatini,

NOTE Confidence: 0.666904327142857

00:12:26.970 --> 00:12:28.230 this is genioglossus.

NOTE Confidence: 0.666904327142857

00:12:28.230 --> 00:12:30.126 They restore air flow very quickly

NOTE Confidence: 0.666904327142857

00:12:30.126 --> 00:12:31.710 and the Airways protected from

NOTE Confidence: 0.666904327142857

00:12:31.710 --> 00:12:33.288 from sleep apnea and you can

NOTE Confidence: 0.666904327142857

00:12:33.288 --> 00:12:34.769 see that there's no arousals.

NOTE Confidence: 0.666904327142857

00:12:34.770 --> 00:12:39.355 I've done this all whilst maintaining sleep.

NOTE Confidence: 0.666904327142857

00:12:39.360 --> 00:12:41.658 Unfortunately, many patients cannot do this.

NOTE Confidence: 0.666904327142857

00:12:41.660 --> 00:12:43.890 Here's the office that excrete

NOTE Confidence: 0.666904327142857

00:12:43.890 --> 00:12:44.952 extreme pressure drop.

NOTE Confidence: 0.666904327142857

00:12:44.952 --> 00:12:46.788 We've gone from about 10 centimetres

NOTE Confidence: 0.666904327142857

00:12:46.788 --> 00:12:48.534 of water down to, you know,

NOTE Confidence: 0.666904327142857

00:12:48.534 --> 00:12:50.556 four or five centimetres of water,

NOTE Confidence: 0.666904327142857

00:12:50.560 --> 00:12:51.850 mild hypopneas occurred.

NOTE Confidence: 0.666904327142857

00:12:51.850 --> 00:12:54.000 We can see those negative

NOTE Confidence: 0.666904327142857

00:12:54.000 --> 00:12:55.600 epiglottic pressure increasing.

NOTE Confidence: 0.666904327142857

00:12:55.600 --> 00:12:58.056 So CO2 is building up and yet there's

NOTE Confidence: 0.666904327142857

00:12:58.056 --> 00:12:59.916 no activation on the genioglossus

NOTE Confidence: 0.666904327142857

00:12:59.916 --> 00:13:01.496 or tensor palatini muscle.

NOTE Confidence: 0.666904327142857

00:13:01.500 --> 00:13:02.552 And for this individual,

NOTE Confidence: 0.666904327142857

00:13:02.552 --> 00:13:04.468 it's not until I have an arousal

NOTE Confidence: 0.666904327142857

00:13:04.468 --> 00:13:06.142 from sleep that they can get

NOTE Confidence: 0.666904327142857

00:13:06.142 --> 00:13:07.730 robust by later muscle activation

NOTE Confidence: 0.666904327142857

00:13:07.730 --> 00:13:09.455 and and reopen that airway.

NOTE Confidence: 0.666904327142857

00:13:09.460 --> 00:13:10.770 So there's the extreme example

NOTE Confidence: 0.666904327142857

00:13:10.770 --> 00:13:11.818 of what we see.

NOTE Confidence: 0.666904327142857

00:13:11.820 --> 00:13:14.124 So here's that first example of

NOTE Confidence: 0.666904327142857

00:13:14.124 --> 00:13:15.660 very good muscle responsiveness.

NOTE Confidence: 0.666904327142857

00:13:15.660 --> 00:13:17.800 So with increasing negative pressure,

NOTE Confidence: 0.666904327142857

00:13:17.800 --> 00:13:19.392 muscle activation is increasing.

NOTE Confidence: 0.666904327142857

00:13:19.392 --> 00:13:21.382 And here's that second example

NOTE Confidence: 0.666904327142857

00:13:21.382 --> 00:13:23.466 of of someone where it really,

NOTE Confidence: 0.666904327142857

00:13:23.470 --> 00:13:24.988 despite the fact they're getting lots

NOTE Confidence: 0.666904327142857

00:13:24.988 --> 00:13:26.499 of negative pressure in the airway,

NOTE Confidence: 0.666904327142857

00:13:26.500 --> 00:13:28.720 there's no activation of the muscles

NOTE Confidence: 0.666904327142857

00:13:28.720 --> 00:13:31.010 until they wake up from sleep.

NOTE Confidence: 0.666904327142857

00:13:31.010 --> 00:13:32.830 Next trait is how easy they wake

NOTE Confidence: 0.666904327142857

00:13:32.830 --> 00:13:34.769 up when that airway narrows off.

NOTE Confidence: 0.666904327142857

00:13:34.770 --> 00:13:35.004 And,

NOTE Confidence: 0.666904327142857

00:13:35.004 --> 00:13:36.876 and this is really at least a good

NOTE Confidence: 0.666904327142857

00:13:36.876 --> 00:13:38.420 surrogate of what's waking people

NOTE Confidence: 0.666904327142857

00:13:38.420 --> 00:13:39.990 up during these respiratory events,

NOTE Confidence: 0.666904327142857

00:13:39.990 --> 00:13:41.766 how hard they're working to breathe.

NOTE Confidence: 0.666904327142857

00:13:41.770 --> 00:13:43.324 And the reason this trade is important.

NOTE Confidence: 0.666904327142857

00:13:43.330 --> 00:13:44.842 You can imagine if an individual

NOTE Confidence: 0.666904327142857

00:13:44.842 --> 00:13:46.150 was waking up right here,

NOTE Confidence: 0.666904327142857

00:13:46.150 --> 00:13:49.846 so just a relatively low arousal threshold,

NOTE Confidence: 0.666904327142857

00:13:49.850 --> 00:13:52.722 waking up at maybe 10 or 15 centimeters

NOTE Confidence: 0.666904327142857

00:13:52.722 --> 00:13:55.127 of negative pressure in the airway.

NOTE Confidence: 0.666904327142857

00:13:55.130 --> 00:13:56.270 If this were the case,

NOTE Confidence: 0.666904327142857

00:13:56.270 --> 00:13:58.048 then they were not having enough time

NOTE Confidence: 0.666904327142857

00:13:58.048 --> 00:13:59.389 to actually activate the muscles,

NOTE Confidence: 0.666904327142857

00:13:59.390 --> 00:14:01.078 assuming they were able to do so and.

NOTE Confidence: 0.666904327142857

00:14:01.080 --> 00:14:03.362 Build up that CO2 and negative pressure

NOTE Confidence: 0.666904327142857

00:14:03.362 --> 00:14:05.528 that's required to recruit the muscles,

NOTE Confidence: 0.666904327142857

00:14:05.530 --> 00:14:06.660 and they're also not able

NOTE Confidence: 0.666904327142857

00:14:06.660 --> 00:14:07.790 to get into deeper sleep.

NOTE Confidence: 0.666904327142857

00:14:07.790 --> 00:14:09.446 We know for reasons that are

NOTE Confidence: 0.666904327142857

00:14:09.446 --> 00:14:10.830 incompletely understood that you know,

NOTE Confidence: 0.666904327142857

00:14:10.830 --> 00:14:13.170 sleep apnea is very rare in slow wave sleep.

NOTE Confidence: 0.666904327142857

00:14:13.170 --> 00:14:14.946 So if people can get off and have

NOTE Confidence: 0.666904327142857

00:14:14.946 --> 00:14:16.209 those deeper stages of sleep,

NOTE Confidence: 0.666904327142857

00:14:16.210 --> 00:14:18.130 the airway is somewhat protected.

NOTE Confidence: 0.666904327142857

00:14:18.130 --> 00:14:20.090 And then finally, every time you wake up,

NOTE Confidence: 0.666904327142857

00:14:20.090 --> 00:14:22.029 you take a deep breath and that

NOTE Confidence: 0.666904327142857

00:14:22.029 --> 00:14:23.170 blows off your CO2.

NOTE Confidence: 0.666904327142857

00:14:23.170 --> 00:14:25.046 And that can not only turn off

NOTE Confidence: 0.666904327142857

00:14:25.046 --> 00:14:25.850 the dilator muscles,

NOTE Confidence: 0.666904327142857

00:14:25.850 --> 00:14:27.626 but it feeds into this final

NOTE Confidence: 0.666904327142857

00:14:27.626 --> 00:14:29.530 trait which is really all about

NOTE Confidence: 0.666904327142857

00:14:29.530 --> 00:14:31.180 the control of breathing and.

NOTE Confidence: 0.666904327142857

00:14:31.180 --> 00:14:31.782 Really it's,

NOTE Confidence: 0.666904327142857

00:14:31.782 --> 00:14:33.588 it's all we're measuring here is

NOTE Confidence: 0.666904327142857

00:14:33.588 --> 00:14:35.538 when we do these pressure drops

NOTE Confidence: 0.666904327142857

00:14:35.538 --> 00:14:37.148 as shown in this schematic,

NOTE Confidence: 0.666904327142857

00:14:37.150 --> 00:14:39.075 we're reducing the minute ventilation

NOTE Confidence: 0.666904327142857

00:14:39.075 --> 00:14:41.000 and we can quantify this.

NOTE Confidence: 0.8486144275

00:14:43.860 --> 00:14:46.164 So here we can reopen the airway and

NOTE Confidence: 0.8486144275

00:14:46.164 --> 00:14:48.009 measure the ventilator response.

NOTE Confidence: 0.8486144275

00:14:48.010 --> 00:14:50.179 And this really just gives us a ratio of

NOTE Confidence: 0.8486144275

00:14:50.179 --> 00:14:52.320 their ventilator response to disturbance.

NOTE Confidence: 0.8486144275

00:14:52.320 --> 00:14:54.000 Some people, they have

NOTE Confidence: 0.8486144275

00:14:54.000 --> 00:14:55.260 very exaggerated responses.

NOTE Confidence: 0.8486144275

00:14:55.260 --> 00:14:56.140 So in this individual,

NOTE Confidence: 0.8486144275

00:14:56.140 --> 00:14:58.433 it's not too bad for any one liter minute

NOTE Confidence: 0.8486144275

00:14:58.433 --> 00:15:00.275 per reduction in their minute ventilation,

NOTE Confidence: 0.8486144275

00:15:00.280 --> 00:15:03.080 they have a 2 litre per minute overshoot.

NOTE Confidence: 0.8486144275

00:15:03.080 --> 00:15:04.921 Some people it can be more like

NOTE Confidence: 0.8486144275

00:15:04.921 --> 00:15:06.720 1011 liters per minute overshoot.

NOTE Confidence: 0.8486144275

00:15:06.720 --> 00:15:09.594 So that's really unstable and it

NOTE Confidence: 0.8486144275

00:15:09.594 --> 00:15:12.206 feeds into that cyclical pattern

NOTE Confidence: 0.8486144275

00:15:12.206 --> 00:15:14.626 of sleep disorder breathing.

NOTE Confidence: 0.8486144275

00:15:14.630 --> 00:15:16.464 So hopefully that's sort of laid out

NOTE Confidence: 0.8486144275

00:15:16.464 --> 00:15:18.255 the foundation of those those different

NOTE Confidence: 0.8486144275

00:15:18.255 --> 00:15:20.467 Ender types that contribute to sleep apnea.

NOTE Confidence: 0.8486144275

00:15:20.470 --> 00:15:21.653 And now I'm just going to switch

NOTE Confidence: 0.8486144275

00:15:21.653 --> 00:15:22.990 a little bit to, you know,

NOTE Confidence: 0.8486144275

00:15:22.990 --> 00:15:25.370 I'll talk a little bit more detail

NOTE Confidence: 0.8486144275

00:15:25.370 --> 00:15:27.732 here about the functional anatomy or

NOTE Confidence: 0.8486144275

00:15:27.732 --> 00:15:30.948 peak credit and then how we can use

NOTE Confidence: 0.8486144275

00:15:30.948 --> 00:15:32.943 that information to target therapy.

NOTE Confidence: 0.8486144275

00:15:32.950 --> 00:15:34.258 So firstly what we see here,

NOTE Confidence: 0.8486144275

00:15:34.260 --> 00:15:35.996 so this is the peak create the

NOTE Confidence: 0.8486144275

00:15:35.996 --> 00:15:37.223 collapsible ability of the airway

NOTE Confidence: 0.8486144275

00:15:37.223 --> 00:15:38.943 and firstly the red dots we can see

NOTE Confidence: 0.8486144275

00:15:38.997 --> 00:15:40.768 are our people with sleep apnea and

NOTE Confidence: 0.8486144275

00:15:40.768 --> 00:15:42.586 immediately we can see those ranges

NOTE Confidence: 0.8486144275

00:15:42.586 --> 00:15:44.346 and pressures some people airway.

NOTE Confidence: 0.8486144275

00:15:44.350 --> 00:15:45.715 Requires you know negative pressure

NOTE Confidence: 0.8486144275

00:15:45.715 --> 00:15:46.932 to close off, you know,

NOTE Confidence: 0.8486144275

00:15:46.932 --> 00:15:48.304 in the order of minus four or

NOTE Confidence: 0.8486144275

00:15:48.304 --> 00:15:49.490 five centimeters of water.

NOTE Confidence: 0.8486144275

00:15:49.490 --> 00:15:51.415 Others there Airways closing at

NOTE Confidence: 0.8486144275

00:15:51.415 --> 00:15:53.740 +5 centimetres of water or more.

NOTE Confidence: 0.8486144275

00:15:53.740 --> 00:15:55.365 These folks down here probably

NOTE Confidence: 0.8486144275

00:15:55.365 --> 00:15:56.990 doesn't matter if they're dilator

NOTE Confidence: 0.8486144275

00:15:57.048 --> 00:15:58.853 muscles aren't working because their

NOTE Confidence: 0.8486144275

00:15:58.853 --> 00:16:00.658 Airways really not an anatomically

NOTE Confidence: 0.8486144275

00:16:00.713 --> 00:16:01.679 compromised airway.

NOTE Confidence: 0.8486144275

00:16:01.680 --> 00:16:02.454 So these people,

NOTE Confidence: 0.8486144275

00:16:02.454 --> 00:16:02.970 you know,

NOTE Confidence: 0.8486144275

00:16:02.970 --> 00:16:05.436 they require some of them minus

NOTE Confidence: 0.8486144275

00:16:05.440 --> 00:16:06.612 15161718 centimeters of water

NOTE Confidence: 0.8486144275

00:16:06.612 --> 00:16:08.077 to close off their airway.

NOTE Confidence: 0.8486144275

00:16:08.080 --> 00:16:09.835 As you can see here on the X axis,

NOTE Confidence: 0.8486144275

00:16:09.840 --> 00:16:11.526 these people do not have sleep

NOTE Confidence: 0.8486144275

00:16:11.526 --> 00:16:13.087 apnea because they got really

NOTE Confidence: 0.8486144275

00:16:13.087 --> 00:16:14.239 no anatomical problem.

NOTE Confidence: 0.8486144275

00:16:14.240 --> 00:16:15.564 Here's the other extreme,

NOTE Confidence: 0.8486144275

00:16:15.564 --> 00:16:17.219 these folks got very severe

NOTE Confidence: 0.8486144275

00:16:17.219 --> 00:16:18.926 sleep apnea Airways closing at

NOTE Confidence: 0.8486144275

00:16:18.926 --> 00:16:20.576 plus 5 centimeters of water,

NOTE Confidence: 0.8486144275

00:16:20.580 --> 00:16:22.120 and invariably they've got

NOTE Confidence: 0.8486144275

00:16:22.120 --> 00:16:23.660 very severe sleep apnea.

NOTE Confidence: 0.8486144275

00:16:23.660 --> 00:16:24.200 With 40.

NOTE Confidence: 0.882917058

00:16:26.780 --> 00:16:27.930 But then there's this group,

NOTE Confidence: 0.882917058

00:16:27.930 --> 00:16:30.254 about 20% of all people sleep apnea,

NOTE Confidence: 0.882917058

00:16:30.260 --> 00:16:32.612 their Airways closing off at a similar

NOTE Confidence: 0.882917058

00:16:32.612 --> 00:16:35.440 level to many people without sleep apnea.

NOTE Confidence: 0.882917058

00:16:35.440 --> 00:16:36.460 So whereas, you know,

NOTE Confidence: 0.882917058

00:16:36.460 --> 00:16:37.990 some of these folks were sleep

NOTE Confidence: 0.882917058

00:16:38.044 --> 00:16:39.419 apnea have got mild disease,

NOTE Confidence: 0.882917058

00:16:39.420 --> 00:16:41.220 others moderate, others very severe

NOTE Confidence: 0.882917058

00:16:41.220 --> 00:16:43.770 sleep apnea and yet they their anatomy

NOTE Confidence: 0.882917058

00:16:43.770 --> 00:16:45.840 issue is really only quite mild.

NOTE Confidence: 0.882917058

00:16:45.840 --> 00:16:47.504 So they they're in the order of minus

NOTE Confidence: 0.882917058

00:16:47.504 --> 00:16:49.338 two to minus 5 centimeters of water.

NOTE Confidence: 0.882917058

00:16:49.340 --> 00:16:52.084 So they require that suction pressure to

NOTE Confidence: 0.882917058

00:16:52.084 --> 00:16:54.900 close off the airway and yet you know,

NOTE Confidence: 0.882917058

00:16:54.900 --> 00:16:56.550 marked differences in terms of their.

NOTE Confidence: 0.882917058

00:16:56.550 --> 00:16:57.606 The pattern is severity.

NOTE Confidence: 0.882917058

00:16:57.606 --> 00:16:59.709 So in these people it turns out that

NOTE Confidence: 0.882917058

00:16:59.709 --> 00:17:01.573 they've all got a problem with one or

NOTE Confidence: 0.882917058

00:17:01.631 --> 00:17:03.455 more of those non anatomical traits.

NOTE Confidence: 0.882917058

00:17:03.460 --> 00:17:04.680 Either the muscles aren't working,

NOTE Confidence: 0.882917058

00:17:04.680 --> 00:17:06.180 they're too sensitive to CO2,

NOTE Confidence: 0.882917058

00:17:06.180 --> 00:17:07.818 or they're waking up too easily,

NOTE Confidence: 0.882917058

00:17:07.820 --> 00:17:10.095 or multiple factors and those

NOTE Confidence: 0.882917058

00:17:10.095 --> 00:17:11.460 non anatomical traits.

NOTE Confidence: 0.882917058

00:17:11.460 --> 00:17:13.252 So in these people we should be able

NOTE Confidence: 0.882917058

00:17:13.252 --> 00:17:15.131 to give them an intervention to fix

NOTE Confidence: 0.882917058

00:17:15.131 --> 00:17:16.801 those issues and and treat their

NOTE Confidence: 0.882917058

00:17:16.801 --> 00:17:18.713 sleep apnea to get them over to this

NOTE Confidence: 0.882917058

00:17:18.713 --> 00:17:20.480 side with these other people that

NOTE Confidence: 0.882917058

00:17:20.480 --> 00:17:22.699 don't have sleep apnea for the same

NOTE Confidence: 0.882917058

00:17:22.699 --> 00:17:24.364 anatomical compromise however if we

NOTE Confidence: 0.882917058

00:17:24.364 --> 00:17:26.808 just gave a non anatomical intervention.

NOTE Confidence: 0.882917058

00:17:26.810 --> 00:17:27.368 These people were,

NOTE Confidence: 0.882917058

00:17:27.368 --> 00:17:28.360 you know, terrible anatomy.

NOTE Confidence: 0.882917058

00:17:28.360 --> 00:17:31.140 Yes, we might lower the HR a little bit,

NOTE Confidence: 0.882917058

00:17:31.140 --> 00:17:34.044 but unless we deal with the anatomical issue,

NOTE Confidence: 0.882917058

00:17:34.050 --> 00:17:36.305 they're still going to have

NOTE Confidence: 0.882917058

00:17:36.305 --> 00:17:37.658 major sleep apnea.

NOTE Confidence: 0.882917058

00:17:37.660 --> 00:17:38.026 Yeah.

NOTE Confidence: 0.882917058

00:17:38.026 --> 00:17:38.392 Here,

NOTE Confidence: 0.882917058

00:17:38.392 --> 00:17:41.320 if we don't go after the anatomy issue

NOTE Confidence: 0.882917058

00:17:41.400 --> 00:17:43.818 as well or or indeed exclusively.

NOTE Confidence: 0.882917058

00:17:43.820 --> 00:17:45.850 So the goal I guess here physiologically

NOTE Confidence: 0.882917058

00:17:45.850 --> 00:17:47.877 at least with all these therapies is

NOTE Confidence: 0.882917058

00:17:47.877 --> 00:17:49.860 either to get them over here into

NOTE Confidence: 0.882917058

00:17:49.860 --> 00:17:51.813 this pocket here or really get them

NOTE Confidence: 0.882917058

00:17:51.813 --> 00:17:54.052 below minus 5 centimeters of water.

NOTE Confidence: 0.882917058

00:17:54.052 --> 00:17:56.142 So whether it's CPAP surgery,

NOTE Confidence: 0.882917058

00:17:56.150 --> 00:17:57.140 mandira advancement,

NOTE Confidence: 0.882917058

00:17:57.140 --> 00:17:59.120 splendor or combination thereof,

NOTE Confidence: 0.882917058

00:17:59.120 --> 00:18:01.292 we're trying to make that airway

NOTE Confidence: 0.882917058

00:18:01.292 --> 00:18:03.653 less collapsible so that we can

NOTE Confidence: 0.882917058

00:18:03.653 --> 00:18:05.345 stabilize breathing during sleep.

NOTE Confidence: 0.882917058

00:18:05.350 --> 00:18:06.778 Right, so it turns out that yes,

NOTE Confidence: 0.882917058

00:18:06.780 --> 00:18:08.348 as I highlighted everyone with sleep apnea,

NOTE Confidence: 0.882917058

00:18:08.350 --> 00:18:10.000 it's got some degree of

NOTE Confidence: 0.882917058

00:18:10.000 --> 00:18:10.660 anatomical compromise,

NOTE Confidence: 0.882917058

00:18:10.660 --> 00:18:13.740 but the range varies minus 5 + 5

NOTE Confidence: 0.882917058

00:18:13.740 --> 00:18:16.896 centimeters of water per credit and beyond.

NOTE Confidence: 0.882917058

00:18:16.900 --> 00:18:18.668 3rd of patients wake up too easily or

NOTE Confidence: 0.882917058

00:18:18.668 --> 00:18:20.288 have this lower arousal threshold.

NOTE Confidence: 0.828537477777778

00:18:22.380 --> 00:18:23.886 Certain patient groups,

NOTE Confidence: 0.828537477777778

00:18:23.886 --> 00:18:26.898 others are too sensitive to see.

NOTE Confidence: 0.828537477777778

00:18:26.900 --> 00:18:28.552 A little gain, at least 1/3 of

NOTE Confidence: 0.828537477777778

00:18:28.552 --> 00:18:30.320 patients and 1/3 of patients just

NOTE Confidence: 0.828537477777778

00:18:30.320 --> 00:18:31.664 cannot activate those dilator

NOTE Confidence: 0.828537477777778

00:18:31.664 --> 00:18:33.482 muscles during sleep and have a

NOTE Confidence: 0.828537477777778

00:18:33.482 --> 00:18:34.988 have a problem with their muscles.

NOTE Confidence: 0.859946123043478

00:18:37.030 --> 00:18:39.325 70% or more of all patients have have one

NOTE Confidence: 0.859946123043478

00:18:39.325 --> 00:18:41.721 or more of these non anatomical factors

NOTE Confidence: 0.859946123043478

00:18:41.721 --> 00:18:44.220 that start feeding into their sleep apnea.

NOTE Confidence: 0.859946123043478

00:18:44.220 --> 00:18:45.613 OK. So now we know a little

NOTE Confidence: 0.859946123043478

00:18:45.613 --> 00:18:47.040 bit about the pathophysiology,

NOTE Confidence: 0.859946123043478

00:18:47.040 --> 00:18:49.200 what are the implications for

NOTE Confidence: 0.859946123043478

00:18:49.200 --> 00:18:50.496 targeted personalized therapy.

NOTE Confidence: 0.859946123043478

00:18:50.500 --> 00:18:52.720 So I'm just going to talk

NOTE Confidence: 0.859946123043478

00:18:52.720 --> 00:18:54.200 about three things here.

NOTE Confidence: 0.859946123043478

00:18:54.200 --> 00:18:55.720 Firstly, if we're going to

NOTE Confidence: 0.859946123043478

00:18:55.720 --> 00:18:56.936 deliver non CPAP therapies,

NOTE Confidence: 0.859946123043478

00:18:56.940 --> 00:19:00.140 we need to know how much they improve,

NOTE Confidence: 0.859946123043478

00:19:00.140 --> 00:19:02.852 the things that we're trying to modify here

NOTE Confidence: 0.859946123043478

00:19:02.852 --> 00:19:05.907 and of course anatomies the major factor.

NOTE Confidence: 0.859946123043478

00:19:05.910 --> 00:19:08.250 Where our current therapies

NOTE Confidence: 0.859946123043478

00:19:08.250 --> 00:19:10.005 are are targeting.

NOTE Confidence: 0.859946123043478

00:19:10.010 --> 00:19:11.810 I'm also going to talk about how we

NOTE Confidence: 0.859946123043478

00:19:11.810 --> 00:19:13.214 can improve outcomes with existing

NOTE Confidence: 0.859946123043478

00:19:13.214 --> 00:19:15.321 therapies if we know about these traits.

NOTE Confidence: 0.859946123043478

00:19:15.330 --> 00:19:18.146 And finally how we can use this information

NOTE Confidence: 0.859946123043478

00:19:18.146 --> 00:19:20.686 for developing new therapies including

NOTE Confidence: 0.859946123043478

00:19:20.686 --> 00:19:23.046 pharmacotherapies and combination therapies.

NOTE Confidence: 0.859946123043478

00:19:23.050 --> 00:19:25.210 So here's that framework again,

NOTE Confidence: 0.859946123043478

00:19:25.210 --> 00:19:28.140 anatomy and these non anatomical

NOTE Confidence: 0.859946123043478

00:19:28.140 --> 00:19:29.898 traits in person.

NOTE Confidence: 0.859946123043478

00:19:29.900 --> 00:19:31.402 Existing interventions,

NOTE Confidence: 0.859946123043478

00:19:31.402 --> 00:19:34.406 we've got oral appliances,

NOTE Confidence: 0.859946123043478

00:19:34.410 --> 00:19:36.090 we've got upper airway surgery,

NOTE Confidence: 0.859946123043478

00:19:36.090 --> 00:19:37.370 position therapy, weight loss.

NOTE Confidence: 0.859946123043478

00:19:37.370 --> 00:19:39.810 So I'm just going to talk through,

NOTE Confidence: 0.859946123043478

00:19:39.810 --> 00:19:40.320 you know,

NOTE Confidence: 0.859946123043478

00:19:40.320 --> 00:19:42.105 what is the effect on the collapsibility

NOTE Confidence: 0.859946123043478

00:19:42.105 --> 00:19:43.945 of the airwave when we put one

NOTE Confidence: 0.859946123043478

00:19:43.945 --> 00:19:45.310 of these interventions in place.

NOTE Confidence: 0.859946123043478

00:19:45.310 --> 00:19:48.319 So here's a study we did with Ahmad,

NOTE Confidence: 0.859946123043478

00:19:48.319 --> 00:19:50.711 a PhD student in the lab and we

NOTE Confidence: 0.859946123043478

00:19:50.711 --> 00:19:52.898 used that rather detailed Physiology

NOTE Confidence: 0.859946123043478

00:19:52.898 --> 00:19:55.616 setup again and we took advantage

NOTE Confidence: 0.859946123043478

00:19:55.686 --> 00:19:58.008 of this device developed by John

NOTE Confidence: 0.859946123043478

00:19:58.008 --> 00:20:00.040 Remmers in Canada where we can.

NOTE Confidence: 0.859946123043478

00:20:00.040 --> 00:20:01.490 Actually sit in the control

NOTE Confidence: 0.859946123043478

00:20:01.490 --> 00:20:03.554 room and move the jaw remotely

NOTE Confidence: 0.859946123043478

00:20:03.554 --> 00:20:05.329 whilst the participant is asleep.

NOTE Confidence: 0.859946123043478

00:20:05.330 --> 00:20:07.388 And that enables us to look at,

NOTE Confidence: 0.859946123043478

00:20:07.390 --> 00:20:07.914 you know,

NOTE Confidence: 0.859946123043478

00:20:07.914 --> 00:20:10.010 what is the effect of moving that mandible.

NOTE Confidence: 0.859946123043478

00:20:10.010 --> 00:20:12.033 And here we did a randomised design

NOTE Confidence: 0.859946123043478

00:20:12.033 --> 00:20:13.849 where we left it at baseline.

NOTE Confidence: 0.859946123043478

00:20:13.850 --> 00:20:15.490 We advanced at 50 percent,

NOTE Confidence: 0.859946123043478

00:20:15.490 --> 00:20:18.166 100% of their maximal protrusive range,

NOTE Confidence: 0.859946123043478

00:20:18.170 --> 00:20:19.905 and looked at the collapsibility

NOTE Confidence: 0.859946123043478

00:20:19.905 --> 00:20:22.130 of the airway along with some

NOTE Confidence: 0.859946123043478

00:20:22.130 --> 00:20:23.408 other other components.

NOTE Confidence: 0.859946123043478

00:20:23.410 --> 00:20:26.122 And essentially what we found the more you

NOTE Confidence: 0.859946123043478

00:20:26.122 --> 00:20:28.758 move that jaw forward here at baseline,

NOTE Confidence: 0.859946123043478

00:20:28.760 --> 00:20:29.750 50 percent, 100%,

NOTE Confidence: 0.859946123043478

00:20:29.750 --> 00:20:31.070 here's our P crit,

NOTE Confidence: 0.859946123043478

00:20:31.070 --> 00:20:33.566 the less collapsible the airway became.

NOTE Confidence: 0.859946123043478

00:20:33.570 --> 00:20:35.898 And you can see that this at baseline

NOTE Confidence: 0.859946123043478

00:20:35.898 --> 00:20:37.331 the collapsibility of the Airwave

NOTE Confidence: 0.859946123043478

00:20:37.331 --> 00:20:39.186 varies again as I showed you before,

NOTE Confidence: 0.859946123043478

00:20:39.190 --> 00:20:40.968 anywhere from minus five and in this

NOTE Confidence: 0.859946123043478

00:20:40.968 --> 00:20:43.009 case up to above 10 centimeters

NOTE Confidence: 0.859946123043478

00:20:43.009 --> 00:20:44.227 of water collapsibility.

NOTE Confidence: 0.859946123043478

00:20:44.230 --> 00:20:46.372 And there is that inter individual

NOTE Confidence: 0.859946123043478

00:20:46.372 --> 00:20:46.729 variability.

NOTE Confidence: 0.859946123043478

00:20:46.730 --> 00:20:48.501 But overall you get a pretty good

NOTE Confidence: 0.859946123043478

00:20:48.501 --> 00:20:49.701 improvement in the collapsibility

NOTE Confidence: 0.859946123043478

00:20:49.701 --> 00:20:51.646 of the airway with mandibular

NOTE Confidence: 0.859946123043478

00:20:51.646 --> 00:20:52.424 advancement splint.

NOTE Confidence: 0.859946123043478

00:20:52.430 --> 00:20:53.750 So when you move it about.

NOTE Confidence: 0.859946123043478

00:20:53.750 --> 00:20:55.060 50% of the productive range,

NOTE Confidence: 0.859946123043478

00:20:55.060 --> 00:20:55.924 it's, you know,

NOTE Confidence: 0.859946123043478

00:20:55.924 --> 00:20:57.652 two or three centimeters of water.

NOTE Confidence: 0.859946123043478

00:20:57.660 --> 00:21:00.100 But when if you can go to 100%,

NOTE Confidence: 0.859946123043478

00:21:00.100 --> 00:21:01.871 you're more like 5 or 6 centimetres

NOTE Confidence: 0.859946123043478

00:21:01.871 --> 00:21:03.320 of water and improvement.

NOTE Confidence: 0.859946123043478

00:21:03.320 --> 00:21:05.035 And this was a small Physiology study,

NOTE Confidence: 0.859946123043478

00:21:05.040 --> 00:21:06.544 but there was a bit of a hint

NOTE Confidence: 0.859946123043478

00:21:06.544 --> 00:21:08.335 that the people that had a less

NOTE Confidence: 0.859946123043478

00:21:08.335 --> 00:21:09.695 collapsible airway to begin with

NOTE Confidence: 0.859946123043478

00:21:09.754 --> 00:21:11.588 tended to do better when we followed.

NOTE Confidence: 0.595572834

00:21:16.180 --> 00:21:17.490 What about upper airway surgery?

NOTE Confidence: 0.595572834

00:21:17.490 --> 00:21:18.826 Now there's a bit of a gap in

NOTE Confidence: 0.595572834

00:21:18.826 --> 00:21:20.546 in knowledge here, but this was

NOTE Confidence: 0.595572834

00:21:20.546 --> 00:21:22.838 some early work by Alan Schwartz.

NOTE Confidence: 0.595572834

00:21:22.840 --> 00:21:23.904 There's now, you know,

NOTE Confidence: 0.595572834

00:21:23.904 --> 00:21:25.796 we've moved beyond the the sort of

NOTE Confidence: 0.595572834

00:21:25.796 --> 00:21:27.518 traditional U triple P and are onto

NOTE Confidence: 0.595572834

00:21:27.518 --> 00:21:29.000 model level surgery and things.

NOTE Confidence: 0.595572834

00:21:29.000 --> 00:21:32.450 So there's an like this, but you know,

NOTE Confidence: 0.595572834

00:21:32.450 --> 00:21:34.550 Alan's early work showed us that

NOTE Confidence: 0.595572834

00:21:34.550 --> 00:21:37.168 with the old new triple P techniques,

NOTE Confidence: 0.595572834

00:21:37.170 --> 00:21:38.688 you improve the collapsibility of the

NOTE Confidence: 0.595572834

00:21:38.688 --> 00:21:40.659 airway about minus 3 centimeters of water.

NOTE Confidence: 0.595572834

00:21:40.660 --> 00:21:42.186 And remember the goal of treatment is

NOTE Confidence: 0.595572834

00:21:42.186 --> 00:21:43.819 to get everyone at least below that

NOTE Confidence: 0.595572834

00:21:43.819 --> 00:21:45.223 minus five and then you're basically.

NOTE Confidence: 0.595572834

00:21:45.230 --> 00:21:48.446 You know, get rid of their sleep apnea.

NOTE Confidence: 0.595572834

00:21:48.450 --> 00:21:51.264 What about putting people on their side?

NOTE Confidence: 0.595572834

00:21:51.270 --> 00:21:52.965 Three studies that I've highlighted

NOTE Confidence: 0.595572834

00:21:52.965 --> 00:21:56.011 here show us that again you get about a

NOTE Confidence: 0.595572834

00:21:56.011 --> 00:21:57.943 two to four centimetre water improvement

NOTE Confidence: 0.595572834

00:21:58.003 --> 00:21:59.727 in that airway collapsibility.

NOTE Confidence: 0.595572834

00:21:59.730 --> 00:22:01.842 When you move someone from the

NOTE Confidence: 0.595572834

00:22:01.842 --> 00:22:03.930 supine to the lateral position,

NOTE Confidence: 0.595572834

00:22:03.930 --> 00:22:05.670 that airway becomes less collapsible.

NOTE Confidence: 0.595572834

00:22:05.670 --> 00:22:06.654 So you've got,

NOTE Confidence: 0.595572834

00:22:06.654 --> 00:22:08.622 you've got a bit of improvement

NOTE Confidence: 0.595572834

00:22:08.622 --> 00:22:10.940 there in there in the airway just

NOTE Confidence: 0.595572834

00:22:10.940 --> 00:22:12.610 moving people off their back.

NOTE Confidence: 0.595572834

00:22:12.610 --> 00:22:14.806 Finally, weight loss.

NOTE Confidence: 0.595572834

00:22:14.806 --> 00:22:17.474 You know, roughly half of all

NOTE Confidence: 0.595572834

00:22:17.474 --> 00:22:18.678 patients with sleep apnea,

NOTE Confidence: 0.595572834

00:22:18.680 --> 00:22:20.528 in fact not overweight or obese,

NOTE Confidence: 0.595572834

00:22:20.530 --> 00:22:22.966 but but many of course are.

NOTE Confidence: 0.595572834

00:22:22.970 --> 00:22:25.609 And and indeed when you are successfully

NOTE Confidence: 0.595572834

00:22:25.609 --> 00:22:28.188 able to get rid of that weight,

NOTE Confidence: 0.595572834

00:22:28.190 --> 00:22:30.365 the airway becomes less collapsible

NOTE Confidence: 0.595572834

00:22:30.365 --> 00:22:31.670 as shown here.

NOTE Confidence: 0.595572834

00:22:31.670 --> 00:22:33.310 So here they had a usual care group

NOTE Confidence: 0.595572834

00:22:33.310 --> 00:22:35.099 and A and a Weight Loss Diet group

NOTE Confidence: 0.595572834

00:22:35.099 --> 00:22:37.007 and you can see what's happening in

NOTE Confidence: 0.595572834

00:22:37.007 --> 00:22:38.945 terms of collapsibility of the airway.

NOTE Confidence: 0.595572834

00:22:38.950 --> 00:22:40.213 It varies here.

NOTE Confidence: 0.595572834

00:22:40.213 --> 00:22:43.840 Here's the reduction in BMI on the X axis.

NOTE Confidence: 0.595572834

00:22:43.840 --> 00:22:45.696 But the more weight you lost in these,

NOTE Confidence: 0.595572834

00:22:45.700 --> 00:22:47.090 you know, morbidly obese folks,

NOTE Confidence: 0.595572834

00:22:47.090 --> 00:22:48.665 the less collapsible the airway we can.

NOTE Confidence: 0.880684968

00:22:50.750 --> 00:22:52.030 OK. So that's just showing,

NOTE Confidence: 0.880684968

00:22:52.030 --> 00:22:54.319 you know, a few examples of how

NOTE Confidence: 0.880684968

00:22:54.319 --> 00:22:55.838 much our existing interventions

NOTE Confidence: 0.880684968

00:22:55.838 --> 00:22:57.706 can improve the collapsibility

NOTE Confidence: 0.880684968

00:22:57.706 --> 00:23:00.450 or that that main anatomy tray.

NOTE Confidence: 0.880684968

00:23:00.450 --> 00:23:02.226 I'm now just going to move on a

NOTE Confidence: 0.880684968

00:23:02.226 --> 00:23:04.082 little bit to this next question of

NOTE Confidence: 0.880684968

00:23:04.082 --> 00:23:06.364 how can we use information if we knew

NOTE Confidence: 0.880684968

00:23:06.364 --> 00:23:07.819 about what these different entity

NOTE Confidence: 0.880684968

00:23:07.819 --> 00:23:09.550 types were and a given individual,

NOTE Confidence: 0.880684968

00:23:09.550 --> 00:23:11.910 how can it help us inform treatment?

NOTE Confidence: 0.7425708475

00:23:14.390 --> 00:23:16.340 Just that this palm scale concept

NOTE Confidence: 0.7425708475

00:23:16.340 --> 00:23:18.362 which is really just again reiterating

NOTE Confidence: 0.7425708475

00:23:18.362 --> 00:23:21.010 that if we knew what the peak credit,

NOTE Confidence: 0.7425708475

00:23:21.010 --> 00:23:23.842 arousal threshold, loop gain and muscle

NOTE Confidence: 0.7425708475

00:23:23.842 --> 00:23:26.246 responsiveness is, how can we use

NOTE Confidence: 0.7425708475

00:23:26.246 --> 00:23:28.066 that information to inform therapy.

NOTE Confidence: 0.7425708475

00:23:28.070 --> 00:23:30.674 So as a whole ideally roughly 20%

NOTE Confidence: 0.7425708475

00:23:30.680 --> 00:23:32.759 of all patients really only have a

NOTE Confidence: 0.7425708475

00:23:32.759 --> 00:23:34.487 mild anatomical issue and for them

NOTE Confidence: 0.7425708475

00:23:34.487 --> 00:23:36.047 it's really driven by a problem

NOTE Confidence: 0.7425708475

00:23:36.047 --> 00:23:37.847 with these non anatomical traits.

NOTE Confidence: 0.7425708475

00:23:37.850 --> 00:23:39.562 So for these folks we should be able

NOTE Confidence: 0.7425708475

00:23:39.562 --> 00:23:41.441 to get one or more non anatomical

NOTE Confidence: 0.7425708475

00:23:41.441 --> 00:23:42.836 interventions and and and get

NOTE Confidence: 0.7425708475

00:23:42.891 --> 00:23:44.446 them treated the opposite.

NOTE Confidence: 0.7425708475

00:23:44.446 --> 00:23:46.880 Scream, you know, 2025% of patients have,

NOTE Confidence: 0.7425708475

00:23:46.880 --> 00:23:48.182 you know, major anatomical

NOTE Confidence: 0.7425708475

00:23:48.182 --> 00:23:50.187 problem Airways collapsing at +2

NOTE Confidence: 0.7425708475

00:23:50.187 --> 00:23:52.019 centimetres of water or beyond.

NOTE Confidence: 0.7425708475

00:23:52.020 --> 00:23:53.472 So these people are really going

NOTE Confidence: 0.7425708475

00:23:53.472 --> 00:23:55.567 to have to go out of there after

NOTE Confidence: 0.7425708475

00:23:55.567 --> 00:23:57.175 the anatomy to get them treated.

NOTE Confidence: 0.7425708475

00:23:57.180 --> 00:23:58.002 The, you know,

NOTE Confidence: 0.7425708475

00:23:58.002 --> 00:23:59.646 the largest group of patients and

NOTE Confidence: 0.7425708475

00:23:59.646 --> 00:24:01.843 most patients are Airways closing at

NOTE Confidence: 0.7425708475

00:24:01.843 --> 00:24:03.335 about atmospheric pressure between

NOTE Confidence: 0.7425708475

00:24:03.335 --> 00:24:05.418 minus two and +2 centimetres of water.

NOTE Confidence: 0.7425708475

00:24:05.420 --> 00:24:06.022 And again,

NOTE Confidence: 0.7425708475

00:24:06.022 --> 00:24:08.430 if we knew what the anatomy was first

NOTE Confidence: 0.7425708475

00:24:08.500 --> 00:24:11.140 that it could help us inform our secondly,

NOTE Confidence: 0.7425708475

00:24:11.140 --> 00:24:12.918 if we need to just go after

NOTE Confidence: 0.7425708475

00:24:12.918 --> 00:24:13.680 the anatomical issue,

NOTE Confidence: 0.7425708475

00:24:13.680 --> 00:24:16.152 or indeed we also might need

NOTE Confidence: 0.7425708475

00:24:16.152 --> 00:24:17.388 to consider them.

NOTE Confidence: 0.7425708475

00:24:17.390 --> 00:24:20.141 Patients is present in about 2/3 of

NOTE Confidence: 0.7425708475

00:24:20.141 --> 00:24:23.565 of the patients with an airway that's

NOTE Confidence: 0.7425708475

00:24:23.565 --> 00:24:26.265 collapsing at about atmospheric pressure.

NOTE Confidence: 0.7425708475

00:24:26.270 --> 00:24:28.265 So that's the sort of conceptual framework.

NOTE Confidence: 0.7425708475

00:24:28.270 --> 00:24:31.250 Now obviously lots of information

NOTE Confidence: 0.7425708475

00:24:31.250 --> 00:24:33.634 on this slide really.

NOTE Confidence: 0.7425708475

00:24:33.640 --> 00:24:35.560 As highlighted in the heading there,

NOTE Confidence: 0.7425708475

00:24:35.560 --> 00:24:37.896 if we know what all these studies show,

NOTE Confidence: 0.7425708475

00:24:37.900 --> 00:24:39.400 if we know about the Physiology,

NOTE Confidence: 0.7425708475

00:24:39.400 --> 00:24:40.846 if we know about these traits,

NOTE Confidence: 0.7425708475

00:24:40.850 --> 00:24:41.854 it can help us.

NOTE Confidence: 0.7425708475

00:24:41.854 --> 00:24:43.659 Instead of it being a 50% success

NOTE Confidence: 0.7425708475

00:24:43.659 --> 00:24:45.453 rate with an oral appliance as

NOTE Confidence: 0.7425708475

00:24:45.453 --> 00:24:47.079 it currently is and recognizing

NOTE Confidence: 0.7425708475

00:24:47.079 --> 00:24:49.101 that many of these patients have

NOTE Confidence: 0.7425708475

00:24:49.101 --> 00:24:50.998 already gone through CPAP therapy.

NOTE Confidence: 0.7425708475

00:24:51.000 --> 00:24:53.508 So they may be already somewhat

NOTE Confidence: 0.7425708475

00:24:53.508 --> 00:24:55.180 disgruntled with the process.

NOTE Confidence: 0.7425708475

00:24:55.180 --> 00:24:56.830 If we use the information about

NOTE Confidence: 0.7425708475

00:24:56.830 --> 00:24:58.582 these end of types and these

NOTE Confidence: 0.7425708475

00:24:58.582 --> 00:25:00.358 sort of proof of concept studies,

NOTE Confidence: 0.7425708475

00:25:00.360 --> 00:25:02.243 turns out that people with a less

NOTE Confidence: 0.7425708475

00:25:02.243 --> 00:25:03.639 collapsible airway to begin with.

NOTE Confidence: 0.7425708475

00:25:03.640 --> 00:25:06.069 And that don't have major non anatomical

NOTE Confidence: 0.7425708475

00:25:06.069 --> 00:25:08.129 issues such as high loop gain.

NOTE Confidence: 0.7425708475

00:25:08.130 --> 00:25:09.770 They're the ones that tend to do better.

NOTE Confidence: 0.7425708475

00:25:09.770 --> 00:25:12.506 So we looked at this at various ways,

NOTE Confidence: 0.7425708475

00:25:12.510 --> 00:25:13.350 but the, the, the,

NOTE Confidence: 0.7425708475

00:25:13.350 --> 00:25:13.560 the,

NOTE Confidence: 0.7425708475

00:25:13.560 --> 00:25:15.674 the story really is if we know

NOTE Confidence: 0.7425708475

00:25:15.674 --> 00:25:16.885 about these enterotypes instead

NOTE Confidence: 0.7425708475

00:25:16.885 --> 00:25:18.490 of being a 50% success rate,

NOTE Confidence: 0.7425708475

00:25:18.490 --> 00:25:21.470 we could probably get it up to north of 80%.

NOTE Confidence: 0.786181326666667

00:25:24.240 --> 00:25:25.550 The same is also true

NOTE Confidence: 0.786181326666667

00:25:25.550 --> 00:25:26.598 with our railway surgery.

NOTE Confidence: 0.786181326666667

00:25:26.600 --> 00:25:28.766 So here's, here's some of the

NOTE Confidence: 0.786181326666667

00:25:28.766 --> 00:25:30.678 initial findings that again much

NOTE Confidence: 0.786181326666667

00:25:30.678 --> 00:25:32.298 like our appliance therapy,

NOTE Confidence: 0.786181326666667

00:25:32.300 --> 00:25:34.034 if you've got a, you know, if you do,

NOTE Confidence: 0.786181326666667

00:25:34.034 --> 00:25:35.480 if you improve the anatomy a little bit,

NOTE Confidence: 0.786181326666667

00:25:35.480 --> 00:25:37.034 but you've still got these residual

NOTE Confidence: 0.786181326666667

00:25:37.034 --> 00:25:38.389 issues with these non anatomical

NOTE Confidence: 0.786181326666667

00:25:38.389 --> 00:25:39.997 traits and you haven't got them

NOTE Confidence: 0.786181326666667

00:25:39.997 --> 00:25:41.400 below that minus 5 threshold.

NOTE Confidence: 0.786181326666667

00:25:41.400 --> 00:25:43.485 Recognizing that these therapies might

NOTE Confidence: 0.786181326666667

00:25:43.485 --> 00:25:46.236 improve your anatomy in the order of

NOTE Confidence: 0.786181326666667

00:25:46.236 --> 00:25:48.315 three to to five or six centimetres

NOTE Confidence: 0.786181326666667

00:25:48.315 --> 00:25:50.543 of water depending on how much move,

NOTE Confidence: 0.786181326666667

00:25:50.543 --> 00:25:52.518 how far you move the jaw forward and

NOTE Confidence: 0.786181326666667

00:25:52.518 --> 00:25:54.597 what type of surgery you do and so forth.

NOTE Confidence: 0.786181326666667

00:25:54.600 --> 00:25:56.096 If you've still got a loop game problem,

NOTE Confidence: 0.786181326666667

00:25:56.100 --> 00:25:58.200 your anatomy hasn't been completely resolved,

NOTE Confidence: 0.786181326666667

00:25:58.200 --> 00:26:01.080 not surprisingly.

NOTE Confidence: 0.786181326666667

00:26:01.080 --> 00:26:04.090 So things like Luke gain are very

NOTE Confidence: 0.786181326666667

00:26:04.090 --> 00:26:06.192 strong predictor of surgical success

NOTE Confidence: 0.786181326666667

00:26:06.192 --> 00:26:09.034 as shown in this study whereby people

NOTE Confidence: 0.786181326666667

00:26:09.034 --> 00:26:11.377 with respiratory construction control

NOTE Confidence: 0.786181326666667

00:26:11.377 --> 00:26:13.857 instability give them surgery,

NOTE Confidence: 0.786181326666667

00:26:13.860 --> 00:26:15.996 they still will have sleep apnea.

NOTE Confidence: 0.786181326666667

00:26:16.000 --> 00:26:18.380 So this is a pretty.

NOTE Confidence: 0.786181326666667

00:26:18.380 --> 00:26:19.790 Want to look at the anatomy?

NOTE Confidence: 0.786181326666667

00:26:19.790 --> 00:26:21.518 And much like oral proliance therapy

NOTE Confidence: 0.786181326666667

00:26:21.518 --> 00:26:23.940 for the Airways less collapsible at baseline,

NOTE Confidence: 0.786181326666667

00:26:23.940 --> 00:26:25.270 they tend to do better.

NOTE Confidence: 0.786181326666667

00:26:25.270 --> 00:26:27.892 And and also other studies showing

NOTE Confidence: 0.786181326666667

00:26:27.892 --> 00:26:29.728 that if you know about the muscle

NOTE Confidence: 0.786181326666667

00:26:29.728 --> 00:26:30.427 activity as well,

NOTE Confidence: 0.786181326666667

00:26:30.430 --> 00:26:33.111 that can also help predict who's going

NOTE Confidence: 0.786181326666667

00:26:33.111 --> 00:26:36.060 to do well at Upper Iowa surgery.

NOTE Confidence: 0.786181326666667

00:26:36.060 --> 00:26:38.232 More recently with hypoglossal

NOTE Confidence: 0.786181326666667

00:26:38.232 --> 00:26:41.210 nerve stimulation, we again,

NOTE Confidence: 0.786181326666667

00:26:41.210 --> 00:26:43.520 if we all these traces show is

NOTE Confidence: 0.786181326666667

00:26:43.520 --> 00:26:45.438 basically if you know all four,

NOTE Confidence: 0.786181326666667

00:26:45.440 --> 00:26:47.288 if you have estimates of all four traits.

NOTE Confidence: 0.786181326666667

00:26:47.290 --> 00:26:49.514 And in this study it was done just

NOTE Confidence: 0.786181326666667

00:26:49.514 --> 00:26:51.596 using estimates using the technique that

NOTE Confidence: 0.786181326666667

00:26:51.596 --> 00:26:53.798 developed in Boston of these enterotypes.

NOTE Confidence: 0.786181326666667

00:26:53.800 --> 00:26:55.435 Again there's various clusters that

NOTE Confidence: 0.786181326666667

00:26:55.435 --> 00:26:57.837 you can use to predict who's going

NOTE Confidence: 0.786181326666667

00:26:57.837 --> 00:26:59.612 to respond to hypoglossal nerve

NOTE Confidence: 0.786181326666667

00:26:59.612 --> 00:27:01.536 stimulation and who you should really

NOTE Confidence: 0.786181326666667

00:27:01.536 --> 00:27:03.424 avoid this therapy in or or at least

NOTE Confidence: 0.786181326666667

00:27:03.424 --> 00:27:05.284 you might need to combine it with

NOTE Confidence: 0.786181326666667

00:27:05.284 --> 00:27:06.789 other therapies if you want to.

NOTE Confidence: 0.786181326666667

00:27:06.790 --> 00:27:10.618 Gets full therapeutic effect.

NOTE Confidence: 0.786181326666667

00:27:10.620 --> 00:27:13.278 And and finally looking at these

NOTE Confidence: 0.786181326666667

00:27:13.278 --> 00:27:15.787 sort of existing therapies and again

NOTE Confidence: 0.786181326666667

00:27:15.787 --> 00:27:17.262 this is Alan Schwartz's earlier

NOTE Confidence: 0.786181326666667

00:27:17.262 --> 00:27:18.949 work and you can see these sort

NOTE Confidence: 0.786181326666667

00:27:18.949 --> 00:27:20.518 of individual differences here.

NOTE Confidence: 0.786181326666667

00:27:20.520 --> 00:27:22.185 So if we if we look at this sort

NOTE Confidence: 0.786181326666667

00:27:22.185 --> 00:27:23.364 of cut off of A0P credit,

NOTE Confidence: 0.786181326666667

00:27:23.364 --> 00:27:24.576 so here's everyone with sort of

NOTE Confidence: 0.786181326666667

00:27:24.576 --> 00:27:26.214 positive P credits, negative P credits,

NOTE Confidence: 0.786181326666667

00:27:26.214 --> 00:27:28.635 you can see that the ones that did

NOTE Confidence: 0.786181326666667

00:27:28.635 --> 00:27:30.592 best on weight loss are within a

NOTE Confidence: 0.786181326666667

00:27:30.592 --> 00:27:32.122 weight loss intervention tended to

NOTE Confidence: 0.786181326666667

00:27:32.122 --> 00:27:34.936 have a less collapsible airway to begin with,

NOTE Confidence: 0.786181326666667

00:27:34.940 --> 00:27:36.250 whereas those that had higher

NOTE Confidence: 0.786181326666667

00:27:36.250 --> 00:27:37.775 peak credits to begin with, yes,

NOTE Confidence: 0.786181326666667

00:27:37.775 --> 00:27:39.065 they might have got some improvement

NOTE Confidence: 0.786181326666667

00:27:39.065 --> 00:27:40.496 in their sleep. Load of breathing.

NOTE Confidence: 0.786181326666667

00:27:40.496 --> 00:27:42.330 But you know it wasn't enough to

NOTE Confidence: 0.786181326666667

00:27:42.383 --> 00:27:43.753 overcome unless they were able

NOTE Confidence: 0.786181326666667

00:27:43.753 --> 00:27:45.670 to get down here, you know,

NOTE Confidence: 0.786181326666667

00:27:45.670 --> 00:27:48.540 below this sort of minus five critical

NOTE Confidence: 0.786181326666667

00:27:48.540 --> 00:27:50.790 threshold as I highlighted earlier.

NOTE Confidence: 0.786181326666667

00:27:50.790 --> 00:27:52.710 Alright, but what? What about CPAP?

NOTE Confidence: 0.786181326666667

00:27:52.710 --> 00:27:53.368 You know,

NOTE Confidence: 0.786181326666667

00:27:53.368 --> 00:27:55.671 how can we use the information from

NOTE Confidence: 0.786181326666667

00:27:55.671 --> 00:27:58.372 these end of types to perhaps predict or

NOTE Confidence: 0.786181326666667

00:27:58.372 --> 00:28:00.849 figure out who's who it will and won't.

NOTE Confidence: 0.786181326666667

00:28:00.850 --> 00:28:01.730 On cpap up front,

NOTE Confidence: 0.786181326666667

00:28:01.730 --> 00:28:03.562 so here's a study we did you know

NOTE Confidence: 0.786181326666667

00:28:03.562 --> 00:28:05.144 five or six years ago now where

NOTE Confidence: 0.786181326666667

00:28:05.144 --> 00:28:07.023 we took people that were coming

NOTE Confidence: 0.786181326666667

00:28:07.023 --> 00:28:08.623 through the clinical service and

NOTE Confidence: 0.78045525

00:28:08.630 --> 00:28:11.948 our in our public hospital and in Sydney and

NOTE Confidence: 0.78045525

00:28:11.948 --> 00:28:14.034 we particularly liked from these folks with

NOTE Confidence: 0.78045525

00:28:14.034 --> 00:28:16.247 these non obese people with sleep apnea.

NOTE Confidence: 0.78045525

00:28:16.250 --> 00:28:18.290 So now the rationale being that yes some

NOTE Confidence: 0.78045525

00:28:18.290 --> 00:28:19.765 might have retrognathia and anatomical

NOTE Confidence: 0.78045525

00:28:19.765 --> 00:28:22.490 issues but many of people who are not obese

NOTE Confidence: 0.78045525

00:28:22.490 --> 00:28:24.650 you know what was driving their sleep apnea.

NOTE Confidence: 0.78045525

00:28:24.650 --> 00:28:26.786 If it's not a major anatomical issue we

NOTE Confidence: 0.78045525

00:28:26.786 --> 00:28:29.048 figured it must be at least non anatomical

NOTE Confidence: 0.78045525

00:28:29.048 --> 00:28:31.180 traits and indeed we we estimated that.

NOTE Confidence: 0.78045525

00:28:31.180 --> 00:28:33.604 About 85% rather than it being a third

NOTE Confidence: 0.78045525

00:28:33.604 --> 00:28:36.214 of the overall population, you know,

NOTE Confidence: 0.78045525

00:28:36.214 --> 00:28:38.790 85% of these people who are not obese

NOTE Confidence: 0.78045525

00:28:38.863 --> 00:28:41.950 actually had a lower arousal threshold trait.

NOTE Confidence: 0.78045525

00:28:41.950 --> 00:28:43.108 And when we followed them up,

NOTE Confidence: 0.78045525

00:28:43.110 --> 00:28:45.708 they did particularly poorly on CPAP.

NOTE Confidence: 0.78045525

00:28:45.710 --> 00:28:46.928 And that kind of makes sense.

NOTE Confidence: 0.78045525

00:28:46.930 --> 00:28:48.568 If you're waking up very easily,

NOTE Confidence: 0.78045525

00:28:48.570 --> 00:28:51.186 you're going to be more sensitive to these

NOTE Confidence: 0.78045525

00:28:51.186 --> 00:28:53.432 pressure changes and perhaps less likely

NOTE Confidence: 0.78045525

00:28:53.432 --> 00:28:55.342 to tolerate that CPAP physiologically.

NOTE Confidence: 0.78045525

00:28:55.350 --> 00:28:57.350 So they're much less likely to be using

NOTE Confidence: 0.78045525

00:28:57.350 --> 00:28:59.803 CPAP at all when we followed them up

NOTE Confidence: 0.78045525

00:28:59.803 --> 00:29:01.330 and their objective compliance was.

NOTE Confidence: 0.78045525

00:29:01.330 --> 00:29:02.723 That was lower at that at that

NOTE Confidence: 0.78045525

00:29:02.723 --> 00:29:03.320 follow up with.

NOTE Confidence: 0.839187674

00:29:05.390 --> 00:29:07.511 Yeah, Andre and the team there at

NOTE Confidence: 0.839187674

00:29:07.511 --> 00:29:09.879 Yale have gone on to show this in

NOTE Confidence: 0.839187674

00:29:09.879 --> 00:29:12.244 other cohorts now both in the in the

NOTE Confidence: 0.839187674

00:29:12.244 --> 00:29:14.062 veteran cohort as well as people

NOTE Confidence: 0.839187674

00:29:14.062 --> 00:29:15.898 with coronary artery disease and

NOTE Confidence: 0.839187674

00:29:15.898 --> 00:29:17.808 effectively found the same thing.

NOTE Confidence: 0.839187674

00:29:17.810 --> 00:29:20.135 People with that lower arousal

NOTE Confidence: 0.839187674

00:29:20.135 --> 00:29:22.362 threshold including those non obese

NOTE Confidence: 0.839187674

00:29:22.362 --> 00:29:25.690 folks really did not do well on CPAP.

NOTE Confidence: 0.839187674

00:29:25.690 --> 00:29:28.970 So I'll get to what can we do about that.

NOTE Confidence: 0.839187674

00:29:28.970 --> 00:29:31.707 I'll highlight that as we move forward.

NOTE Confidence: 0.839187674

00:29:31.710 --> 00:29:35.230 So I might now.

NOTE Confidence: 0.839187674

00:29:35.230 --> 00:29:38.020 Maybe I'll just before I get to that uh,

NOTE Confidence: 0.839187674

00:29:38.020 --> 00:29:39.658 here's a review article that we wrote,

NOTE Confidence: 0.839187674

00:29:39.660 --> 00:29:41.879 recently wrote just so trying to I

NOTE Confidence: 0.839187674

00:29:41.879 --> 00:29:44.219 outline how can we use this information

NOTE Confidence: 0.839187674

00:29:44.219 --> 00:29:46.700 about end of types to better deliver

NOTE Confidence: 0.839187674

00:29:46.700 --> 00:29:48.870 targeted therapy with John Lewis,

NOTE Confidence: 0.839187674

00:29:48.870 --> 00:29:50.259 Peppin and Perrywood.

NOTE Confidence: 0.839187674

00:29:50.259 --> 00:29:52.574 Obviously very small font here,

NOTE Confidence: 0.839187674

00:29:52.580 --> 00:29:53.540 so I don't expect you to read it,

NOTE Confidence: 0.839187674

00:29:53.540 --> 00:29:55.150 but just to say that we went

NOTE Confidence: 0.839187674

00:29:55.150 --> 00:29:55.840 through the advantages,

NOTE Confidence: 0.839187674

00:29:55.840 --> 00:29:57.072 disadvantages of these therapies

NOTE Confidence: 0.839187674

00:29:57.072 --> 00:29:59.883 and and how we might be able to use

NOTE Confidence: 0.839187674

00:29:59.883 --> 00:30:01.695 this enter type information to move

NOTE Confidence: 0.839187674

00:30:01.695 --> 00:30:03.599 towards her a personalized approach.

NOTE Confidence: 0.839187674

00:30:03.600 --> 00:30:04.713 So encourage folks.

NOTE Confidence: 0.839187674

00:30:04.713 --> 00:30:05.826 To take it,

NOTE Confidence: 0.839187674

00:30:05.830 --> 00:30:08.770 take a look at that one if if of interest,

NOTE Confidence: 0.839187674

00:30:08.770 --> 00:30:12.928 alright, so development of new therapies.

NOTE Confidence: 0.839187674

00:30:12.930 --> 00:30:14.010 Off the back of this,

NOTE Confidence: 0.839187674

00:30:14.010 --> 00:30:16.054 this conceptual endotype framework,

NOTE Confidence: 0.839187674

00:30:16.054 --> 00:30:19.527 if we know about these four traits

NOTE Confidence: 0.839187674

00:30:19.527 --> 00:30:22.034 what can we do to develop therapies.

NOTE Confidence: 0.839187674

00:30:22.034 --> 00:30:24.686 So just to recap a bit,

NOTE Confidence: 0.839187674

00:30:24.690 --> 00:30:26.447 we first looked at use that model

NOTE Confidence: 0.839187674

00:30:26.447 --> 00:30:28.509 to figure out how much they are

NOTE Confidence: 0.839187674

00:30:28.509 --> 00:30:29.448 non CPAP interventions,

NOTE Confidence: 0.839187674

00:30:29.450 --> 00:30:31.838 noting that most of them are

NOTE Confidence: 0.839187674

00:30:31.838 --> 00:30:34.309 focused on anatomy at this time.

NOTE Confidence: 0.839187674

00:30:34.310 --> 00:30:36.207 Then we've looked at if we have

NOTE Confidence: 0.839187674

00:30:36.207 --> 00:30:37.583 information about the end of

NOTE Confidence: 0.839187674

00:30:37.583 --> 00:30:39.368 types how can they help us improve

NOTE Confidence: 0.839187674

00:30:39.368 --> 00:30:40.909 outcomes with existing therapies.

NOTE Confidence: 0.839187674

00:30:40.910 --> 00:30:42.908 So again trying to avoid people.

NOTE Confidence: 0.839187674

00:30:42.910 --> 00:30:44.530 With with major non anatomical

NOTE Confidence: 0.839187674

00:30:44.530 --> 00:30:46.570 issues really trying to hone down

NOTE Confidence: 0.839187674

00:30:46.570 --> 00:30:48.742 on the people with minor anatomical

NOTE Confidence: 0.839187674

00:30:48.742 --> 00:30:50.440 compromise perhaps people with CPAP.

NOTE Confidence: 0.839187674

00:30:50.440 --> 00:30:51.960 Sorry people with lower arousal

NOTE Confidence: 0.839187674

00:30:51.960 --> 00:30:53.480 threshold might need some more

NOTE Confidence: 0.839187674

00:30:53.532 --> 00:30:55.142 help getting on to CPAP or indeed

NOTE Confidence: 0.839187674

00:30:55.142 --> 00:30:56.818 look at other therapies for them.

NOTE Confidence: 0.839187674

00:30:56.820 --> 00:30:59.459 But and what are these new therapies

NOTE Confidence: 0.839187674

00:30:59.459 --> 00:31:02.728 you know what can we use to develop you

NOTE Confidence: 0.839187674

00:31:02.728 --> 00:31:05.780 know based on this framework develop the.

NOTE Confidence: 0.839187674

00:31:05.780 --> 00:31:08.172 They're going to switch to you know

NOTE Confidence: 0.839187674

00:31:08.172 --> 00:31:10.769 looking at these these non anatomical traits.

NOTE Confidence: 0.839187674

00:31:10.770 --> 00:31:12.387 So what can we do down here?

NOTE Confidence: 0.839187674

00:31:12.390 --> 00:31:13.394 As I've alluded to,

NOTE Confidence: 0.839187674

00:31:13.394 --> 00:31:15.296 you know these people that where their

NOTE Confidence: 0.839187674

00:31:15.296 --> 00:31:17.330 muscles really aren't working during sleep,

NOTE Confidence: 0.839187674

00:31:17.330 --> 00:31:19.142 you know we've got things like

NOTE Confidence: 0.839187674

00:31:19.142 --> 00:31:20.048 hypoglossal nerve stimulation,

NOTE Confidence: 0.839187674

00:31:20.050 --> 00:31:21.905 upper airway muscle training potentially

NOTE Confidence: 0.839187674

00:31:21.905 --> 00:31:24.309 can help some patients and I'm really

NOTE Confidence: 0.839187674

00:31:24.309 --> 00:31:26.261 going to focus in on you know the

NOTE Confidence: 0.839187674

00:31:26.317 --> 00:31:28.477 role of potential pharmacotherapy here.

NOTE Confidence: 0.839187674

00:31:28.480 --> 00:31:30.202 And and so you know theoretically

NOTE Confidence: 0.839187674

00:31:30.202 --> 00:31:32.240 this should be pretty straightforward.

NOTE Confidence: 0.839187674

00:31:32.240 --> 00:31:34.557 You know we've got out there later

NOTE Confidence: 0.839187674

00:31:34.557 --> 00:31:35.963 muscle function working nicely

NOTE Confidence: 0.839187674

00:31:35.963 --> 00:31:38.087 whilst awake and here's an alpha

NOTE Confidence: 0.839187674

00:31:38.087 --> 00:31:39.540 Theta transition where you know

NOTE Confidence: 0.839187674

00:31:39.540 --> 00:31:40.515 they've gone off to sleep.

NOTE Confidence: 0.839187674

00:31:40.520 --> 00:31:42.716 We see this profound reduction in

NOTE Confidence: 0.839187674

00:31:42.716 --> 00:31:44.598 tensor palatini and genioglossus muscle

NOTE Confidence: 0.839187674

00:31:44.598 --> 00:31:46.740 activity and a reduction in breathing.

NOTE Confidence: 0.839187674

00:31:46.740 --> 00:31:48.468 And so theoretically if we knew

NOTE Confidence: 0.839187674

00:31:48.468 --> 00:31:50.016 sort of neurochemically what was

NOTE Confidence: 0.839187674

00:31:50.016 --> 00:31:51.060 driving these reductions,

NOTE Confidence: 0.839187674

00:31:51.060 --> 00:31:53.580 these brisk reductions that occur with

NOTE Confidence: 0.839187674

00:31:53.580 --> 00:31:55.700 the transition transition of sleep,

NOTE Confidence: 0.839187674

00:31:55.700 --> 00:31:57.588 we should be able to give a drug

NOTE Confidence: 0.839187674

00:31:57.588 --> 00:31:58.060 and theoretically

NOTE Confidence: 0.787572858461538

00:31:58.116 --> 00:31:59.882 if we can. Going down on this

NOTE Confidence: 0.787572858461538

00:31:59.882 --> 00:32:01.174 upper airway motor neurons,

NOTE Confidence: 0.787572858461538

00:32:01.180 --> 00:32:03.126 we should be able to crank up

NOTE Confidence: 0.787572858461538

00:32:03.126 --> 00:32:04.938 these muscles and, you know,

NOTE Confidence: 0.787572858461538

00:32:04.938 --> 00:32:07.383 restore airway patency by giving

NOTE Confidence: 0.787572858461538

00:32:07.383 --> 00:32:08.850 a drug intervention.

NOTE Confidence: 0.787572858461538

00:32:08.850 --> 00:32:10.378 And here, you know,

NOTE Confidence: 0.787572858461538

00:32:10.378 --> 00:32:12.450 we and others have been looking at this

NOTE Confidence: 0.787572858461538

00:32:12.450 --> 00:32:14.218 for a long time and initially they were

NOTE Confidence: 0.787572858461538

00:32:14.218 --> 00:32:15.826 sort of looking at serotonergic agents.

NOTE Confidence: 0.787572858461538

00:32:15.830 --> 00:32:17.020 But thanks to, you know,

NOTE Confidence: 0.787572858461538

00:32:17.020 --> 00:32:19.225 beautiful animal work from Richard

NOTE Confidence: 0.787572858461538

00:32:19.225 --> 00:32:21.430 Horner and colleagues in Toronto

NOTE Confidence: 0.787572858461538

00:32:21.430 --> 00:32:24.090 have really LED us to believe that

NOTE Confidence: 0.787572858461538

00:32:24.090 --> 00:32:26.099 the noradrenergic and the muscarinic

NOTE Confidence: 0.787572858461538

00:32:26.099 --> 00:32:28.499 systems are very important both in

NOTE Confidence: 0.787572858461538

00:32:28.499 --> 00:32:31.338 R.E.M and non REM sleep for driving

NOTE Confidence: 0.787572858461538

00:32:31.338 --> 00:32:33.303 these reductions in muscle tone.

NOTE Confidence: 0.787572858461538

00:32:33.310 --> 00:32:34.370 So with this in mind,

NOTE Confidence: 0.787572858461538

00:32:34.370 --> 00:32:37.022 Luigi and the Boston team took

NOTE Confidence: 0.787572858461538

00:32:37.022 --> 00:32:38.910 these two agents, atomoxetine.

NOTE Confidence: 0.787572858461538

00:32:38.910 --> 00:32:41.470 Oxybutynin that had these properties

NOTE Confidence: 0.787572858461538

00:32:41.470 --> 00:32:42.938 and noradrenergic reuptake inhibitor

NOTE Confidence: 0.787572858461538

00:32:42.938 --> 00:32:45.541 and A and an anti muscarinic put

NOTE Confidence: 0.787572858461538

00:32:45.541 --> 00:32:46.917 them together measured upper

NOTE Confidence: 0.787572858461538

00:32:46.917 --> 00:32:49.035 airway Physiology and HIV in this

NOTE Confidence: 0.787572858461538

00:32:49.035 --> 00:32:50.725 initial proof of concept study.

NOTE Confidence: 0.787572858461538

00:32:50.730 --> 00:32:52.592 And what they found was that about

NOTE Confidence: 0.787572858461538

00:32:52.592 --> 00:32:54.569 a three or four fold activation

NOTE Confidence: 0.787572858461538

00:32:54.569 --> 00:32:56.429 of the Virginia glossus muscle

NOTE Confidence: 0.787572858461538

00:32:56.429 --> 00:32:58.375 response to those negative pressure

NOTE Confidence: 0.787572858461538

00:32:58.375 --> 00:33:00.265 swings when the drug intervention

NOTE Confidence: 0.787572858461538

00:33:00.265 --> 00:33:02.622 was in place compared to placebo.

NOTE Confidence: 0.787572858461538

00:33:02.622 --> 00:33:05.582 And you know this result in quite

NOTE Confidence: 0.787572858461538

00:33:05.582 --> 00:33:08.546 major reductions saying a single night

NOTE Confidence: 0.787572858461538

00:33:08.546 --> 00:33:11.462 acute Physiology study in in in HIV

NOTE Confidence: 0.787572858461538

00:33:11.462 --> 00:33:13.496 is shown here and improvements in

NOTE Confidence: 0.787572858461538

00:33:13.500 --> 00:33:16.180 oxygenation and in this particular

NOTE Confidence: 0.787572858461538

00:33:16.180 --> 00:33:18.324 study these improvements occurred

NOTE Confidence: 0.787572858461538

00:33:18.324 --> 00:33:20.916 both in non R.E.M and REM sleep.

NOTE Confidence: 0.787572858461538

00:33:20.920 --> 00:33:24.464 Akia Ashar and in our group PhD student

NOTE Confidence: 0.787572858461538

00:33:24.464 --> 00:33:27.659 who's just finished her PhD studies,

NOTE Confidence: 0.787572858461538

00:33:27.660 --> 00:33:30.488 you know went on to study these

NOTE Confidence: 0.787572858461538

00:33:30.488 --> 00:33:32.493 atomoxetine and oxybutynin at different

NOTE Confidence: 0.787572858461538

00:33:32.493 --> 00:33:35.027 dose regimes over a one month period

NOTE Confidence: 0.787572858461538

00:33:35.027 --> 00:33:37.549 to see what happens over a month.

NOTE Confidence: 0.787572858461538

00:33:37.550 --> 00:33:39.242 Recognizing that initial study

NOTE Confidence: 0.787572858461538

00:33:39.242 --> 00:33:41.357 was a single night study,

NOTE Confidence: 0.787572858461538

00:33:41.360 --> 00:33:43.965 she's actually just commenced to

NOTE Confidence: 0.787572858461538

00:33:43.965 --> 00:33:47.155 a postdoc studies over in Boston

NOTE Confidence: 0.787572858461538

00:33:47.155 --> 00:33:50.119 there and what Acura found was

NOTE Confidence: 0.787572858461538

00:33:50.119 --> 00:33:52.679 roughly a halving of the HIV.

NOTE Confidence: 0.787572858461538

00:33:52.680 --> 00:33:53.838 With the with the same dose

NOTE Confidence: 0.787572858461538

00:33:53.838 --> 00:33:55.340 that was in the original study,

NOTE Confidence: 0.787572858461538

00:33:55.340 --> 00:33:57.700 the lower doses that were not as efficacious,

NOTE Confidence: 0.787572858461538

00:33:57.700 --> 00:34:00.416 we had like 1/2 dose of atomoxetine

NOTE Confidence: 0.787572858461538

00:34:00.416 --> 00:34:03.018 and 1/2 dose of oxybutynin compared

NOTE Confidence: 0.787572858461538

00:34:03.018 --> 00:34:06.182 to baseline in this in this case.

NOTE Confidence: 0.787572858461538

00:34:06.190 --> 00:34:08.794 And there was also those improvements

NOTE Confidence: 0.787572858461538

00:34:08.794 --> 00:34:11.210 in hypoxic burden and these study

NOTE Confidence: 0.787572858461538

00:34:11.210 --> 00:34:13.512 and these findings are now impressed

NOTE Confidence: 0.787572858461538

00:34:13.512 --> 00:34:14.868 in the annals.

NOTE Confidence: 0.787572858461538

00:34:14.868 --> 00:34:18.145 We also in parallel this is Richard

NOTE Confidence: 0.787572858461538

00:34:18.145 --> 00:34:20.892 Lim's PhD work in the Sydney lab

NOTE Confidence: 0.787572858461538

00:34:20.892 --> 00:34:22.860 and what he did was take.

NOTE Confidence: 0.787572858461538

00:34:22.860 --> 00:34:24.617 Another jar, a drug in this class.

NOTE Confidence: 0.787572858461538

00:34:24.620 --> 00:34:26.280 So um, reboxetine, you know,

NOTE Confidence: 0.787572858461538

00:34:26.280 --> 00:34:28.360 not particularly good any antidepressant,

NOTE Confidence: 0.787572858461538

00:34:28.360 --> 00:34:30.860 but a pretty good NRI.

NOTE Confidence: 0.787572858461538

00:34:30.860 --> 00:34:35.320 And a different a muscarinic higher scene,

NOTE Confidence: 0.787572858461538

00:34:35.320 --> 00:34:36.360 beautiful bromide.

NOTE Confidence: 0.787572858461538

00:34:36.360 --> 00:34:38.600 And what if we looked at the upper

NOTE Confidence: 0.787572858461538

00:34:38.600 --> 00:34:40.367 muscle activity and what he found

NOTE Confidence: 0.787572858461538

00:34:40.367 --> 00:34:42.083 was indeed the tonic component of

NOTE Confidence: 0.787572858461538

00:34:42.142 --> 00:34:44.187 genioglossus improved in this small

NOTE Confidence: 0.787572858461538

00:34:44.187 --> 00:34:46.232 randomised Physiology study and again

NOTE Confidence: 0.787572858461538

00:34:46.240 --> 00:34:50.416 saw pretty consistent reductions in HIV.

NOTE Confidence: 0.787572858461538

00:34:50.420 --> 00:34:51.995 Gave this reboxetine

NOTE Confidence: 0.787572858461538

00:34:51.995 --> 00:34:54.095 combination with high seen,

NOTE Confidence: 0.787572858461538

00:34:54.100 --> 00:34:57.520 beautiful bromide and again you know

NOTE Confidence: 0.787572858461538

00:34:57.520 --> 00:35:00.950 quite marked improvements in oxygenation.

NOTE Confidence: 0.787572858461538

00:35:00.950 --> 00:35:02.980 Independently group in Italy went

NOTE Confidence: 0.787572858461538

00:35:02.980 --> 00:35:05.743 on to look at Reboxetine on the

NOTE Confidence: 0.787572858461538

00:35:05.743 --> 00:35:07.717 back of our work with Oxybutynin

NOTE Confidence: 0.787572858461538

00:35:07.717 --> 00:35:09.358 and you can see here,

NOTE Confidence: 0.787572858461538

00:35:09.360 --> 00:35:11.565 you know quite major improvements in HIV.

NOTE Confidence: 0.787572858461538

00:35:11.570 --> 00:35:14.510 This is now one week trial and they also saw

NOTE Confidence: 0.801738377142857

00:35:14.583 --> 00:35:16.187 improvements in the PvP.

NOTE Confidence: 0.801738377142857

00:35:16.190 --> 00:35:17.850 That's a psychomotor vigilance

NOTE Confidence: 0.801738377142857

00:35:17.850 --> 00:35:20.726 performance task next day and again they

NOTE Confidence: 0.801738377142857

00:35:20.726 --> 00:35:22.966 saw improvements in non R.E.M and REM

NOTE Confidence: 0.801738377142857

00:35:22.966 --> 00:35:27.098 sleep in this small randomized trial.

NOTE Confidence: 0.801738377142857

00:35:27.100 --> 00:35:28.675 We we were all singing this question.

NOTE Confidence: 0.801738377142857

00:35:28.680 --> 00:35:29.800 So when in that study,

NOTE Confidence: 0.801738377142857

00:35:29.800 --> 00:35:32.215 this is Tom Altree, he's a pulmonologist

NOTE Confidence: 0.801738377142857

00:35:32.215 --> 00:35:33.880 who's just finishing up his pH.

NOTE Confidence: 0.801738377142857

00:35:33.880 --> 00:35:35.398 D In the lab in Adelaide.

NOTE Confidence: 0.801738377142857

00:35:35.400 --> 00:35:37.616 And what we're interested in here was when

NOTE Confidence: 0.801738377142857

00:35:37.616 --> 00:35:40.313 we did those earlier studies with high aroma,

NOTE Confidence: 0.801738377142857

00:35:40.313 --> 00:35:42.574 not particularly good at crossing the blood

NOTE Confidence: 0.801738377142857

00:35:42.574 --> 00:35:44.839 brain barrier that particular muscular in it.

NOTE Confidence: 0.801738377142857

00:35:44.840 --> 00:35:46.680 So here we did a 3 way crossover

NOTE Confidence: 0.801738377142857

00:35:46.680 --> 00:35:48.300 to really answer the question.

NOTE Confidence: 0.801738377142857

00:35:48.300 --> 00:35:51.054 You know is it the noradrenergic

NOTE Confidence: 0.801738377142857

00:35:51.054 --> 00:35:53.350 agent that's largely leading from.

NOTE Confidence: 0.801738377142857

00:35:53.350 --> 00:35:53.617 Yeah.

NOTE Confidence: 0.801738377142857

00:35:53.617 --> 00:35:55.219 As well as Reboxetine alone in

NOTE Confidence: 0.801738377142857

00:35:55.219 --> 00:35:57.084 this 3 way crossover study and

NOTE Confidence: 0.801738377142857

00:35:57.084 --> 00:35:59.094 effectively what we found was really

NOTE Confidence: 0.801738377142857

00:35:59.094 --> 00:36:01.306 it was the Norwegian education that

NOTE Confidence: 0.801738377142857

00:36:01.306 --> 00:36:03.121 was driving the improvements in

NOTE Confidence: 0.801738377142857

00:36:03.130 --> 00:36:04.466 in sleep disorder breathing.

NOTE Confidence: 0.801738377142857

00:36:04.466 --> 00:36:07.024 And you can see you know similar

NOTE Confidence: 0.801738377142857

00:36:07.024 --> 00:36:09.776 improvements in oxygenation and ODI

NOTE Confidence: 0.801738377142857

00:36:09.776 --> 00:36:14.492 343 as shown here with Oxybutynin

NOTE Confidence: 0.801738377142857

00:36:14.492 --> 00:36:16.850 and REBOXETINE alone.

NOTE Confidence: 0.801738377142857

00:36:16.850 --> 00:36:19.410 And think about the end of type approach,

NOTE Confidence: 0.801738377142857

00:36:19.410 --> 00:36:21.258 the other thing that these these

NOTE Confidence: 0.801738377142857

00:36:21.258 --> 00:36:23.008 noradrenergic agents do is they lower

NOTE Confidence: 0.801738377142857

00:36:23.008 --> 00:36:24.848 the loop gain by about 10 or 20%.

NOTE Confidence: 0.801738377142857

00:36:24.850 --> 00:36:26.978 And in this particular study it seemed

NOTE Confidence: 0.801738377142857

00:36:26.978 --> 00:36:29.060 that the people with high look going

NOTE Confidence: 0.801738377142857

00:36:29.060 --> 00:36:31.042 to begin with and this study was

NOTE Confidence: 0.801738377142857

00:36:31.042 --> 00:36:33.652 mainly men that had the high loop game

NOTE Confidence: 0.801738377142857

00:36:33.652 --> 00:36:36.134 tended to have the greatest reductions

NOTE Confidence: 0.801738377142857

00:36:36.134 --> 00:36:38.945 in the HIV with reboxetine. OK.

NOTE Confidence: 0.801738377142857

00:36:38.945 --> 00:36:41.145 Uh, just to change tax a little bit.

NOTE Confidence: 0.801738377142857

00:36:41.150 --> 00:36:45.070 So he, he's a, he's a different target.

NOTE Confidence: 0.801738377142857

00:36:45.070 --> 00:36:47.506 We've got these robust reflex responses.

NOTE Confidence: 0.801738377142857

00:36:47.510 --> 00:36:49.554 So here if you deliver a negative

NOTE Confidence: 0.801738377142857

00:36:49.554 --> 00:36:51.528 pressure pulse to the airway you get

NOTE Confidence: 0.801738377142857

00:36:51.530 --> 00:36:53.014 marked activation of genioglossus

NOTE Confidence: 0.801738377142857

00:36:53.014 --> 00:36:54.869 and tensor palatini via these,

NOTE Confidence: 0.801738377142857

00:36:54.870 --> 00:36:55.660 you know,

NOTE Confidence: 0.801738377142857

00:36:55.660 --> 00:36:57.635 pressure sensitive McKenna receptors that

NOTE Confidence: 0.801738377142857

00:36:57.635 --> 00:36:59.790 are located throughout the upper airway.

NOTE Confidence: 0.801738377142857

00:36:59.790 --> 00:37:01.622 And so really what we wanted to ask

NOTE Confidence: 0.801738377142857

00:37:01.622 --> 00:37:03.579 are the question here was you know,

NOTE Confidence: 0.801738377142857

00:37:03.580 --> 00:37:04.775 rather than giving lignocaine which

NOTE Confidence: 0.801738377142857

00:37:04.775 --> 00:37:06.551 we know is knocks off these these

NOTE Confidence: 0.801738377142857

00:37:06.551 --> 00:37:08.153 reflexes and makes your sleep disorder.

NOTE Confidence: 0.801738377142857

00:37:08.160 --> 00:37:08.998 Getting worse.

NOTE Confidence: 0.801738377142857

00:37:08.998 --> 00:37:11.931 Can we give a a topical application

NOTE Confidence: 0.801738377142857

00:37:11.931 --> 00:37:15.232 that enhances this mechanism and so

NOTE Confidence: 0.801738377142857

00:37:15.232 --> 00:37:17.862 colleagues at Bayer had developed

NOTE Confidence: 0.801738377142857

00:37:17.862 --> 00:37:21.397 this agent and we did I guess the

NOTE Confidence: 0.801738377142857

00:37:21.397 --> 00:37:23.563 1st in human Physiology proof of

NOTE Confidence: 0.801738377142857

00:37:23.563 --> 00:37:25.669 concept studies that I'll show you

NOTE Confidence: 0.801738377142857

00:37:25.669 --> 00:37:27.957 here that's just been accepted for

NOTE Confidence: 0.801738377142857

00:37:27.957 --> 00:37:30.250 publication and we delivered this agent.

NOTE Confidence: 0.801738377142857

00:37:30.250 --> 00:37:32.770 It's a potassium channel blocker

NOTE Confidence: 0.801738377142857

00:37:32.770 --> 00:37:34.820 in this sort of randomized.

NOTE Confidence: 0.8451083075

00:37:39.380 --> 00:37:41.116 Sebo and then we went on to deliver

NOTE Confidence: 0.8451083075

00:37:41.116 --> 00:37:43.146 it in different forms, nasal drops,

NOTE Confidence: 0.8451083075

00:37:43.146 --> 00:37:45.547 half dose nasal spray and then finally

NOTE Confidence: 0.8451083075

00:37:45.547 --> 00:37:47.711 we actually put an endoscope down

NOTE Confidence: 0.8451083075

00:37:47.711 --> 00:37:50.480 and used an open channel to spray it

NOTE Confidence: 0.8451083075

00:37:50.480 --> 00:37:52.388 directly in the area of interest.

NOTE Confidence: 0.8451083075

00:37:52.390 --> 00:37:53.602 Here's our group.

NOTE Confidence: 0.8451083075

00:37:53.602 --> 00:37:55.218 They were predominantly severe

NOTE Confidence: 0.8451083075

00:37:55.218 --> 00:37:57.209 sleep apnea as shown here.

NOTE Confidence: 0.8451083075

00:37:57.210 --> 00:37:59.107 They all came back from multiple peak

NOTE Confidence: 0.8451083075

00:37:59.107 --> 00:38:01.043 visits and this is really this was

NOTE Confidence: 0.8451083075

00:38:01.043 --> 00:38:02.639 our primary outcome and the study

NOTE Confidence: 0.8451083075

00:38:02.696 --> 00:38:04.478 can we change the collapsibility of

NOTE Confidence: 0.8451083075

00:38:04.478 --> 00:38:06.456 the airway by spraying this topical

NOTE Confidence: 0.8451083075

00:38:06.456 --> 00:38:09.207 agent into the airway prior to sleep.

NOTE Confidence: 0.8451083075

00:38:09.210 --> 00:38:10.610 This is Amal Osman's work.

NOTE Confidence: 0.8451083075

00:38:10.610 --> 00:38:13.162 She very talented postdoc in the in the

NOTE Confidence: 0.8451083075

00:38:13.162 --> 00:38:16.012 lab that's been doing a lot of this

NOTE Confidence: 0.8451083075

00:38:16.012 --> 00:38:17.878 Physiology work and effectively that

NOTE Confidence: 0.8451083075

00:38:17.878 --> 00:38:20.068 the summary findings are shown here

NOTE Confidence: 0.8451083075

00:38:20.070 --> 00:38:22.026 delivering this spray we're able to.

NOTE Confidence: 0.8451083075

00:38:22.030 --> 00:38:23.038 Decrease the collapsibility of

NOTE Confidence: 0.8451083075

00:38:23.038 --> 00:38:24.550 the airway on average about two

NOTE Confidence: 0.8451083075

00:38:24.597 --> 00:38:25.817 or three centimetres of water.

NOTE Confidence: 0.8451083075

00:38:25.820 --> 00:38:27.140 So about about equivalent to

NOTE Confidence: 0.8451083075

00:38:27.140 --> 00:38:28.790 what we saw with you know,

NOTE Confidence: 0.8451083075

00:38:28.790 --> 00:38:30.308 position therapy if you like and

NOTE Confidence: 0.8451083075

00:38:30.308 --> 00:38:32.260 and so here are the individual and

NOTE Confidence: 0.8451083075

00:38:32.260 --> 00:38:34.325 group findings as shown here with the

NOTE Confidence: 0.8451083075

00:38:34.382 --> 00:38:35.987 various interventions and it didn't

NOTE Confidence: 0.8451083075

00:38:35.987 --> 00:38:39.859 seem to matter whether we go for high.

NOTE Confidence: 0.8451083075

00:38:39.860 --> 00:38:44.235 Try the drops or the endoscope application.

NOTE Confidence: 0.8451083075

00:38:44.240 --> 00:38:46.028 All the applications tended to improve

NOTE Confidence: 0.8451083075

00:38:46.028 --> 00:38:47.799 the collapse of believe the airway,

NOTE Confidence: 0.8451083075

00:38:47.800 --> 00:38:49.168 although it varied between

NOTE Confidence: 0.8451083075

00:38:49.168 --> 00:38:50.536 individuals as shown here.

NOTE Confidence: 0.8451083075

00:38:50.540 --> 00:38:56.356 So these findings are now impressed at chest.

NOTE Confidence: 0.8451083075

00:38:56.360 --> 00:38:56.782 What about,

NOTE Confidence: 0.8451083075

00:38:56.782 --> 00:38:57.837 you know these folks that

NOTE Confidence: 0.8451083075

00:38:57.837 --> 00:38:59.150 are that are light sleepers,

NOTE Confidence: 0.8451083075

00:38:59.150 --> 00:39:01.320 what can we do to help them?

NOTE Confidence: 0.8451083075

00:39:01.320 --> 00:39:03.182 Here's an initial study I did while

NOTE Confidence: 0.8451083075

00:39:03.182 --> 00:39:05.650 I was in Boston with the team and

NOTE Confidence: 0.8451083075

00:39:05.650 --> 00:39:07.688 we just gave Eszopiclone and these

NOTE Confidence: 0.8451083075

00:39:07.688 --> 00:39:09.920 individuals who did not have profound

NOTE Confidence: 0.8451083075

00:39:09.920 --> 00:39:11.445 hypoxemia to begin with because

NOTE Confidence: 0.8451083075

00:39:11.445 --> 00:39:13.365 the risk there of giving hypnotic

NOTE Confidence: 0.8451083075

00:39:13.365 --> 00:39:15.696 to people with already have a high

NOTE Confidence: 0.8451083075

00:39:15.696 --> 00:39:17.749 arousal threshold as you'll make the

NOTE Confidence: 0.8451083075

00:39:17.749 --> 00:39:19.414 events longer and oxygenation worse.

NOTE Confidence: 0.8451083075

00:39:19.420 --> 00:39:21.177 So excluded them to begin with and

NOTE Confidence: 0.8451083075

00:39:21.177 --> 00:39:22.981 we're left with people with sort

NOTE Confidence: 0.8451083075

00:39:22.981 --> 00:39:24.309 of moderate respiratory arousal

NOTE Confidence: 0.8451083075

00:39:24.309 --> 00:39:26.300 threshold and low and what we found

NOTE Confidence: 0.8451083075

00:39:26.300 --> 00:39:27.716 is an improvement in the HIV.

NOTE Confidence: 0.8451083075

00:39:27.720 --> 00:39:30.168 In those people with lower arousal

NOTE Confidence: 0.8451083075

00:39:30.168 --> 00:39:32.610 threshold without worsening the oxygenation,

NOTE Confidence: 0.8451083075

00:39:32.610 --> 00:39:34.170 we've since gone on to do lots of

NOTE Confidence: 0.8451083075

00:39:34.170 --> 00:39:35.590 work looking at the Physiology and

NOTE Confidence: 0.8451083075

00:39:35.590 --> 00:39:37.066 looking at lots of different agents.

NOTE Confidence: 0.8451083075

00:39:37.070 --> 00:39:38.438 I don't have time to sort of go

NOTE Confidence: 0.8451083075

00:39:38.438 --> 00:39:38.990 into those now,

NOTE Confidence: 0.8451083075

00:39:38.990 --> 00:39:40.316 but if you're interested in this,

NOTE Confidence: 0.8451083075

00:39:40.320 --> 00:39:41.620 Sophie and I again,

NOTE Confidence: 0.8451083075

00:39:41.620 --> 00:39:43.570 another PhD student in the lab,

NOTE Confidence: 0.8451083075

00:39:43.570 --> 00:39:44.977 wrote a review on all of this.

NOTE Confidence: 0.8451083075

00:39:44.980 --> 00:39:47.050 These recent finance was really challenged.

NOTE Confidence: 0.8451083075

00:39:47.050 --> 00:39:49.042 Some of those sort of preconceptions

NOTE Confidence: 0.8451083075

00:39:49.042 --> 00:39:51.550 you might have about the role of

NOTE Confidence: 0.8451083075

00:39:51.550 --> 00:39:53.410 hypnotics and sleep disorder breathing,

NOTE Confidence: 0.8451083075

00:39:53.410 --> 00:39:55.582 but potentially you can also get

NOTE Confidence: 0.8451083075

00:39:55.582 --> 00:39:58.222 there without drugs. So this is.

NOTE Confidence: 0.8451083075

00:39:58.222 --> 00:39:59.626 Alex Sweetman's work,

NOTE Confidence: 0.8451083075

00:39:59.626 --> 00:40:02.184 uh again a talent postdoc in

NOTE Confidence: 0.8451083075

00:40:02.184 --> 00:40:03.240 the Adelaide lab.

NOTE Confidence: 0.8451083075

00:40:03.240 --> 00:40:05.360 And and what he's gone and done is

NOTE Confidence: 0.8451083075

00:40:05.360 --> 00:40:07.395 actually in these people with comorbid

NOTE Confidence: 0.8451083075

00:40:07.395 --> 00:40:09.567 sleep apnea and insomnia is actually

NOTE Confidence: 0.8451083075

00:40:09.634 --> 00:40:11.879 give them cognitive behavioral therapy.

NOTE Confidence: 0.8451083075

00:40:11.880 --> 00:40:13.987 And when you just give them cognitive

NOTE Confidence: 0.8451083075

00:40:13.987 --> 00:40:15.749 behavioral therapy and bring them back

NOTE Confidence: 0.8451083075

00:40:15.749 --> 00:40:17.392 and measure their their HIV turns

NOTE Confidence: 0.8451083075

00:40:17.392 --> 00:40:19.144 out that that improves their sleep

NOTE Confidence: 0.8451083075

00:40:19.144 --> 00:40:20.900 apnea across all stages of sleep.

NOTE Confidence: 0.8451083075

00:40:20.900 --> 00:40:22.292 So we think that what's going

NOTE Confidence: 0.8451083075

00:40:22.292 --> 00:40:23.220 on there is the

NOTE Confidence: 0.833860755217391

00:40:23.281 --> 00:40:25.091 therapy is you know behaviorally

NOTE Confidence: 0.833860755217391

00:40:25.091 --> 00:40:26.539 and improving their arousal

NOTE Confidence: 0.833860755217391

00:40:26.539 --> 00:40:27.990 threshold and improving their.

NOTE Confidence: 0.833860755217391

00:40:27.990 --> 00:40:30.576 Have to sort of breathing with

NOTE Confidence: 0.833860755217391

00:40:30.576 --> 00:40:31.995 this intervention. So, you know,

NOTE Confidence: 0.833860755217391

00:40:31.995 --> 00:40:33.734 and and and just wanted to, you know,

NOTE Confidence: 0.833860755217391

00:40:33.734 --> 00:40:35.294 here's 2 epidemiological studies that

NOTE Confidence: 0.833860755217391

00:40:35.294 --> 00:40:37.319 we've done looking at their sleep health,

NOTE Confidence: 0.833860755217391

00:40:37.320 --> 00:40:40.900 heart sleep, heart health start.

NOTE Confidence: 0.833860755217391

00:40:40.900 --> 00:40:41.836 And it turns out, you know,

NOTE Confidence: 0.833860755217391

00:40:41.840 --> 00:40:43.484 people with insomnia and

NOTE Confidence: 0.833860755217391

00:40:43.484 --> 00:40:44.717 sleep apnea symptoms,

NOTE Confidence: 0.833860755217391

00:40:44.720 --> 00:40:47.461 mortality risk is you know, not so good.

NOTE Confidence: 0.833860755217391

00:40:47.461 --> 00:40:49.352 So we really do have to look after

NOTE Confidence: 0.833860755217391

00:40:49.352 --> 00:40:51.254 these patients and think about them.

NOTE Confidence: 0.833860755217391

00:40:51.260 --> 00:40:52.805 And so potentially no cognitive

NOTE Confidence: 0.833860755217391

00:40:52.805 --> 00:40:54.880 behavioural therapy if they do have a

NOTE Confidence: 0.833860755217391

00:40:54.880 --> 00:40:56.546 bit of insomnia going on or perhaps,

NOTE Confidence: 0.833860755217391

00:40:56.550 --> 00:40:58.251 you know, short period of of a

NOTE Confidence: 0.833860755217391

00:40:58.251 --> 00:41:00.013 hypnotic to help them get on CPAP

NOTE Confidence: 0.833860755217391

00:41:00.013 --> 00:41:01.471 in these people that you know,

NOTE Confidence: 0.833860755217391

00:41:01.480 --> 00:41:04.056 probably also have a lower arousal threshold,

NOTE Confidence: 0.833860755217391

00:41:04.060 --> 00:41:07.970 maybe a sensible path forward.

NOTE Confidence: 0.833860755217391

00:41:07.970 --> 00:41:08.252 Finally,

NOTE Confidence: 0.833860755217391

00:41:08.252 --> 00:41:10.226 what about combining all of these therapies?

NOTE Confidence: 0.833860755217391

00:41:10.230 --> 00:41:10.856 You know,

NOTE Confidence: 0.833860755217391

00:41:10.856 --> 00:41:12.734 we hopefully have now shown you

NOTE Confidence: 0.833860755217391

00:41:12.734 --> 00:41:14.740 that there's these different causes

NOTE Confidence: 0.833860755217391

00:41:14.740 --> 00:41:16.496 that vary between individuals.

NOTE Confidence: 0.833860755217391

00:41:16.500 --> 00:41:17.300 You know, can we,

NOTE Confidence: 0.833860755217391

00:41:17.300 --> 00:41:19.198 can we go after one or two of these,

NOTE Confidence: 0.833860755217391

00:41:19.200 --> 00:41:19.588 sorry,

NOTE Confidence: 0.833860755217391

00:41:19.588 --> 00:41:22.304 at least a couple of these traits

NOTE Confidence: 0.833860755217391

00:41:22.304 --> 00:41:24.605 to deliver therapy and these people

NOTE Confidence: 0.833860755217391

00:41:24.605 --> 00:41:26.510 that have got multiple issues

NOTE Confidence: 0.833860755217391

00:41:26.574 --> 00:41:28.478 are driving their pathogenesis.

NOTE Confidence: 0.833860755217391

00:41:28.480 --> 00:41:30.349 So here just a couple of examples

NOTE Confidence: 0.833860755217391

00:41:30.349 --> 00:41:32.241 quickly to show this study that Brad

NOTE Confidence: 0.833860755217391

00:41:32.241 --> 00:41:34.220 Edwards did when he was in Boston.

NOTE Confidence: 0.833860755217391

00:41:34.220 --> 00:41:36.436 And so really he's doing nothing to the

NOTE Confidence: 0.833860755217391

00:41:36.436 --> 00:41:37.816 anatomy, just giving oxygen therapy.

NOTE Confidence: 0.833860755217391

00:41:37.816 --> 00:41:39.460 To lower the loop gain and

NOTE Confidence: 0.833860755217391

00:41:39.517 --> 00:41:41.292 hypnotic dystopic line again so

NOTE Confidence: 0.833860755217391

00:41:41.292 --> 00:41:42.712 increase the arousal threshold.

NOTE Confidence: 0.833860755217391

00:41:42.720 --> 00:41:43.928 These were unselected patients.

NOTE Confidence: 0.833860755217391

00:41:43.928 --> 00:41:46.026 So we didn't know about that endo

NOTE Confidence: 0.833860755217391

00:41:46.026 --> 00:41:47.678 types ahead of time and you could

NOTE Confidence: 0.833860755217391

00:41:47.678 --> 00:41:49.654 see that overall just with these

NOTE Confidence: 0.833860755217391

00:41:49.654 --> 00:41:51.102 two interventions of combination

NOTE Confidence: 0.833860755217391

00:41:51.102 --> 00:41:52.986 therapy roughly half the hi you

NOTE Confidence: 0.833860755217391

00:41:52.986 --> 00:41:54.142 know with that intervention

NOTE Confidence: 0.833860755217391

00:41:54.142 --> 00:41:55.784 alone and many patients were you

NOTE Confidence: 0.833860755217391

00:41:55.784 --> 00:41:57.984 know now in the sort of what we

NOTE Confidence: 0.833860755217391

00:41:57.984 --> 00:41:59.256 consider the treated range.

NOTE Confidence: 0.918470275

00:42:01.300 --> 00:42:03.316 Last few years we've been working

NOTE Confidence: 0.918470275

00:42:03.320 --> 00:42:04.384 with these oral appliances.

NOTE Confidence: 0.918470275

00:42:04.384 --> 00:42:06.592 Amal and Ben Tong have been doing this

NOTE Confidence: 0.918470275

00:42:06.592 --> 00:42:08.272 work across the Adelaide and Sydney

NOTE Confidence: 0.918470275

00:42:08.272 --> 00:42:09.878 sites where we've brought you know

NOTE Confidence: 0.918470275

00:42:09.878 --> 00:42:11.650 a large group of people over 100.

NOTE Confidence: 0.918470275

00:42:11.650 --> 00:42:13.390 We've instrumented them with all the

NOTE Confidence: 0.918470275

00:42:13.390 --> 00:42:15.159 equipment we've then brought them back.

NOTE Confidence: 0.918470275

00:42:15.160 --> 00:42:17.086 We've we've seen if we've worked

NOTE Confidence: 0.918470275

00:42:17.086 --> 00:42:18.849 with the dentist and giving

NOTE Confidence: 0.918470275

00:42:18.849 --> 00:42:20.497 them oral appliance device,

NOTE Confidence: 0.918470275

00:42:20.500 --> 00:42:22.788 roughly half of them you know had a.

NOTE Confidence: 0.8201665775

00:42:26.380 --> 00:42:27.520 After therapy and so

NOTE Confidence: 0.8201665775

00:42:27.520 --> 00:42:28.660 they're they're all done.

NOTE Confidence: 0.8201665775

00:42:28.660 --> 00:42:30.228 But the question is and you know

NOTE Confidence: 0.8201665775

00:42:30.228 --> 00:42:31.617 again a big clinical problem

NOTE Confidence: 0.8201665775

00:42:31.617 --> 00:42:33.603 recognizing that many of these people

NOTE Confidence: 0.8201665775

00:42:33.603 --> 00:42:35.340 might have already failed CPAP,

NOTE Confidence: 0.8201665775

00:42:35.340 --> 00:42:37.350 now we've brought them through roughly

NOTE Confidence: 0.8201665775

00:42:37.350 --> 00:42:40.136 half of them don't get a full therapeutic

NOTE Confidence: 0.8201665775

00:42:40.136 --> 00:42:41.866 response on an oral appliance.

NOTE Confidence: 0.8201665775

00:42:41.870 --> 00:42:44.000 We use the phenotype information and

NOTE Confidence: 0.8201665775

00:42:44.000 --> 00:42:46.791 use this sort of stage protocol to

NOTE Confidence: 0.8201665775

00:42:46.791 --> 00:42:49.318 deliver targeted therapy and this kind of

NOTE Confidence: 0.8201665775

00:42:49.318 --> 00:42:52.227 proof of concept study also led by Aqua.

NOTE Confidence: 0.8201665775

00:42:52.230 --> 00:42:53.940 So here's we specifically brought

NOTE Confidence: 0.8201665775

00:42:53.940 --> 00:42:56.047 back these people that didn't have

NOTE Confidence: 0.8201665775

00:42:56.047 --> 00:42:57.757 resolution with their ISA just

NOTE Confidence: 0.8201665775

00:42:57.757 --> 00:42:59.468 with oral appliance therapy alone

NOTE Confidence: 0.8201665775

00:42:59.468 --> 00:43:01.190 and mass therapy is shown here.

NOTE Confidence: 0.8201665775

00:43:01.190 --> 00:43:02.942 So they've all gone HF 10, yes,

NOTE Confidence: 0.8201665775

00:43:02.942 --> 00:43:04.452 they've had some improvement and

NOTE Confidence: 0.8201665775

00:43:04.452 --> 00:43:06.579 then we just added on things like

NOTE Confidence: 0.8201665775

00:43:06.579 --> 00:43:08.295 position therapy and so just adding

NOTE Confidence: 0.8201665775

00:43:08.295 --> 00:43:09.936 an additional anatomical intervention

NOTE Confidence: 0.8201665775

00:43:09.936 --> 00:43:12.096 roughly half of these people.

NOTE Confidence: 0.8201665775

00:43:12.100 --> 00:43:13.408 Weren't treated beforehand.

NOTE Confidence: 0.8201665775

00:43:13.408 --> 00:43:14.280 Now where?

NOTE Confidence: 0.8201665775

00:43:14.280 --> 00:43:16.394 And then again if that didn't work,

NOTE Confidence: 0.8201665775

00:43:16.400 --> 00:43:17.830 we added on either oxygen,

NOTE Confidence: 0.8201665775

00:43:17.830 --> 00:43:19.854 the lower the lip gain or some drug

NOTE Confidence: 0.8201665775

00:43:19.854 --> 00:43:21.580 therapy to activate the muscles.

NOTE Confidence: 0.8201665775

00:43:21.580 --> 00:43:22.966 And then finally we added a bit

NOTE Confidence: 0.8201665775

00:43:22.966 --> 00:43:24.475 of CPAP to the oral appliance

NOTE Confidence: 0.8201665775

00:43:24.475 --> 00:43:25.920 device if nothing else worked.

NOTE Confidence: 0.8201665775

00:43:25.920 --> 00:43:27.236 And Long story short,

NOTE Confidence: 0.8201665775

00:43:27.236 --> 00:43:29.210 aside from this individual who really

NOTE Confidence: 0.8201665775

00:43:29.267 --> 00:43:31.217 could not tolerate CPAP and wasn't,

NOTE Confidence: 0.8201665775

00:43:31.220 --> 00:43:33.740 it wasn't a candidate for drug therapy.

NOTE Confidence: 0.8201665775

00:43:33.740 --> 00:43:35.486 We managed to treat all the

NOTE Confidence: 0.8201665775

00:43:35.486 --> 00:43:37.653 patients with this sort of targeted

NOTE Confidence: 0.8201665775

00:43:37.653 --> 00:43:39.060 combination therapy approach.

NOTE Confidence: 0.8201665775

00:43:39.060 --> 00:43:41.115 So hopefully we're building up

NOTE Confidence: 0.8201665775

00:43:41.115 --> 00:43:43.170 this toolkit off the different.

NOTE Confidence: 0.8201665775

00:43:43.170 --> 00:43:43.976 Therapies, yes,

NOTE Confidence: 0.8201665775

00:43:43.976 --> 00:43:45.185 traditionally we're focused

NOTE Confidence: 0.8201665775

00:43:45.185 --> 00:43:47.200 on the the anatomy side,

NOTE Confidence: 0.8201665775

00:43:47.200 --> 00:43:49.027 but now we're building up this toolkit

NOTE Confidence: 0.8201665775

00:43:49.027 --> 00:43:51.450 of the of the sort of non anatomical

NOTE Confidence: 0.8201665775

00:43:51.450 --> 00:43:53.030 approaches that we can combine.

NOTE Confidence: 0.8201665775

00:43:53.030 --> 00:43:54.890 So rather than I guess using

NOTE Confidence: 0.8201665775

00:43:54.890 --> 00:43:57.006 largely this sort of single night

NOTE Confidence: 0.8201665775

00:43:57.006 --> 00:43:59.436 hi measures to inform our treatment

NOTE Confidence: 0.8201665775

00:43:59.436 --> 00:44:01.448 decisions which we know aren't

NOTE Confidence: 0.8201665775

00:44:01.448 --> 00:44:03.343 aren't particularly good at working

NOTE Confidence: 0.8201665775

00:44:03.343 --> 00:44:05.230 out who's going to respond to which

NOTE Confidence: 0.8201665775

00:44:05.230 --> 00:44:06.665 therapy and who's going to have

NOTE Confidence: 0.8201665775

00:44:06.665 --> 00:44:08.025 an improvement in their symptoms.

NOTE Confidence: 0.8201665775

00:44:08.030 --> 00:44:09.530 Uh with the various treatments

NOTE Confidence: 0.8201665775

00:44:09.530 --> 00:44:11.322 we have available today it's very

NOTE Confidence: 0.8201665775

00:44:11.322 --> 00:44:12.507 much a trial and error.

NOTE Confidence: 0.8201665775

00:44:12.510 --> 00:44:14.846 Process if we could use this sort of

NOTE Confidence: 0.8201665775

00:44:14.846 --> 00:44:16.780 more Physiology or palm scale approach.

NOTE Confidence: 0.8201665775

00:44:16.780 --> 00:44:17.042 Firstly,

NOTE Confidence: 0.8201665775

00:44:17.042 --> 00:44:19.138 if we know how bad the anatomy was,

NOTE Confidence: 0.8201665775

00:44:19.140 --> 00:44:20.646 that won't help us initially decide

NOTE Confidence: 0.8201665775

00:44:20.646 --> 00:44:22.299 whether we need to go for CPAP

NOTE Confidence: 0.8201665775

00:44:22.299 --> 00:44:23.289 or one of these other.

NOTE Confidence: 0.71452084

00:44:25.440 --> 00:44:27.636 That's position therapy and so forth.

NOTE Confidence: 0.71452084

00:44:27.640 --> 00:44:30.064 Uh, we could hopefully get to the successful

NOTE Confidence: 0.71452084

00:44:30.064 --> 00:44:31.558 treatment upfront rather than this,

NOTE Confidence: 0.71452084

00:44:31.560 --> 00:44:34.140 you know, trial and error approach.

NOTE Confidence: 0.71452084

00:44:34.140 --> 00:44:36.282 So I'm just gonna spend a few minutes to

NOTE Confidence: 0.71452084

00:44:36.282 --> 00:44:38.976 to finish now to just whiz through some

NOTE Confidence: 0.71452084

00:44:38.976 --> 00:44:40.370 simplified approaches for translating

NOTE Confidence: 0.71452084

00:44:40.370 --> 00:44:42.842 these concepts to the to the clinic and

NOTE Confidence: 0.71452084

00:44:42.842 --> 00:44:45.720 then allow some time for questions.

NOTE Confidence: 0.71452084

00:44:45.720 --> 00:44:47.616 And and really you know this is obviously

NOTE Confidence: 0.71452084

00:44:47.616 --> 00:44:49.569 the big question you know all well and

NOTE Confidence: 0.71452084

00:44:49.569 --> 00:44:51.299 good to figure out this Physiology but

NOTE Confidence: 0.71452084

00:44:51.299 --> 00:44:53.764 how can you actually use it in the clinic.

NOTE Confidence: 0.71452084

00:44:53.764 --> 00:44:56.438 So here's a little test that we've

NOTE Confidence: 0.71452084

00:44:56.440 --> 00:44:58.260 further developed again our mouse

NOTE Confidence: 0.71452084

00:44:58.260 --> 00:45:01.466 LED much of this work where you know

NOTE Confidence: 0.71452084

00:45:01.466 --> 00:45:04.108 rather than doing a sort of looking at.

NOTE Confidence: 0.2517227108

00:45:06.910 --> 00:45:09.480 And uh, awakened oscopy, uh,

NOTE Confidence: 0.2517227108

00:45:09.480 --> 00:45:10.607 we can do a little test here,

NOTE Confidence: 0.2517227108

00:45:10.610 --> 00:45:13.042 15 minutes in the lab where we just

NOTE Confidence: 0.2517227108

00:45:13.042 --> 00:45:14.705 deliver brief pulses of suction

NOTE Confidence: 0.2517227108

00:45:14.705 --> 00:45:16.679 to the airway with this device

NOTE Confidence: 0.2517227108

00:45:16.679 --> 00:45:18.713 here and we can get a pretty

NOTE Confidence: 0.2517227108

00:45:18.713 --> 00:45:20.236 good estimate of the P credit.

NOTE Confidence: 0.2517227108

00:45:20.236 --> 00:45:21.088 So in this study,

NOTE Confidence: 0.2517227108

00:45:21.090 --> 00:45:22.898 we did these little pulses to the airway,

NOTE Confidence: 0.2517227108

00:45:22.900 --> 00:45:24.508 about 1/4 of a second pressure.

NOTE Confidence: 0.2517227108

00:45:24.510 --> 00:45:26.760 We do about 50 pulses or?

NOTE Confidence: 0.740339829666666

00:45:28.990 --> 00:45:31.150 The difference throughout the airway

NOTE Confidence: 0.740339829666666

00:45:31.150 --> 00:45:34.131 to see how collapsible that airway is

NOTE Confidence: 0.740339829666666

00:45:34.131 --> 00:45:36.363 and that's simple awake testing lines

NOTE Confidence: 0.740339829666666

00:45:36.363 --> 00:45:38.499 up very nicely with the overnight

NOTE Confidence: 0.740339829666666

00:45:38.499 --> 00:45:41.262 peak as shown here in a mile study.

NOTE Confidence: 0.740339829666666

00:45:41.262 --> 00:45:43.578 And here's our sort of receiver

NOTE Confidence: 0.740339829666666

00:45:43.578 --> 00:45:44.810 operating characteristic curves.

NOTE Confidence: 0.740339829666666

00:45:44.810 --> 00:45:46.525 So very good if that first thing,

NOTE Confidence: 0.740339829666666

00:45:46.530 --> 00:45:48.672 if all you want to do is

NOTE Confidence: 0.740339829666666

00:45:48.672 --> 00:45:50.707 differentiate between who has a + a

NOTE Confidence: 0.740339829666666

00:45:50.707 --> 00:45:52.285 positive P credit and a negative,

NOTE Confidence: 0.740339829666666

00:45:52.290 --> 00:45:54.226 this technique is pretty good at doing that.

NOTE Confidence: 0.740339829666666

00:45:54.230 --> 00:45:56.926 Or if you want to go further minus

NOTE Confidence: 0.740339829666666

00:45:56.926 --> 00:45:58.920 two versus you know that minus 2.

NOTE Confidence: 0.740339829666666

00:45:58.920 --> 00:46:00.380 Threshold, so that 20% of

NOTE Confidence: 0.740339829666666

00:46:00.380 --> 00:46:01.548 patients that really don't,

NOTE Confidence: 0.740339829666666

00:46:01.550 --> 00:46:03.839 you only have a mild anatomical problem.

NOTE Confidence: 0.740339829666666

00:46:03.840 --> 00:46:05.808 And here's the area under the curve as

NOTE Confidence: 0.740339829666666

00:46:05.808 --> 00:46:07.908 shown here for those different approaches.

NOTE Confidence: 0.740339829666666

00:46:07.910 --> 00:46:09.830 But if you know obviously

NOTE Confidence: 0.740339829666666

00:46:09.830 --> 00:46:11.366 that's work in development.

NOTE Confidence: 0.740339829666666

00:46:11.370 --> 00:46:12.710 Many of these patients have

NOTE Confidence: 0.740339829666666

00:46:12.710 --> 00:46:14.050 already had a CPAP trial.

NOTE Confidence: 0.740339829666666

00:46:14.050 --> 00:46:15.994 Turns out that information gives you a pretty

NOTE Confidence: 0.740339829666666

00:46:15.994 --> 00:46:17.805 good idea of their peak credit as well.

NOTE Confidence: 0.740339829666666

00:46:17.810 --> 00:46:19.346 So people with a pity credit,

NOTE Confidence: 0.740339829666666

00:46:19.350 --> 00:46:20.626 you know,

NOTE Confidence: 0.740339829666666

00:46:20.626 --> 00:46:22.540 above atmospheric pressure

NOTE Confidence: 0.740339829666666

00:46:22.540 --> 00:46:26.390 tend to be on require CPAP.

NOTE Confidence: 0.740339829666666

00:46:26.390 --> 00:46:28.735 That you know 10 centimeters of water

NOTE Confidence: 0.740339829666666

00:46:28.735 --> 00:46:31.288 and again we've shown this in a follow-up

NOTE Confidence: 0.740339829666666

00:46:31.288 --> 00:46:33.752 study as well here in a couple of

NOTE Confidence: 0.740339829666666

00:46:33.752 --> 00:46:36.050 follow up studies as well as that ratio,

NOTE Confidence: 0.740339829666666

00:46:36.050 --> 00:46:38.598 if you got more apneas compared

NOTE Confidence: 0.740339829666666

00:46:38.598 --> 00:46:40.068 to hypopneas than you're likely

NOTE Confidence: 0.740339829666666

00:46:40.068 --> 00:46:42.088 to have a more collapsible AOI,

NOTE Confidence: 0.740339829666666

00:46:42.090 --> 00:46:45.438 which also kind of makes sense.

NOTE Confidence: 0.740339829666666

00:46:45.440 --> 00:46:46.872 We've also got tools,

NOTE Confidence: 0.740339829666666

00:46:46.872 --> 00:46:49.473 and Andre and the team have been

NOTE Confidence: 0.740339829666666

00:46:49.473 --> 00:46:51.729 using these over there in Yale.

NOTE Confidence: 0.740339829666666

00:46:51.730 --> 00:46:53.242 3 measures from a standard sleep

NOTE Confidence: 0.740339829666666

00:46:53.242 --> 00:46:55.014 study can give you a pretty good

NOTE Confidence: 0.740339829666666

00:46:55.014 --> 00:46:56.673 idea of whether or not with pretty

NOTE Confidence: 0.740339829666666

00:46:56.727 --> 00:46:58.359 good sensitivity and specificity.

NOTE Confidence: 0.740339829666666

00:46:58.360 --> 00:47:00.421 So you just look at the HIV Nadia sat

NOTE Confidence: 0.740339829666666

00:47:00.421 --> 00:47:02.244 and the fraction about the hypotenuse

NOTE Confidence: 0.740339829666666

00:47:02.244 --> 00:47:04.627 and that can give you a pretty good

NOTE Confidence: 0.740339829666666

00:47:04.627 --> 00:47:06.886 idea of who's got a lower arousal threshold.

NOTE Confidence: 0.740339829666666

00:47:06.886 --> 00:47:08.966 And the type Boston team,

NOTE Confidence: 0.740339829666666

00:47:08.970 --> 00:47:09.774 as I mentioned,

NOTE Confidence: 0.740339829666666

00:47:09.774 --> 00:47:12.356 we've done a great job at trying to do

NOTE Confidence: 0.740339829666666

00:47:12.356 --> 00:47:13.976 some signal processing techniques where

NOTE Confidence: 0.740339829666666

00:47:13.976 --> 00:47:16.678 they look at the end of the PSG recordings,

NOTE Confidence: 0.740339829666666

00:47:16.680 --> 00:47:18.530 the flow signal in particular,

NOTE Confidence: 0.740339829666666

00:47:18.530 --> 00:47:20.666 and estimate each of those traits

NOTE Confidence: 0.740339829666666

00:47:20.666 --> 00:47:22.690 as outlined in these various.

NOTE Confidence: 0.740339829666666

00:47:22.690 --> 00:47:24.010 Type is here now.

NOTE Confidence: 0.740339829666666

00:47:24.010 --> 00:47:26.791 Trouble with that of course is you need

NOTE Confidence: 0.740339829666666

00:47:26.791 --> 00:47:29.353 an engineer and it's not automated yet.

NOTE Confidence: 0.740339829666666

00:47:29.360 --> 00:47:30.672 Standard Sleep study reports.

NOTE Confidence: 0.740339829666666

00:47:30.672 --> 00:47:32.312 But just to finish on,

NOTE Confidence: 0.740339829666666

00:47:32.320 --> 00:47:33.620 here's some work that we've

NOTE Confidence: 0.740339829666666

00:47:33.620 --> 00:47:34.920 done with my colleague really.

NOTE Confidence: 0.740339829666666

00:47:34.920 --> 00:47:35.392 Bandata,

NOTE Confidence: 0.740339829666666

00:47:35.392 --> 00:47:37.752 who's a data scientist and

NOTE Confidence: 0.740339829666666

00:47:37.752 --> 00:47:39.640 a machine learning expert,

NOTE Confidence: 0.740339829666666

00:47:39.640 --> 00:47:41.180 works with our government

NOTE Confidence: 0.740339829666666

00:47:41.180 --> 00:47:42.720 agency called the Csro.

NOTE Confidence: 0.740339829666666

00:47:42.720 --> 00:47:45.331 Basically what we did was just take

NOTE Confidence: 0.740339829666666

00:47:45.331 --> 00:47:47.697 simple variables from a sleep study age,

NOTE Confidence: 0.740339829666666

00:47:47.700 --> 00:47:48.981 plus clinical outputs,

NOTE Confidence: 0.740339829666666

00:47:48.981 --> 00:47:51.543 age, BMI and and develop a

NOTE Confidence: 0.740339829666666

00:47:51.543 --> 00:47:53.480 machine learning algorithm.

NOTE Confidence: 0.740339829666666

00:47:53.480 --> 00:47:56.216 And effectively what we're able to do was

NOTE Confidence: 0.740339829666666

00:47:56.216 --> 00:47:58.680 estimate the traits using this approach,

NOTE Confidence: 0.740339829666666

00:47:58.680 --> 00:48:00.204 just plugging this information

NOTE Confidence: 0.740339829666666

00:48:00.204 --> 00:48:01.347 into the algorithm.

NOTE Confidence: 0.740339829666666

00:48:01.350 --> 00:48:03.506 And this can help us predict who's

NOTE Confidence: 0.740339829666666

00:48:03.506 --> 00:48:05.480 going to respond to oral appliance

NOTE Confidence: 0.740339829666666

00:48:05.480 --> 00:48:07.769 therapy as shown in this paper here.

NOTE Confidence: 0.740339829666666

00:48:07.770 --> 00:48:10.420 And we've also gone on,

NOTE Confidence: 0.740339829666666

00:48:10.420 --> 00:48:12.055 we've just presented this stuff

NOTE Confidence: 0.740339829666666

00:48:12.055 --> 00:48:14.144 at these findings at our recent

NOTE Confidence: 0.740339829666666

00:48:14.144 --> 00:48:16.410 sleep meeting in Australia in a

NOTE Confidence: 0.740339829666666

00:48:16.410 --> 00:48:18.210 prospective cohort of 90 people.

NOTE Confidence: 0.740339829666666

00:48:18.210 --> 00:48:19.475 Here's the sort of success

NOTE Confidence: 0.740339829666666

00:48:19.475 --> 00:48:20.740 rates that we got when

NOTE Confidence: 0.861716302307692

00:48:20.795 --> 00:48:22.430 we applied the, the algorithm

NOTE Confidence: 0.861716302307692

00:48:22.430 --> 00:48:24.580 prospectively in this cohort here.

NOTE Confidence: 0.861716302307692

00:48:24.580 --> 00:48:26.360 Similarly, we've been working on

NOTE Confidence: 0.861716302307692

00:48:26.360 --> 00:48:27.784 different therapies using this,

NOTE Confidence: 0.861716302307692

00:48:27.790 --> 00:48:29.990 in this case children with

NOTE Confidence: 0.861716302307692

00:48:29.990 --> 00:48:31.790 removal of adenoids and tonsils.

NOTE Confidence: 0.861716302307692

00:48:31.790 --> 00:48:33.834 Work with Jordan in in Hong Kong.

NOTE Confidence: 0.861716302307692

00:48:33.840 --> 00:48:36.143 He's now doing a postdoc in Toronto

NOTE Confidence: 0.861716302307692

00:48:36.143 --> 00:48:38.673 and he is the success rates in

NOTE Confidence: 0.861716302307692

00:48:38.673 --> 00:48:40.730 this initial proof of concept work.

NOTE Confidence: 0.861716302307692

00:48:40.730 --> 00:48:43.058 Using the model that we developed,

NOTE Confidence: 0.861716302307692

00:48:43.060 --> 00:48:44.420 we've also built an interface

NOTE Confidence: 0.861716302307692

00:48:44.420 --> 00:48:46.372 that we can sort of apply this

NOTE Confidence: 0.861716302307692

00:48:46.372 --> 00:48:47.956 so you can securely log in,

NOTE Confidence: 0.861716302307692

00:48:47.960 --> 00:48:49.715 put in the information and

NOTE Confidence: 0.861716302307692

00:48:49.715 --> 00:48:51.470 make predictions not only about

NOTE Confidence: 0.861716302307692

00:48:51.536 --> 00:48:53.372 whether their ender types are,

NOTE Confidence: 0.861716302307692

00:48:53.372 --> 00:48:56.325 but also whether or not they're going to

NOTE Confidence: 0.861716302307692

00:48:56.325 --> 00:48:59.020 respond to these various non CPAP therapies.

NOTE Confidence: 0.861716302307692

00:48:59.020 --> 00:49:00.300 So just to summarize,

NOTE Confidence: 0.861716302307692

00:49:00.300 --> 00:49:01.900 what can we do immediately?

NOTE Confidence: 0.861716302307692

00:49:01.900 --> 00:49:04.690 Clinically to implement this car,

NOTE Confidence: 0.861716302307692

00:49:04.690 --> 00:49:06.305 our palm scale category or

NOTE Confidence: 0.861716302307692

00:49:06.305 --> 00:49:07.597 OSA under typing concepts,

NOTE Confidence: 0.861716302307692

00:49:07.600 --> 00:49:09.212 so just to summarize,

NOTE Confidence: 0.861716302307692

00:49:09.212 --> 00:49:11.870 it can help with improving outcomes

NOTE Confidence: 0.861716302307692

00:49:11.870 --> 00:49:13.430 of existing therapies.

NOTE Confidence: 0.861716302307692

00:49:13.430 --> 00:49:15.335 Fabral characteristics for non CPAP

NOTE Confidence: 0.861716302307692

00:49:15.335 --> 00:49:18.240 therapies tend to be mild to moderate

NOTE Confidence: 0.861716302307692

00:49:18.240 --> 00:49:20.112 collapsibility without major problems

NOTE Confidence: 0.861716302307692

00:49:20.112 --> 00:49:22.490 with these non anatomical traits.

NOTE Confidence: 0.861716302307692

00:49:22.490 --> 00:49:24.362 People with a lower alcohol threshold

NOTE Confidence: 0.861716302307692

00:49:24.362 --> 00:49:27.006 endotype do not do well on CPAP and general

NOTE Confidence: 0.861716302307692

00:49:27.010 --> 00:49:30.538 and as I've highlighted we can also.

NOTE Confidence: 0.861716302307692

00:49:30.540 --> 00:49:31.749 New fair piece.

NOTE Confidence: 0.861716302307692

00:49:31.749 --> 00:49:33.764 But in terms of translations,

NOTE Confidence: 0.861716302307692

00:49:33.770 --> 00:49:35.030 some of these approaches can be

NOTE Confidence: 0.861716302307692

00:49:35.030 --> 00:49:36.309 applied in the clinic right now.

NOTE Confidence: 0.861716302307692

00:49:36.310 --> 00:49:37.183 So for example,

NOTE Confidence: 0.861716302307692

00:49:37.183 --> 00:49:38.929 that happened to hypopnea ratio gives

NOTE Confidence: 0.861716302307692

00:49:38.929 --> 00:49:40.779 us an idea of how collapsible the

NOTE Confidence: 0.861716302307692

00:49:40.779 --> 00:49:42.518 airway is or your CPAP therapeutic

NOTE Confidence: 0.861716302307692

00:49:42.518 --> 00:49:44.576 pressure talked about those 3 parameters

NOTE Confidence: 0.861716302307692

00:49:44.576 --> 00:49:46.980 that you can use to estimate the

NOTE Confidence: 0.861716302307692

00:49:46.980 --> 00:49:49.080 lower arousal threshold end of type.

NOTE Confidence: 0.861716302307692

00:49:49.080 --> 00:49:51.048 And hopefully I've shown you some of the

NOTE Confidence: 0.861716302307692

00:49:51.048 --> 00:49:53.165 work that we're doing to move forward for,

NOTE Confidence: 0.861716302307692

00:49:53.170 --> 00:49:53.862 you know,

NOTE Confidence: 0.861716302307692

00:49:53.862 --> 00:49:56.284 being able to get these tools readily

NOTE Confidence: 0.861716302307692

00:49:56.284 --> 00:49:58.524 available and simply in the clinic

NOTE Confidence: 0.861716302307692

00:49:58.524 --> 00:50:00.349 to inform clinical decision making.

NOTE Confidence: 0.861716302307692

00:50:00.350 --> 00:50:01.388 OK, very big.

NOTE Confidence: 0.861716302307692

00:50:01.388 --> 00:50:03.810 Thank you to my team and collaborators

NOTE Confidence: 0.861716302307692

00:50:03.885 --> 00:50:05.457 at Neuroscience Research Australia

NOTE Confidence: 0.861716302307692

00:50:05.457 --> 00:50:07.815 and my my lab in Sydney,

NOTE Confidence: 0.861716302307692

00:50:07.820 --> 00:50:09.486 as well as our fantastic team at

NOTE Confidence: 0.861716302307692

00:50:09.486 --> 00:50:11.078 the LA Institute for Sleep Health.

NOTE Confidence: 0.861716302307692

00:50:11.080 --> 00:50:12.910 Over 60 people in the team

NOTE Confidence: 0.861716302307692

00:50:12.910 --> 00:50:14.378 and they're a fantastic group.

NOTE Confidence: 0.861716302307692

00:50:14.378 --> 00:50:15.808 So thank you very much.

NOTE Confidence: 0.874395286363637

00:50:18.340 --> 00:50:20.392 Amazing. Thank you so much Doctor

NOTE Confidence: 0.874395286363637

00:50:20.392 --> 00:50:22.580 Eckert for this excellent presentation.

NOTE Confidence: 0.874395286363637

00:50:22.580 --> 00:50:24.784 Was very thought provoking

NOTE Confidence: 0.874395286363637

00:50:24.784 --> 00:50:26.437 and super informative.

NOTE Confidence: 0.874395286363637

00:50:26.440 --> 00:50:28.960 If anyone has any questions you

NOTE Confidence: 0.874395286363637

00:50:28.960 --> 00:50:31.990 can either put it in the chat

NOTE Confidence: 0.874395286363637

00:50:31.990 --> 00:50:34.504 or feel free to unmute yourself.

NOTE Confidence: 0.874395286363637

00:50:34.510 --> 00:50:35.470 I have a question.

NOTE Confidence: 0.874395286363637

00:50:35.470 --> 00:50:36.430 So as you mentioned,

NOTE Confidence: 0.874395286363637

00:50:36.430 --> 00:50:39.167 you know we do have all these

NOTE Confidence: 0.874395286363637

00:50:39.167 --> 00:50:40.865 alternative meds approved for OSA,

NOTE Confidence: 0.874395286363637

00:50:40.865 --> 00:50:43.000 but you know these are as we

NOTE Confidence: 0.874395286363637

00:50:43.075 --> 00:50:45.070 all know less frequently used.

NOTE Confidence: 0.874395286363637

00:50:45.070 --> 00:50:47.458 Any thoughts on what would help

NOTE Confidence: 0.874395286363637

00:50:47.458 --> 00:50:49.050 clinicians in day-to-day practice

NOTE Confidence: 0.874395286363637

00:50:49.115 --> 00:50:50.707 to utilize these alternatives

NOTE Confidence: 0.874395286363637

00:50:50.707 --> 00:50:52.697 on patients who meet criteria

NOTE Confidence: 0.874395286363637

00:50:52.697 --> 00:50:54.570 these alternative treatments?

NOTE Confidence: 0.847014442857143

00:50:55.810 --> 00:50:58.390 Yeah, look, hopefully just applying some

NOTE Confidence: 0.847014442857143

00:50:58.390 --> 00:51:01.449 of these concepts so you can get close.

NOTE Confidence: 0.847014442857143

00:51:01.450 --> 00:51:03.088 Just looking at the sleep studies

NOTE Confidence: 0.847014442857143

00:51:03.088 --> 00:51:04.808 as I've alluded to at the end,

NOTE Confidence: 0.847014442857143

00:51:04.810 --> 00:51:06.306 you know, in terms of what's going on

NOTE Confidence: 0.847014442857143

00:51:06.306 --> 00:51:07.749 in terms of their pathophysiology,

NOTE Confidence: 0.847014442857143

00:51:07.750 --> 00:51:10.474 how collapsible is this airway? You know,

NOTE Confidence: 0.847014442857143

00:51:10.474 --> 00:51:12.209 are they predominantly having hypopneas,

NOTE Confidence: 0.847014442857143

00:51:12.210 --> 00:51:13.614 in which case the Airways probably

NOTE Confidence: 0.847014442857143

00:51:13.614 --> 00:51:15.309 not going to be so collapsible.

NOTE Confidence: 0.847014442857143

00:51:15.310 --> 00:51:17.926 So you can start to just look at

NOTE Confidence: 0.847014442857143

00:51:17.926 --> 00:51:20.010 the recordings and that way if you

NOTE Confidence: 0.847014442857143

00:51:20.010 --> 00:51:22.209 do happen to have a CPAP trial,

NOTE Confidence: 0.847014442857143

00:51:22.210 --> 00:51:24.466 you can look at what pressures they require,

NOTE Confidence: 0.847014442857143

00:51:24.470 --> 00:51:25.990 so you can start to map this out.

NOTE Confidence: 0.847014442857143

00:51:25.990 --> 00:51:27.790 Like OK, this person may be a candidate

NOTE Confidence: 0.847014442857143

00:51:27.790 --> 00:51:29.655 for for some of these non CPAP

NOTE Confidence: 0.847014442857143

00:51:29.655 --> 00:51:31.020 interventions just from looking at

NOTE Confidence: 0.847014442857143

00:51:31.068 --> 00:51:32.768 information that we're already collecting

NOTE Confidence: 0.847014442857143

00:51:32.768 --> 00:51:34.875 and you know potentially plug some

NOTE Confidence: 0.847014442857143

00:51:34.875 --> 00:51:37.305 of those variables into that simple.

NOTE Confidence: 0.847014442857143

00:51:37.310 --> 00:51:39.487 Whether or not they gonna lower our

NOTE Confidence: 0.847014442857143

00:51:39.487 --> 00:51:41.463 threshold in terms of the readily

NOTE Confidence: 0.847014442857143

00:51:41.463 --> 00:51:43.103 available or the availability of

NOTE Confidence: 0.847014442857143

00:51:43.103 --> 00:51:45.405 these non CPAP therapies particularly

NOTE Confidence: 0.847014442857143

00:51:45.405 --> 00:51:46.989 pharmacotherapy and others.

NOTE Confidence: 0.847014442857143

00:51:46.990 --> 00:51:49.102 Of course the the work workup

NOTE Confidence: 0.847014442857143

00:51:49.102 --> 00:51:50.510 needs to take place.

NOTE Confidence: 0.847014442857143

00:51:50.510 --> 00:51:52.286 You know we need to see those trials

NOTE Confidence: 0.847014442857143

00:51:52.286 --> 00:51:54.004 through make sure all they're safe and

NOTE Confidence: 0.847014442857143

00:51:54.004 --> 00:51:55.998 efficacious in the long term and so forth so.

NOTE Confidence: 0.847014442857143

00:51:56.000 --> 00:51:57.164 You know unfortunately that's

NOTE Confidence: 0.847014442857143

00:51:57.164 --> 00:51:59.178 that'll takes time but you know we

NOTE Confidence: 0.847014442857143

00:51:59.178 --> 00:52:00.683 and others are working hard to try

NOTE Confidence: 0.847014442857143

00:52:00.683 --> 00:52:02.256 and try and make that the case.

NOTE Confidence: 0.847014442857143

00:52:02.260 --> 00:52:04.826 But you know I think it is as I

NOTE Confidence: 0.847014442857143

00:52:04.826 --> 00:52:06.164 showed you know we're quite excited

NOTE Confidence: 0.847014442857143

00:52:06.164 --> 00:52:07.352 about those targeted therapy ones

NOTE Confidence: 0.847014442857143

00:52:07.352 --> 00:52:08.976 where we you know you start with

NOTE Confidence: 0.847014442857143

00:52:09.019 --> 00:52:10.349 an oral appliance doesn't work.

NOTE Confidence: 0.847014442857143

00:52:10.350 --> 00:52:11.758 You can add on some of these other

NOTE Confidence: 0.847014442857143

00:52:11.758 --> 00:52:13.045 things you know just adding position

NOTE Confidence: 0.847014442857143

00:52:13.045 --> 00:52:14.649 therapy alone we've got most of the

NOTE Confidence: 0.847014442857143

00:52:14.649 --> 00:52:15.987 people treated there and these were

NOTE Confidence: 0.847014442857143

00:52:15.987 --> 00:52:17.293 people that would otherwise be left

NOTE Confidence: 0.847014442857143

00:52:17.293 --> 00:52:19.240 you know kind of done you know if they

NOTE Confidence: 0.847014442857143

00:52:19.240 --> 00:52:20.717 if you didn't get them treated with

NOTE Confidence: 0.847014442857143

00:52:20.717 --> 00:52:22.648 CPAP or oral appliance then what do you do.

NOTE Confidence: 0.847014442857143

00:52:22.650 --> 00:52:24.630 Well just adding a bit of and this is

NOTE Confidence: 0.847014442857143

00:52:24.630 --> 00:52:26.087 regardless of whether or not they'll.

NOTE Confidence: 0.847014442857143

00:52:26.090 --> 00:52:27.182 Position dependent because you

NOTE Confidence: 0.847014442857143

00:52:27.182 --> 00:52:28.820 know you're still getting about 2

NOTE Confidence: 0.847014442857143

00:52:28.865 --> 00:52:30.530 centimetres of water improvement there,

NOTE Confidence: 0.847014442857143

00:52:30.530 --> 00:52:31.484 collapsibility like that.

NOTE Confidence: 0.847014442857143

00:52:31.484 --> 00:52:33.392 So I think just thinking about

NOTE Confidence: 0.847014442857143

00:52:33.392 --> 00:52:34.230 these concepts,

NOTE Confidence: 0.847014442857143

00:52:34.230 --> 00:52:34.804 you know,

NOTE Confidence: 0.847014442857143

00:52:34.804 --> 00:52:36.813 using what we've got and as more

NOTE Confidence: 0.847014442857143

00:52:36.813 --> 00:52:38.989 of these things come onto line

NOTE Confidence: 0.847014442857143

00:52:38.989 --> 00:52:40.809 and a sensible strategic way,

NOTE Confidence: 0.847014442857143

00:52:40.810 --> 00:52:42.539 we'll be able to get more solutions

NOTE Confidence: 0.847014442857143

00:52:42.539 --> 00:52:43.928 for these patients that otherwise

NOTE Confidence: 0.847014442857143

00:52:43.928 --> 00:52:45.120 fall through the cracks.

NOTE Confidence: 0.700703575

00:52:46.620 --> 00:52:47.110 So much.

NOTE Confidence: 0.911083218

00:52:49.690 --> 00:52:51.290 We have a question here.

NOTE Confidence: 0.911083218

00:52:51.290 --> 00:52:53.966 Excellent talk updated in the theme,

NOTE Confidence: 0.911083218

00:52:53.970 --> 00:52:55.490 maybe I failed to listen.

NOTE Confidence: 0.911083218

00:52:55.490 --> 00:52:57.828 Is there any data in terms of

NOTE Confidence: 0.911083218

00:52:57.828 --> 00:53:00.159 ethnicity and peak Ridge variability?

NOTE Confidence: 0.80790419

00:53:01.650 --> 00:53:05.636 Yes, they look, there is and in

NOTE Confidence: 0.80790419

00:53:05.636 --> 00:53:08.520 particular they've studied the, you know,

NOTE Confidence: 0.80790419

00:53:08.520 --> 00:53:11.523 the airway anatomy traits in in Asian

NOTE Confidence: 0.80790419

00:53:11.523 --> 00:53:13.969 populations where there tends to be

NOTE Confidence: 0.80790419

00:53:13.969 --> 00:53:16.129 a little bit more retrognathia or,

NOTE Confidence: 0.80790419

00:53:16.130 --> 00:53:18.686 you know, skeletal differences going on.

NOTE Confidence: 0.80790419

00:53:18.690 --> 00:53:22.083 But what I will say in terms of this,

NOTE Confidence: 0.80790419

00:53:22.090 --> 00:53:25.975 you know, in terms of the ethnic

NOTE Confidence: 0.80790419

00:53:25.980 --> 00:53:29.544 differences ultimately, you know,

NOTE Confidence: 0.80790419

00:53:29.544 --> 00:53:32.217 racist social constructs.

NOTE Confidence: 0.80790419

00:53:32.220 --> 00:53:34.420 So this is not, this is not anatomy,

NOTE Confidence: 0.80790419

00:53:34.420 --> 00:53:36.968 so, so or Physiology.

NOTE Confidence: 0.80790419

00:53:36.968 --> 00:53:42.320 So if we can measure the Physiology

NOTE Confidence: 0.80790419

00:53:42.320 --> 00:53:44.678 in the way that I've described,

NOTE Confidence: 0.80790419

00:53:44.680 --> 00:53:46.690 then yes, certain features as I

NOTE Confidence: 0.80790419

00:53:46.690 --> 00:53:48.515 just highlighted in the Asian

NOTE Confidence: 0.80790419

00:53:48.515 --> 00:53:50.600 population might be more prominent,

NOTE Confidence: 0.80790419

00:53:50.600 --> 00:53:53.310 but there's much more physiological

NOTE Confidence: 0.80790419

00:53:53.310 --> 00:53:56.278 variability than there is, you know,

NOTE Confidence: 0.80790419

00:53:56.278 --> 00:53:58.273 race driven variability in the

NOTE Confidence: 0.80790419

00:53:58.273 --> 00:53:59.960 physiological traits that we see.

NOTE Confidence: 0.80790419

00:53:59.960 --> 00:54:02.813 So I think it comes back to you know.

NOTE Confidence: 0.80790419

00:54:02.820 --> 00:54:03.603 Regardless of race,

NOTE Confidence: 0.80790419

00:54:03.603 --> 00:54:05.788 you want to know what is their Physiology

NOTE Confidence: 0.80790419

00:54:05.788 --> 00:54:07.909 and then you can use that information

NOTE Confidence: 0.80790419

00:54:07.909 --> 00:54:10.038 and treat them as an individual to

NOTE Confidence: 0.80790419

00:54:10.038 --> 00:54:13.029 target their therapy in this case.

NOTE Confidence: 0.80790419

00:54:13.030 --> 00:54:13.600 Great.

NOTE Confidence: 0.795054250625

00:54:13.690 --> 00:54:15.804 Thank you. And we have a question

NOTE Confidence: 0.795054250625

00:54:15.804 --> 00:54:17.562 from Doctor Yagi to one on

NOTE Confidence: 0.795054250625

00:54:17.562 --> 00:54:18.870 you to yourself. Doctor yagi.

NOTE Confidence: 0.865690943888889

00:54:21.230 --> 00:54:22.736 Sorry, Danny. Thank you so much

NOTE Confidence: 0.865690943888889

00:54:22.736 --> 00:54:24.243 for taking time out of your

NOTE Confidence: 0.865690943888889

00:54:24.243 --> 00:54:25.605 schedule to talk to us today.

NOTE Confidence: 0.865690943888889

00:54:25.610 --> 00:54:27.670 It was really clear

NOTE Confidence: 0.865690943888889

00:54:27.670 --> 00:54:30.760 presentation I put in the chat.

NOTE Confidence: 0.865690943888889

00:54:30.760 --> 00:54:32.984 How we might be able to use data

NOTE Confidence: 0.865690943888889

00:54:32.984 --> 00:54:35.390 from home sleep apnea testing and

NOTE Confidence: 0.865690943888889

00:54:35.390 --> 00:54:37.166 whether the clinical prognostic

NOTE Confidence: 0.865690943888889

00:54:37.166 --> 00:54:39.719 system that your group has developed

NOTE Confidence: 0.865690943888889

00:54:39.720 --> 00:54:41.778 whether data from HSAT could could

NOTE Confidence: 0.865690943888889

00:54:41.778 --> 00:54:44.499 inform in the in the types and

NOTE Confidence: 0.865690943888889

00:54:44.499 --> 00:54:46.107 and treatment decisions. Yeah.

NOTE Confidence: 0.865690943888889

00:54:46.107 --> 00:54:48.723 Let me look thanks very much for the

NOTE Confidence: 0.865690943888889

00:54:48.723 --> 00:54:50.863 question it it's really important

NOTE Confidence: 0.865690943888889

00:54:50.863 --> 00:54:52.607 obviously there's that balance

NOTE Confidence: 0.865690943888889

00:54:52.607 --> 00:54:54.638 between huge burden of disease

NOTE Confidence: 0.865690943888889

00:54:54.640 --> 00:54:56.705 and what I've talked about is very

NOTE Confidence: 0.865690943888889

00:54:56.705 --> 00:54:58.700 much relying on these more more

NOTE Confidence: 0.865690943888889

00:54:58.700 --> 00:55:00.788 detailed measurements or in lab PSGS.

NOTE Confidence: 0.865690943888889

00:55:00.790 --> 00:55:02.190 But of course the world is moving on.

NOTE Confidence: 0.865690943888889

00:55:02.190 --> 00:55:04.078 We've got to diagnose and and and and

NOTE Confidence: 0.865690943888889

00:55:04.078 --> 00:55:06.125 do this in in in more efficient ways.

NOTE Confidence: 0.865690943888889

00:55:06.130 --> 00:55:09.478 Now it turns out that in some of the.

NOTE Confidence: 0.857330567142857

00:55:12.900 --> 00:55:14.979 And when you do get those neurophysiological

NOTE Confidence: 0.857330567142857

00:55:14.979 --> 00:55:16.698 information with the egg and so forth,

NOTE Confidence: 0.857330567142857

00:55:16.700 --> 00:55:19.340 but actually there's probably a

NOTE Confidence: 0.857330567142857

00:55:19.340 --> 00:55:21.552 few drivers that you can get.

NOTE Confidence: 0.857330567142857

00:55:21.552 --> 00:55:24.004 So if you can get that as oxygen

NOTE Confidence: 0.857330567142857

00:55:24.004 --> 00:55:26.902 measures and in the home as well as the

NOTE Confidence: 0.857330567142857

00:55:26.902 --> 00:55:28.714 key parameters from the SLEEP study,

NOTE Confidence: 0.857330567142857

00:55:28.720 --> 00:55:30.442 you can probably still get pretty good

NOTE Confidence: 0.857330567142857

00:55:30.442 --> 00:55:31.979 estimates of what their endo types

NOTE Confidence: 0.857330567142857

00:55:31.979 --> 00:55:33.473 are from those home sleep studies.

NOTE Confidence: 0.857330567142857

00:55:33.480 --> 00:55:35.755 And very importantly I think that there's

NOTE Confidence: 0.857330567142857

00:55:35.755 --> 00:55:37.519 information in multi night testing.

NOTE Confidence: 0.857330567142857

00:55:37.520 --> 00:55:40.100 You know we know that if we do a single

NOTE Confidence: 0.857330567142857

00:55:40.173 --> 00:55:42.908 night sleep study 20 to 50% of the time.

NOTE Confidence: 0.857330567142857

00:55:42.910 --> 00:55:44.225 They're going to get the

NOTE Confidence: 0.857330567142857

00:55:44.225 --> 00:55:45.014 diagnostic category wrong.

NOTE Confidence: 0.857330567142857

00:55:45.020 --> 00:55:47.796 So, so using this technology in the home,

NOTE Confidence: 0.857330567142857

00:55:47.800 --> 00:55:48.700 even if it's simplified,

NOTE Confidence: 0.857330567142857

00:55:48.700 --> 00:55:50.050 but we could start to do

NOTE Confidence: 0.857330567142857

00:55:50.097 --> 00:55:51.197 it over multiple nights,

NOTE Confidence: 0.857330567142857

00:55:51.200 --> 00:55:53.932 we might be able to get as good

NOTE Confidence: 0.857330567142857

00:55:53.932 --> 00:55:55.864 or in fact in some cases better

NOTE Confidence: 0.857330567142857

00:55:55.864 --> 00:55:57.608 information to inform these sort

NOTE Confidence: 0.857330567142857

00:55:57.608 --> 00:55:59.016 of targeted therapy approaches.

NOTE Confidence: 0.857330567142857

00:55:59.020 --> 00:56:01.588 So absolutely that's the way of the future.

NOTE Confidence: 0.7549492

00:56:05.380 --> 00:56:08.720 Great. Thank you.

NOTE Confidence: 0.949038681428571

00:56:08.720 --> 00:56:11.597 If we don't have any other questions,

NOTE Confidence: 0.949038681428571

00:56:11.600 --> 00:56:14.736 we will wrap it up here and.

NOTE Confidence: 0.949038681428571

00:56:14.740 --> 00:56:16.700 Thank you Doctor Eckert again,

NOTE Confidence: 0.949038681428571

00:56:16.700 --> 00:56:18.000 and thank you everyone.

NOTE Confidence: 0.749264082571429

00:56:18.780 --> 00:56:22.440 She looks like Andre has a question. Oh.

NOTE Confidence: 0.85472835

00:56:23.810 --> 00:56:24.640 Is he?

NOTE Confidence: 0.7372416525

00:56:27.490 --> 00:56:29.080 Andrew, can you unmute yourself?

NOTE Confidence: 0.83695333

00:56:32.690 --> 00:56:33.870 I don't see the question.

NOTE Confidence: 0.0701561

00:56:41.510 --> 00:56:43.180 Hi, I have a question

NOTE Confidence: 0.89676687

00:56:43.190 --> 00:56:45.290 that's there. You see it?

NOTE Confidence: 0.85223052125

00:56:50.240 --> 00:56:56.520 I am. I can't see the question myself, but.

NOTE Confidence: 0.85223052125

00:56:56.520 --> 00:56:58.898 No, here was the question does

NOTE Confidence: 0.85223052125

00:56:58.900 --> 00:57:01.854 the use of oxygen and hypnotics.

NOTE Confidence: 0.85223052125

00:57:01.854 --> 00:57:05.012 Likely lead to increasing the

NOTE Confidence: 0.85223052125

00:57:05.012 --> 00:57:08.176 duration of the apnea events and and

NOTE Confidence: 0.870701435

00:57:08.190 --> 00:57:10.338 is O2 available through

NOTE Confidence: 0.936820095

00:57:10.350 --> 00:57:13.510 insurance in Australia it's.

NOTE Confidence: 0.936820095

00:57:13.510 --> 00:57:15.399 Pretty difficult for us to

NOTE Confidence: 0.792493975

00:57:15.530 --> 00:57:17.750 use O2. With sleep

NOTE Confidence: 0.733158168333333

00:57:17.760 --> 00:57:20.824 apnea. Yeah, yeah, yeah.

NOTE Confidence: 0.733158168333333

00:57:20.824 --> 00:57:22.356 Good questions.

NOTE Confidence: 0.733158168333333

00:57:22.360 --> 00:57:24.394 Look, we we have not if you take out,

NOTE Confidence: 0.733158168333333

00:57:24.400 --> 00:57:27.081 if you do not study people with

NOTE Confidence: 0.733158168333333

00:57:27.081 --> 00:57:29.099 profound hypoxemia to begin with,

NOTE Confidence: 0.733158168333333

00:57:29.100 --> 00:57:32.314 we have never seen you know.

NOTE Confidence: 0.733158168333333

00:57:32.314 --> 00:57:34.899 Major worsening in terms of

NOTE Confidence: 0.733158168333333

00:57:34.899 --> 00:57:36.916 prolongation of respiratory events

NOTE Confidence: 0.733158168333333

00:57:36.916 --> 00:57:39.614 or oxygen dips with a, you know,

NOTE Confidence: 0.733158168333333

00:57:39.614 --> 00:57:41.936 common dose of of standard hypnotics.

NOTE Confidence: 0.733158168333333

00:57:41.940 --> 00:57:45.480 The same obviously is true in

NOTE Confidence: 0.733158168333333

00:57:45.480 --> 00:57:47.935 terms of prolongation with oxygen.

NOTE Confidence: 0.733158168333333

00:57:47.935 --> 00:57:51.348 Again we have not seen that when we

NOTE Confidence: 0.733158168333333

00:57:51.348 --> 00:57:54.212 combine the two either in in those cases.

NOTE Confidence: 0.733158168333333

00:57:54.220 --> 00:57:57.178 So and to your second question,

NOTE Confidence: 0.733158168333333

00:57:57.180 --> 00:57:59.184 no, you know there there lies

NOTE Confidence: 0.733158168333333

00:57:59.184 --> 00:58:00.186 the practical issues.

NOTE Confidence: 0.733158168333333

00:58:00.190 --> 00:58:01.638 Yes, there's oxygen concentrators

NOTE Confidence: 0.733158168333333

00:58:01.638 --> 00:58:03.448 and things that are available.

NOTE Confidence: 0.733158168333333

00:58:03.450 --> 00:58:05.880 But it's not particularly um,

NOTE Confidence: 0.733158168333333

00:58:05.880 --> 00:58:07.224 yeah, well, you know,

NOTE Confidence: 0.733158168333333

00:58:07.224 --> 00:58:08.904 the costs are somewhat similar

NOTE Confidence: 0.733158168333333

00:58:08.904 --> 00:58:10.580 to a CPAP machine, but.

NOTE Confidence: 0.733158168333333

00:58:10.580 --> 00:58:12.740 We're still in this position of

NOTE Confidence: 0.733158168333333

00:58:12.740 --> 00:58:14.829 not knowing who's gonna respond,

NOTE Confidence: 0.733158168333333

00:58:14.830 --> 00:58:16.356 what the long term outcomes with it

NOTE Confidence: 0.733158168333333

00:58:16.356 --> 00:58:17.807 is with oxygen therapy and I mean

NOTE Confidence: 0.733158168333333

00:58:17.807 --> 00:58:19.425 we know it does a pretty good job

NOTE Confidence: 0.733158168333333

00:58:19.425 --> 00:58:20.757 of you know roughly halving your

NOTE Confidence: 0.733158168333333

00:58:20.757 --> 00:58:22.830 loop gain and and and can roughly

NOTE Confidence: 0.733158168333333

00:58:22.830 --> 00:58:24.450 half your sleep apnea severity.

NOTE Confidence: 0.733158168333333

00:58:24.450 --> 00:58:27.210 But in terms of that translation

NOTE Confidence: 0.733158168333333

00:58:27.210 --> 00:58:30.400 question insurance and rolling.

NOTE Confidence: 0.733158168333333

00:58:30.400 --> 00:58:33.767 As a viable uh and and economically

NOTE Confidence: 0.733158168333333

00:58:33.767 --> 00:58:36.480 yeah viable therapy you know that

NOTE Confidence: 0.733158168333333

00:58:36.480 --> 00:58:39.564 remains to be done but you know these

NOTE Confidence: 0.733158168333333

00:58:39.564 --> 00:58:41.184 this technology is always improving

NOTE Confidence: 0.733158168333333

00:58:41.184 --> 00:58:42.480 these concentrators against smaller

NOTE Confidence: 0.733158168333333

00:58:42.524 --> 00:58:44.036 and smaller and lighter and lighter.

NOTE Confidence: 0.733158168333333

00:58:44.040 --> 00:58:45.792 So conceptually you know it it

NOTE Confidence: 0.733158168333333

00:58:45.792 --> 00:58:47.513 it could be possible down the

NOTE Confidence: 0.733158168333333

00:58:47.513 --> 00:58:49.249 line but no not at the moment.

NOTE Confidence: 0.827508383

00:58:59.500 --> 00:59:01.292 Any more questions, Andre?

NOTE Confidence: 0.827508383

00:59:01.292 --> 00:59:03.980 I still can't see your question.

NOTE Confidence: 0.825591395833333

00:59:30.570 --> 00:59:32.159 Look, I know Andre said he was

NOTE Confidence: 0.825591395833333

00:59:32.159 --> 00:59:33.872 in the ICU this week, so he,

NOTE Confidence: 0.825591395833333

00:59:33.872 --> 00:59:35.349 he may have had to fly off.

NOTE Confidence: 0.825591395833333

00:59:35.350 --> 00:59:36.550 So he sent me, sent me,

NOTE Confidence: 0.825591395833333

00:59:36.550 --> 00:59:37.510 he sent me a note.

NOTE Confidence: 0.825591395833333

00:59:37.510 --> 00:59:38.998 Yeah, yeah, yeah.

NOTE Confidence: 0.888672927

00:59:39.510 --> 00:59:41.874 OK. Alright then. Thank you again

NOTE Confidence: 0.888672927

00:59:41.874 --> 00:59:44.022 so much Doctor Eckert, and thank

NOTE Confidence: 0.888672927

00:59:44.022 --> 00:59:45.738 you everyone for joining in today.

NOTE Confidence: 0.838928738333333

00:59:46.770 --> 00:59:48.738 You're very welcome. Thanks so much.

NOTE Confidence: 0.9670232575

00:59:48.890 --> 00:59:51.998 Thank you. Bye, bye.