

WEBVTT

NOTE duration:"01:02:41.2480000"

NOTE language:en-us

NOTE Confidence: 0.87638587

00:00:00.000 --> 00:00:01.950 Thank you and.

NOTE Confidence: 0.8383747

00:00:24.930 --> 00:00:26.650 Alright, I think we're ready

NOTE Confidence: 0.8383747

00:00:26.650 --> 00:00:28.026 to get started everybody.

NOTE Confidence: 0.8383747

00:00:28.030 --> 00:00:30.086 Hello, my name is Lauren Tobias

NOTE Confidence: 0.8383747

00:00:30.086 --> 00:00:32.150 and I'd like to welcome you.

NOTE Confidence: 0.8383747

00:00:32.150 --> 00:00:33.870 Doris Yale State Sleep seminar,

NOTE Confidence: 0.8383747

00:00:33.870 --> 00:00:34.719 Yale sleep seminar.

NOTE Confidence: 0.8383747

00:00:34.719 --> 00:00:36.417 This afternoon I have a few

NOTE Confidence: 0.8383747

00:00:36.417 --> 00:00:38.067 quick announcements before I

NOTE Confidence: 0.8383747

00:00:38.067 --> 00:00:39.375 introduce today's speaker.

NOTE Confidence: 0.8383747

00:00:39.380 --> 00:00:41.100 First, please take a moment

NOTE Confidence: 0.8383747

00:00:41.100 --> 00:00:42.820 to ensure that you're muted.

NOTE Confidence: 0.8383747

00:00:42.820 --> 00:00:44.535 Also, in order to receive

NOTE Confidence: 0.8383747

00:00:44.535 --> 00:00:45.907 CME credit for attendance,

NOTE Confidence: 0.8383747

00:00:45.910 --> 00:00:48.318 please see the chat room for instructions.

NOTE Confidence: 0.8383747

00:00:48.320 --> 00:00:50.665 You can text the unique ID for

NOTE Confidence: 0.8383747

00:00:50.665 --> 00:00:52.099 this conference anytime until

NOTE Confidence: 0.8383747

00:00:52.099 --> 00:00:54.295 3:15 PM if you're not already

NOTE Confidence: 0.8383747

00:00:54.295 --> 00:00:55.890 registered with Chelsea and me,

NOTE Confidence: 0.8383747

00:00:55.890 --> 00:00:58.536 you will need to do that first.

NOTE Confidence: 0.8383747

00:00:58.540 --> 00:01:00.175 If you have any questions

NOTE Confidence: 0.8383747

00:01:00.175 --> 00:01:01.156 during the presentation,

NOTE Confidence: 0.8383747

00:01:01.160 --> 00:01:03.328 I encourage you to make use of the

NOTE Confidence: 0.8383747

00:01:03.328 --> 00:01:05.512 chat room throughout the hour and

NOTE Confidence: 0.8383747

00:01:05.512 --> 00:01:07.482 recorded versions of these lectures

NOTE Confidence: 0.8383747

00:01:07.482 --> 00:01:09.759 will be available on line within two

NOTE Confidence: 0.8383747

00:01:09.759 --> 00:01:12.274 weeks at the link provided in the chat.

NOTE Confidence: 0.8383747

00:01:12.274 --> 00:01:12.600 Finally,

NOTE Confidence: 0.8383747

00:01:12.600 --> 00:01:14.544 please feel free to share the

NOTE Confidence: 0.8383747

00:01:14.544 --> 00:01:16.224 announcements for our weekly lecture  
NOTE Confidence: 0.8383747

00:01:16.224 --> 00:01:18.808 series to anyone else who may be interested,  
NOTE Confidence: 0.8383747

00:01:18.810 --> 00:01:20.415 or contact Debbie Lovejoy to  
NOTE Confidence: 0.8383747

00:01:20.415 --> 00:01:22.410 be added to our email list.  
NOTE Confidence: 0.8383747

00:01:22.410 --> 00:01:24.664 So now I'm delighted to introduce Doctor  
NOTE Confidence: 0.8383747

00:01:24.664 --> 00:01:26.658 Ulysses Magalang as our speaker today.  
NOTE Confidence: 0.8383747

00:01:26.660 --> 00:01:29.089 Doctor Magalong is a professor of medicine.  
NOTE Confidence: 0.8383747

00:01:29.090 --> 00:01:31.300 And neuroscience in the division  
NOTE Confidence: 0.8383747

00:01:31.300 --> 00:01:33.510 of pulmonary critical care and  
NOTE Confidence: 0.8383747

00:01:33.582 --> 00:01:36.066 Sleep Medicine at the Ohio State  
NOTE Confidence: 0.8383747

00:01:36.066 --> 00:01:38.229 University and director of the  
NOTE Confidence: 0.8383747

00:01:38.229 --> 00:01:39.969 OSU Sleep Medicine program.  
NOTE Confidence: 0.8383747

00:01:39.970 --> 00:01:42.938 He is a member of the American  
NOTE Confidence: 0.8383747

00:01:42.938 --> 00:01:44.210 Thoracic Society Scientific  
NOTE Confidence: 0.8383747

00:01:44.283 --> 00:01:46.473 Advisory Committee and a founding  
NOTE Confidence: 0.8383747

00:01:46.473 --> 00:01:48.663 member of the Sleep Apnea,

NOTE Confidence: 0.8383747

00:01:48.670 --> 00:01:49.972 Global Interdiscipline or

NOTE Confidence: 0.8383747

00:01:49.972 --> 00:01:50.840 Interdisciplinary Consortium,

NOTE Confidence: 0.8383747

00:01:50.840 --> 00:01:52.475 which promotes collaboration

NOTE Confidence: 0.8383747

00:01:52.475 --> 00:01:54.110 between international experts

NOTE Confidence: 0.8383747

00:01:54.110 --> 00:01:57.148 working in the field of genetics

NOTE Confidence: 0.8383747

00:01:57.148 --> 00:01:59.118 and genomics of sleep apnea.

NOTE Confidence: 0.8383747

00:01:59.120 --> 00:02:01.585 Doctor Magalong's is in an

NOTE Confidence: 0.8383747

00:02:01.585 --> 00:02:03.557 accomplished researcher whose work

NOTE Confidence: 0.8383747

00:02:03.557 --> 00:02:06.062 examines the effects of intermittent

NOTE Confidence: 0.8383747

00:02:06.062 --> 00:02:08.487 hypoxia on adipose tissue biology,

NOTE Confidence: 0.8383747

00:02:08.490 --> 00:02:10.955 particularly its effects on glucose

NOTE Confidence: 0.8383747

00:02:10.955 --> 00:02:13.420 control and diabetes and atherogenesis.

NOTE Confidence: 0.8383747

00:02:13.420 --> 00:02:16.864 His funding sources include the NIH an,

NOTE Confidence: 0.8383747

00:02:16.870 --> 00:02:18.325 the ASM Foundation,

NOTE Confidence: 0.8383747

00:02:18.325 --> 00:02:20.750 and he has projects including

NOTE Confidence: 0.8383747

00:02:20.750 --> 00:02:22.780 looking at the genetic,  
NOTE Confidence: 0.8383747

00:02:22.780 --> 00:02:23.273 epigenetic,  
NOTE Confidence: 0.8383747

00:02:23.273 --> 00:02:25.738 and metabolomic basis of different  
NOTE Confidence: 0.8383747

00:02:25.738 --> 00:02:27.217 subtypes of OSA,  
NOTE Confidence: 0.8383747

00:02:27.220 --> 00:02:29.790 and another project looking at.  
NOTE Confidence: 0.8383747

00:02:29.790 --> 00:02:31.538 Transcranial direct current stimulation  
NOTE Confidence: 0.8383747

00:02:31.538 --> 00:02:33.286 therapy for central hypersomnia.  
NOTE Confidence: 0.8383747

00:02:33.290 --> 00:02:35.034 He regularly speaks nationally  
NOTE Confidence: 0.8383747

00:02:35.034 --> 00:02:35.906 and internationally,  
NOTE Confidence: 0.8383747

00:02:35.910 --> 00:02:38.335 and topics including phenotypes of  
NOTE Confidence: 0.8383747

00:02:38.335 --> 00:02:40.760 sleep apnea and the neurobiology  
NOTE Confidence: 0.8383747

00:02:40.835 --> 00:02:43.091 of breathing and I am delighted  
NOTE Confidence: 0.8383747

00:02:43.091 --> 00:02:46.410 that he's here today to give a talk  
NOTE Confidence: 0.8383747

00:02:46.410 --> 00:02:48.146 entitled RCT's of cardiovascular  
NOTE Confidence: 0.8383747

00:02:48.146 --> 00:02:50.292 outcomes and obstructive sleep apnea.  
NOTE Confidence: 0.8383747

00:02:50.292 --> 00:02:53.830 Is it time for an alternative trial design,

NOTE Confidence: 0.8383747

00:02:53.830 --> 00:02:59.780 and with that I will turn it over to you.

NOTE Confidence: 0.8383747

00:02:59.780 --> 00:03:00.160 Thanks,

NOTE Confidence: 0.8716507

00:03:00.160 --> 00:03:01.303 Lauren, good afternoon.

NOTE Confidence: 0.8716507

00:03:01.303 --> 00:03:02.827 Thanks for inviting me.

NOTE Confidence: 0.8716507

00:03:02.830 --> 00:03:05.050 So when I first received the

NOTE Confidence: 0.8716507

00:03:05.050 --> 00:03:07.001 invitation I thought about presenting

NOTE Confidence: 0.8716507

00:03:07.001 --> 00:03:09.383 some of the animal studies that

NOTE Confidence: 0.8716507

00:03:09.383 --> 00:03:11.589 we're doing here at Ohio State.

NOTE Confidence: 0.8716507

00:03:11.590 --> 00:03:12.733 However, you know,

NOTE Confidence: 0.8716507

00:03:12.733 --> 00:03:15.400 given the audience of this seminar series,

NOTE Confidence: 0.8716507

00:03:15.400 --> 00:03:17.310 I quickly changed my mind.

NOTE Confidence: 0.8716507

00:03:17.310 --> 00:03:19.482 So this afternoon we're going to

NOTE Confidence: 0.8716507

00:03:19.482 --> 00:03:21.880 talk about humans and that rodents.

NOTE Confidence: 0.9003723

00:03:24.420 --> 00:03:27.066 So this is my first slide.

NOTE Confidence: 0.9003723

00:03:27.070 --> 00:03:30.500 I have no conflict of interest to

NOTE Confidence: 0.9003723

00:03:30.500 --> 00:03:34.049 report in relation to this presentation.  
NOTE Confidence: 0.9003723

00:03:34.050 --> 00:03:39.026 Let me start with this headline from 2017.  
NOTE Confidence: 0.9003723

00:03:39.030 --> 00:03:43.440 From CNN Health stating that sleep apnea's  
NOTE Confidence: 0.9003723

00:03:43.440 --> 00:03:47.040 CPAP machine doesn't cut heart risks.  
NOTE Confidence: 0.9003723

00:03:47.040 --> 00:03:51.376 And of course the article is referring to.  
NOTE Confidence: 0.9003723

00:03:51.380 --> 00:03:53.920 The now famous Safe Study,  
NOTE Confidence: 0.9003723

00:03:53.920 --> 00:03:59.198 its largest trial so far up CPAP.  
NOTE Confidence: 0.9003723

00:03:59.200 --> 00:04:01.585 In in cardiovascular disease that  
NOTE Confidence: 0.9003723

00:04:01.585 --> 00:04:04.538 was published in the New England  
NOTE Confidence: 0.9003723

00:04:04.538 --> 00:04:07.430 Journal of Medicine in late 2016,  
NOTE Confidence: 0.9003723

00:04:07.430 --> 00:04:10.944 and the studies show that CPAP did  
NOTE Confidence: 0.9003723

00:04:10.944 --> 00:04:13.438 not prevent cardiovascular events in  
NOTE Confidence: 0.9003723

00:04:13.438 --> 00:04:16.150 patients with moderate to severe OSA  
NOTE Confidence: 0.9003723

00:04:16.150 --> 00:04:19.449 and stab Lish cardiovascular disease.  
NOTE Confidence: 0.9003723

00:04:19.450 --> 00:04:22.502 It did confirm results of prior studies  
NOTE Confidence: 0.9003723

00:04:22.502 --> 00:04:25.339 that CPAP improve daytime sleepiness,

NOTE Confidence: 0.9003723

00:04:25.340 --> 00:04:28.740 health related quality of life.

NOTE Confidence: 0.9003723

00:04:28.740 --> 00:04:31.020 And mood.

NOTE Confidence: 0.9003723

00:04:31.020 --> 00:04:33.996 So in the next 40 minutes or So

NOTE Confidence: 0.9003723

00:04:33.996 --> 00:04:36.698 what I'm going to talk about?

NOTE Confidence: 0.9003723

00:04:36.700 --> 00:04:38.948 RCT's cardiovascular outcomes in

NOTE Confidence: 0.9003723

00:04:38.948 --> 00:04:42.320 OSA and biases in this RCT's.

NOTE Confidence: 0.9003723

00:04:42.320 --> 00:04:44.560 However, before before that,

NOTE Confidence: 0.9003723

00:04:44.560 --> 00:04:47.920 I'm gonna that's on a little

NOTE Confidence: 0.9003723

00:04:48.026 --> 00:04:50.190 bit about OSA disease,

NOTE Confidence: 0.9003723

00:04:50.190 --> 00:04:53.015 heterogeneity as well as some

NOTE Confidence: 0.9003723

00:04:53.015 --> 00:04:55.840 of the preclinical and large

NOTE Confidence: 0.9003723

00:04:55.944 --> 00:04:58.672 epidemiological studies that have

NOTE Confidence: 0.9003723

00:04:58.672 --> 00:05:02.764 been done and published that you're.

NOTE Confidence: 0.9003723

00:05:02.770 --> 00:05:06.016 All familiar with just as a

NOTE Confidence: 0.9003723

00:05:06.016 --> 00:05:08.180 review to put the.

NOTE Confidence: 0.9003723



00:05:08.180 --> 00:05:10.930 Results of the RCT's in  
NOTE Confidence: 0.9003723

00:05:10.930 --> 00:05:12.580 the proper perspective.  
NOTE Confidence: 0.9003723

00:05:12.580 --> 00:05:15.298 And then finally we will discuss  
NOTE Confidence: 0.9003723

00:05:15.298 --> 00:05:17.760 alternative designs for future studies.  
NOTE Confidence: 0.9003723

00:05:17.760 --> 00:05:19.078 In particular,  
NOTE Confidence: 0.9003723

00:05:19.078 --> 00:05:22.373 we're going to touch on  
NOTE Confidence: 0.9003723

00:05:22.373 --> 00:05:24.350 propensity score matching.  
NOTE Confidence: 0.9003723

00:05:24.350 --> 00:05:27.790 So this is the famous Sir Bradford Hill  
NOTE Confidence: 0.9003723

00:05:27.790 --> 00:05:31.692 who in the 60s published the criteria  
NOTE Confidence: 0.9003723

00:05:31.692 --> 00:05:34.637 for the assessment of causation.  
NOTE Confidence: 0.9003723

00:05:34.640 --> 00:05:38.222 What I have listed here are some of the  
NOTE Confidence: 0.9003723

00:05:38.222 --> 00:05:40.861 criteria as well as the corresponding  
NOTE Confidence: 0.9003723

00:05:40.861 --> 00:05:44.628 types of studies in the right side to  
NOTE Confidence: 0.9003723

00:05:44.628 --> 00:05:47.168 fulfill the criteria for causation.  
NOTE Confidence: 0.9003723

00:05:47.170 --> 00:05:49.622 So mechanistic and preclinical  
NOTE Confidence: 0.9003723

00:05:49.622 --> 00:05:52.074 experiments both in animals.

NOTE Confidence: 0.9003723

00:05:52.080 --> 00:05:55.881 In humans are typically done to explore

NOTE Confidence: 0.9003723

00:05:55.881 --> 00:05:58.680 the biologic plausibility of causation.

NOTE Confidence: 0.9003723

00:05:58.680 --> 00:06:00.945 Epidemiological cross sectional

NOTE Confidence: 0.9003723

00:06:00.945 --> 00:06:03.965 studies showed the strength.

NOTE Confidence: 0.9003723

00:06:03.970 --> 00:06:08.422 Consistency and dose response of the

NOTE Confidence: 0.9003723

00:06:08.422 --> 00:06:11.390 Association while longitudinal studies.

NOTE Confidence: 0.9003723

00:06:11.390 --> 00:06:13.778 Show that the timing is right,

NOTE Confidence: 0.9003723

00:06:13.780 --> 00:06:16.180 you know the chronology is right,

NOTE Confidence: 0.9003723

00:06:16.180 --> 00:06:18.170 and then finally you have.

NOTE Confidence: 0.9003723

00:06:18.170 --> 00:06:19.770 Of course interventional studies

NOTE Confidence: 0.9003723

00:06:19.770 --> 00:06:21.370 which can be observation,

NOTE Confidence: 0.9003723

00:06:21.370 --> 00:06:24.156 ull or in the form of RCT.

NOTE Confidence: 0.9003723

00:06:24.160 --> 00:06:26.320 So randomized control trials that are

NOTE Confidence: 0.9003723

00:06:26.320 --> 00:06:28.950 used to evaluate the treatment effects.

NOTE Confidence: 0.82505476

00:06:31.230 --> 00:06:34.198 As far as treatment trials are concerned,

NOTE Confidence: 0.82505476

00:06:34.200 --> 00:06:37.350 you know proponents, of course of evidence  
NOTE Confidence: 0.82505476

00:06:37.350 --> 00:06:40.257 based medicine state that there is a  
NOTE Confidence: 0.82505476

00:06:40.257 --> 00:06:42.483 hierarchy of evidence with RCT's and  
NOTE Confidence: 0.82505476

00:06:42.561 --> 00:06:44.736 systematic reviews and meta analysis  
NOTE Confidence: 0.82505476

00:06:44.736 --> 00:06:47.470 occupying the top of the triangle.  
NOTE Confidence: 0.82505476

00:06:47.470 --> 00:06:51.320 And the reason for that is indeed  
NOTE Confidence: 0.82505476

00:06:51.320 --> 00:06:54.528 the quality of evidence shown with  
NOTE Confidence: 0.82505476

00:06:54.528 --> 00:06:58.568 the error on the right hand side is  
NOTE Confidence: 0.82505476

00:06:58.568 --> 00:07:01.837 higher from the bottom to the top.  
NOTE Confidence: 0.82505476

00:07:01.840 --> 00:07:06.736 And mainly because of the effects  
NOTE Confidence: 0.82505476

00:07:06.736 --> 00:07:08.368 of confounding.  
NOTE Confidence: 0.82505476

00:07:08.370 --> 00:07:10.050 As shown on the left,  
NOTE Confidence: 0.82505476

00:07:10.050 --> 00:07:12.730 the increasing arrows on the left hand side.  
NOTE Confidence: 0.90453327

00:07:15.290 --> 00:07:18.235 However, there are situations where  
NOTE Confidence: 0.90453327

00:07:18.235 --> 00:07:21.970 randomization is not possible or ethical.  
NOTE Confidence: 0.90453327

00:07:21.970 --> 00:07:23.515 So for example,

NOTE Confidence: 0.90453327

00:07:23.515 --> 00:07:27.120 it would be unethical to randomize to

NOTE Confidence: 0.90453327

00:07:27.226 --> 00:07:31.120 no smoking versus versus smoking.

NOTE Confidence: 0.90453327

00:07:31.120 --> 00:07:33.808 And this is to illustrate this point.

NOTE Confidence: 0.90453327

00:07:33.810 --> 00:07:36.192 This is an article published in

NOTE Confidence: 0.90453327

00:07:36.192 --> 00:07:38.419 the Christmas edition of The BMJ.

NOTE Confidence: 0.90453327

00:07:38.420 --> 00:07:41.492 You know there they are known to publish

NOTE Confidence: 0.90453327

00:07:41.492 --> 00:07:44.948 this kind of articles around Christmas time.

NOTE Confidence: 0.90453327

00:07:44.950 --> 00:07:47.956 And this manuscript addresses the issue

NOTE Confidence: 0.90453327

00:07:47.956 --> 00:07:51.155 that parachutes reduces the risk of

NOTE Confidence: 0.90453327

00:07:51.155 --> 00:07:53.395 injury after gravitational challenge,

NOTE Confidence: 0.90453327

00:07:53.400 --> 00:07:56.120 but their effectiveness has

NOTE Confidence: 0.90453327

00:07:56.120 --> 00:07:59.520 not been proven by RCT's.

NOTE Confidence: 0.90453327

00:07:59.520 --> 00:08:01.884 So they perform a systematic review

NOTE Confidence: 0.90453327

00:08:01.884 --> 00:08:04.370 and found of course that know

NOTE Confidence: 0.90453327

00:08:04.370 --> 00:08:06.465 our cities have been performed,

NOTE Confidence: 0.90453327

00:08:06.470 --> 00:08:09.067 and they conclude that the basis for  
NOTE Confidence: 0.90453327

00:08:09.067 --> 00:08:11.789 power should use is purely observation.  
NOTE Confidence: 0.90453327

00:08:11.790 --> 00:08:13.850 ULL and it's apparent efficacy  
NOTE Confidence: 0.90453327

00:08:13.850 --> 00:08:15.498 could potentially be explained  
NOTE Confidence: 0.90453327

00:08:15.498 --> 00:08:17.519 by a healthy cohort effect.  
NOTE Confidence: 0.90453327

00:08:17.520 --> 00:08:18.474 That is,  
NOTE Confidence: 0.90453327

00:08:18.474 --> 00:08:21.336 those individuals who jumped from an  
NOTE Confidence: 0.90453327

00:08:21.336 --> 00:08:23.806 airplane without without a parachute  
NOTE Confidence: 0.90453327

00:08:23.806 --> 00:08:26.680 are likely to be mentally unhealthy.  
NOTE Confidence: 0.90453327

00:08:26.680 --> 00:08:29.329 And that individuals.  
NOTE Confidence: 0.90453327

00:08:29.330 --> 00:08:31.160 Who insist that all intervention  
NOTE Confidence: 0.90453327

00:08:31.160 --> 00:08:33.248 interventions need to be validated by  
NOTE Confidence: 0.90453327

00:08:33.248 --> 00:08:36.488 our CPS? Need to come down to earth.  
NOTE Confidence: 0.90453327

00:08:36.490 --> 00:08:37.249 With a bomb.  
NOTE Confidence: 0.8304738

00:08:39.290 --> 00:08:41.870 Of course they could have answered  
NOTE Confidence: 0.8304738

00:08:41.870 --> 00:08:44.609 your question had they included all

NOTE Confidence: 0.8304738

00:08:44.609 --> 00:08:47.892 observational data and not only are cities,

NOTE Confidence: 0.8304738

00:08:47.900 --> 00:08:51.050 so it turns out that the US

NOTE Confidence: 0.8304738

00:08:51.050 --> 00:08:52.400 Parachute Association registers

NOTE Confidence: 0.8304738

00:08:52.479 --> 00:08:55.149 every single jump from an airplane.

NOTE Confidence: 0.80246806

00:08:57.230 --> 00:08:59.660 Of course, with the parachute.

NOTE Confidence: 0.80246806

00:08:59.660 --> 00:09:04.160 And in 2007 there were over 2 million jumps,

NOTE Confidence: 0.80246806

00:09:04.160 --> 00:09:07.660 resulting in 821 injuries and 18 deaths,

NOTE Confidence: 0.80246806

00:09:07.660 --> 00:09:10.485 so that's a relative risk

NOTE Confidence: 0.80246806

00:09:10.485 --> 00:09:12.745 reduction of about 99.9%.

NOTE Confidence: 0.80246806

00:09:12.750 --> 00:09:14.540 A huge can argue so.

NOTE Confidence: 0.80246806

00:09:14.540 --> 00:09:18.180 Huge effect size that cannot be ignored.

NOTE Confidence: 0.80246806

00:09:18.180 --> 00:09:20.400 So I have to be honest,

NOTE Confidence: 0.80246806

00:09:20.400 --> 00:09:22.290 I hesitated to use example

NOTE Confidence: 0.80246806

00:09:22.290 --> 00:09:24.180 because now it's probably the

NOTE Confidence: 0.80246806

00:09:24.251 --> 00:09:26.357 only the only slide that you

NOTE Confidence: 0.80246806

00:09:26.357 --> 00:09:28.170 will remember from this talk.  
NOTE Confidence: 0.8445632

00:09:30.890 --> 00:09:33.548 But observation ULL study set value,  
NOTE Confidence: 0.8445632

00:09:33.550 --> 00:09:36.220 but they still have to be.  
NOTE Confidence: 0.8445632

00:09:36.220 --> 00:09:39.540 The methods should be rigorous.  
NOTE Confidence: 0.8445632

00:09:39.540 --> 00:09:43.229 And I I would present argument that  
NOTE Confidence: 0.8445632

00:09:43.229 --> 00:09:45.563 perhaps propensity score matching  
NOTE Confidence: 0.8445632

00:09:45.563 --> 00:09:49.517 provides as meta methodology to robustly  
NOTE Confidence: 0.8445632

00:09:49.517 --> 00:09:52.290 assess the cardiovascular benefit.  
NOTE Confidence: 0.8445632

00:09:52.290 --> 00:09:55.335 Of CPAP in in real world patients.  
NOTE Confidence: 0.6602841

00:09:57.430 --> 00:10:00.118 So let's talk about OSA disease heterogen.  
NOTE Confidence: 0.6602841

00:10:00.120 --> 00:10:04.630 Nyati we've been at Ohio State.  
NOTE Confidence: 0.6602841

00:10:04.630 --> 00:10:07.264 We've been actively participating in an  
NOTE Confidence: 0.6602841

00:10:07.264 --> 00:10:09.020 international consortium called Sajik.  
NOTE Confidence: 0.6602841

00:10:09.020 --> 00:10:12.248 As Lauren alluded to.  
NOTE Confidence: 0.6602841

00:10:12.250 --> 00:10:13.642 You know there's there's.  
NOTE Confidence: 0.6602841

00:10:13.642 --> 00:10:15.730 There's two sides in the US.

NOTE Confidence: 0.6602841  
00:10:15.730 --> 00:10:17.118 There's two in Australia,  
NOTE Confidence: 0.6602841  
00:10:17.118 --> 00:10:18.506 a couple in Europe,  
NOTE Confidence: 0.6602841  
00:10:18.510 --> 00:10:21.898 and then the rest in in Asia.  
NOTE Confidence: 0.6602841  
00:10:21.900 --> 00:10:24.876 And one of the object objectives of Sajik  
NOTE Confidence: 0.6602841  
00:10:24.876 --> 00:10:28.274 is to establish a large multinational  
NOTE Confidence: 0.6602841  
00:10:28.274 --> 00:10:30.846 cohort with detailed phenotyping.  
NOTE Confidence: 0.6602841  
00:10:30.850 --> 00:10:34.648 To understand common and ethnicity specific  
NOTE Confidence: 0.6602841  
00:10:34.648 --> 00:10:38.499 always say presentations and risk profiles.  
NOTE Confidence: 0.6602841  
00:10:38.500 --> 00:10:40.790 So sleep apnea, of course,  
NOTE Confidence: 0.6602841  
00:10:40.790 --> 00:10:43.526 is a heterogeneous disease that's that.  
NOTE Confidence: 0.6602841  
00:10:43.530 --> 00:10:46.519 Is 2 patients with the same severity  
NOTE Confidence: 0.6602841  
00:10:46.519 --> 00:10:49.065 of the condition may present  
NOTE Confidence: 0.6602841  
00:10:49.065 --> 00:10:51.429 with totally different symptoms.  
NOTE Confidence: 0.6602841  
00:10:51.430 --> 00:10:55.138 And using cluster analysis we published  
NOTE Confidence: 0.6602841  
00:10:55.138 --> 00:10:59.762 an article about two years ago showing  
NOTE Confidence: 0.6602841



00:10:59.762 --> 00:11:03.162 that indeed there are different  
NOTE Confidence: 0.6602841

00:11:03.162 --> 00:11:06.178 symptom clusters of sleep apnea.  
NOTE Confidence: 0.6602841

00:11:06.180 --> 00:11:10.128 And they are the consist of  
NOTE Confidence: 0.6602841

00:11:10.128 --> 00:11:13.893 obstructive sleep apnea patients with  
NOTE Confidence: 0.6602841

00:11:13.893 --> 00:11:16.938 predominantly insomnia symptoms.  
NOTE Confidence: 0.6602841

00:11:16.940 --> 00:11:19.600 The typical OSA with excessive  
NOTE Confidence: 0.6602841

00:11:19.600 --> 00:11:23.775 sleepiness as well as the third class  
NOTE Confidence: 0.6602841

00:11:23.775 --> 00:11:27.305 are composed of relatively asymptomatic.  
NOTE Confidence: 0.6602841

00:11:27.310 --> 00:11:30.748 Always say patience.  
NOTE Confidence: 0.6602841

00:11:30.750 --> 00:11:32.430 So what is clustering?  
NOTE Confidence: 0.6602841

00:11:32.430 --> 00:11:34.530 I probably don't need to.  
NOTE Confidence: 0.6602841

00:11:34.530 --> 00:11:39.570 Tell this group about this since.  
NOTE Confidence: 0.6602841

00:11:39.570 --> 00:11:42.550 Claire and doctors in truck.  
NOTE Confidence: 0.6602841

00:11:42.550 --> 00:11:46.852 Actually at Publix up articles about  
NOTE Confidence: 0.6602841

00:11:46.852 --> 00:11:50.369 clustering cluster analysis begins with  
NOTE Confidence: 0.6602841

00:11:50.369 --> 00:11:53.639 a predefined set of input variables

NOTE Confidence: 0.6602841

00:11:53.639 --> 00:11:57.199 targeted to a specific question.

NOTE Confidence: 0.6602841

00:11:57.200 --> 00:12:01.680 Example other symptom based subtypes of OSA.

NOTE Confidence: 0.6602841

00:12:01.680 --> 00:12:04.770 You then apply a clustering algorithm

NOTE Confidence: 0.6602841

00:12:04.770 --> 00:12:09.224 and an many are available to group the

NOTE Confidence: 0.6602841

00:12:09.224 --> 00:12:12.662 patients such that within a cluster.

NOTE Confidence: 0.6602841

00:12:12.670 --> 00:12:15.784 Patients are as similar as possible

NOTE Confidence: 0.6602841

00:12:15.784 --> 00:12:18.446 and then between clastres they

NOTE Confidence: 0.6602841

00:12:18.446 --> 00:12:20.926 are as dissimilar as possible.

NOTE Confidence: 0.6602841

00:12:20.930 --> 00:12:23.990 The clustering method is unbiased,

NOTE Confidence: 0.6602841

00:12:23.990 --> 00:12:26.862 meaning it is unsupervised

NOTE Confidence: 0.6602841

00:12:26.862 --> 00:12:30.452 and typically uses the lowest.

NOTE Confidence: 0.6602841

00:12:30.460 --> 00:12:34.204 Value of the so-called BICR valuation

NOTE Confidence: 0.6602841

00:12:34.204 --> 00:12:37.332 information criteria to define the

NOTE Confidence: 0.6602841

00:12:37.332 --> 00:12:40.554 optimal number of number of clusters.

NOTE Confidence: 0.6602841

00:12:40.560 --> 00:12:42.888 So this table is is busy,

NOTE Confidence: 0.6602841

00:12:42.890 --> 00:12:46.994 but it's just meant to simply show the  
NOTE Confidence: 0.6602841

00:12:46.994 --> 00:12:50.130 symptom questions and there's a variety.  
NOTE Confidence: 0.6602841

00:12:50.130 --> 00:12:52.560 To define the clusters that  
NOTE Confidence: 0.6602841

00:12:52.560 --> 00:12:54.990 was used in our study.  
NOTE Confidence: 0.6602841

00:12:54.990 --> 00:12:57.195 Shows the characteristic's of the  
NOTE Confidence: 0.6602841

00:12:57.195 --> 00:12:59.885 three clusters with the value side  
NOTE Confidence: 0.6602841

00:12:59.885 --> 00:13:01.930 light that that helped define.  
NOTE Confidence: 0.6602841

00:13:01.930 --> 00:13:04.035 You know this this clusters  
NOTE Confidence: 0.6602841

00:13:04.035 --> 00:13:05.719 in different colors there.  
NOTE Confidence: 0.86681

00:13:09.490 --> 00:13:12.080 So the first clustering study was actually  
NOTE Confidence: 0.86681

00:13:12.080 --> 00:13:15.477 done in a clinical population in Iceland,  
NOTE Confidence: 0.86681

00:13:15.480 --> 00:13:17.928 and the results are shown here  
NOTE Confidence: 0.86681

00:13:17.928 --> 00:13:21.050 in the on the left hand side.  
NOTE Confidence: 0.86681

00:13:21.050 --> 00:13:25.594 What is known as the Ice Axe study?  
NOTE Confidence: 0.86681

00:13:25.600 --> 00:13:29.275 Showing indeed that there are three clusters  
NOTE Confidence: 0.86681

00:13:29.275 --> 00:13:32.947 and that that's shown on the left side.

NOTE Confidence: 0.86681

00:13:32.950 --> 00:13:36.374 And what is not known after that article,

NOTE Confidence: 0.86681

00:13:36.380 --> 00:13:39.082 as Publius is that if the classes

NOTE Confidence: 0.86681

00:13:39.082 --> 00:13:42.429 are unique to Iceland with its

NOTE Confidence: 0.86681

00:13:42.429 --> 00:13:44.526 relatively homogeneous population?

NOTE Confidence: 0.86681

00:13:44.530 --> 00:13:47.450 We did find in our paper that the

NOTE Confidence: 0.86681

00:13:47.450 --> 00:13:50.950 same 3 classes generalize in an

NOTE Confidence: 0.86681

00:13:50.950 --> 00:13:54.295 international sample of clinic patients,

NOTE Confidence: 0.86681

00:13:54.300 --> 00:13:57.378 although with some what you know,

NOTE Confidence: 0.86681

00:13:57.380 --> 00:14:00.770 different prevalence of the insomnia

NOTE Confidence: 0.86681

00:14:00.770 --> 00:14:03.482 and minimally symptomatic groups

NOTE Confidence: 0.86681

00:14:03.482 --> 00:14:06.618 as shown in the figure here.

NOTE Confidence: 0.86681

00:14:06.620 --> 00:14:08.068 The sleeping group remained

NOTE Confidence: 0.86681

00:14:08.068 --> 00:14:09.516 constant at about 40%,

NOTE Confidence: 0.86681

00:14:09.520 --> 00:14:10.676 and by the way,

NOTE Confidence: 0.86681

00:14:10.676 --> 00:14:12.891 I just want to point out that

NOTE Confidence: 0.86681

00:14:12.891 --> 00:14:14.916 the responses that defined the  
NOTE Confidence: 0.86681

00:14:14.916 --> 00:14:17.741 sleepy group was not solely on the  
NOTE Confidence: 0.86681

00:14:17.741 --> 00:14:20.003 basis of the Epworth score score,  
NOTE Confidence: 0.86681

00:14:20.010 --> 00:14:22.558 but that was all that was that  
NOTE Confidence: 0.86681

00:14:22.558 --> 00:14:24.000 was part of it.  
NOTE Confidence: 0.81988186

00:14:26.510 --> 00:14:29.470 So this three symptoms sub  
NOTE Confidence: 0.81988186

00:14:29.470 --> 00:14:32.430 subtypes are found in both.  
NOTE Confidence: 0.81988186

00:14:32.430 --> 00:14:35.860 In both clinical and community  
NOTE Confidence: 0.81988186

00:14:35.860 --> 00:14:37.918 based samples worldwide.  
NOTE Confidence: 0.81988186

00:14:37.920 --> 00:14:39.628 So that's the original  
NOTE Confidence: 0.81988186

00:14:39.628 --> 00:14:41.763 I sax study in Iceland.  
NOTE Confidence: 0.81988186

00:14:41.770 --> 00:14:44.770 This is our study in Sajik  
NOTE Confidence: 0.81988186

00:14:44.770 --> 00:14:46.770 which we compared to.  
NOTE Confidence: 0.81988186

00:14:46.770 --> 00:14:50.010 Up the the nine Iceland,  
NOTE Confidence: 0.81988186

00:14:50.010 --> 00:14:53.496 we also have a in the paper.  
NOTE Confidence: 0.81988186

00:14:53.500 --> 00:14:57.028 There was a second group of Iceland

NOTE Confidence: 0.81988186

00:14:57.028 --> 00:14:59.290 patients that basically reproduced

NOTE Confidence: 0.81988186

00:14:59.290 --> 00:15:02.570 their their their original finding.

NOTE Confidence: 0.81988186

00:15:02.570 --> 00:15:06.850 And this is been shown also in a

NOTE Confidence: 0.81988186

00:15:06.850 --> 00:15:10.050 population based cohort in South Korea

NOTE Confidence: 0.81988186

00:15:10.050 --> 00:15:14.709 as well as in Europe and most recently,

NOTE Confidence: 0.81988186

00:15:14.710 --> 00:15:18.028 although this is not published yet,

NOTE Confidence: 0.81988186

00:15:18.030 --> 00:15:21.189 but it's been.

NOTE Confidence: 0.81988186

00:15:21.190 --> 00:15:23.038 Found and generalized,

NOTE Confidence: 0.81988186

00:15:23.038 --> 00:15:25.502 the three subtypes generalized

NOTE Confidence: 0.81988186

00:15:25.502 --> 00:15:28.869 to the Canadian biobank samples.

NOTE Confidence: 0.8828786

00:15:33.080 --> 00:15:37.805 And most importantly, so this is a.

NOTE Confidence: 0.8828786

00:15:37.810 --> 00:15:39.790 A study that was published

NOTE Confidence: 0.8828786

00:15:39.790 --> 00:15:42.273 in the Blue Journal by Diego

NOTE Confidence: 0.8828786

00:15:42.273 --> 00:15:44.769 Mazzotti out of the pen group.

NOTE Confidence: 0.8828786

00:15:44.770 --> 00:15:46.782 In 2019, recent analysis.

NOTE Confidence: 0.8828786

00:15:46.782 --> 00:15:50.444 So this is a re analysis of  
NOTE Confidence: 0.8828786

00:15:50.444 --> 00:15:53.129 the Sleep Heart Health study.  
NOTE Confidence: 0.8828786

00:15:53.130 --> 00:15:57.990 And this indicates that the  
NOTE Confidence: 0.8828786

00:15:57.990 --> 00:16:00.906 increased cardiovascular risk.  
NOTE Confidence: 0.8828786

00:16:00.910 --> 00:16:03.997 Would always say is driven by patients  
NOTE Confidence: 0.8828786

00:16:03.997 --> 00:16:06.559 in the excessively sleepy subtype.  
NOTE Confidence: 0.8828786

00:16:06.560 --> 00:16:10.879 So these are survival plots of knew,  
NOTE Confidence: 0.8828786

00:16:10.880 --> 00:16:11.497 incident.  
NOTE Confidence: 0.8828786

00:16:11.497 --> 00:16:13.348 Coronary heart disease,  
NOTE Confidence: 0.8828786

00:16:13.348 --> 00:16:15.816 knew incident cardiovascular disease,  
NOTE Confidence: 0.8828786

00:16:15.820 --> 00:16:19.110 and knew incident heart failure  
NOTE Confidence: 0.8828786

00:16:19.110 --> 00:16:22.400 and after adjusting for covariates  
NOTE Confidence: 0.8828786

00:16:22.500 --> 00:16:25.686 in the in the adjusted analysis,  
NOTE Confidence: 0.8828786

00:16:25.690 --> 00:16:28.595 it's only this excessively sleepy  
NOTE Confidence: 0.8828786

00:16:28.595 --> 00:16:31.500 subtype that predicted the occurrence  
NOTE Confidence: 0.8828786

00:16:31.582 --> 00:16:33.709 of cardiovascular disease,

NOTE Confidence: 0.8828786

00:16:33.710 --> 00:16:37.838 and that's perhaps shown better here.

NOTE Confidence: 0.8828786

00:16:37.840 --> 00:16:40.279 In this figure.

NOTE Confidence: 0.8828786

00:16:40.280 --> 00:16:44.879 In the sleep part field study there was a.

NOTE Confidence: 0.8828786

00:16:44.880 --> 00:16:48.230 Another group called moderately sleepy,

NOTE Confidence: 0.8828786

00:16:48.230 --> 00:16:51.085 but it's the excessively sleepy

NOTE Confidence: 0.8828786

00:16:51.085 --> 00:16:55.004 subgroup where that had the increased

NOTE Confidence: 0.8828786

00:16:55.004 --> 00:16:58.194 cardiovascular risk, Interestingly.

NOTE Confidence: 0.8828786

00:16:58.194 --> 00:17:05.718 Sleepy patients or subjects without OSA?

NOTE Confidence: 0.8828786

00:17:05.720 --> 00:17:07.046 That wasn't there,

NOTE Confidence: 0.8828786

00:17:07.046 --> 00:17:09.698 not at risk for future garbage.

NOTE Confidence: 0.8828786

00:17:09.700 --> 00:17:12.090 Cardiovascular events.

NOTE Confidence: 0.8828786

00:17:12.090 --> 00:17:14.138 So, just to summarize,

NOTE Confidence: 0.8828786

00:17:14.138 --> 00:17:16.698 there are three symptom clusters

NOTE Confidence: 0.8828786

00:17:16.698 --> 00:17:19.512 that generalize the moderate severe

NOTE Confidence: 0.8828786

00:17:19.512 --> 00:17:22.282 OSA patients in both community

NOTE Confidence: 0.8828786



00:17:22.282 --> 00:17:24.379 and clinical samples.  
NOTE Confidence: 0.8828786

00:17:24.380 --> 00:17:27.338 The OSA cardiovascular risk comes from  
NOTE Confidence: 0.8828786

00:17:27.338 --> 00:17:29.990 only the excessively sleepy subtype.  
NOTE Confidence: 0.8828786

00:17:29.990 --> 00:17:33.140 And sleepiness in those without OSA  
NOTE Confidence: 0.8828786

00:17:33.140 --> 00:17:35.720 did not increase cardiovascular risk.  
NOTE Confidence: 0.8828786

00:17:35.720 --> 00:17:38.445 Anne Anne it's conceivable that  
NOTE Confidence: 0.8828786

00:17:38.445 --> 00:17:41.170 distinct molecular responses to OSA  
NOTE Confidence: 0.8828786

00:17:41.259 --> 00:17:44.069 result in sleepiness and increased  
NOTE Confidence: 0.8828786

00:17:44.069 --> 00:17:46.879 risk of cardiovascular disease in.  
NOTE Confidence: 0.8828786

00:17:46.880 --> 00:17:49.140 And in certain patients,  
NOTE Confidence: 0.8828786

00:17:49.140 --> 00:17:50.835 to this end,  
NOTE Confidence: 0.8828786

00:17:50.840 --> 00:17:55.558 this was actually the basis of a.  
NOTE Confidence: 0.8828786

00:17:55.560 --> 00:17:58.590 Dot Med grant application between Penn,  
NOTE Confidence: 0.8828786

00:17:58.590 --> 00:18:01.620 Ohio State and University of British  
NOTE Confidence: 0.8828786

00:18:01.620 --> 00:18:04.617 Columbia with innogy bias and Alan  
NOTE Confidence: 0.8828786

00:18:04.617 --> 00:18:07.305 Pack that's looking at the molecular

NOTE Confidence: 0.8828786

00:18:07.305 --> 00:18:10.463 basis for differences between or say

NOTE Confidence: 0.8828786

00:18:10.463 --> 00:18:13.733 subtypes because that's not known right,

NOTE Confidence: 0.8828786

00:18:13.740 --> 00:18:15.525 we just this.

NOTE Confidence: 0.8828786

00:18:15.525 --> 00:18:17.905 This just got funded.

NOTE Confidence: 0.8828786

00:18:17.910 --> 00:18:20.796 And we got funded for 3000

NOTE Confidence: 0.8828786

00:18:20.796 --> 00:18:23.180 samples from patients with OSA.

NOTE Confidence: 0.8828786

00:18:23.180 --> 00:18:26.295 So basically the idea is a thousands

NOTE Confidence: 0.8828786

00:18:26.295 --> 00:18:29.408 of samples in its three subtypes,

NOTE Confidence: 0.8828786

00:18:29.410 --> 00:18:32.330 and the top Med program

NOTE Confidence: 0.8828786

00:18:32.330 --> 00:18:34.666 doesn't give you resources.

NOTE Confidence: 0.8828786

00:18:34.670 --> 00:18:36.910 For collection that they collecting

NOTE Confidence: 0.8828786

00:18:36.910 --> 00:18:40.230 the samples but it does give you

NOTE Confidence: 0.8828786

00:18:40.230 --> 00:18:42.735 resources for the following whole

NOTE Confidence: 0.8828786

00:18:42.735 --> 00:18:45.380 whole genome sequencing DNA methylation

NOTE Confidence: 0.8828786

00:18:45.380 --> 00:18:48.035 patterns as well as metabolomics,

NOTE Confidence: 0.8828786

00:18:48.040 --> 00:18:51.420 so they'll do that.  
NOTE Confidence: 0.8828786

00:18:51.420 --> 00:18:54.995 Those three things in in  
NOTE Confidence: 0.8828786

00:18:54.995 --> 00:18:57.855 all the 3000 samples.  
NOTE Confidence: 0.8828786

00:18:57.860 --> 00:19:00.659 I believe this is going to be a good  
NOTE Confidence: 0.8828786

00:19:00.659 --> 00:19:02.976 resource because you know that that  
NOTE Confidence: 0.8828786

00:19:02.976 --> 00:19:05.420 Med program releases the data for  
NOTE Confidence: 0.8828786

00:19:05.420 --> 00:19:07.610 two other two other investigators.  
NOTE Confidence: 0.77920747

00:19:09.900 --> 00:19:13.148 So just quickly I'm going to touch on  
NOTE Confidence: 0.77920747

00:19:13.148 --> 00:19:15.880 preclinical and epidemiological studies.  
NOTE Confidence: 0.77920747

00:19:15.880 --> 00:19:19.730 You guys all know this.  
NOTE Confidence: 0.77920747

00:19:19.730 --> 00:19:22.645 Numerous studies looking at biological  
NOTE Confidence: 0.77920747

00:19:22.645 --> 00:19:24.977 plausibility of obstructive sleep  
NOTE Confidence: 0.77920747

00:19:24.977 --> 00:19:27.659 apnea and cardiovascular disease,  
NOTE Confidence: 0.77920747

00:19:27.660 --> 00:19:30.846 just to name a few increased  
NOTE Confidence: 0.77920747

00:19:30.846 --> 00:19:32.970 oxidative stress through impaired  
NOTE Confidence: 0.77920747

00:19:33.064 --> 00:19:36.409 vasoreactivity increase catecholamines.

NOTE Confidence: 0.77920747

00:19:36.410 --> 00:19:40.106 Increase platelet aggregation and

NOTE Confidence: 0.77920747

00:19:40.106 --> 00:19:43.802 increase inflammation and this

NOTE Confidence: 0.77920747

00:19:43.802 --> 00:19:48.239 been shown in many animals and.

NOTE Confidence: 0.77920747

00:19:48.240 --> 00:19:49.779 And human studies.

NOTE Confidence: 0.77920747

00:19:49.779 --> 00:19:53.824 They are small, but it does show

NOTE Confidence: 0.77920747

00:19:53.824 --> 00:19:56.954 a biological plausibility of the.

NOTE Confidence: 0.77920747

00:19:56.960 --> 00:19:59.460 Of obstructive sleep apnea

NOTE Confidence: 0.77920747

00:19:59.460 --> 00:20:00.710 causing cardiovascular.

NOTE Confidence: 0.77920747

00:20:00.710 --> 00:20:04.700 Events just to give you an example,

NOTE Confidence: 0.77920747

00:20:04.700 --> 00:20:08.214 you guys are very familiar with Seabass.

NOTE Confidence: 0.77920747

00:20:08.220 --> 00:20:09.334 Apollo skis.

NOTE Confidence: 0.77920747

00:20:09.334 --> 00:20:13.790 A paper that was published in the Blue

NOTE Confidence: 0.77920747

00:20:13.906 --> 00:20:18.274 Journal many years ago where he exposed.

NOTE Confidence: 0.77920747

00:20:18.280 --> 00:20:21.444 C57 Black 6 mice.

NOTE Confidence: 0.77920747

00:20:21.444 --> 00:20:26.190 Two chronic intermittent hypoxia and found.

NOTE Confidence: 0.77920747

00:20:26.190 --> 00:20:29.361 In panel D here that if you  
NOTE Confidence: 0.77920747

00:20:29.361 --> 00:20:30.720 combine intermittent hypoxia,  
NOTE Confidence: 0.77920747

00:20:30.720 --> 00:20:32.956 exposure with high cholesterol  
NOTE Confidence: 0.77920747

00:20:32.956 --> 00:20:36.310 diet that the this is sections  
NOTE Confidence: 0.77920747

00:20:36.405 --> 00:20:40.122 of the order that you will find  
NOTE Confidence: 0.77920747

00:20:40.122 --> 00:20:42.235 atherosclerotic plaques or as  
NOTE Confidence: 0.77920747

00:20:42.235 --> 00:20:44.749 all the other groups did not.  
NOTE Confidence: 0.77920747

00:20:44.750 --> 00:20:46.935 This is our own metaanalysis  
NOTE Confidence: 0.77920747

00:20:46.935 --> 00:20:50.280 also from out of the Sajik group,  
NOTE Confidence: 0.77920747

00:20:50.280 --> 00:20:52.758 showing that the effects of CPAP  
NOTE Confidence: 0.77920747

00:20:52.758 --> 00:20:55.543 on blood pressure in patients with  
NOTE Confidence: 0.77920747

00:20:55.543 --> 00:20:58.158 resistant hypertension and the forest  
NOTE Confidence: 0.77920747

00:20:58.158 --> 00:21:01.298 flat shown here shows the results  
NOTE Confidence: 0.77920747

00:21:01.298 --> 00:21:03.783 of the randomized control trials.  
NOTE Confidence: 0.77920747

00:21:03.790 --> 00:21:07.678 On 24 hour systolic blood pressure.  
NOTE Confidence: 0.77920747

00:21:07.680 --> 00:21:10.879 And in this analysis we found that

NOTE Confidence: 0.77920747

00:21:10.879 --> 00:21:14.792 there is a large decreases in systolic

NOTE Confidence: 0.77920747

00:21:14.792 --> 00:21:19.200 blood pressure after CPAP use in the

NOTE Confidence: 0.77920747

00:21:19.200 --> 00:21:22.415 order about 7 millimeters Mercury.

NOTE Confidence: 0.8820883

00:21:24.870 --> 00:21:29.894 Just to summarize, in the interest of time.

NOTE Confidence: 0.8820883

00:21:29.900 --> 00:21:33.414 See you all know that large epidemiological

NOTE Confidence: 0.8820883

00:21:33.414 --> 00:21:36.812 studies consistently find that OSA is an

NOTE Confidence: 0.8820883

00:21:36.812 --> 00:21:39.077 independent risk factor for hypertension,

NOTE Confidence: 0.8820883

00:21:39.080 --> 00:21:41.490 coronary artery disease, heart failure,

NOTE Confidence: 0.8820883

00:21:41.490 --> 00:21:47.106 stroke and death, and death due to CBT.

NOTE Confidence: 0.8820883

00:21:47.110 --> 00:21:49.042 And that individuals effectively

NOTE Confidence: 0.8820883

00:21:49.042 --> 00:21:52.482 treated with CPAP have the same rate

NOTE Confidence: 0.8820883

00:21:52.482 --> 00:21:54.807 of cardiovascular events as age,

NOTE Confidence: 0.8820883

00:21:54.810 --> 00:21:57.215 sex and weight match controls

NOTE Confidence: 0.8820883

00:21:57.215 --> 00:21:59.620 with no apnea or snoring.

NOTE Confidence: 0.8820883

00:21:59.620 --> 00:22:02.020 I'm referring, of course,

NOTE Confidence: 0.8820883

00:22:02.020 --> 00:22:07.209 to the very famous study of Doctor Marin.  
NOTE Confidence: 0.8820883

00:22:07.210 --> 00:22:10.633 Where he showed that severe always saying  
NOTE Confidence: 0.8820883

00:22:10.633 --> 00:22:13.241 Christmas trees of cardiovascular events  
NOTE Confidence: 0.8820883

00:22:13.241 --> 00:22:16.944 and that CPAP use reduces this risk  
NOTE Confidence: 0.8820883

00:22:16.944 --> 00:22:19.599 because those patients and always say  
NOTE Confidence: 0.8820883

00:22:19.599 --> 00:22:23.564 we'd always say on C pap have the same  
NOTE Confidence: 0.8820883

00:22:23.564 --> 00:22:25.969 cardiovascular event rate as controls,  
NOTE Confidence: 0.8820883

00:22:25.970 --> 00:22:27.578 an inflamed snores,  
NOTE Confidence: 0.8820883

00:22:27.578 --> 00:22:30.794 and the more important thing is  
NOTE Confidence: 0.8820883

00:22:30.794 --> 00:22:34.378 that I believe this is in a follow  
NOTE Confidence: 0.8820883

00:22:34.378 --> 00:22:37.370 up paper where they showed that.  
NOTE Confidence: 0.8820883

00:22:37.370 --> 00:22:40.700 Medication refill rates are similar  
NOTE Confidence: 0.8820883

00:22:40.700 --> 00:22:44.969 in users and nonusers subsea of CPAP.  
NOTE Confidence: 0.8820883

00:22:44.970 --> 00:22:47.100 Suggesting that healthy user bias,  
NOTE Confidence: 0.8820883

00:22:47.100 --> 00:22:50.068 which is of course a big confounder  
NOTE Confidence: 0.8820883

00:22:50.068 --> 00:22:50.916 in observation.

NOTE Confidence: 0.8820883

00:22:50.920 --> 00:22:53.885 ULL studies does not explain

NOTE Confidence: 0.8820883

00:22:53.885 --> 00:22:56.850 the observed benefit of CPAP.

NOTE Confidence: 0.8820883

00:22:56.850 --> 00:23:00.962 So if you then look at Sir Bradford

NOTE Confidence: 0.8820883

00:23:00.962 --> 00:23:05.038 Hill's criteria, you'll find that.

NOTE Confidence: 0.8820883

00:23:05.040 --> 00:23:10.503 All of this things had been have been shown.

NOTE Confidence: 0.8820883

00:23:10.510 --> 00:23:13.480 And except for our cities.

NOTE Confidence: 0.8820883

00:23:13.480 --> 00:23:16.050 So.

NOTE Confidence: 0.8820883

00:23:16.050 --> 00:23:18.978 Why is it that the three major are

NOTE Confidence: 0.8820883

00:23:18.978 --> 00:23:21.572 cities that have been published so

NOTE Confidence: 0.8820883

00:23:21.572 --> 00:23:24.242 far have been have been negative,

NOTE Confidence: 0.8820883

00:23:24.250 --> 00:23:27.530 and I'm talking about course the SAFE study,

NOTE Confidence: 0.8820883

00:23:27.530 --> 00:23:29.250 which is the largest?

NOTE Confidence: 0.8820883

00:23:29.250 --> 00:23:31.830 There's the re courage to study

NOTE Confidence: 0.8820883

00:23:31.914 --> 00:23:34.542 and then there's a dissect study

NOTE Confidence: 0.8820883

00:23:34.542 --> 00:23:36.960 that was published in Lancet

NOTE Confidence: 0.8820883



00:23:36.960 --> 00:23:39.865 respiratory medicine just this year.  
NOTE Confidence: 0.8820883

00:23:39.870 --> 00:23:41.991 So I'm going to send a review  
NOTE Confidence: 0.8820883

00:23:41.991 --> 00:23:42.900 real real quick.  
NOTE Confidence: 0.8820883

00:23:42.900 --> 00:23:44.934 This three RCP's and we're going  
NOTE Confidence: 0.8820883

00:23:44.934 --> 00:23:47.090 to discuss some of the biases.  
NOTE Confidence: 0.8820883

00:23:47.090 --> 00:23:49.970 That we believe are present.  
NOTE Confidence: 0.8820883

00:23:49.970 --> 00:23:52.840 So the same, of course,  
NOTE Confidence: 0.8820883

00:23:52.840 --> 00:23:53.974 very briefly,  
NOTE Confidence: 0.8820883

00:23:53.974 --> 00:23:57.943 is a study multicenter study of roughly  
NOTE Confidence: 0.8820883

00:23:57.943 --> 00:24:02.040 2700 adults with moderate to severe OSA.  
NOTE Confidence: 0.8820883

00:24:02.040 --> 00:24:06.174 And it's they have coronary or  
NOTE Confidence: 0.8820883

00:24:06.174 --> 00:24:08.930 cerebral cerebral vascular disease.  
NOTE Confidence: 0.8820883

00:24:08.930 --> 00:24:12.946 They were randomized to see Pap less use,  
NOTE Confidence: 0.8820883

00:24:12.950 --> 00:24:16.457 less useful care versus usual care alone.  
NOTE Confidence: 0.8820883

00:24:16.460 --> 00:24:20.142 And of course the primacy of the  
NOTE Confidence: 0.8820883

00:24:20.142 --> 00:24:22.987 primary composite endpoint scuse me

NOTE Confidence: 0.8820883

00:24:22.987 --> 00:24:25.917 was death from cardiovascular causes.

NOTE Confidence: 0.8820883

00:24:25.920 --> 00:24:28.941 Am I stroke?

NOTE Confidence: 0.8820883

00:24:28.941 --> 00:24:33.976 Or hospitalization for unstable angina.

NOTE Confidence: 0.8820883

00:24:33.980 --> 00:24:36.878 Heart failure or the mean follow-up

NOTE Confidence: 0.8820883

00:24:36.878 --> 00:24:40.614 was 3.7 years and the incidence of

NOTE Confidence: 0.8820883

00:24:40.614 --> 00:24:44.034 the primary endpoint did not differ

NOTE Confidence: 0.8820883

00:24:44.034 --> 00:24:46.520 significantly in patients who did

NOTE Confidence: 0.8820883

00:24:46.520 --> 00:24:49.895 versus those that did not receive C

NOTE Confidence: 0.8820883

00:24:49.895 --> 00:24:54.895 Pap with a hazard ratio of 1.1.

NOTE Confidence: 0.8820883

00:24:54.900 --> 00:24:57.215 And I mentioned earlier CPAP

NOTE Confidence: 0.8820883

00:24:57.215 --> 00:24:59.067 did improve daytime sleepiness,

NOTE Confidence: 0.8820883

00:24:59.070 --> 00:25:03.814 health related quality of life and mood.

NOTE Confidence: 0.8820883

00:25:03.820 --> 00:25:06.830 The records study was published in the

NOTE Confidence: 0.8820883

00:25:06.830 --> 00:25:09.329 Blue Journal about four years ago.

NOTE Confidence: 0.8820883

00:25:09.330 --> 00:25:12.578 The single center RCT.

NOTE Confidence: 0.8820883

00:25:12.580 --> 00:25:14.940 There's it's a smaller study.  
NOTE Confidence: 0.8820883

00:25:14.940 --> 00:25:15.902 Of course,  
NOTE Confidence: 0.8820883

00:25:15.902 --> 00:25:18.307 there's 244 patients with newly  
NOTE Confidence: 0.8820883

00:25:18.307 --> 00:25:19.750 revascularized coronary artery  
NOTE Confidence: 0.8820883

00:25:19.821 --> 00:25:22.091 disease and moderate to severe  
NOTE Confidence: 0.8820883

00:25:22.091 --> 00:25:23.907 OSA without daytime sleepiness.  
NOTE Confidence: 0.8820883

00:25:23.910 --> 00:25:27.678 So this this patient also had stab Lish,  
NOTE Confidence: 0.8820883

00:25:27.680 --> 00:25:29.261 coronary artery disease,  
NOTE Confidence: 0.8820883

00:25:29.261 --> 00:25:31.896 and obviously they were randomized  
NOTE Confidence: 0.8820883

00:25:31.896 --> 00:25:35.446 to sipat versus no see bat and the  
NOTE Confidence: 0.8820883

00:25:35.446 --> 00:25:37.600 primary endpoint is listed there.  
NOTE Confidence: 0.8820883

00:25:37.600 --> 00:25:38.542 It's again,  
NOTE Confidence: 0.8820883

00:25:38.542 --> 00:25:40.897 it's a composite endpoint endpoint.  
NOTE Confidence: 0.8820883

00:25:40.900 --> 00:25:43.828 Little bit longer follow up of.  
NOTE Confidence: 0.8820883

00:25:43.830 --> 00:25:45.714 4.75 years and again,  
NOTE Confidence: 0.8820883

00:25:45.714 --> 00:25:48.540 the incidence of the primary endpoint

NOTE Confidence: 0.8930136

00:25:48.626 --> 00:25:51.548 did not differ significantly in patients

NOTE Confidence: 0.8930136

00:25:51.548 --> 00:25:55.019 who did versus those who did not receive

NOTE Confidence: 0.8930136

00:25:55.019 --> 00:25:58.960 a seat back with a hazard ratio of a .8.

NOTE Confidence: 0.82090217

00:26:02.280 --> 00:26:04.790 And in the third study,

NOTE Confidence: 0.82090217

00:26:04.790 --> 00:26:08.213 is that uh, is the Isak study

NOTE Confidence: 0.82090217

00:26:08.213 --> 00:26:10.810 that was published this year.

NOTE Confidence: 0.82090217

00:26:10.810 --> 00:26:13.320 It's a multi center RCT.

NOTE Confidence: 0.82090217

00:26:13.320 --> 00:26:15.830 This patients have were admitted

NOTE Confidence: 0.82090217

00:26:15.830 --> 00:26:17.838 for acute coronary syndrome.

NOTE Confidence: 0.82090217

00:26:17.840 --> 00:26:21.856 They were found to have moderate severe OSA,

NOTE Confidence: 0.82090217

00:26:21.860 --> 00:26:24.968 diagnosed during the first 24 to

NOTE Confidence: 0.82090217

00:26:24.968 --> 00:26:28.366 72 hours after admission and we

NOTE Confidence: 0.82090217

00:26:28.366 --> 00:26:30.738 without daytime sleepiness. Um?

NOTE Confidence: 0.82090217

00:26:30.738 --> 00:26:34.364 Of course you can question you know

NOTE Confidence: 0.82090217

00:26:34.364 --> 00:26:37.497 there's some data that says that.

NOTE Confidence: 0.82090217

00:26:37.500 --> 00:26:40.045 When you follow patients where  
NOTE Confidence: 0.82090217

00:26:40.045 --> 00:26:42.590 admitted for acute coronary syndrome  
NOTE Confidence: 0.82090217

00:26:42.666 --> 00:26:44.981 that perhaps there hi changes  
NOTE Confidence: 0.82090217

00:26:44.981 --> 00:26:47.296 but nonetheless that was there.  
NOTE Confidence: 0.84707826

00:26:49.580 --> 00:26:52.609 Entry criteria. Again,  
NOTE Confidence: 0.84707826

00:26:52.609 --> 00:26:55.663 randomized to see that versus know  
NOTE Confidence: 0.84707826

00:26:55.663 --> 00:26:58.737 Steve at about 600 in each arm.  
NOTE Confidence: 0.84707826

00:26:58.740 --> 00:27:01.288 Again, it composite endpoint  
NOTE Confidence: 0.84707826

00:27:01.288 --> 00:27:04.473 that's listed there with a  
NOTE Confidence: 0.84707826

00:27:04.473 --> 00:27:07.576 median follow up of 3.3 years.  
NOTE Confidence: 0.84707826

00:27:07.580 --> 00:27:10.100 And again, the primary endpoint  
NOTE Confidence: 0.84707826

00:27:10.100 --> 00:27:12.116 did not differ significantly  
NOTE Confidence: 0.84707826

00:27:12.116 --> 00:27:14.482 in patients who did versus  
NOTE Confidence: 0.84707826

00:27:14.482 --> 00:27:16.702 those who did not receive.  
NOTE Confidence: 0.84707826

00:27:16.710 --> 00:27:18.030 C pap therapy.  
NOTE Confidence: 0.7654318

00:27:20.140 --> 00:27:23.398 So what are the biases in the in this

NOTE Confidence: 0.7654318

00:27:23.398 --> 00:27:26.378 published RCT's of cardiovascular outcomes?

NOTE Confidence: 0.7654318

00:27:26.380 --> 00:27:30.404 In no essay I I'm just going to

NOTE Confidence: 0.7654318

00:27:30.404 --> 00:27:34.128 touch on a couple. We believe that

NOTE Confidence: 0.7654318

00:27:34.128 --> 00:27:37.044 there is a sample selection bias.

NOTE Confidence: 0.7654318

00:27:37.050 --> 00:27:41.478 And and and there are a few things to

NOTE Confidence: 0.7654318

00:27:41.478 --> 00:27:44.968 consider here. But first thing is,

NOTE Confidence: 0.7654318

00:27:44.968 --> 00:27:47.316 are they recruited participants

NOTE Confidence: 0.7654318

00:27:47.316 --> 00:27:50.617 representative of real world and patients?

NOTE Confidence: 0.7654318

00:27:50.620 --> 00:27:56.794 And we believe the answer to this is no.

NOTE Confidence: 0.7654318

00:27:56.800 --> 00:28:00.022 Based on the data that I presented to you,

NOTE Confidence: 0.7654318

00:28:00.030 --> 00:28:01.754 they included.

NOTE Confidence: 0.7654318

00:28:01.754 --> 00:28:06.064 Non sleepy patients and excluded.

NOTE Confidence: 0.7654318

00:28:06.070 --> 00:28:09.740 The sleepy patients who are.

NOTE Confidence: 0.7654318

00:28:09.740 --> 00:28:11.264 The ones.

NOTE Confidence: 0.7654318

00:28:11.264 --> 00:28:15.836 That are primarily at risk of

NOTE Confidence: 0.7654318

00:28:15.836 --> 00:28:18.300 developing cardiovascular events.

NOTE Confidence: 0.7654318

00:28:18.300 --> 00:28:21.541 All these prior our cities were secondary

NOTE Confidence: 0.7654318

00:28:21.541 --> 00:28:24.359 prevention studies and and really that

NOTE Confidence: 0.7654318

00:28:24.359 --> 00:28:26.619 was done deliberately because she,

NOTE Confidence: 0.7654318

00:28:26.620 --> 00:28:28.925 you know they wanted a

NOTE Confidence: 0.7654318

00:28:28.925 --> 00:28:30.769 higher event rates force.

NOTE Confidence: 0.7654318

00:28:30.770 --> 00:28:33.675 But one of the downside of that

NOTE Confidence: 0.7654318

00:28:33.675 --> 00:28:37.792 would be that you know a lot of this

NOTE Confidence: 0.7654318

00:28:37.792 --> 00:28:40.222 patients were already being managed

NOTE Confidence: 0.7654318

00:28:40.222 --> 00:28:43.645 actively and they they are on statins

NOTE Confidence: 0.7654318

00:28:43.645 --> 00:28:47.222 and and perhaps the effect of.

NOTE Confidence: 0.7654318

00:28:47.222 --> 00:28:50.260 Uh, partly the reason why it's

NOTE Confidence: 0.7654318

00:28:50.260 --> 00:28:53.010 negative is that the effect of.

NOTE Confidence: 0.7654318

00:28:53.010 --> 00:28:57.060 Of C PAP may have invented.

NOTE Confidence: 0.7654318

00:28:57.060 --> 00:29:00.200 The largest issue, we believe,

NOTE Confidence: 0.7654318

00:29:00.200 --> 00:29:04.190 is that you know where and how

NOTE Confidence: 0.7654318

00:29:04.190 --> 00:29:07.090 this participants were recruited.

NOTE Confidence: 0.7654318

00:29:07.090 --> 00:29:12.698 So all these RCT's focus and diagnosing OSA.

NOTE Confidence: 0.7654318

00:29:12.700 --> 00:29:15.520 Among relatively asymptomatic individuals

NOTE Confidence: 0.7654318

00:29:15.520 --> 00:29:19.045 with stab Lish cardiovascular disease.

NOTE Confidence: 0.7654318

00:29:19.050 --> 00:29:22.615 As opposed to identifying adults

NOTE Confidence: 0.7654318

00:29:22.615 --> 00:29:24.754 with clinically diagnose.

NOTE Confidence: 0.7654318

00:29:24.760 --> 00:29:28.250 Always saying, then randomizing them.

NOTE Confidence: 0.7654318

00:29:28.250 --> 00:29:32.066 So there they are not from the sleep clinics.

NOTE Confidence: 0.85450685

00:29:34.460 --> 00:29:37.666 And we believe that symptomatic the bias

NOTE Confidence: 0.85450685

00:29:37.666 --> 00:29:39.837 occurs because symptomatic patients are

NOTE Confidence: 0.85450685

00:29:39.837 --> 00:29:42.733 less willing to be randomized to a study

NOTE Confidence: 0.85450685

00:29:42.808 --> 00:29:45.489 arm that receives no treatment for an

NOTE Confidence: 0.85450685

00:29:45.489 --> 00:29:47.810 extended period of time of follow-up,

NOTE Confidence: 0.85450685

00:29:47.810 --> 00:29:50.540 which is what you need for a

NOTE Confidence: 0.85450685

00:29:50.626 --> 00:29:53.198 study of cardiovascular events.

NOTE Confidence: 0.85450685



00:29:53.200 --> 00:29:55.860 Or their providers are less  
NOTE Confidence: 0.85450685

00:29:55.860 --> 00:29:57.988 likely to recommend participation  
NOTE Confidence: 0.85450685

00:29:57.988 --> 00:30:00.250 and such was the expiry.  
NOTE Confidence: 0.85450685

00:30:00.250 --> 00:30:02.230 As in some NH sponsored trials.  
NOTE Confidence: 0.85450685

00:30:02.230 --> 00:30:04.540 So for example, the Apple study had.  
NOTE Confidence: 0.6423485

00:30:07.070 --> 00:30:10.222 You know, according to clip, Kushida had.  
NOTE Confidence: 0.6423485

00:30:10.222 --> 00:30:13.302 Terrible time with recruitment in  
NOTE Confidence: 0.6423485

00:30:13.302 --> 00:30:17.439 the sleep clinics and they had to  
NOTE Confidence: 0.6423485

00:30:17.439 --> 00:30:20.169 resort to really large advertising.  
NOTE Confidence: 0.6423485

00:30:20.170 --> 00:30:24.362 The other trial that comes to mind is  
NOTE Confidence: 0.6423485

00:30:24.362 --> 00:30:26.889 nalaka Gooneratne's memories trial.  
NOTE Confidence: 0.6423485

00:30:26.890 --> 00:30:28.693 Were he actually?  
NOTE Confidence: 0.6423485

00:30:28.693 --> 00:30:31.698 You know providers were not  
NOTE Confidence: 0.6423485

00:30:31.698 --> 00:30:34.080 willing to randomize.  
NOTE Confidence: 0.6423485

00:30:34.080 --> 00:30:36.644 Their subjects with cognitive  
NOTE Confidence: 0.6423485

00:30:36.644 --> 00:30:39.849 impairment if they have they

NOTE Confidence: 0.6423485  
00:30:39.849 --> 00:30:43.246 were found to have sleep apnea.  
NOTE Confidence: 0.6423485  
00:30:43.250 --> 00:30:45.356 So we believe that these are  
NOTE Confidence: 0.6423485  
00:30:45.356 --> 00:30:46.409 not our patients.  
NOTE Confidence: 0.6423485  
00:30:46.410 --> 00:30:49.553 If you look at the exclusion criteria  
NOTE Confidence: 0.6423485  
00:30:49.553 --> 00:30:52.142 there that's listed and then the  
NOTE Confidence: 0.6423485  
00:30:52.142 --> 00:30:54.452 average on the right hand side.  
NOTE Confidence: 0.6423485  
00:30:54.460 --> 00:30:58.778 The. The average effort,  
NOTE Confidence: 0.6423485  
00:30:58.778 --> 00:30:59.434 sleepiness,  
NOTE Confidence: 0.6423485  
00:30:59.434 --> 00:31:03.995 scale score that all the recent RCT  
NOTE Confidence: 0.6423485  
00:31:03.995 --> 00:31:07.115 sub C Pap on cardiovascular events  
NOTE Confidence: 0.6423485  
00:31:07.115 --> 00:31:10.658 had had had had the same bias.  
NOTE Confidence: 0.6423485  
00:31:10.660 --> 00:31:11.662 And of course,  
NOTE Confidence: 0.6423485  
00:31:11.662 --> 00:31:14.000 you know they had to exclude this  
NOTE Confidence: 0.6423485  
00:31:14.078 --> 00:31:15.946 patients because it's unethical  
NOTE Confidence: 0.6423485  
00:31:15.946 --> 00:31:18.281 to randomize sleepy OSA patients  
NOTE Confidence: 0.6423485

00:31:18.281 --> 00:31:20.566 to no treatment in cardiovascular  
NOTE Confidence: 0.6423485

00:31:20.566 --> 00:31:22.310 trials of seed Bab,  
NOTE Confidence: 0.6423485

00:31:22.310 --> 00:31:25.946 basically because of fear of automobile.  
NOTE Confidence: 0.6423485

00:31:25.950 --> 00:31:32.268 Accidents as well as workplace accidents.  
NOTE Confidence: 0.6423485

00:31:32.270 --> 00:31:34.964 But but the sample bias likely  
NOTE Confidence: 0.6423485

00:31:34.964 --> 00:31:37.978 led to the very low adherence  
NOTE Confidence: 0.6423485

00:31:37.978 --> 00:31:40.768 to CPAP that was reported.  
NOTE Confidence: 0.6423485

00:31:40.770 --> 00:31:42.734 So that's another bias,  
NOTE Confidence: 0.6423485

00:31:42.734 --> 00:31:45.680 because low adherence to therapy would  
NOTE Confidence: 0.6423485

00:31:45.760 --> 00:31:48.766 tend to underestimate the effect size.  
NOTE Confidence: 0.6423485

00:31:48.770 --> 00:31:52.530 And this is the summary.  
NOTE Confidence: 0.6423485

00:31:52.530 --> 00:31:56.878 Of the adherence data.  
NOTE Confidence: 0.6423485

00:31:56.880 --> 00:32:00.100 In in the three trials in the  
NOTE Confidence: 0.6423485

00:32:00.100 --> 00:32:02.038 records actually separated their  
NOTE Confidence: 0.6423485

00:32:02.038 --> 00:32:04.368 users and all patients here,  
NOTE Confidence: 0.6423485

00:32:04.370 --> 00:32:06.150 so all patients here,

NOTE Confidence: 0.6423485

00:32:06.150 --> 00:32:08.820 these are the CPAP users in

NOTE Confidence: 0.6423485

00:32:08.919 --> 00:32:10.919 the regards the trial.

NOTE Confidence: 0.6423485

00:32:10.920 --> 00:32:15.078 The bottom line is after 20 four

NOTE Confidence: 0.6423485

00:32:15.078 --> 00:32:18.529 months roughly in the range of.

NOTE Confidence: 0.6423485

00:32:18.530 --> 00:32:22.088 2.8 to 3 hours per nine.

NOTE Confidence: 0.8543448

00:32:25.400 --> 00:32:27.032 And you'd say, well, that's what

NOTE Confidence: 0.8543448

00:32:27.032 --> 00:32:28.750 you're going to get with C pap,

NOTE Confidence: 0.8543448

00:32:28.750 --> 00:32:31.270 but but there's some.

NOTE Confidence: 0.8543448

00:32:31.270 --> 00:32:33.450 Evidence that they may not

NOTE Confidence: 0.8543448

00:32:33.450 --> 00:32:35.630 be in our patients so.

NOTE Confidence: 0.8543448

00:32:35.630 --> 00:32:39.344 This is Peter's studies study that

NOTE Confidence: 0.8543448

00:32:39.344 --> 00:32:43.787 was published in 2019 using big data

NOTE Confidence: 0.8543448

00:32:43.787 --> 00:32:48.120 looking at CPAP usage in clinic patients.

NOTE Confidence: 0.8543448

00:32:48.120 --> 00:32:51.557 .6 million patients and and you can

NOTE Confidence: 0.8543448

00:32:51.557 --> 00:32:55.098 see that that indeed the device usage

NOTE Confidence: 0.8543448

00:32:55.098 --> 00:32:59.050 is roughly in the area of about 62.  
NOTE Confidence: 0.8543448

00:32:59.050 --> 00:33:02.394 To 70% now, I mean this this study  
NOTE Confidence: 0.8543448

00:33:02.394 --> 00:33:05.128 of course is limited because.  
NOTE Confidence: 0.8543448

00:33:05.130 --> 00:33:07.446 You know these are they didn't.  
NOTE Confidence: 0.8543448

00:33:07.450 --> 00:33:09.958 They didn't include those who did  
NOTE Confidence: 0.8543448

00:33:09.958 --> 00:33:13.178 not drop up or return their seat  
NOTE Confidence: 0.8543448

00:33:13.178 --> 00:33:16.082 that because that's going to be.  
NOTE Confidence: 0.8543448

00:33:16.090 --> 00:33:20.325 They won't have the data and then.  
NOTE Confidence: 0.8543448

00:33:20.330 --> 00:33:21.990 And and and it is.  
NOTE Confidence: 0.8543448

00:33:21.990 --> 00:33:25.617 In addition, this was only the 90 days so.  
NOTE Confidence: 0.8543448

00:33:25.620 --> 00:33:29.596 Off of therapy. But still some some evidence.  
NOTE Confidence: 0.8543448

00:33:29.600 --> 00:33:33.086 Not great that perhaps our clinic patients.  
NOTE Confidence: 0.8543448

00:33:33.090 --> 00:33:36.576 If you if you enroll them in  
NOTE Confidence: 0.8543448

00:33:36.576 --> 00:33:41.058 a in a in a trial of C pap.  
NOTE Confidence: 0.7898935

00:33:43.070 --> 00:33:48.568 Would perhaps use? Their seat belt  
NOTE Confidence: 0.7898935

00:33:48.568 --> 00:33:52.360 more and then you know as I mentioned,

NOTE Confidence: 0.7898935

00:33:52.360 --> 00:33:56.728 likely some of the selection bias that accord

NOTE Confidence: 0.7898935

00:33:56.728 --> 00:34:00.506 resulted in the lowest seat belt usage.

NOTE Confidence: 0.7898935

00:34:00.510 --> 00:34:03.982 The two of these studies in fact did

NOTE Confidence: 0.7898935

00:34:03.982 --> 00:34:07.102 a propensity score matching in those

NOTE Confidence: 0.7898935

00:34:07.102 --> 00:34:10.342 who are adherent versus non adherent.

NOTE Confidence: 0.7898935

00:34:10.350 --> 00:34:14.995 Um? So the Save and Isaac did this

NOTE Confidence: 0.7898935

00:34:14.995 --> 00:34:18.657 and they got a point estimate of a .8.

NOTE Confidence: 0.7898935

00:34:18.660 --> 00:34:22.564 I would just point out and this is.

NOTE Confidence: 0.7898935

00:34:22.570 --> 00:34:26.035 This was I think it was Dan Gottlieb who,

NOTE Confidence: 0.7898935

00:34:26.040 --> 00:34:28.254 in an editorial in JAMA pointed

NOTE Confidence: 0.7898935

00:34:28.254 --> 00:34:30.270 this out at this point,

NOTE Confidence: 0.7898935

00:34:30.270 --> 00:34:33.854 estimates similar to the meta analysis of.

NOTE Confidence: 0.7898935

00:34:33.860 --> 00:34:36.060 That that's that's off of

NOTE Confidence: 0.7898935

00:34:36.060 --> 00:34:38.260 our cities Anstatt in trials.

NOTE Confidence: 0.8753948

00:34:40.670 --> 00:34:45.901 And but at the end of the day, you know this.

NOTE Confidence: 0.8753948

00:34:45.901 --> 00:34:48.436 This post hoc analysis using  
NOTE Confidence: 0.8753948

00:34:48.436 --> 00:34:50.300 propensity score matching.  
NOTE Confidence: 0.8753948

00:34:50.300 --> 00:34:53.475 Where or underpowered because of  
NOTE Confidence: 0.8753948

00:34:53.475 --> 00:34:57.936 the event rate, the recruits a study  
NOTE Confidence: 0.8753948

00:34:57.936 --> 00:35:02.737 did show that they if you separate  
NOTE Confidence: 0.8753948

00:35:02.737 --> 00:35:08.456 out the users versus non users that.  
NOTE Confidence: 0.8753948

00:35:08.460 --> 00:35:11.400 There was a difference in in  
NOTE Confidence: 0.8753948

00:35:11.400 --> 00:35:14.155 cardiovascular events in a different  
NOTE Confidence: 0.8753948

00:35:14.155 --> 00:35:16.939 versus non adherent subjects.  
NOTE Confidence: 0.8753948

00:35:16.940 --> 00:35:20.420 So the question is.  
NOTE Confidence: 0.8753948

00:35:20.420 --> 00:35:22.760 What are the alternative  
NOTE Confidence: 0.8753948

00:35:22.760 --> 00:35:25.100 designs for future studies?  
NOTE Confidence: 0.8753948

00:35:25.100 --> 00:35:26.452 If you think about,  
NOTE Confidence: 0.8753948

00:35:26.452 --> 00:35:28.480 we believe there are three three  
NOTE Confidence: 0.8753948

00:35:28.552 --> 00:35:30.972 ways of doing this. One is.  
NOTE Confidence: 0.8753948

00:35:30.972 --> 00:35:33.927 We can include the excessive

NOTE Confidence: 0.8753948

00:35:33.927 --> 00:35:37.019 sleep patients in the trials,

NOTE Confidence: 0.8753948

00:35:37.020 --> 00:35:39.470 include them in the useful

NOTE Confidence: 0.8753948

00:35:39.470 --> 00:35:42.300 RCT you know the question is,

NOTE Confidence: 0.8753948

00:35:42.300 --> 00:35:43.557 is this ethical?

NOTE Confidence: 0.8753948

00:35:43.557 --> 00:35:46.071 And then there's also the question

NOTE Confidence: 0.8753948

00:35:46.071 --> 00:35:48.160 of whether symptomatic patients

NOTE Confidence: 0.8753948

00:35:48.160 --> 00:35:50.800 and their providers agreed to

NOTE Confidence: 0.8753948

00:35:50.800 --> 00:35:53.339 not being treated for years.

NOTE Confidence: 0.8753948

00:35:53.340 --> 00:35:56.268 The second one was actually published

NOTE Confidence: 0.8753948

00:35:56.268 --> 00:35:59.099 and was written by a doctor,

NOTE Confidence: 0.8753948

00:35:59.100 --> 00:36:00.570 Javaherian colleagues in,

NOTE Confidence: 0.8753948

00:36:00.570 --> 00:36:02.530 and they suggested that.

NOTE Confidence: 0.8753948

00:36:02.530 --> 00:36:06.418 Let's do the RCT with pharmacological

NOTE Confidence: 0.8753948

00:36:06.418 --> 00:36:09.867 management of sleepiness using using

NOTE Confidence: 0.8753948

00:36:09.867 --> 00:36:13.426 Modafinil. We don't think this to wait.

NOTE Confidence: 0.8753948



00:36:13.430 --> 00:36:16.220 Wait, are the way to go.  
NOTE Confidence: 0.8753948

00:36:16.220 --> 00:36:17.453 It's probably we.  
NOTE Confidence: 0.8753948

00:36:17.453 --> 00:36:20.330 We believe that using a study design  
NOTE Confidence: 0.8753948

00:36:20.411 --> 00:36:23.151 using propensity score matching that  
NOTE Confidence: 0.8753948

00:36:23.151 --> 00:36:25.891 allows the inclusion of excessively  
NOTE Confidence: 0.8753948

00:36:25.973 --> 00:36:28.029 sleepy or Safeway patients.  
NOTE Confidence: 0.8753948

00:36:28.030 --> 00:36:30.658 Most likely to show a cardiovascular  
NOTE Confidence: 0.8753948

00:36:30.658 --> 00:36:33.349 benefit from CPAP and not only  
NOTE Confidence: 0.8753948

00:36:33.349 --> 00:36:35.929 that because you're in a propensity  
NOTE Confidence: 0.8753948

00:36:35.929 --> 00:36:38.608 score design and real world patient,  
NOTE Confidence: 0.8753948

00:36:38.610 --> 00:36:40.815 you're going to compare users  
NOTE Confidence: 0.8753948

00:36:40.815 --> 00:36:42.138 versus non users.  
NOTE Confidence: 0.8753948

00:36:42.140 --> 00:36:44.762 You could examine the true benefit  
NOTE Confidence: 0.8753948

00:36:44.762 --> 00:36:47.953 of C pap therapy on cardiovascular  
NOTE Confidence: 0.8753948

00:36:47.953 --> 00:36:52.003 outcomes within real world clinical patients.  
NOTE Confidence: 0.8753948

00:36:52.010 --> 00:36:55.098 And this is the the paper that I

NOTE Confidence: 0.8753948

00:36:55.098 --> 00:36:57.849 was alluding to that was published.

NOTE Confidence: 0.8753948

00:36:57.850 --> 00:36:59.930 They estimate that they would

NOTE Confidence: 0.8753948

00:36:59.930 --> 00:37:01.594 need a sample size,

NOTE Confidence: 0.8753948

00:37:01.600 --> 00:37:04.519 about 24,000 with 12,000 in each arm.

NOTE Confidence: 0.8753948

00:37:04.520 --> 00:37:06.920 Using pharmacological management of.

NOTE Confidence: 0.8753948

00:37:06.920 --> 00:37:08.120 Of sleepiness.

NOTE Confidence: 0.8505913

00:37:10.240 --> 00:37:13.607 This is the way we think that

NOTE Confidence: 0.8505913

00:37:13.607 --> 00:37:17.019 this the using propensity score.

NOTE Confidence: 0.8505913

00:37:17.020 --> 00:37:18.646 Should be done.

NOTE Confidence: 0.8505913

00:37:18.646 --> 00:37:21.356 You know you have include.

NOTE Confidence: 0.8505913

00:37:21.360 --> 00:37:24.006 Subjects who are seen in the clinic.

NOTE Confidence: 0.8505913

00:37:24.010 --> 00:37:26.670 So you have the inclusion criteria there.

NOTE Confidence: 0.8505913

00:37:26.670 --> 00:37:29.246 Of course there will be sleepy subjects

NOTE Confidence: 0.8505913

00:37:29.246 --> 00:37:32.263 based on the sleepy subtype and they will

NOTE Confidence: 0.8505913

00:37:32.263 --> 00:37:35.379 be treated with CPAP in all the patients.

NOTE Confidence: 0.8505913

00:37:35.380 --> 00:37:37.858 But the most important thing there  
NOTE Confidence: 0.8505913

00:37:37.858 --> 00:37:40.782 in any propensity score design is to  
NOTE Confidence: 0.8505913

00:37:40.782 --> 00:37:43.176 obtain the covariates and I'll explain  
NOTE Confidence: 0.8505913

00:37:43.176 --> 00:37:46.000 that in a little bit and then you can.  
NOTE Confidence: 0.8505913

00:37:46.000 --> 00:37:50.304 You can then compare those who are adherents.  
NOTE Confidence: 0.8505913

00:37:50.310 --> 00:37:51.798 Versus those who declined  
NOTE Confidence: 0.8505913

00:37:51.798 --> 00:37:53.286 therapy or non users.  
NOTE Confidence: 0.8505913

00:37:53.290 --> 00:37:55.810 You could define this as less than  
NOTE Confidence: 0.8505913

00:37:55.810 --> 00:37:58.655 two hours per night or you could say  
NOTE Confidence: 0.8505913

00:37:58.655 --> 00:38:01.235 less than one hour per night without  
NOTE Confidence: 0.8505913

00:38:01.235 --> 00:38:03.665 using the without CPAP you states  
NOTE Confidence: 0.8505913

00:38:03.665 --> 00:38:07.414 in the last 30 days and then you  
NOTE Confidence: 0.8505913

00:38:07.414 --> 00:38:10.899 can do a propensity score design.  
NOTE Confidence: 0.8505913

00:38:10.900 --> 00:38:15.476 With an annual follow up of CPAP adherence,  
NOTE Confidence: 0.8505913

00:38:15.480 --> 00:38:19.190 an major adverse cardiovascular events.  
NOTE Confidence: 0.8505913

00:38:19.190 --> 00:38:22.118 For for a number of years.

NOTE Confidence: 0.8505913

00:38:22.120 --> 00:38:25.936 So this is crucial for any PS design study.

NOTE Confidence: 0.8505913

00:38:25.940 --> 00:38:28.484 You need to include a rich

NOTE Confidence: 0.8505913

00:38:28.484 --> 00:38:30.180 set of clinical relevant,

NOTE Confidence: 0.8505913

00:38:30.180 --> 00:38:32.040 clinically relevant covariates.

NOTE Confidence: 0.8505913

00:38:32.040 --> 00:38:33.280 Associated with.

NOTE Confidence: 0.8505913

00:38:33.280 --> 00:38:35.292 Basically we do things,

NOTE Confidence: 0.8505913

00:38:35.292 --> 00:38:38.310 the CPAP adherence and the outcome,

NOTE Confidence: 0.8505913

00:38:38.310 --> 00:38:41.460 and this reduces the bias associated

NOTE Confidence: 0.8505913

00:38:41.460 --> 00:38:44.530 with observed and unobserved covariates.

NOTE Confidence: 0.8505913

00:38:44.530 --> 00:38:47.407 And just in the interest of time,

NOTE Confidence: 0.8505913

00:38:47.410 --> 00:38:51.658 I'll you know these are the useful things.

NOTE Confidence: 0.8505913

00:38:51.660 --> 00:38:54.740 That we would think would be important

NOTE Confidence: 0.8505913

00:38:54.740 --> 00:38:57.350 as predictors of CPAP adherence.

NOTE Confidence: 0.8505913

00:38:57.350 --> 00:39:00.524 Including educational attainment.

NOTE Confidence: 0.8505913

00:39:00.524 --> 00:39:03.698 Social economic factors.

NOTE Confidence: 0.8505913

00:39:03.700 --> 00:39:04.558 Insoft,  
NOTE Confidence: 0.8505913

00:39:04.558 --> 00:39:08.848 presence of insomnia and psychological  
NOTE Confidence: 0.8505913

00:39:08.848 --> 00:39:13.840 problems but also include measures of.  
NOTE Confidence: 0.8505913

00:39:13.840 --> 00:39:16.280 Self efficacy as well  
NOTE Confidence: 0.8505913

00:39:16.280 --> 00:39:18.110 as medication adherence.  
NOTE Confidence: 0.8403714

00:39:21.430 --> 00:39:23.866 The predictors of the events obviously  
NOTE Confidence: 0.8403714

00:39:23.866 --> 00:39:26.708 are the useful things that we consider.  
NOTE Confidence: 0.69759923

00:39:28.980 --> 00:39:34.080 Gender, obesity, prevalence, CVD, smoking.  
NOTE Confidence: 0.69759923

00:39:34.080 --> 00:39:36.872 Lipids, family history and  
NOTE Confidence: 0.69759923

00:39:36.872 --> 00:39:41.060 physical activity as well as Dyett.  
NOTE Confidence: 0.69759923

00:39:41.060 --> 00:39:46.880 Assessment so what's propensity score?  
NOTE Confidence: 0.69759923

00:39:46.880 --> 00:39:48.800 So the definition,  
NOTE Confidence: 0.69759923

00:39:48.800 --> 00:39:52.000 the PS is the probability.  
NOTE Confidence: 0.69759923

00:39:52.000 --> 00:39:55.528 Or being in the treated group conditional  
NOTE Confidence: 0.69759923

00:39:55.528 --> 00:39:58.899 on all relevant baseline covariates.  
NOTE Confidence: 0.69759923

00:39:58.900 --> 00:40:00.444 And at here's the.

NOTE Confidence: 0.69759923

00:40:00.444 --> 00:40:02.760 Is the formula there and basically

NOTE Confidence: 0.69759923

00:40:02.838 --> 00:40:05.694 it says that given two subjects with

NOTE Confidence: 0.69759923

00:40:05.694 --> 00:40:08.600 identical values of your propensity score,

NOTE Confidence: 0.69759923

00:40:08.600 --> 00:40:11.576 one from the treated group and

NOTE Confidence: 0.69759923

00:40:11.576 --> 00:40:14.250 one from the control group.

NOTE Confidence: 0.69759923

00:40:14.250 --> 00:40:17.090 If it's the same then analysis may proceed

NOTE Confidence: 0.69759923

00:40:17.090 --> 00:40:20.019 as if the subjects were randomized.

NOTE Confidence: 0.69759923

00:40:20.020 --> 00:40:23.728 And of course the key assumption is that no,

NOTE Confidence: 0.69759923

00:40:23.730 --> 00:40:27.170 there are no observed confounders.

NOTE Confidence: 0.69759923

00:40:27.170 --> 00:40:30.128 There's three types of PS design.

NOTE Confidence: 0.69759923

00:40:30.130 --> 00:40:32.220 She used stratification by PSR

NOTE Confidence: 0.69759923

00:40:32.220 --> 00:40:35.472 subclasses at one to one matching or

NOTE Confidence: 0.69759923

00:40:35.472 --> 00:40:38.172 there's a technique called inverse

NOTE Confidence: 0.69759923

00:40:38.172 --> 00:40:40.480 probability of treatment waiting,

NOTE Confidence: 0.69759923

00:40:40.480 --> 00:40:43.370 but the fondle fundamental considerations

NOTE Confidence: 0.69759923

00:40:43.370 --> 00:40:47.550 of this science is that the outcome days  
NOTE Confidence: 0.69759923

00:40:47.550 --> 00:40:51.329 that data is not used in the PS design.  
NOTE Confidence: 0.69759923

00:40:51.330 --> 00:40:54.738 So in regulatory studies.  
NOTE Confidence: 0.69759923

00:40:54.740 --> 00:40:59.168 So FDA actually uses these two.  
NOTE Confidence: 0.69759923

00:40:59.170 --> 00:41:02.368 To make a decision whether to  
NOTE Confidence: 0.69759923

00:41:02.368 --> 00:41:04.500 approve surgeries or devices.  
NOTE Confidence: 0.69759923

00:41:04.500 --> 00:41:09.156 It must be documented that the PS design.  
NOTE Confidence: 0.69759923

00:41:09.160 --> 00:41:12.597 Start decision had no access to the  
NOTE Confidence: 0.69759923

00:41:12.597 --> 00:41:15.802 outcome data and therefore the PS  
NOTE Confidence: 0.69759923

00:41:15.802 --> 00:41:19.072 design faces a second design phase.  
NOTE Confidence: 0.69759923

00:41:19.080 --> 00:41:22.727 Very briefly, this is just a schematic.  
NOTE Confidence: 0.69759923

00:41:22.730 --> 00:41:24.778 You perform a observation,  
NOTE Confidence: 0.69759923

00:41:24.778 --> 00:41:28.576 ULL study and you have the developed  
NOTE Confidence: 0.69759923

00:41:28.576 --> 00:41:31.088 propensity scores using this  
NOTE Confidence: 0.69759923

00:41:31.088 --> 00:41:35.657 techniques and then at the end of the  
NOTE Confidence: 0.69759923

00:41:35.657 --> 00:41:38.765 day you got PS based matched pairs.

NOTE Confidence: 0.69759923  
00:41:38.770 --> 00:41:41.750 So this is nothing new.  
NOTE Confidence: 0.69759923  
00:41:41.750 --> 00:41:44.928 Independent group has used this to assess  
NOTE Confidence: 0.69759923  
00:41:44.928 --> 00:41:47.509 CPAP treatment and fasting lipids.  
NOTE Confidence: 0.69759923  
00:41:47.510 --> 00:41:48.462 For example,  
NOTE Confidence: 0.69759923  
00:41:48.462 --> 00:41:53.270 and you'll see this is known as the lab plot,  
NOTE Confidence: 0.69759923  
00:41:53.270 --> 00:41:55.982 and here are the cold marriage  
NOTE Confidence: 0.69759923  
00:41:55.982 --> 00:41:58.550 and the PS design sample.  
NOTE Confidence: 0.69759923  
00:41:58.550 --> 00:42:00.542 As you can see,  
NOTE Confidence: 0.69759923  
00:42:00.542 --> 00:42:03.530 simulates that of us if you've  
NOTE Confidence: 0.69759923  
00:42:03.643 --> 00:42:07.108 done a randomized control trial.  
NOTE Confidence: 0.69759923  
00:42:07.110 --> 00:42:10.392 So we believe that the benefits  
NOTE Confidence: 0.69759923  
00:42:10.392 --> 00:42:12.580 of a PS assign.  
NOTE Confidence: 0.69759923  
00:42:12.580 --> 00:42:15.418 And obtain valid estimates of causal  
NOTE Confidence: 0.69759923  
00:42:15.418 --> 00:42:17.310 treatment effects in observation.  
NOTE Confidence: 0.69759923  
00:42:17.310 --> 00:42:19.415 ULL Data Bay creating covariate  
NOTE Confidence: 0.69759923



00:42:19.415 --> 00:42:22.184 balance similar to or even better  
NOTE Confidence: 0.69759923

00:42:22.184 --> 00:42:23.930 than under randomization.  
NOTE Confidence: 0.69759923

00:42:23.930 --> 00:42:27.276 You can use real world patient data  
NOTE Confidence: 0.69759923

00:42:27.276 --> 00:42:30.799 that is often not well represented in  
NOTE Confidence: 0.69759923

00:42:30.799 --> 00:42:34.960 those that you choose to be randomized.  
NOTE Confidence: 0.69759923

00:42:34.960 --> 00:42:37.816 You can include patients that cannot be  
NOTE Confidence: 0.69759923

00:42:37.816 --> 00:42:40.429 otherwise ethically be randomized in RCT's,  
NOTE Confidence: 0.69759923

00:42:40.430 --> 00:42:42.860 and you can evaluate benefits of  
NOTE Confidence: 0.69759923

00:42:42.860 --> 00:42:45.060 treatment efficiently in larger samples.  
NOTE Confidence: 0.69759923

00:42:45.060 --> 00:42:47.165 Because this is a pragmatic  
NOTE Confidence: 0.69759923

00:42:47.165 --> 00:42:50.254 trial so you can just, you know,  
NOTE Confidence: 0.69759923

00:42:50.254 --> 00:42:53.206 you can easily insert this within  
NOTE Confidence: 0.69759923

00:42:53.206 --> 00:42:56.169 the context of clinical practice.  
NOTE Confidence: 0.69759923

00:42:56.170 --> 00:42:57.076 And so,  
NOTE Confidence: 0.69759923

00:42:57.076 --> 00:42:59.794 while an RCT provides the preferred  
NOTE Confidence: 0.69759923

00:42:59.794 --> 00:43:02.877 level of evidence in ideal world,

NOTE Confidence: 0.69759923

00:43:02.880 --> 00:43:06.126 PS designs can achieve the same

NOTE Confidence: 0.69759923

00:43:06.126 --> 00:43:07.749 level of evidence.

NOTE Confidence: 0.69759923

00:43:07.750 --> 00:43:12.356 For treatment effects in the real world.

NOTE Confidence: 0.69759923

00:43:12.360 --> 00:43:13.299 And you know,

NOTE Confidence: 0.69759923

00:43:13.299 --> 00:43:13.612 I,

NOTE Confidence: 0.69759923

00:43:13.612 --> 00:43:16.347 I certainly am not an expert on the

NOTE Confidence: 0.69759923

00:43:16.347 --> 00:43:18.693 propensity score matching at the sign.

NOTE Confidence: 0.69759923

00:43:18.700 --> 00:43:21.859 Greg Maislin in our group is the one that.

NOTE Confidence: 0.7878788

00:43:23.950 --> 00:43:27.170 That that has worked with Donald Rubin,

NOTE Confidence: 0.7878788

00:43:27.170 --> 00:43:29.930 who is the inventor of the

NOTE Confidence: 0.7878788

00:43:29.930 --> 00:43:31.310 propensity score matching,

NOTE Confidence: 0.7878788

00:43:31.310 --> 00:43:32.922 and this this manuscript.

NOTE Confidence: 0.7878788

00:43:32.922 --> 00:43:36.830 He did a good job in explaining this.

NOTE Confidence: 0.7878788

00:43:36.830 --> 00:43:39.130 If you're interested, there's a

NOTE Confidence: 0.7878788

00:43:39.130 --> 00:43:41.430 recently accepted paper in sleep.

NOTE Confidence: 0.9005558

00:43:43.540 --> 00:43:46.980 That was accepted just.  
NOTE Confidence: 0.9005558

00:43:46.980 --> 00:43:49.770 Last last week I believe,  
NOTE Confidence: 0.9005558

00:43:49.770 --> 00:43:53.940 where he explained in detail more  
NOTE Confidence: 0.9005558

00:43:53.940 --> 00:43:56.720 the propensity score matching.  
NOTE Confidence: 0.9005558

00:43:56.720 --> 00:43:59.312 So the proposed clinical trial would  
NOTE Confidence: 0.9005558

00:43:59.312 --> 00:44:02.484 be a multi center RCT of patients  
NOTE Confidence: 0.9005558

00:44:02.484 --> 00:44:05.202 with moderate to severe severe OSA.  
NOTE Confidence: 0.9005558

00:44:05.210 --> 00:44:08.479 We believe we can do this with  
NOTE Confidence: 0.9005558

00:44:08.479 --> 00:44:12.219 either 10 or 1310 to 13 sites you  
NOTE Confidence: 0.9005558

00:44:12.219 --> 00:44:15.540 offer seat up to all patients.  
NOTE Confidence: 0.9005558

00:44:15.540 --> 00:44:18.403 The primary would be similar to the  
NOTE Confidence: 0.9005558

00:44:18.403 --> 00:44:21.478 same a composet endpoint follow up of.  
NOTE Confidence: 0.9005558

00:44:21.480 --> 00:44:23.960 Two to five years.  
NOTE Confidence: 0.9005558

00:44:23.960 --> 00:44:27.056 And we believe that we with 11,000 subjects,  
NOTE Confidence: 0.9005558

00:44:27.060 --> 00:44:29.407 and that includes additional 10% to  
NOTE Confidence: 0.9005558

00:44:29.407 --> 00:44:31.849 maintain power after loss to follow

NOTE Confidence: 0.9005558

00:44:31.849 --> 00:44:34.564 up or trimming of patients in the

NOTE Confidence: 0.9005558

00:44:34.564 --> 00:44:37.150 PS design that you could do this.

NOTE Confidence: 0.9005558

00:44:37.150 --> 00:44:40.633 Now you say, well, that's a lot of subjects.

NOTE Confidence: 0.9005558

00:44:40.640 --> 00:44:42.368 We actually did a.

NOTE Confidence: 0.9005558

00:44:42.368 --> 00:44:47.120 So if you look at the number of subjects.

NOTE Confidence: 0.9005558

00:44:47.120 --> 00:44:49.780 We included this data in in a

NOTE Confidence: 0.9005558

00:44:49.780 --> 00:44:52.059 recent grant that we submitted.

NOTE Confidence: 0.9005558

00:44:52.060 --> 00:44:55.196 The total here is like this is the

NOTE Confidence: 0.9005558

00:44:55.196 --> 00:44:57.859 annual number of subjects in the centers

NOTE Confidence: 0.9005558

00:44:57.859 --> 00:45:01.129 and you have 7 to 6000 potentially.

NOTE Confidence: 0.77396494

00:45:03.770 --> 00:45:05.144 And rollable patients.

NOTE Confidence: 0.77396494

00:45:05.144 --> 00:45:07.892 So we believe that we could

NOTE Confidence: 0.77396494

00:45:07.892 --> 00:45:10.168 we could do this study.

NOTE Confidence: 0.77396494

00:45:10.170 --> 00:45:14.630 It's going to be a heavy lift. We we, we,

NOTE Confidence: 0.77396494

00:45:14.630 --> 00:45:18.390 we we think but but it's worth trying.

NOTE Confidence: 0.77396494

00:45:18.390 --> 00:45:20.919 So to summarize.  
NOTE Confidence: 0.77396494

00:45:20.920 --> 00:45:24.180 Get few minutes for questions.  
NOTE Confidence: 0.77396494

00:45:24.180 --> 00:45:27.792 Sleep apnea is heterogeneous disease symptom  
NOTE Confidence: 0.77396494

00:45:27.792 --> 00:45:32.000 clusters of those with daytime sleepiness,  
NOTE Confidence: 0.77396494

00:45:32.000 --> 00:45:34.472 insomnia, and asymptomatic groups.  
NOTE Confidence: 0.77396494

00:45:34.472 --> 00:45:37.562 Are consistently shown in community  
NOTE Confidence: 0.77396494

00:45:37.562 --> 00:45:40.518 and clinical samples worldwide.  
NOTE Confidence: 0.77396494

00:45:40.520 --> 00:45:42.590 It's important because EDS we  
NOTE Confidence: 0.77396494

00:45:42.590 --> 00:45:45.216 believe is a marker of cardiovascular  
NOTE Confidence: 0.77396494

00:45:45.216 --> 00:45:48.018 risk in in those with OSA,  
NOTE Confidence: 0.77396494

00:45:48.020 --> 00:45:51.919 but not in those without always say.  
NOTE Confidence: 0.77396494

00:45:51.920 --> 00:45:55.202 And Publix are cities of cardio  
NOTE Confidence: 0.77396494

00:45:55.202 --> 00:45:57.390 cardiovascular outcomes in OSA  
NOTE Confidence: 0.77396494

00:45:57.483 --> 00:46:00.613 have been negative and inconsistent  
NOTE Confidence: 0.77396494

00:46:00.613 --> 00:46:03.117 with the large epidemiological  
NOTE Confidence: 0.77396494

00:46:03.117 --> 00:46:05.957 data because of major biases.

NOTE Confidence: 0.77396494

00:46:05.960 --> 00:46:09.662 That's primarily the sample selection bias

NOTE Confidence: 0.77396494

00:46:09.662 --> 00:46:14.468 and bias due to adherence to therapy.

NOTE Confidence: 0.77396494

00:46:14.470 --> 00:46:17.470 In future studies need to include

NOTE Confidence: 0.77396494

00:46:17.470 --> 00:46:20.420 and focus on sleepy subjects.

NOTE Confidence: 0.77396494

00:46:20.420 --> 00:46:21.899 Ethical lamp limitations,

NOTE Confidence: 0.77396494

00:46:21.899 --> 00:46:23.871 including this patients can

NOTE Confidence: 0.77396494

00:46:23.871 --> 00:46:26.270 be overcome with observation.

NOTE Confidence: 0.77396494

00:46:26.270 --> 00:46:29.180 ULL designs using propensity scores an

NOTE Confidence: 0.77396494

00:46:29.180 --> 00:46:32.660 to obtain a robust treatment effect.

NOTE Confidence: 0.77396494

00:46:32.660 --> 00:46:35.135 This designs need to directly

NOTE Confidence: 0.77396494

00:46:35.135 --> 00:46:37.610 ensure balance of covariates related

NOTE Confidence: 0.77396494

00:46:37.692 --> 00:46:39.570 to cardiovascular events,

NOTE Confidence: 0.77396494

00:46:39.570 --> 00:46:41.994 including measures of healthy

NOTE Confidence: 0.77396494

00:46:41.994 --> 00:46:45.024 used userin healthy adhere bias.

NOTE Confidence: 0.77396494

00:46:45.030 --> 00:46:47.682 In patients who are very compliant

NOTE Confidence: 0.77396494

00:46:47.682 --> 00:46:50.286 seat back compared to non users

NOTE Confidence: 0.77396494

00:46:50.286 --> 00:46:52.536 and I'm going to stop there.

NOTE Confidence: 0.77396494

00:46:52.540 --> 00:46:53.130 Thank you.

NOTE Confidence: 0.8320763

00:46:55.240 --> 00:46:57.748 Thank you so much Doctor Magalong,

NOTE Confidence: 0.8320763

00:46:57.750 --> 00:47:00.138 that was really a fantastic talk

NOTE Confidence: 0.8320763

00:47:00.138 --> 00:47:03.115 and I think really help to clarify

NOTE Confidence: 0.8320763

00:47:03.115 --> 00:47:05.719 some of the the residual questions

NOTE Confidence: 0.8320763

00:47:05.720 --> 00:47:09.488 that a lot of us had about how we

NOTE Confidence: 0.8320763

00:47:09.488 --> 00:47:11.578 should be characterizing the benefit.

NOTE Confidence: 0.8320763

00:47:11.580 --> 00:47:13.770 The cardiovascular benefit of CPAP

NOTE Confidence: 0.8320763

00:47:13.770 --> 00:47:16.420 for patients after these these recent

NOTE Confidence: 0.8320763

00:47:16.420 --> 00:47:19.157 trials I want to invite people to

NOTE Confidence: 0.8320763

00:47:19.157 --> 00:47:21.219 unmute themselves and ask questions.

NOTE Confidence: 0.8320763

00:47:21.220 --> 00:47:24.980 I expect there probably are some. Not

NOTE Confidence: 0.7751113

00:47:24.980 --> 00:47:27.180 really, I was going to say I'm not

NOTE Confidence: 0.7751113

00:47:27.180 --> 00:47:29.746 sure I have access to the chat room,

NOTE Confidence: 0.7751113

00:47:29.750 --> 00:47:33.490 but you could just tell us up, Garth. How

NOTE Confidence: 0.87652886

00:47:33.490 --> 00:47:35.830 are you? Thank you so much.

NOTE Confidence: 0.87652886

00:47:35.830 --> 00:47:38.170 That was a really thoughtful presentation.

NOTE Confidence: 0.87652886

00:47:38.170 --> 00:47:40.120 I'm so sorry we can't

NOTE Confidence: 0.87652886

00:47:40.120 --> 00:47:42.070 have you here in person,

NOTE Confidence: 0.87652886

00:47:42.070 --> 00:47:44.776 but we really appreciate you making

NOTE Confidence: 0.87652886

00:47:44.776 --> 00:47:47.239 the time and congratulations on the

NOTE Confidence: 0.87652886

00:47:47.239 --> 00:47:49.408 top Med project and I, you know,

NOTE Confidence: 0.87652886

00:47:49.408 --> 00:47:52.240 I agree with with so much of what

NOTE Confidence: 0.87652886

00:47:52.325 --> 00:47:55.552 you were saying and I think the

NOTE Confidence: 0.87652886

00:47:55.552 --> 00:47:57.359 propensity score matched approach

NOTE Confidence: 0.87652886

00:47:57.359 --> 00:48:00.392 is a great is a great idea and I

NOTE Confidence: 0.87652886

00:48:00.400 --> 00:48:03.368 I think I also want to emphasize.

NOTE Confidence: 0.87652886

00:48:03.370 --> 00:48:07.240 A point that you made which is you know,

NOTE Confidence: 0.87652886

00:48:07.240 --> 00:48:10.040 the trials that have been the three

NOTE Confidence: 0.87652886



00:48:10.040 --> 00:48:12.231 trials that you referenced that  
NOTE Confidence: 0.87652886

00:48:12.231 --> 00:48:15.402 would really have been done to date,  
NOTE Confidence: 0.87652886

00:48:15.410 --> 00:48:17.811 and I think we're really in the  
NOTE Confidence: 0.87652886

00:48:17.811 --> 00:48:19.809 the infancy of doing randomized  
NOTE Confidence: 0.87652886

00:48:19.809 --> 00:48:22.491 control trials in our field compared  
NOTE Confidence: 0.87652886

00:48:22.491 --> 00:48:25.883 to the size of the trials that  
NOTE Confidence: 0.87652886

00:48:25.883 --> 00:48:27.819 typically occur in cardiovascular  
NOTE Confidence: 0.87652886

00:48:27.819 --> 00:48:31.802 disease are tiny and with so many  
NOTE Confidence: 0.87652886

00:48:31.802 --> 00:48:33.548 pharmacological treatments available.  
NOTE Confidence: 0.87652886

00:48:33.550 --> 00:48:36.266 That that actually reflects some of the  
NOTE Confidence: 0.87652886

00:48:36.266 --> 00:48:38.783 biologic pathways by which sleep apnea  
NOTE Confidence: 0.87652886

00:48:38.783 --> 00:48:40.923 can lead to cardiovascular disease.  
NOTE Confidence: 0.87652886

00:48:40.930 --> 00:48:43.170 You really need so those large sample  
NOTE Confidence: 0.87652886

00:48:43.170 --> 00:48:45.737 sizes to to demonstrate an additional  
NOTE Confidence: 0.87652886

00:48:45.737 --> 00:48:48.307 benefit associated with CPAP therapy.  
NOTE Confidence: 0.87652886

00:48:48.310 --> 00:48:50.838 But I think one point I would add

NOTE Confidence: 0.87652886

00:48:50.838 --> 00:48:53.674 is that I think the outcomes may

NOTE Confidence: 0.87652886

00:48:53.674 --> 00:48:56.395 be also different depending on the

NOTE Confidence: 0.87652886

00:48:56.395 --> 00:48:58.970 cardiovascular event that is chosen,

NOTE Confidence: 0.87652886

00:48:58.970 --> 00:49:01.763 and I think save may have pointed

NOTE Confidence: 0.87652886

00:49:01.763 --> 00:49:04.080 to this a little bit.

NOTE Confidence: 0.87652886

00:49:04.080 --> 00:49:06.824 Some of our studies and stroke have

NOTE Confidence: 0.87652886

00:49:06.824 --> 00:49:09.172 suggested this as well that there

NOTE Confidence: 0.87652886

00:49:09.172 --> 00:49:12.170 there may be a more robust affect in

NOTE Confidence: 0.87652886

00:49:12.170 --> 00:49:14.830 stroke for some reason compared to MI,

NOTE Confidence: 0.87652886

00:49:14.830 --> 00:49:17.518 and I think some of the observation.

NOTE Confidence: 0.87652886

00:49:17.520 --> 00:49:21.240 ULL data support that but.

NOTE Confidence: 0.87652886

00:49:21.240 --> 00:49:24.498 Another another approach I think to

NOTE Confidence: 0.87652886

00:49:24.498 --> 00:49:27.260 doing a randomized controlled trial.

NOTE Confidence: 0.87652886

00:49:27.260 --> 00:49:30.382 We've done is is more of a

NOTE Confidence: 0.87652886

00:49:30.382 --> 00:49:31.720 comparative effectiveness approach,

NOTE Confidence: 0.87652886

00:49:31.720 --> 00:49:34.204 and so you're not randomizing a  
NOTE Confidence: 0.87652886

00:49:34.204 --> 00:49:36.420 patient that you have diagnosed  
NOTE Confidence: 0.87652886

00:49:36.420 --> 00:49:39.300 with sleep apnea and not treated,  
NOTE Confidence: 0.87652886

00:49:39.300 --> 00:49:42.296 but but rather randomizing to a diagnosis  
NOTE Confidence: 0.87652886

00:49:42.296 --> 00:49:44.210 and treatment intervention strategy,  
NOTE Confidence: 0.87652886

00:49:44.210 --> 00:49:46.880 trial versus the usual care approach,  
NOTE Confidence: 0.87652886

00:49:46.880 --> 00:49:49.414 and I think that that might help  
NOTE Confidence: 0.87652886

00:49:49.414 --> 00:49:52.333 to get through some of the ethical  
NOTE Confidence: 0.87652886

00:49:52.333 --> 00:49:54.967 challenges and could be a potentially  
NOTE Confidence: 0.87652886

00:49:55.045 --> 00:49:58.225 useful strategy in a very high  
NOTE Confidence: 0.87652886

00:49:58.225 --> 00:49:59.815 pretest probability population.  
NOTE Confidence: 0.8163701

00:50:00.640 --> 00:50:01.690 Thank you Clark.  
NOTE Confidence: 0.8163701

00:50:01.690 --> 00:50:04.280 With it, you know I just didn't have  
NOTE Confidence: 0.8163701

00:50:04.280 --> 00:50:07.270 the time to to go into those details,  
NOTE Confidence: 0.8163701

00:50:07.270 --> 00:50:09.020 but that was those points.  
NOTE Confidence: 0.8163701

00:50:09.020 --> 00:50:10.756 Your point about Cerebro

NOTE Confidence: 0.8163701

00:50:10.756 --> 00:50:12.058 vascular disease versus.

NOTE Confidence: 0.8163701

00:50:12.060 --> 00:50:14.700 You know, ameißen all those

NOTE Confidence: 0.8163701

00:50:14.700 --> 00:50:16.812 those kind of events?

NOTE Confidence: 0.8163701

00:50:16.820 --> 00:50:19.922 Certainly there is data to suggest

NOTE Confidence: 0.8163701

00:50:19.922 --> 00:50:23.093 that you'll have probably a greater

NOTE Confidence: 0.8163701

00:50:23.093 --> 00:50:25.633 effect on cerebral vascular effect

NOTE Confidence: 0.8163701

00:50:25.633 --> 00:50:29.428 events and and and the other issue

NOTE Confidence: 0.8163701

00:50:29.428 --> 00:50:32.153 of doing a comparative effectiveness.

NOTE Confidence: 0.8163701

00:50:32.160 --> 00:50:34.810 I didn't list it here,

NOTE Confidence: 0.8163701

00:50:34.810 --> 00:50:39.388 it was actually in the paper.

NOTE Confidence: 0.8163701

00:50:39.390 --> 00:50:40.822 Potentially you could say,

NOTE Confidence: 0.8163701

00:50:40.822 --> 00:50:43.248 well, let's do an enhance.

NOTE Confidence: 0.8163701

00:50:43.248 --> 00:50:48.096 Add CPAP adherence so that that way you can

NOTE Confidence: 0.8163701

00:50:48.096 --> 00:50:51.925 have a separation between with usage right.

NOTE Confidence: 0.8163701

00:50:51.930 --> 00:50:53.850 We believe that they may.

NOTE Confidence: 0.8163701

00:50:53.850 --> 00:50:56.524 That might actually affect the sample size,

NOTE Confidence: 0.8163701

00:50:56.530 --> 00:50:58.440 and you're going to because

NOTE Confidence: 0.8163701

00:50:58.440 --> 00:50:59.968 it's you're going to.

NOTE Confidence: 0.8163701

00:50:59.970 --> 00:51:02.870 You're probably going to need.

NOTE Confidence: 0.8163701

00:51:02.870 --> 00:51:04.430 A very large sample size,

NOTE Confidence: 0.8163701

00:51:04.430 --> 00:51:07.886 if that's the approach that you're going to.

NOTE Confidence: 0.8163701

00:51:07.890 --> 00:51:12.126 That you are going to take.

NOTE Confidence: 0.8163701

00:51:12.130 --> 00:51:16.897 But but those are very good points.

NOTE Confidence: 0.7638806

00:51:18.500 --> 00:51:19.658 Can I hire

NOTE Confidence: 0.7638806

00:51:19.660 --> 00:51:20.818 lease is high

NOTE Confidence: 0.7638806

00:51:20.820 --> 00:51:22.742 High made Nelson? How are

NOTE Confidence: 0.7638806

00:51:22.742 --> 00:51:25.058 you good? Thanks oh that was

NOTE Confidence: 0.7638806

00:51:25.060 --> 00:51:26.608 a great insightful talk.

NOTE Confidence: 0.7638806

00:51:26.610 --> 00:51:28.540 I'm just going to ask

NOTE Confidence: 0.7638806

00:51:28.540 --> 00:51:29.689 it kind of

NOTE Confidence: 0.7638806

00:51:29.690 --> 00:51:30.848 a different question.

NOTE Confidence: 0.7638806

00:51:30.850 --> 00:51:33.938 We're going to treat all patients with OSA

NOTE Confidence: 0.7638806

00:51:33.940 --> 00:51:36.640 that are sleepy because we have no

NOTE Confidence: 0.7638806

00:51:36.640 --> 00:51:38.568 other better treatment than CPAP.

NOTE Confidence: 0.851808

00:51:39.580 --> 00:51:41.168 If that's a statement,

NOTE Confidence: 0.851808

00:51:41.170 --> 00:51:43.155 then who cares about whether

NOTE Confidence: 0.851808

00:51:43.155 --> 00:51:45.928 CPAP is going to reduce or not

NOTE Confidence: 0.851808

00:51:45.928 --> 00:51:47.520 reduce cardiovascular events? OK,

NOTE Confidence: 0.851808

00:51:47.520 --> 00:51:49.510 so the question is the

NOTE Confidence: 0.851808

00:51:49.510 --> 00:51:51.490 non sleeping group that we

NOTE Confidence: 0.851808

00:51:51.490 --> 00:51:53.474 don't really have the full

NOTE Confidence: 0.851808

00:51:53.474 --> 00:51:55.860 confidence that whether they do or

NOTE Confidence: 0.851808

00:51:55.860 --> 00:51:57.840 they do not have that

NOTE Confidence: 0.8431091833333333

00:51:57.840 --> 00:52:00.540 increase risk. And that's the

NOTE Confidence: 0.8431091833333333

00:52:00.540 --> 00:52:03.074 tough rope to trade with something

NOTE Confidence: 0.8431091833333333

00:52:03.074 --> 00:52:05.620 like super, which lends itself to

NOTE Confidence: 0.82571155

00:52:05.620 --> 00:52:06.880 suboptimal adherence on

NOTE Confidence: 0.82571155

00:52:06.880 --> 00:52:08.149 a long term

NOTE Confidence: 0.82571155

00:52:08.150 --> 00:52:11.050 basis. How we gonna actually.

NOTE Confidence: 0.82571155

00:52:11.050 --> 00:52:12.800 Answered that question.

NOTE Confidence: 0.82571155

00:52:13.760 --> 00:52:16.325 Well, to the point of so the the first

NOTE Confidence: 0.82571155

00:52:16.325 --> 00:52:18.535 point or question is where are you

NOTE Confidence: 0.82571155

00:52:18.535 --> 00:52:20.949 going to treat this patient's anyway?

NOTE Confidence: 0.82571155

00:52:20.950 --> 00:52:23.239 Because they're sleepy is that is that,

NOTE Confidence: 0.82571155

00:52:23.240 --> 00:52:26.467 is that correct? Well, you know,

NOTE Confidence: 0.82571155

00:52:26.467 --> 00:52:28.910 we believe that there is a reason

NOTE Confidence: 0.82571155

00:52:28.987 --> 00:52:31.269 and one of them there are other.

NOTE Confidence: 0.82571155

00:52:31.270 --> 00:52:33.328 You know. There are several reasons,

NOTE Confidence: 0.82571155

00:52:33.330 --> 00:52:36.738 but the major one is that.

NOTE Confidence: 0.82571155

00:52:36.740 --> 00:52:38.917 You know right now I should know.

NOTE Confidence: 0.835407286

00:52:41.840 --> 00:52:45.520 Screening for or identifying.

NOTE Confidence: 0.835407286

00:52:45.520 --> 00:52:48.075 UH, patients, for example,

NOTE Confidence: 0.835407286

00:52:48.075 --> 00:52:51.345 a large scale in primary practice

NOTE Confidence: 0.835407286

00:52:51.345 --> 00:52:54.368 is is not recommended, right?

NOTE Confidence: 0.835407286

00:52:54.368 --> 00:52:57.458 So we believe that showing

NOTE Confidence: 0.835407286

00:52:57.458 --> 00:52:59.930 that sifat indeed impacts.

NOTE Confidence: 0.835407286

00:52:59.930 --> 00:53:02.674 On whether sudrow basket

NOTE Confidence: 0.835407286

00:53:02.674 --> 00:53:05.418 or or cardiovascular event

NOTE Confidence: 0.835407286

00:53:05.418 --> 00:53:08.428 would would sway you know.

NOTE Confidence: 0.835407286

00:53:08.430 --> 00:53:10.170 A people too.

NOTE Confidence: 0.82042664

00:53:12.820 --> 00:53:16.684 To identify more cases of sleep apnea and

NOTE Confidence: 0.82042664

00:53:16.684 --> 00:53:19.985 perhaps towards towards screening, although

NOTE Confidence: 0.82042664

00:53:19.985 --> 00:53:24.335 that's a different entirely different topic.

NOTE Confidence: 0.82042664

00:53:24.340 --> 00:53:28.876 The other thing is, as in other studies.

NOTE Confidence: 0.82042664

00:53:28.880 --> 00:53:32.396 That show that you know physician

NOTE Confidence: 0.82042664

00:53:32.396 --> 00:53:35.250 advocacy of treatment. For example,

NOTE Confidence: 0.82042664

00:53:35.250 --> 00:53:39.610 if if if they know that the treatment

NOTE Confidence: 0.82042664



00:53:39.719 --> 00:53:43.734 makes a difference, they would indeed.  
NOTE Confidence: 0.82042664

00:53:43.734 --> 00:53:47.622 Outside of the excessive daytime sleepiness,  
NOTE Confidence: 0.82042664

00:53:47.630 --> 00:53:50.990 they would indeed encourage identification of  
NOTE Confidence: 0.82042664

00:53:50.990 --> 00:53:55.468 patients as well as US treatment of patients,  
NOTE Confidence: 0.82042664

00:53:55.470 --> 00:53:59.198 in that I think that's well known in  
NOTE Confidence: 0.82042664

00:53:59.198 --> 00:54:03.488 the in the cardiovascular literature.  
NOTE Confidence: 0.82042664

00:54:03.490 --> 00:54:09.266 Your second point is about the non sleepy.  
NOTE Confidence: 0.82042664

00:54:09.270 --> 00:54:10.878 Patients out how we're going to,  
NOTE Confidence: 0.82042664

00:54:10.880 --> 00:54:16.230 how we're going to treat them. I.  
NOTE Confidence: 0.82042664

00:54:16.230 --> 00:54:20.559 It's. I mean, that's as far as there  
NOTE Confidence: 0.82042664

00:54:20.559 --> 00:54:23.379 are others who will argue with you.  
NOTE Confidence: 0.82042664

00:54:23.380 --> 00:54:28.908 That if they are asymptomatic.  
NOTE Confidence: 0.82042664

00:54:28.910 --> 00:54:31.250 Up at the present time,  
NOTE Confidence: 0.82042664

00:54:31.250 --> 00:54:34.820 there is no rationale to treat them.  
NOTE Confidence: 0.82042664

00:54:34.820 --> 00:54:36.856 I mean, I know,  
NOTE Confidence: 0.82042664

00:54:36.856 --> 00:54:40.880 I know that's probably a very controversial

NOTE Confidence: 0.82042664

00:54:40.880 --> 00:54:46.016 statement given some of the guidelines.

NOTE Confidence: 0.82042664

00:54:46.020 --> 00:54:51.564 About at least the data that we have.

NOTE Confidence: 0.82042664

00:54:51.570 --> 00:54:52.641 In the Sleep,

NOTE Confidence: 0.82042664

00:54:52.641 --> 00:54:54.783 Heart tells Saudi and of course

NOTE Confidence: 0.82042664

00:54:54.783 --> 00:54:56.860 that needs to be replicated.

NOTE Confidence: 0.82042664

00:54:56.860 --> 00:54:57.734 It's it's.

NOTE Confidence: 0.82042664

00:54:57.734 --> 00:54:59.919 It's actually only the sleepy

NOTE Confidence: 0.82042664

00:54:59.919 --> 00:55:02.657 group that was that was at risk,

NOTE Confidence: 0.82042664

00:55:02.660 --> 00:55:05.138 or at least that was what

NOTE Confidence: 0.8487515

00:55:05.140 --> 00:55:07.625 was shown by the panel group.

NOTE Confidence: 0.8487515

00:55:07.625 --> 00:55:10.109 Yeah, the problem with the Epworth,

NOTE Confidence: 0.8487515

00:55:10.110 --> 00:55:13.834 which we use all of us use for assessing

NOTE Confidence: 0.8487515

00:55:13.834 --> 00:55:15.490 subjective sleepiness is very,

NOTE Confidence: 0.8487515

00:55:15.490 --> 00:55:16.729 very susceptible to

NOTE Confidence: 0.8487515

00:55:16.730 --> 00:55:17.969 false negative scores.

NOTE Confidence: 0.8487515

00:55:17.969 --> 00:55:20.034 Yeah, I pointed that out.  
NOTE Confidence: 0.8487515

00:55:20.040 --> 00:55:22.465 I specifically said that actually  
NOTE Confidence: 0.8487515

00:55:22.465 --> 00:55:25.819 that the subtype of sleep apnea is  
NOTE Confidence: 0.8487515

00:55:25.819 --> 00:55:28.345 not only does that only include.  
NOTE Confidence: 0.8487515

00:55:28.350 --> 00:55:30.978 The The Epworth Sleepiness Scale score.  
NOTE Confidence: 0.8487515

00:55:30.980 --> 00:55:33.872 So determining those subtypes is actually  
NOTE Confidence: 0.8487515

00:55:33.872 --> 00:55:37.038 there are other questions that were included  
NOTE Confidence: 0.8487515

00:55:37.038 --> 00:55:39.754 that although it's it's the F word,  
NOTE Confidence: 0.8487515

00:55:39.760 --> 00:55:42.400 was a component of defining the  
NOTE Confidence: 0.8487515

00:55:42.400 --> 00:55:45.336 sleepy subtype. But it's it's not.  
NOTE Confidence: 0.8487515

00:55:45.336 --> 00:55:49.830 It's not the F word. Alone.  
NOTE Confidence: 0.8487515

00:55:49.830 --> 00:55:51.980 That defines the sleepy subtype.  
NOTE Confidence: 0.8487515

00:55:51.980 --> 00:55:54.990 At least you know in, in, in,  
NOTE Confidence: 0.8487515

00:55:54.990 --> 00:55:57.570 in the papers that we have  
NOTE Confidence: 0.809432

00:55:57.570 --> 00:56:00.150 established what we have popped. It  
NOTE Confidence: 0.809432

00:56:00.150 --> 00:56:02.730 have worked their real world situation.

NOTE Confidence: 0.809432  
00:56:02.730 --> 00:56:05.310 We use Epworth Aurora comperable type  
NOTE Confidence: 0.809432  
00:56:05.310 --> 00:56:07.460 of a self administered questionnaire  
NOTE Confidence: 0.809432  
00:56:07.460 --> 00:56:08.750 as opposed in  
NOTE Confidence: 0.809432  
00:56:08.750 --> 00:56:11.330 a research based type of tools.  
NOTE Confidence: 0.809432  
00:56:11.330 --> 00:56:14.340 So identifying those people with or without  
NOTE Confidence: 0.809432  
00:56:14.340 --> 00:56:16.490 sleepiness is going to be  
NOTE Confidence: 0.809432  
00:56:16.490 --> 00:56:19.930 prone to bias against or in favor of  
NOTE Confidence: 0.809432  
00:56:19.930 --> 00:56:21.220 selecting people for  
NOTE Confidence: 0.770240916666667  
00:56:21.220 --> 00:56:23.964 treatments. Right after that,  
NOTE Confidence: 0.770240916666667  
00:56:23.964 --> 00:56:28.080 and then we actually so Brendan  
NOTE Confidence: 0.770240916666667  
00:56:28.197 --> 00:56:31.503 Keenan at Penn actually has created  
NOTE Confidence: 0.770240916666667  
00:56:31.503 --> 00:56:35.892 a so based on the on the studies  
NOTE Confidence: 0.770240916666667  
00:56:35.892 --> 00:56:41.052 that we publish it is there is a an  
NOTE Confidence: 0.770240916666667  
00:56:41.052 --> 00:56:45.840 app Web type app that you could.  
NOTE Confidence: 0.770240916666667  
00:56:45.840 --> 00:56:48.174 Plug in the answers to the  
NOTE Confidence: 0.770240916666667

00:56:48.174 --> 00:56:50.549 questions and it will give you.  
NOTE Confidence: 0.770240916666667

00:56:50.550 --> 00:56:52.645 The answer whether that patient  
NOTE Confidence: 0.770240916666667

00:56:52.645 --> 00:56:54.740 belongs to a sleepy subtype,  
NOTE Confidence: 0.770240916666667

00:56:54.740 --> 00:56:57.330 but you know whether that lends itself  
NOTE Confidence: 0.770240916666667

00:56:57.330 --> 00:57:00.190 to the usual busy clinical practice.  
NOTE Confidence: 0.770240916666667

00:57:00.190 --> 00:57:04.810 I I I agree with you. Yes,  
NOTE Confidence: 0.88995653

00:57:04.810 --> 00:57:07.330 so why aren't we using objective  
NOTE Confidence: 0.88995653

00:57:07.330 --> 00:57:08.590 measures of sleepiness?  
NOTE Confidence: 0.88995653

00:57:08.590 --> 00:57:11.957 I mean, there's a big literature showing  
NOTE Confidence: 0.88995653

00:57:11.957 --> 00:57:14.439 that subjective measures are terrible.  
NOTE Confidence: 0.88995653

00:57:14.440 --> 00:57:17.592 An an an an so that's like, uh,  
NOTE Confidence: 0.88995653

00:57:17.592 --> 00:57:19.824 that's that's a real problem and  
NOTE Confidence: 0.88995653

00:57:19.824 --> 00:57:22.478 I think the other problem in a  
NOTE Confidence: 0.88995653

00:57:22.478 --> 00:57:25.212 lot of these studies is that they  
NOTE Confidence: 0.88995653

00:57:25.212 --> 00:57:27.537 are studying patients too late.  
NOTE Confidence: 0.88995653

00:57:27.540 --> 00:57:29.530 So in the safe trial,

NOTE Confidence: 0.88995653

00:57:29.530 --> 00:57:31.510 the average patient was over,

NOTE Confidence: 0.88995653

00:57:31.510 --> 00:57:33.500 you know, 61 years old.

NOTE Confidence: 0.88995653

00:57:33.500 --> 00:57:34.824 By then the patient,

NOTE Confidence: 0.88995653

00:57:34.824 --> 00:57:36.479 already his cardiovasc he or

NOTE Confidence: 0.88995653

00:57:36.479 --> 00:57:38.260 her cardiovascular system,

NOTE Confidence: 0.88995653

00:57:38.260 --> 00:57:39.848 is already really abnormal.

NOTE Confidence: 0.88995653

00:57:39.848 --> 00:57:41.039 And for example,

NOTE Confidence: 0.88995653

00:57:41.040 --> 00:57:43.819 in in an art clinic in Canada,

NOTE Confidence: 0.88995653

00:57:43.820 --> 00:57:47.376 our average patient was 48 years old.

NOTE Confidence: 0.88995653

00:57:47.380 --> 00:57:49.940 And and and and and at the age

NOTE Confidence: 0.88995653

00:57:49.940 --> 00:57:52.301 of 48 they had already had

NOTE Confidence: 0.88995653

00:57:52.301 --> 00:57:55.380 symptoms for like 5 to 10 years.

NOTE Confidence: 0.88995653

00:57:55.380 --> 00:57:57.510 They already were very heavy

NOTE Confidence: 0.88995653

00:57:57.510 --> 00:57:59.640 users of health care resource

NOTE Confidence: 0.88995653

00:57:59.716 --> 00:58:01.480 is for five to 10 years,

NOTE Confidence: 0.88995653

00:58:01.480 --> 00:58:03.385 and that's the group that  
NOTE Confidence: 0.88995653

00:58:03.385 --> 00:58:05.290 we ought to be studying,  
NOTE Confidence: 0.88995653

00:58:05.290 --> 00:58:07.195 not the ones that already  
NOTE Confidence: 0.88995653

00:58:07.195 --> 00:58:09.100 have a bunch of diseases.  
NOTE Confidence: 0.8474037

00:58:10.120 --> 00:58:11.864 Yeah, that's certainly true.  
NOTE Confidence: 0.8474037

00:58:11.864 --> 00:58:14.344 I mean, again, that May contributes  
NOTE Confidence: 0.8474037

00:58:14.344 --> 00:58:16.349 to remember these are all  
NOTE Confidence: 0.8474037

00:58:16.349 --> 00:58:18.772 secondary prevention trials, right?  
NOTE Confidence: 0.8474037

00:58:18.772 --> 00:58:21.980 They had to have.  
NOTE Confidence: 0.8474037

00:58:21.980 --> 00:58:24.700 CVD in order to be enrolled in in  
NOTE Confidence: 0.8474037

00:58:24.700 --> 00:58:27.713 the in the in the Safe study and  
NOTE Confidence: 0.8474037

00:58:27.713 --> 00:58:30.703 the other ones are they had acute  
NOTE Confidence: 0.8474037

00:58:30.703 --> 00:58:33.043 coronary syndrome and then the  
NOTE Confidence: 0.8474037

00:58:33.043 --> 00:58:35.935 the other study they you have to  
NOTE Confidence: 0.8474037

00:58:35.935 --> 00:58:38.372 have a cast proven coronary artery  
NOTE Confidence: 0.8474037

00:58:38.372 --> 00:58:41.179 disease and and I agree with that.

NOTE Confidence: 0.8474037

00:58:41.180 --> 00:58:44.200 Perhaps you know the the.

NOTE Confidence: 0.8474037

00:58:44.200 --> 00:58:46.018 Although I think the entry criteria

NOTE Confidence: 0.8474037

00:58:46.018 --> 00:58:48.220 of the age is about is is 18,

NOTE Confidence: 0.8474037

00:58:48.220 --> 00:58:50.440 but you're saying that the.

NOTE Confidence: 0.8474037

00:58:50.440 --> 00:58:53.086 The the the average age is there,

NOTE Confidence: 0.8474037

00:58:53.090 --> 00:58:54.598 they're older, they're older.

NOTE Confidence: 0.8348341

00:58:54.600 --> 00:58:57.160 Yeah, I mean it. It reminds me of

NOTE Confidence: 0.8348341

00:58:57.160 --> 00:58:59.162 the Women's Health Initiative study

NOTE Confidence: 0.8348341

00:58:59.162 --> 00:59:02.151 where the you know they were giving.

NOTE Confidence: 0.8348341

00:59:02.160 --> 00:59:03.672 They were treating women.

NOTE Confidence: 0.8348341

00:59:03.672 --> 00:59:06.315 You know, for menopause like 15 years

NOTE Confidence: 0.8348341

00:59:06.315 --> 00:59:08.584 after their menopause, Ann and Dan.

NOTE Confidence: 0.8348341

00:59:08.584 --> 00:59:11.231 And that's you know. In other words,

NOTE Confidence: 0.8348341

00:59:11.231 --> 00:59:13.493 we're treating patients way too late.

NOTE Confidence: 0.8348341

00:59:13.500 --> 00:59:16.139 We ought to be screening them earlier,

NOTE Confidence: 0.8348341



00:59:16.140 --> 00:59:18.570 and that's where I think the  
NOTE Confidence: 0.8348341

00:59:18.570 --> 00:59:20.949 RTC should focus an in fact.  
NOTE Confidence: 0.8348341

00:59:20.950 --> 00:59:22.750 There are several studies early,  
NOTE Confidence: 0.8348341

00:59:22.750 --> 00:59:24.652 you know years ago that showed  
NOTE Confidence: 0.8348341

00:59:24.652 --> 00:59:26.406 that that that the mortality  
NOTE Confidence: 0.8348341

00:59:26.406 --> 00:59:28.506 of patients with sleep apnea,  
NOTE Confidence: 0.8348341

00:59:28.510 --> 00:59:31.390 the older patients actually don't do so bad.  
NOTE Confidence: 0.8348341

00:59:31.390 --> 00:59:34.086 You know it's the younger ones that have  
NOTE Confidence: 0.8348341

00:59:34.086 --> 00:59:36.788 that seem to have the higher mortality.  
NOTE Confidence: 0.87799215

00:59:37.430 --> 00:59:40.010 Yeah, that's because of this.  
NOTE Confidence: 0.87799215

00:59:40.010 --> 00:59:42.066 Basically as survival effect,  
NOTE Confidence: 0.87799215

00:59:42.066 --> 00:59:44.710 right? Yeah, yeah. Ulysses  
NOTE Confidence: 0.79342604

00:59:44.710 --> 00:59:46.098 I have a question.  
NOTE Confidence: 0.79342604

00:59:46.100 --> 00:59:49.228 This is Nancy Rediker High we met. I think  
NOTE Confidence: 0.79342604

00:59:49.230 --> 00:59:50.280 that grant reviews.  
NOTE Confidence: 0.79342604

00:59:50.280 --> 00:59:52.364 Hi, my question is about the

NOTE Confidence: 0.79342604

00:59:52.364 --> 00:59:54.448 mechanisms of the sleepy patients and

NOTE Confidence: 0.79342604

00:59:54.450 --> 00:59:55.500 CVD. So you've

NOTE Confidence: 0.79342604

00:59:55.500 --> 00:59:57.240 mentioned this study about the

NOTE Confidence: 0.79342604

00:59:57.240 --> 00:59:59.326 looking at genetics and and what

NOTE Confidence: 0.79342604

00:59:59.326 --> 01:00:01.312 could you let? You know there's,

NOTE Confidence: 0.79342604

01:00:01.312 --> 01:00:02.927 so there's obviously all different

NOTE Confidence: 0.8757959

01:00:02.930 --> 01:00:04.170 kind of genetic pathways,

NOTE Confidence: 0.8757959

01:00:04.170 --> 01:00:05.100 but is it

NOTE Confidence: 0.8757959

01:00:05.100 --> 01:00:06.640 possible that this is just,

NOTE Confidence: 0.8757959

01:00:06.640 --> 01:00:08.181 you know, the sleepy patient,

NOTE Confidence: 0.8757959

01:00:08.181 --> 01:00:09.730 it's just it's inflammatory or

NOTE Confidence: 0.8757959

01:00:09.730 --> 01:00:11.280 it's some other underlying process.

NOTE Confidence: 0.8757959

01:00:11.280 --> 01:00:12.376 It's causing the connections,

NOTE Confidence: 0.8757959

01:00:12.376 --> 01:00:13.746 so that's really just an

NOTE Confidence: 0.8757959

01:00:13.746 --> 01:00:15.121 epic phenomenon that there's

NOTE Confidence: 0.8757959

01:00:15.121 --> 01:00:16.525 inflammation going on anyway,  
NOTE Confidence: 0.8757959

01:00:16.530 --> 01:00:17.758 or it matches what  
NOTE Confidence: 0.8757959

01:00:17.760 --> 01:00:18.690 I'm guessing, but  
NOTE Confidence: 0.8757959

01:00:18.690 --> 01:00:19.930 what? What kind of  
NOTE Confidence: 0.8757959

01:00:19.930 --> 01:00:21.778 genetic pathways are you looking at?  
NOTE Confidence: 0.8684457

01:00:22.730 --> 01:00:26.224 Well, that that that Grant is, we don't know.  
NOTE Confidence: 0.8684457

01:00:26.224 --> 01:00:28.940 Basically, you see that it's it's there,  
NOTE Confidence: 0.8684457

01:00:28.940 --> 01:00:31.267 but there are possible mechanisms and  
NOTE Confidence: 0.8684457

01:00:31.267 --> 01:00:33.976 and the number one suspect will be.  
NOTE Confidence: 0.8684457

01:00:33.980 --> 01:00:36.696 Of course what you mentioned is inflammation,  
NOTE Confidence: 0.8684457

01:00:36.700 --> 01:00:39.550 right? There is some evidence of  
NOTE Confidence: 0.8684457

01:00:39.550 --> 01:00:41.450 inflammation activity may cause  
NOTE Confidence: 0.8684457

01:00:41.527 --> 01:00:43.679 you to be to be to be sleepy.  
NOTE Confidence: 0.8684457

01:00:43.680 --> 01:00:47.550 Now to the point of.  
NOTE Confidence: 0.8684457

01:00:47.550 --> 01:00:53.507 The PV, the objective evidence of sleepiness.  
NOTE Confidence: 0.8684457

01:00:53.510 --> 01:00:55.976 We could potentially add results of,

NOTE Confidence: 0.8684457  
01:00:55.980 --> 01:00:58.035 although it's not really sleeping  
NOTE Confidence: 0.8684457  
01:00:58.035 --> 01:00:59.679 as its vigilance would.  
NOTE Confidence: 0.8684457  
01:00:59.680 --> 01:01:02.140 That would be easy to incorporate,  
NOTE Confidence: 0.8684457  
01:01:02.140 --> 01:01:04.195 would be psycho motor vigilance  
NOTE Confidence: 0.8684457  
01:01:04.195 --> 01:01:05.428 testing for example.  
NOTE Confidence: 0.8684457  
01:01:05.430 --> 01:01:06.558 That might be.  
NOTE Confidence: 0.8684457  
01:01:06.558 --> 01:01:09.190 That that might be a that might  
NOTE Confidence: 0.8684457  
01:01:09.277 --> 01:01:12.047 provide really confidence on the  
NOTE Confidence: 0.8684457  
01:01:12.047 --> 01:01:14.263 defining the sleepy subtype.  
NOTE Confidence: 0.8684457  
01:01:14.270 --> 01:01:17.750 One Pvt is so easy to do now.  
NOTE Confidence: 0.8684457  
01:01:17.750 --> 01:01:19.930 I mean, we could do  
NOTE Confidence: 0.80611736  
01:01:19.930 --> 01:01:21.670 it on an iPad.  
NOTE Confidence: 0.80611736  
01:01:21.670 --> 01:01:24.280 We don't need a special device.  
NOTE Confidence: 0.80611736  
01:01:24.280 --> 01:01:26.455 Yeah, it feels like something  
NOTE Confidence: 0.80611736  
01:01:26.455 --> 01:01:28.630 that could readily be incorporated  
NOTE Confidence: 0.80611736

01:01:28.630 --> 01:01:29.929 into clinical encounters.  
NOTE Confidence: 0.86336946

01:01:31.610 --> 01:01:34.013 It is just going back to the to the  
NOTE Confidence: 0.86336946

01:01:34.013 --> 01:01:36.555 top match of the the way that would  
NOTE Confidence: 0.86336946

01:01:36.555 --> 01:01:38.938 that Grant was structured was that.  
NOTE Confidence: 0.86336946

01:01:38.940 --> 01:01:41.040 We you know, it's basically  
NOTE Confidence: 0.86336946

01:01:41.040 --> 01:01:44.400 we're going to do a whole genome.  
NOTE Confidence: 0.86336946

01:01:44.400 --> 01:01:48.144 All all the mix an all the all the  
NOTE Confidence: 0.86336946

01:01:48.144 --> 01:01:51.440 epigenetic things and see if there are  
NOTE Confidence: 0.86336946

01:01:51.440 --> 01:01:54.870 any differences in the in the subtypes.  
NOTE Confidence: 0.86336946

01:01:54.870 --> 01:01:57.775 Of course, when when the data is  
NOTE Confidence: 0.86336946

01:01:57.775 --> 01:01:59.870 published in publicly available,  
NOTE Confidence: 0.86336946

01:01:59.870 --> 01:02:02.971 there's a bunch of things that you  
NOTE Confidence: 0.86336946

01:02:02.971 --> 01:02:06.238 could do with that with that data.  
NOTE Confidence: 0.8460196

01:02:08.340 --> 01:02:10.328 Thank you so much for the accounts.  
NOTE Confidence: 0.8460196

01:02:10.330 --> 01:02:12.250 I think as there are a few minutes  
NOTE Confidence: 0.8460196

01:02:12.250 --> 01:02:14.180 past the hour and people hung around

NOTE Confidence: 0.8460196

01:02:14.180 --> 01:02:16.579 because this is such a compelling topic,

NOTE Confidence: 0.8460196

01:02:16.580 --> 01:02:19.420 but we should still cut it off here and thank

NOTE Confidence: 0.8460196

01:02:19.420 --> 01:02:20.552 you again. Needless yeah.

NOTE Confidence: 0.8460196

01:02:20.552 --> 01:02:21.684 Thanks for inviting me,

NOTE Confidence: 0.8460196

01:02:21.690 --> 01:02:26.150 I appreciate it. Thank you. Thanks.

NOTE Confidence: 0.8460196

01:02:26.150 --> 01:02:27.950 You like Michelle? Take care.