WEBVTT

NOTE duration:"01:16:06"

NOTE recognizability:0.784

NOTE language:en-us

NOTE Confidence: 0.746227261666667

00:00:00.000 --> 00:00:01.080 And and they were both OK.

NOTE Confidence: 0.6382003

00:00:03.360 --> 00:00:05.158 All right. Hello everyone. Thank

NOTE Confidence: 0.96179443

 $00{:}00{:}05{.}160 \dashrightarrow 00{:}00{:}06{.}685$  you for coming to our

NOTE Confidence: 0.96179443

 $00:00:06.685 \rightarrow 00:00:08.120$  psychedelic seminar for December.

NOTE Confidence: 0.96179443

 $00:00:08.120 \dashrightarrow 00:00:11.352$  We have our own Jerry Sanacora and

NOTE Confidence: 0.96179443

00:00:11.352 --> 00:00:14.510 Ben Kilmendi here today who ran our

NOTE Confidence: 0.96179443

 $00{:}00{:}14.510 \dashrightarrow 00{:}00{:}17.090$  sites Yale sites contribution to

NOTE Confidence: 0.96179443

 $00{:}00{:}17.090 \dashrightarrow 00{:}00{:}20.970$  the bona funded study of multi site

NOTE Confidence: 0.96179443

 $00{:}00{:}20{.}970 \dashrightarrow 00{:}00{:}23{.}520$  study of psilocybin in the treatment

NOTE Confidence: 0.96179443

 $00{:}00{:}23.520$  -->  $00{:}00{:}25.680$  of depression which was published in

NOTE Confidence: 0.96179443

 $00{:}00{:}25.680 \dashrightarrow 00{:}00{:}28.480$  JAMA Psychiatry earlier this year.

NOTE Confidence: 0.96179443

 $00{:}00{:}28.480 \dashrightarrow 00{:}00{:}30.940$  And so I I thought it'd be great to have NOTE Confidence: 0.96179443

00:00:31.001 --> 00:00:33.393 Jerry and Ben tell us about that study, NOTE Confidence: 0.96179443

1

00:00:33.400 --> 00:00:35.140 the design, the results and some

NOTE Confidence: 0.96179443

 $00{:}00{:}35{.}140 \dashrightarrow 00{:}00{:}37{.}154$  of the the issues that come up in

NOTE Confidence: 0.96179443

 $00:00:37.154 \dashrightarrow 00:00:38.666$  next steps from that program of NOTE Confidence: 0.96179443

 $00:00:38.666 \rightarrow 00:00:40.724$  research which is one of the sort of NOTE Confidence: 0.96179443

 $00{:}00{:}40{.}724 \dashrightarrow 00{:}00{:}42{.}416$  one of the leading programs that's

NOTE Confidence: 0.96179443

 $00:00:42.416 \dashrightarrow 00:00:44.320$  moving towards the potential for

NOTE Confidence: 0.96179443

 $00{:}00{:}44.320 \dashrightarrow 00{:}00{:}46.358$  approval of psychedelic treatments.

NOTE Confidence: 0.96179443

00:00:46.358 --> 00:00:48.204 So very current, very important.

NOTE Confidence: 0.96179443

 $00{:}00{:}48.204 \dashrightarrow 00{:}00{:}49.314$  Thank you for being here.

NOTE Confidence: 0.466014546

00:00:49.520 --> 00:00:52.160 All right, thank you. Thanks Chris. Well,

NOTE Confidence: 0.944610498461538

00:00:52.160 --> 00:00:54.368 thank you all. Let me just make sure

NOTE Confidence: 0.944610498461538

00:00:54.368 --> 00:00:56.485 we can share our screen. Jessica,

NOTE Confidence: 0.944610498461538

 $00{:}00{:}56{.}485 \dashrightarrow 00{:}00{:}59{.}160$  I don't know if there's a there we

NOTE Confidence: 0.750009934

 $00:00:59.360 \longrightarrow 00:01:00.880$  go should be able to

NOTE Confidence: 0.6428473275

 $00{:}01{:}01{.}760 \dashrightarrow 00{:}01{:}02{.}920$  looks good now and.

NOTE Confidence: 0.59666913625

 $00:01:10.240 \longrightarrow 00:01:12.080$  OK, all right. That should be a Ben.

00:01:12.360 --> 00:01:14.397 OK yeah. I'm going to start up.

NOTE Confidence: 0.629248604285714

 $00:01:14.400 \longrightarrow 00:01:16.764$  So we're going to do something

NOTE Confidence: 0.629248604285714

00:01:16.764 --> 00:01:18.980 differently in a sense that Jerry

NOTE Confidence: 0.629248604285714

 $00:01:18.980 \rightarrow 00:01:21.427$  and I are going to split the talk.

NOTE Confidence: 0.629248604285714

 $00{:}01{:}21{.}427 \dashrightarrow 00{:}01{:}23{.}138$  I'm going to go over the first half

NOTE Confidence: 0.629248604285714

 $00:01:23.138 \longrightarrow 00:01:24.640$  of the talk, which is going to,

NOTE Confidence: 0.629248604285714

 $00:01:24.640 \longrightarrow 00:01:26.020$  it's going to cover more or

NOTE Confidence: 0.629248604285714

 $00:01:26.070 \longrightarrow 00:01:27.516$  less the same things that are

NOTE Confidence: 0.939710803333333

 $00{:}01{:}29.640 \dashrightarrow 00{:}01{:}32.316$  no longer unfamiliar to this group.

NOTE Confidence: 0.939710803333333

00:01:32.320 --> 00:01:34.511 And so I'm going to cruise through

NOTE Confidence: 0.939710803333333

00:01:34.511 -> 00:01:37.239 so we can get to sort of the data.

NOTE Confidence: 0.939710803333333

 $00:01:37.240 \rightarrow 00:01:38.840$  And the more interesting part of this, we

NOTE Confidence: 0.613679365

00:01:41.000 --> 00:01:41.960 have time for discussion

NOTE Confidence: 0.830800422

 $00{:}01{:}41.960 \dashrightarrow 00{:}01{:}42.728$  and then Oh yeah,

NOTE Confidence: 0.830800422

 $00{:}01{:}42.728 \dashrightarrow 00{:}01{:}44.225$  we want to leave as much time

 $00{:}01{:}44.225 \dashrightarrow 00{:}01{:}45.397$  as possible for discussion.

NOTE Confidence: 0.830800422

00:01:45.400 --> 00:01:47.955 Let me just see how this works.

NOTE Confidence: 0.830800422

 $00:01:47.960 \longrightarrow 00:01:50.640$  OK, so disclosures,

NOTE Confidence: 0.830800422

 $00:01:50.640 \longrightarrow 00:01:53.196$  all of these above are Jerry's

NOTE Confidence: 0.830800422

 $00:01:53.200 \dashrightarrow 00:01:56.238$  and I have this measly one liner

NOTE Confidence: 0.582320838571428

 $00{:}01{:}58{.}800 \dashrightarrow 00{:}02{:}01{.}880$  skip. So psilocybin as as I said,

NOTE Confidence: 0.582320838571428

 $00:02:01.880 \rightarrow 00:02:04.640$  I'm not going to go into detail about what

NOTE Confidence: 0.582320838571428

 $00:02:04.640 \longrightarrow 00:02:06.600$  psilocybin is and where it comes from.

NOTE Confidence: 0.582320838571428

 $00{:}02{:}06.600 \dashrightarrow 00{:}02{:}11.112$  It's a natural occurring compound found

NOTE Confidence: 0.582320838571428

 $00:02:11.112 \rightarrow 00:02:14.800$  in psilocybin mushrooms. It's found in.

NOTE Confidence: 0.691371978571429

 $00{:}02{:}17.120 \dashrightarrow 00{:}02{:}19.380$  The particular extract comes

NOTE Confidence: 0.691371978571429

00:02:19.380 --> 00:02:21.075 from psilocybin kubensis,

NOTE Confidence: 0.691371978571429

 $00:02:21.080 \longrightarrow 00:02:25.000$  that the number of psychoactive

NOTE Confidence: 0.691371978571429

00:02:25.000 --> 00:02:25.744 species of mushrooms,

NOTE Confidence: 0.691371978571429

 $00:02:25.744 \longrightarrow 00:02:27.232$  at least in the United States,

NOTE Confidence: 0.691371978571429

 $00:02:27.240 \longrightarrow 00:02:30.000$  is in the range of 60.

- NOTE Confidence: 0.691371978571429
- 00:02:30.000 --> 00:02:32.447 Briefly here I thought would
- NOTE Confidence: 0.691371978571429
- $00:02:32.447 \longrightarrow 00:02:34.781$  be really useful to review the
- NOTE Confidence: 0.691371978571429
- 00:02:34.781 --> 00:02:36.199 metabolism of psilocybin.
- NOTE Confidence: 0.691371978571429
- $00:02:36.200 \longrightarrow 00:02:39.035$  As you can see psilocybin in its
- NOTE Confidence: 0.691371978571429
- 00:02:39.040 --> 00:02:43.259 natural form it's not it's not active,
- NOTE Confidence: 0.691371978571429
- $00:02:43.259 \longrightarrow 00:02:44.798$  it actually is.
- NOTE Confidence: 0.691371978571429
- $00:02:44.800 \longrightarrow 00:02:46.918$  Once it's ingested that it is
- NOTE Confidence: 0.29092836
- $00{:}02{:}51{.}640 \dashrightarrow 00{:}02{:}53{.}840$  mute and turn off your your speaker
- NOTE Confidence: 0.59558175
- $00:02:54.240 \longrightarrow 00:02:55.359$  it's so it
- NOTE Confidence: 0.83852712125
- $00:02:57.440 \dashrightarrow 00:03:00.730$  GI once it actually hits the stomach
- NOTE Confidence: 0.83852712125
- $00:03:00.730 \rightarrow 00:03:03.315$  it's dephospholarated as you can see
- NOTE Confidence: 0.83852712125
- $00{:}03{:}03{.}315 \dashrightarrow 00{:}03{:}06{.}399$  here and it becomes silos silos in or
- NOTE Confidence: 0.83852712125
- $00:03:06.399 \rightarrow 00:03:09.069$  silosin is the active ingredient and
- NOTE Confidence: 0.83852712125
- $00:03:09.069 \rightarrow 00:03:12.536$  the capsules that we use in our study
- NOTE Confidence: 0.83852712125
- $00:03:12.536 \dashrightarrow 00:03:16.226$  actually contain silos in rather than silos.
- NOTE Confidence: 0.83852712125

 $00:03:16.226 \rightarrow 00:03:21.496$  Cyben the much of the metabolism is actually

NOTE Confidence: 0.83852712125

 $00:03:21.496 \dashrightarrow 00:03:25.812$  in the IT undergoes hepatic metabolism.

NOTE Confidence: 0.83852712125

 $00{:}03{:}25.812 \dashrightarrow 00{:}03{:}27.917$  So it's glucurini,

NOTE Confidence: 0.83852712125

 $00{:}03{:}27{.}917 \dashrightarrow 00{:}03{:}30{.}702$  Glucurini needed that it's broken

NOTE Confidence: 0.83852712125

 $00:03:30.702 \longrightarrow 00:03:33.992$  down into four hydroxy indole acetyl

NOTE Confidence: 0.83852712125

 $00{:}03{:}33{.}992 \dashrightarrow 00{:}03{:}37{.}240$  hydrate and then the four HDP and four NOTE Confidence: 0.3454221

00:03:39.400 --> 00:03:44.939 HAIAAR excreted urinary and it's

NOTE Confidence: 0.3454221

 $00:03:44.939 \rightarrow 00:03:48.120$  the half life Typically this is out

NOTE Confidence: 0.3454221

 $00{:}03{:}48.120 \dashrightarrow 00{:}03{:}50.074$  of your system within 24 hours.

NOTE Confidence: 0.3454221

 $00:03:50.074 \longrightarrow 00:03:54.238$  The half life is 4 to 6 hours.

NOTE Confidence: 0.3454221

 $00{:}03{:}54{.}240$  -->  $00{:}03{:}56{.}733$  So just a little, I guess this is more NOTE Confidence: 0.3454221

00:03:56.733 --> 00:03:59.108 what I said earlier that sell us you

NOTE Confidence: 0.3454221

 $00{:}03{:}59{.}108 \dashrightarrow 00{:}04{:}01{.}158$  know the use of psilocybin in various

NOTE Confidence: 0.849401545

00:04:03.760 --> 00:04:06.735 cultures throughout the world goes

NOTE Confidence: 0.849401545

 $00:04:06.735 \longrightarrow 00:04:10.440$  back to a couple of 1000 years.

NOTE Confidence: 0.849401545

 $00{:}04{:}10.440 \dashrightarrow 00{:}04{:}13.666$  But it's most prominent use that at

- NOTE Confidence: 0.849401545
- $00:04:13.666 \longrightarrow 00:04:15.805$  least in the United States that's
- NOTE Confidence: 0.849401545
- $00:04:15.805 \rightarrow 00:04:18.235$  had an influence really comes from
- NOTE Confidence: 0.849401545
- 00:04:18.235 --> 00:04:21.944 the indigenous use in Central
- NOTE Confidence: 0.849401545
- 00:04:21.944 --> 00:04:24.932 America and Sierra Mastic region,
- NOTE Confidence: 0.849401545
- $00{:}04{:}24.932 \dashrightarrow 00{:}04{:}26.708$  particularly the Sierra Mastic
- NOTE Confidence: 0.849401545
- 00:04:26.708 --> 00:04:29.240 region in Mexico. It came.
- NOTE Confidence: 0.849401545
- $00{:}04{:}29{.}240 \dashrightarrow 00{:}04{:}33{.}584$  It was first introduced to the States
- NOTE Confidence: 0.849401545
- $00:04:33.584 \longrightarrow 00:04:36.935$  in 1950s and shortly thereafter
- NOTE Confidence: 0.849401545
- $00:04:36.935 \rightarrow 00:04:40.360$  studies with psilocybin were underway,
- NOTE Confidence: 0.849401545
- $00:04:40.360 \longrightarrow 00:04:43.765$  particularly late 1950s and 1960s
- NOTE Confidence: 0.849401545
- 00:04:43.765 --> 00:04:46.025 Psilocybin became a scheduled
- NOTE Confidence: 0.849401545
- $00{:}04{:}46.025 \dashrightarrow 00{:}04{:}50.440$  one compound in 1974.
- NOTE Confidence: 0.849401545
- $00:04:50.440 \rightarrow 00:04:56.160$  Here is just a quick Since recently with,
- NOTE Confidence: 0.849401545
- 00:04:56.160 --> 00:04:59.280 you know, what's been dubbed as
- NOTE Confidence: 0.849401545
- $00:04:59.280 \rightarrow 00:05:01.465$  the Renaissance of psychedelics,
- NOTE Confidence: 0.849401545

00:05:01.465 - 00:05:04.746 there's been an interest in doing

NOTE Confidence: 0.849401545

 $00{:}05{:}04.746 \dashrightarrow 00{:}05{:}07.276$  some more work with psilocybin.

NOTE Confidence: 0.849401545

 $00:05:07.280 \longrightarrow 00:05:10.520$  And this table summarizes the recent,

NOTE Confidence: 0.849401545

 $00:05:10.520 \longrightarrow 00:05:12.752$  most recent studies looking at the

NOTE Confidence: 0.849401545

 $00:05:12.752 \rightarrow 00:05:15.000$  effect of psilocybin and depression.

NOTE Confidence: 0.849401545

 $00:05:15.000 \rightarrow 00:05:16.995$  So there's been quite a few studies.

NOTE Confidence: 0.849401545

 $00{:}05{:}17{.}000 \dashrightarrow 00{:}05{:}19{.}542$  This is actually not a comprehensive table.

NOTE Confidence: 0.849401545

 $00:05:19.542 \rightarrow 00:05:21.252$  There's some studies that actually

NOTE Confidence: 0.849401545

 $00{:}05{:}21{.}252 \dashrightarrow 00{:}05{:}25{.}160$  go back to 2016 that were done in

NOTE Confidence: 0.849401545

 $00{:}05{:}25{.}160 \dashrightarrow 00{:}05{:}28{.}240$  patients with anxiety and depressive

NOTE Confidence: 0.849401545

 $00:05:28.240 \rightarrow 00:05:31.320$  symptoms in palliative care setting,

NOTE Confidence: 0.849401545

 $00:05:31.320 \longrightarrow 00:05:33.140$  but those patients did not

NOTE Confidence: 0.849401545

 $00:05:33.140 \rightarrow 00:05:34.960$  necessarily meet criteria for MD.

NOTE Confidence: 0.849401545

 $00:05:34.960 \rightarrow 00:05:35.794$  These studies are,

NOTE Confidence: 0.849401545

 $00:05:35.794 \rightarrow 00:05:37.740$  this one does not actually include the

NOTE Confidence: 0.849401545

 $00:05:37.793 \rightarrow 00:05:39.599$  study that we're going to talk about,

 $00:05:39.600 \dashrightarrow 00:05:42.155$  but these are the studies that have

NOTE Confidence: 0.849401545

 $00{:}05{:}42.160 \dashrightarrow 00{:}05{:}46.280$  looked at psilocybin and MDD or and

NOTE Confidence: 0.849401545

 $00:05:46.280 \rightarrow 00:05:50.560$  as well as PRD though this table

NOTE Confidence: 0.849401545

 $00:05:50.560 \rightarrow 00:05:53.160$  doesn't differentiate between the two.

NOTE Confidence: 0.849401545

 $00{:}05{:}53{.}160 \dashrightarrow 00{:}05{:}56{.}040$  And here in this I think we're going

NOTE Confidence: 0.849401545

 $00{:}05{:}56.040 \dashrightarrow 00{:}05{:}59.680$  to spend most of the talk looking at

NOTE Confidence: 0.849401545

 $00{:}05{:}59{.}680 \dashrightarrow 00{:}06{:}02{.}830$  the talking about the study at hand

NOTE Confidence: 0.849401545

 $00:06:02.830 \longrightarrow 00:06:05.932$  which is a single dose of 25 milligram

NOTE Confidence: 0.849401545

 $00:06:05.932 \dashrightarrow 00:06:09.000$  of psilocybin in major depressive disorder.

NOTE Confidence: 0.849401545

 $00{:}06{:}09{.}000 \dashrightarrow 00{:}06{:}11{.}100$  And as Chris mentioned earlier

NOTE Confidence: 0.849401545

 $00:06:11.100 \rightarrow 00:06:13.460$  that we were Doctor Senecora and I,

NOTE Confidence: 0.849401545

 $00{:}06{:}13.460 \dashrightarrow 00{:}06{:}15.580$  we were one of the sites here

NOTE Confidence: 0.849401545

 $00{:}06{:}15{.}580 \dashrightarrow 00{:}06{:}17{.}800$  at Yale and ran the study.

NOTE Confidence: 0.849401545

 $00{:}06{:}17.800 \dashrightarrow 00{:}06{:}19.360$  And with that any further ado,

NOTE Confidence: 0.849401545

 $00:06:19.360 \longrightarrow 00:06:21.142$  I'm going to hand this over

- $00:06:21.142 \rightarrow 00:06:22.033$  to Doctor Senecora,
- NOTE Confidence: 0.849401545
- $00:06:22.040 \longrightarrow 00:06:24.240$  He will review the details of the study.
- NOTE Confidence: 0.819302645
- $00{:}06{:}24.760 \dashrightarrow 00{:}06{:}26.950$  Great. Thanks Ben.
- NOTE Confidence: 0.819302645
- $00:06:26.950 \longrightarrow 00:06:30.940$  So just to go through the
- NOTE Confidence: 0.819302645
- $00:06:30.940 \longrightarrow 00:06:32.640$  the purpose of the study,
- NOTE Confidence: 0.819302645
- $00{:}06{:}32{.}640 \dashrightarrow 00{:}06{:}35{.}041$  as as Ben said there have been
- NOTE Confidence: 0.819302645
- $00{:}06{:}35{.}041 \dashrightarrow 00{:}06{:}36{.}866$  several studies prior to when
- NOTE Confidence: 0.819302645
- $00:06:36.866 \longrightarrow 00:06:38.318$  this study was initiated.
- NOTE Confidence: 0.819302645
- $00:06:38.320 \longrightarrow 00:06:41.350$  But many of the problems with
- NOTE Confidence: 0.819302645
- $00{:}06{:}41.350 \dashrightarrow 00{:}06{:}42.750$  those studies surrounded the
- NOTE Confidence: 0.819302645
- $00:06:42.750 \rightarrow 00:06:44.800$  small sample sizes that we use,
- NOTE Confidence: 0.819302645
- $00:06:44.800 \longrightarrow 00:06:46.584$  the relatively short term
- NOTE Confidence: 0.819302645
- $00:06:46.584 \rightarrow 00:06:49.760$  follow up that was used,
- NOTE Confidence: 0.819302645
- $00:06:49.760 \dashrightarrow 00:06:53.500$  the the comparative that was used
- NOTE Confidence: 0.819302645
- $00:06:53.500 \rightarrow 00:06:55.990$  and and the frequent unblinding
- NOTE Confidence: 0.819302645
- $00:06:55.990 \dashrightarrow 00:06:59.680$  of the assessors or the raters.

 $00:06:59.680 \longrightarrow 00:07:03.061$  So this study aimed to try to

NOTE Confidence: 0.819302645

 $00:07:03.061 \rightarrow 00:07:05.543$  address many of those concerns

NOTE Confidence: 0.819302645

 $00:07:05.543 \dashrightarrow 00:07:07.458$  with the original studies when

NOTE Confidence: 0.819302645

 $00:07:07.458 \rightarrow 00:07:09.680$  when it was originally initiated.

NOTE Confidence: 0.819302645

00:07:09.680 --> 00:07:12.952 So we'll take quite a bit of time

NOTE Confidence: 0.819302645

 $00{:}07{:}12.952 \dashrightarrow 00{:}07{:}15.086$  just going through I'm there.

NOTE Confidence: 0.819302645

 $00:07:15.086 \dashrightarrow 00:07:16.501$  I'm getting a message saying

NOTE Confidence: 0.819302645

 $00:07:16.501 \longrightarrow 00:07:17.680$  it's hard to hear.

NOTE Confidence: 0.819302645

00:07:17.680 --> 00:07:19.217 So I don't know if anything

NOTE Confidence: 0.819302645

 $00:07:19.217 \longrightarrow 00:07:21.479$  we can do about the volume,

NOTE Confidence: 0.819302645

 $00{:}07{:}21.480 \dashrightarrow 00{:}07{:}24.024$  but so I wanted to just take

NOTE Confidence: 0.819302645

 $00:07:24.024 \rightarrow 00:07:25.000$  some time going through this,

NOTE Confidence: 0.799821575238095

 $00{:}07{:}25{.}320 \dashrightarrow 00{:}07{:}26{.}888$  sorry. We can turn off the room

NOTE Confidence: 0.799821575238095

 $00{:}07{:}26.888 \dashrightarrow 00{:}07{:}28.616$  mics and you can turn on your

NOTE Confidence: 0.799821575238095

 $00{:}07{:}28.616 \dashrightarrow 00{:}07{:}30.320$  computer mic and then it'll make it.

- 00:07:57.480 --> 00:07:59.639 OK. I don't know
- NOTE Confidence: 0.6061673075
- $00:08:01.800 \longrightarrow 00:08:02.280$  if that's that that
- NOTE Confidence: 0.580640235
- 00:08:12.450 --> 00:08:14.810 that you were getting. I don't know.
- NOTE Confidence: 0.94073075
- $00:08:15.970 \longrightarrow 00:08:17.894$  We didn't get any complaints from others, so.
- NOTE Confidence: 0.94073075
- $00{:}08{:}17.894 \dashrightarrow 00{:}08{:}20.486$  OK. So I I'm assuming people can hear.
- NOTE Confidence: 0.94073075
- $00{:}08{:}20{.}490 \dashrightarrow 00{:}08{:}22{.}290$  So I'm going to move forward.
- NOTE Confidence: 0.94073075
- 00:08:22.290 --> 00:08:24.050 It sounds good. OK.
- NOTE Confidence: 0.94073075
- 00:08:24.050 --> 00:08:25.283 Thanks, Jess. Thank you. Good.
- NOTE Confidence: 0.94073075
- $00{:}08{:}25{.}283 \dashrightarrow 00{:}08{:}26{.}770$  So we're going to spend a little
- NOTE Confidence: 0.94073075
- $00:08:26.770 \longrightarrow 00:08:27.985$  bit of time going through.
- NOTE Confidence: 0.94073075
- $00:08:27.985 \longrightarrow 00:08:30.860$  This was actually the study
- NOTE Confidence: 0.94073075
- $00{:}08{:}30{.}860 \dashrightarrow 00{:}08{:}34{.}960$  design and this was a randomized
- NOTE Confidence: 0.94073075
- 00:08:34.960 --> 00:08:38.293 2 group which was psilocybin 25
- NOTE Confidence: 0.94073075
- $00:08:38.293 \dashrightarrow 00:08:40.558$  milligrams or niacin 100 milligrams.
- NOTE Confidence: 0.94073075
- $00:08:40.560 \rightarrow 00:08:42.880$  Phase two clinical trial designed
- NOTE Confidence: 0.94073075
- $00:08:42.880 \longrightarrow 00:08:45.760$  to evaluate both the efficacy of

 $00:08:45.760 \rightarrow 00:08:48.332$  psilocybin as compared to niacin

NOTE Confidence: 0.94073075

 $00{:}08{:}48{.}332 \dashrightarrow 00{:}08{:}50{.}424$  what it's administered with

NOTE Confidence: 0.94073075

 $00:08:50.424 \rightarrow 00:08:52.605$  psychological support in patients

NOTE Confidence: 0.94073075

 $00:08:52.605 \rightarrow 00:08:54.717$  with major depressive disorder.

NOTE Confidence: 0.94073075

 $00{:}08{:}54{.}720 \dashrightarrow 00{:}08{:}58{.}920$  It was run at 11 US sites between

NOTE Confidence: 0.94073075

 $00{:}08{:}58{.}920 \dashrightarrow 00{:}09{:}02{.}106$  December 2019 and June 2022 and we'll

NOTE Confidence: 0.94073075

 $00:09:02.106 \dashrightarrow 00:09:05.118$  get a chance to talk a little bit later.

NOTE Confidence: 0.94073075

 $00{:}09{:}05{.}120 \dashrightarrow 00{:}09{:}07{.}495$  That's kind of a interesting

NOTE Confidence: 0.94073075

 $00:09:07.495 \longrightarrow 00:09:09.395$  period of history.

NOTE Confidence: 0.94073075

 $00:09:09.400 \dashrightarrow 00:09:11.668$  So we'll get a chance to talk about how

NOTE Confidence: 0.94073075

 $00:09:11.668 \dashrightarrow 00:09:15.440$  that could have had impact on the study.

NOTE Confidence: 0.94073075

 $00{:}09{:}15{.}440 \dashrightarrow 00{:}09{:}18{.}800$  The inclusion criteria for the study,

NOTE Confidence: 0.94073075

00:09:18.800 --> 00:09:21.166 the main the key inclusion criteria was

NOTE Confidence: 0.94073075

 $00:09:21.166 \rightarrow 00:09:23.839$  patients had to be medically healthy or NOTE Confidence: 0.94073075

 $00:09:23.839 \dashrightarrow 00:09:26.233$  participants had to be medically healthy.

 $00{:}09{:}26.240 \dashrightarrow 00{:}09{:}28.112$  It was for a dults between the

NOTE Confidence: 0.94073075

00:09:28.112 --> 00:09:30.000 ages of 21 and 65 with,

NOTE Confidence: 0.94073075

00:09:30.000 --> 00:09:31.215 as I said,

NOTE Confidence: 0.94073075

 $00{:}09{:}31{.}215 \dashrightarrow 00{:}09{:}34{.}322$  a diagnosis of MDD with the current

NOTE Confidence: 0.94073075

 $00{:}09{:}34{.}322 \dashrightarrow 00{:}09{:}36{.}298$  major depressive episode lasting

NOTE Confidence: 0.94073075

 $00:09:36.298 \dashrightarrow 00:09:38.958$  of two months or or 60 days.

NOTE Confidence: 0.94073075

 $00:09:38.960 \longrightarrow 00:09:43.000$  They had to have a rating of over

NOTE Confidence: 0.94073075

 $00{:}09{:}43{.}000 \dashrightarrow 00{:}09{:}47{.}212$  28 but equal to or above 28 on the

NOTE Confidence: 0.94073075

 $00{:}09{:}47{.}212 \dashrightarrow 00{:}09{:}49{.}700$  Madras by the Central Rater and

NOTE Confidence: 0.94073075

00:09:49.700 --> 00:09:52.280 they couldn't have more than a 30%

NOTE Confidence: 0.94073075

 $00:09:52.280 \dashrightarrow 00:09:54.680$  drop from the screening to baseline.

NOTE Confidence: 0.94073075

 $00{:}09{:}54.680 \dashrightarrow 00{:}09{:}56.080$  So that's the inclusion criteria.

NOTE Confidence: 0.94073075

 $00{:}09{:}56{.}080 \dashrightarrow 00{:}09{:}57{.}400$  Key exclusion criteria which are

NOTE Confidence: 0.94073075

 $00{:}09{:}57{.}400 \dashrightarrow 00{:}09{:}59{.}280$  going to be important to remember is

NOTE Confidence: 0.899353404

 $00{:}10{:}01{.}960 \dashrightarrow 00{:}10{:}03{.}340$  the patients had to be

NOTE Confidence: 0.899353404

 $00:10:03.340 \longrightarrow 00:10:04.720$  able to be medication free.

- NOTE Confidence: 0.899353404
- $00:10:04.720 \longrightarrow 00:10:06.640$  So either not on a medication
- NOTE Confidence: 0.899353404
- $00:10:06.640 \longrightarrow 00:10:08.720$  at the time of screening,
- NOTE Confidence: 0.899353404
- $00:10:08.720 \longrightarrow 00:10:11.921$  or being able to tolerate a taper
- NOTE Confidence: 0.899353404
- $00{:}10{:}11{.}921 \dashrightarrow 00{:}10{:}14{.}567$  and a washout during the screening
- NOTE Confidence: 0.899353404
- $00{:}10{:}14.567 \dashrightarrow 00{:}10{:}16.697$  period and remain off antidepressant
- NOTE Confidence: 0.899353404
- $00:10:16.697 \rightarrow 00:10:19.679$  medications during that period of time.
- NOTE Confidence: 0.899353404
- $00:10:19.680 \longrightarrow 00:10:22.456$  They also needed to be able to go
- NOTE Confidence: 0.899353404
- $00:10:22.456 \rightarrow 00:10:24.958$  without seeing an outpatient therapist.
- NOTE Confidence: 0.899353404
- $00:10:24.960 \longrightarrow 00:10:26.857$  So if they have not had an
- NOTE Confidence: 0.899353404
- 00:10:26.857 --> 00:10:27.946 outpatient therapist, that was OK,
- NOTE Confidence: 0.899353404
- $00:10:27.946 \rightarrow 00:10:29.038$  but if they were seeing one,
- NOTE Confidence: 0.899353404
- $00:10:29.040 \longrightarrow 00:10:31.238$  they would have to be able to
- NOTE Confidence: 0.899353404
- 00:10:31.240 --> 00:10:32.535 at least take a hiatus or a
- NOTE Confidence: 0.899353404
- $00:10:32.535 \longrightarrow 00:10:33.884$  pause in their treatment with
- NOTE Confidence: 0.899353404
- $00:10:33.884 \rightarrow 00:10:34.997$  their outpatient the rapist.
- NOTE Confidence: 0.952799308461538

 $00:10:37.120 \longrightarrow 00:10:39.451$  The other part that was important to

NOTE Confidence: 0.952799308461538

 $00:10:39.451 \longrightarrow 00:10:41.760$  think about is the family history.

NOTE Confidence: 0.952799308461538

 $00:10:41.760 \longrightarrow 00:10:43.884$  So there was no personal history

NOTE Confidence: 0.952799308461538

 $00:10:43.884 \rightarrow 00:10:45.760$  of either psychosis or mania,

NOTE Confidence: 0.952799308461538

 $00{:}10{:}45.760 \dashrightarrow 00{:}10{:}48.436$  but also no first degree relative

NOTE Confidence: 0.952799308461538

 $00{:}10{:}48{.}440 \dashrightarrow 00{:}10{:}51{.}384$  with psychosis or mania.

NOTE Confidence: 0.952799308461538

 $00:10:51.384 \rightarrow 00:10:55.750$  And then the other major important two

NOTE Confidence: 0.952799308461538

 $00:10:55.750 \rightarrow 00:10:58.900$  exclusion criterias was having psychedelic

NOTE Confidence: 0.952799308461538

 $00:10:58.900 \rightarrow 00:11:01.640$  drug use in the past five years,

NOTE Confidence: 0.952799308461538

 $00:11:01.640 \longrightarrow 00:11:04.125$  or more than 10 lifetime

NOTE Confidence: 0.952799308461538

 $00{:}11{:}04{.}125 \dashrightarrow 00{:}11{:}06{.}113$  uses of a psyched elic.

NOTE Confidence: 0.952799308461538

 $00:11:06.120 \longrightarrow 00:11:07.320$  And then finally the last one,

NOTE Confidence: 0.952799308461538

 $00:11:07.320 \longrightarrow 00:11:09.590$  was anybody with active suicidal

NOTE Confidence: 0.952799308461538

 $00{:}11{:}09{.}590 \dashrightarrow 00{:}11{:}12{.}695$  ideation with intent or a plan within

NOTE Confidence: 0.952799308461538

 $00:11:12.695 \rightarrow 00:11:15.313$  the past six months or or self,

NOTE Confidence: 0.952799308461538

00:11:15.320 --> 00:11:17.228 I'm sorry, or suicidal behavior in

 $00:11:17.228 \rightarrow 00:11:19.400$  the past 12 months were excluded.

NOTE Confidence: 0.952799308461538

 $00{:}11{:}19{.}400 \dashrightarrow 00{:}11{:}22{.}352$  So just to give you a general sense that

NOTE Confidence: 0.952799308461538

 $00:11:22.352 \rightarrow 00:11:25.317$  this was a generally healthy population,

NOTE Confidence: 0.952799308461538

 $00:11:25.320 \rightarrow 00:11:26.680$  really screened pretty carefully

NOTE Confidence: 0.952799308461538

 $00:11:26.680 \longrightarrow 00:11:28.040$  not to have psychosis,

NOTE Confidence: 0.952799308461538

00:11:28.040 --> 00:11:30.060 not even a family history

NOTE Confidence: 0.952799308461538

 $00:11:30.060 \rightarrow 00:11:31.676$  of psychosis or mania.

NOTE Confidence: 0.952799308461538

 $00:11:31.680 \longrightarrow 00:11:33.360$  So well this is the population

NOTE Confidence: 0.952799308461538

 $00:11:33.360 \longrightarrow 00:11:35.000$  that it was geared towards.

NOTE Confidence: 0.952799308461538

00:11:35.000 --> 00:11:36.000 As you can see here,

NOTE Confidence: 0.952799308461538

 $00{:}11{:}36{.}000 \dashrightarrow 00{:}11{:}39{.}598$  the original plan was to run 80

NOTE Confidence: 0.952799308461538

 $00{:}11{:}39{.}600 \dashrightarrow 00{:}11{:}42{.}680$  participants that was actually updated

NOTE Confidence: 0.530287529

 $00{:}11{:}44{.}720 \dashrightarrow 00{:}11{:}47{.}924$  see if I can. So it was updated to

NOTE Confidence: 0.530287529

 $00{:}11{:}47{.}924 \dashrightarrow 00{:}11{:}49{.}438$  100 in the beginning of the study.

NOTE Confidence: 0.530287529

 $00{:}11{:}49{.}440 \dashrightarrow 00{:}11{:}52{.}824$  The the there was a reanalysis and the and

00:11:52.824 --> 00:11:56.637 the idea to run 100 patients was was changed.

NOTE Confidence: 0.530287529

00:11:56.640 --> 00:11:58.830 So patients were screened and

NOTE Confidence: 0.530287529

 $00:11:58.830 \longrightarrow 00:12:01.426$  then after a screening period of

NOTE Confidence: 0.530287529

 $00:12:01.426 \longrightarrow 00:12:03.400$  lasting either 7 to 35 days,

NOTE Confidence: 0.530287529

 $00:12:03.400 \longrightarrow 00:12:04.954$  largely depending on if they needed

NOTE Confidence: 0.530287529

 $00{:}12{:}04{.}954 \dashrightarrow 00{:}12{:}06{.}760$  to do a medication washout or not,

NOTE Confidence: 0.530287529

 $00:12:06.760 \longrightarrow 00:12:10.724$  they would then go into a baseline period.

NOTE Confidence: 0.530287529

 $00:12:10.724 \longrightarrow 00:12:12.544$  And during that baseline period

NOTE Confidence: 0.530287529

 $00{:}12{:}12{.}544 \dashrightarrow 00{:}12{:}14.000$  they would be reassessed.

NOTE Confidence: 0.530287529

 $00{:}12{:}14.000 \dashrightarrow 00{:}12{:}14.880$  And as I said,

NOTE Confidence: 0.530287529

 $00:12:14.880 \longrightarrow 00:12:17.079$  if they had more than a 30 point drop,

NOTE Confidence: 0.530287529

 $00:12:17.080 \longrightarrow 00:12:18.880 a 30\%$  drop in their ratings,

NOTE Confidence: 0.530287529

 $00:12:18.880 \longrightarrow 00:12:20.160$  that would be an exclusion,

NOTE Confidence: 0.530287529

 $00:12:20.160 \longrightarrow 00:12:22.599$  but otherwise they can move on and that would

NOTE Confidence: 0.530287529

 $00:12:22.599 \rightarrow 00:12:25.076$  be their baseline ratings moving forward.

NOTE Confidence: 0.530287529

 $00{:}12{:}25{.}080 \dashrightarrow 00{:}12{:}27{.}240$  And then before actual treatment

- NOTE Confidence: 0.530287529
- $00:12:27.240 \rightarrow 00:12:29.400$  or randomization was a preparatory

 $00{:}12{:}29{.}466 \dashrightarrow 00{:}12{:}31{.}466$  session and these preparatory sessions

NOTE Confidence: 0.530287529

00:12:31.466 --> 00:12:34.238 were designed to last 6 to 8 hours,

NOTE Confidence: 0.530287529

 $00:12:34.240 \longrightarrow 00:12:37.438$  usually two sessions prior to the.

NOTE Confidence: 0.530287529

 $00{:}12{:}37{.}440 \dashrightarrow 00{:}12{:}40{.}040$  Originally in this design it was meant to

NOTE Confidence: 0.530287529

 $00:12:40.040 \longrightarrow 00:12:42.997$  be the person with the two facilitators.

NOTE Confidence: 0.530287529

00:12:43.000 --> 00:12:43.472 The two,

NOTE Confidence: 0.530287529

 $00:12:43.472 \rightarrow 00:12:45.360$  the two people in the room in these

NOTE Confidence: 0.530287529

 $00{:}12{:}45{.}423 \dashrightarrow 00{:}12{:}47{.}199$  studies were called facilitators.

NOTE Confidence: 0.530287529

 $00{:}12{:}47{.}200 \dashrightarrow 00{:}12{:}49{.}927$  But again if we go back and look at

NOTE Confidence: 0.530287529

 $00:12:49.927 \rightarrow 00:12:52.877$  the timing starting in December 2019,

NOTE Confidence: 0.530287529

 $00{:}12{:}52{.}880 \dashrightarrow 00{:}12{:}53{.}840$  the pandemic hit.

NOTE Confidence: 0.530287529

 $00{:}12{:}53{.}840 \dashrightarrow 00{:}12{:}55{.}760$  So the prep sessions were altered

NOTE Confidence: 0.530287529

 $00{:}12{:}55.760 \dashrightarrow 00{:}12{:}57.719$  where many of these prep sessions,

NOTE Confidence: 0.530287529

 $00{:}12{:}57{.}720 \dashrightarrow 00{:}13{:}02{.}400$  at least one of them was done virtually.

 $00:13:02.400 \longrightarrow 00:13:04.160$  So that little bit different

NOTE Confidence: 0.530287529

00:13:04.160 --> 00:13:05.920 than the original study design.

NOTE Confidence: 0.530287529

 $00{:}13{:}05{.}920 \dashrightarrow 00{:}13{:}07{.}915$  And then there was day one

NOTE Confidence: 0.530287529

00:13:07.915 --> 00:13:10.102 and that was actually the dosing

NOTE Confidence: 0.530287529

 $00{:}13{:}10.102 \dashrightarrow 00{:}13{:}12.207$  day and that's where patients

NOTE Confidence: 0.530287529

 $00{:}13{:}12{.}207 \dashrightarrow 00{:}13{:}14{.}093$  or participants were randomized

NOTE Confidence: 0.530287529

00:13:14.093 --> 00:13:16.526 either receive the psilocybin 25

NOTE Confidence: 0.530287529

 $00{:}13{:}16.526$  -->  $00{:}13{:}18.956$  milligrams or niacin 100 milligrams.

NOTE Confidence: 0.530287529

 $00:13:18.960 \longrightarrow 00:13:21.284$  And I'll just say briefly that the

NOTE Confidence: 0.530287529

 $00:13:21.284 \longrightarrow 00:13:23.597$  idea of using niacin was to have

NOTE Confidence: 0.530287529

 $00{:}13{:}23.600 \dashrightarrow 00{:}13{:}26.639$  an attempt of at an active placebo,

NOTE Confidence: 0.530287529

 $00:13:26.639 \rightarrow 00:13:29.992$  meaning that there may be some sensation

NOTE Confidence: 0.530287529

00:13:29.992 --> 00:13:32.998 from taking 100 milligrams of niacin,

NOTE Confidence: 0.530287529

 $00:13:33.000 \longrightarrow 00:13:35.238$  there's some flushing.

NOTE Confidence: 0.530287529

 $00:13:35.240 \rightarrow 00:13:37.100$  It also offered us the opportunity

NOTE Confidence: 0.530287529

 $00{:}13{:}37{.}100 \dashrightarrow 00{:}13{:}39{.}024$  to provide some equipoise by saying

- NOTE Confidence: 0.530287529
- $00:13:39.024 \rightarrow 00:13:40.914$  'cause there were there are some
- NOTE Confidence: 0.530287529
- 00:13:40.914 --> 00:13:42.306 studies suggesting niac<br/>in may
- NOTE Confidence: 0.530287529
- $00{:}13{:}42.306 \dashrightarrow 00{:}13{:}43.718$  have an antidepressant effect.
- NOTE Confidence: 0.530287529
- $00{:}13{:}43.720 \dashrightarrow 00{:}13{:}45.472$  So you could legitimately tell patients
- NOTE Confidence: 0.530287529
- $00{:}13{:}45{.}472 \dashrightarrow 00{:}13{:}47{.}755$  that there is some evidence that they
- NOTE Confidence: 0.530287529
- $00:13:47.755 \longrightarrow 00:13:49.520$  both may have antidepressant effects,
- NOTE Confidence: 0.530287529
- $00:13:49.520 \rightarrow 00:13:53.872$  but it was still was listed as a placebo,
- NOTE Confidence: 0.530287529
- $00{:}13{:}53{.}872 \dashrightarrow 00{:}13{:}57{.}960$  what would be called an active placebo.
- NOTE Confidence: 0.530287529
- $00{:}13{:}57{.}960 \dashrightarrow 00{:}14{:}00{.}991$  So dosing was provided on that day
- NOTE Confidence: 0.530287529
- $00:14:00.991 \longrightarrow 00:14:03.559$  and dosing typically lasted 6 hours.
- NOTE Confidence: 0.530287529
- $00:14:03.560 \rightarrow 00:14:05.906$  And then patients were seen again
- NOTE Confidence: 0.530287529
- $00:14:05.906 \longrightarrow 00:14:08.260$  the day after, which was day two.
- NOTE Confidence: 0.530287529
- $00{:}14{:}08{.}260 \dashrightarrow 00{:}14{:}09{.}440$  And on day two,
- NOTE Confidence: 0.530287529
- $00{:}14{:}09{.}440 \dashrightarrow 00{:}14{:}12{.}038$  they had their first integration session
- NOTE Confidence: 0.530287529
- $00{:}14{:}12{.}040 \dashrightarrow 00{:}14{:}13{.}462$  along with the ratings that were
- NOTE Confidence: 0.530287529

- $00:14:13.462 \rightarrow 00:14:15.359$  performed And in the integration session,
- NOTE Confidence: 0.530287529
- $00:14:15.360 \longrightarrow 00:14:16.640$  typically lasting about an hour,
- NOTE Confidence: 0.530287529
- 00:14:16.640 --> 00:14:21.320 then I think an hour to two hours depending,
- NOTE Confidence: 0.530287529
- $00:14:21.320 \rightarrow 00:14:22.784$  they were seen again.
- NOTE Confidence: 0.530287529
- $00{:}14{:}22.784 \dashrightarrow 00{:}14{:}26.208$  And then day five was a telephone interview.
- NOTE Confidence: 0.530287529
- $00{:}14{:}26{.}208 \dashrightarrow 00{:}14{:}28{.}656$  The day eight was one of
- NOTE Confidence: 0.530287529
- $00:14:28.656 \longrightarrow 00:14:29.880$  the secondary measures,
- NOTE Confidence: 0.530287529
- $00:14:29.880 \longrightarrow 00:14:31.160$  an outcome at day eight.
- NOTE Confidence: 0.530287529
- $00{:}14{:}31{.}160 \dashrightarrow 00{:}14{:}32{.}786$  And again they had their rating
- NOTE Confidence: 0.530287529
- $00{:}14{:}32.786 \dashrightarrow 00{:}14{:}34.944$  scales and you can see all the
- NOTE Confidence: 0.530287529
- $00:14:34.944 \rightarrow 00:14:36.639$  individual rating skills listed there.
- NOTE Confidence: 0.530287529
- $00:14:36.640 \rightarrow 00:14:37.440$  Day nine,
- NOTE Confidence: 0.530287529
- $00:14:37.440 \longrightarrow 00:14:39.440$  they came back for another
- NOTE Confidence: 0.530287529
- $00:14:39.440 \longrightarrow 00:14:40.240$  integration session.
- NOTE Confidence: 0.530287529
- $00{:}14{:}40{.}240 \dashrightarrow 00{:}14{:}42{.}928$  So this is again a meeting with
- NOTE Confidence: 0.530287529
- $00:14:42.928 \rightarrow 00:14:44.504$  the two facilitators lasting

- NOTE Confidence: 0.530287529
- $00:14:44.504 \longrightarrow 00:14:46.954$  about an hour to to two hours.
- NOTE Confidence: 0.530287529
- $00:14:46.960 \longrightarrow 00:14:49.676$  And then day 15 were more assessments.
- NOTE Confidence: 0.530287529
- $00:14:49.680 \rightarrow 00:14:52.039$  And then on day 16 was the
- NOTE Confidence: 0.530287529
- $00:14:52.039 \longrightarrow 00:14:53.050$  3rd integration session
- NOTE Confidence: 0.956447876
- $00{:}14{:}53{.}120 \dashrightarrow 00{:}14{:}55{.}480$  meeting with the facilitators again
- NOTE Confidence: 0.956447876
- $00{:}14{:}55{.}480 \dashrightarrow 00{:}14{:}56{.}926$  and then there was another exploratory
- NOTE Confidence: 0.956447876
- $00:14:56.926 \rightarrow 00:14:58.478$  endpoint at the end of the month.
- NOTE Confidence: 0.956447876
- 00:14:58.480 --> 00:15:00.120 And then the primary endpoint,
- NOTE Confidence: 0.956447876
- $00:15:00.120 \longrightarrow 00:15:02.584$  the, the main goal of the study
- NOTE Confidence: 0.956447876
- $00:15:02.584 \longrightarrow 00:15:04.650$  was the look at the response.
- NOTE Confidence: 0.956447876
- $00:15:04.650 \rightarrow 00:15:08.101$  There were the change in the Madras score on
- NOTE Confidence: 0.956447876
- $00:15:08.101 \rightarrow 00:15:11.160 \text{ day } 43 \text{ that was really look at six weeks out.}$
- NOTE Confidence: 0.956447876
- $00:15:11.160 \longrightarrow 00:15:13.876$  That's the primary endpoint for the study.
- NOTE Confidence: 0.956447876
- 00:15:13.880 --> 00:15:16.757 So let's just look a little bit.
- NOTE Confidence: 0.956447876
- $00{:}15{:}16.760 \dashrightarrow 00{:}15{:}20.158$  The idea of using this, as I said,
- NOTE Confidence: 0.956447876

 $00:15:20.160 \rightarrow 00:15:21.580$  along with psychological support goes

NOTE Confidence: 0.956447876

 $00:15:21.580 \rightarrow 00:15:24.000$  back to the set and setting principles.

NOTE Confidence: 0.956447876

00:15:24.000 --> 00:15:25.176 And then I don't know if you want

NOTE Confidence: 0.956447876

 $00:15:25.176 \longrightarrow 00:15:26.476$  to talk a little bit about this or.

NOTE Confidence: 0.956447876

 $00:15:26.480 \longrightarrow 00:15:29.440$  Sure, yeah, yeah. The idea

NOTE Confidence: 0.853937831428571

 $00{:}15{:}29{.}440 \dashrightarrow 00{:}15{:}31{.}477$  behind set and setting is something that NOTE Confidence: 0.853937831428571

 $00:15:31.477 \rightarrow 00:15:33.680$  was taken very seriously in this study.

NOTE Confidence: 0.853937831428571

 $00{:}15{:}33.680 \dashrightarrow 00{:}15{:}39.720$  And set is defined as mindset sort of the

NOTE Confidence: 0.853937831428571

 $00:15:39.720 \rightarrow 00:15:44.006$  your sort of baseline thinking process,

NOTE Confidence: 0.853937831428571

 $00{:}15{:}44.006 \dashrightarrow 00{:}15{:}46.805$  your mood at the time of dosing and the

NOTE Confidence: 0.853937831428571

 $00:15:46.805 \rightarrow 00:15:48.811$  setting typically referred to the environment

NOTE Confidence: 0.853937831428571

 $00:15:48.811 \dashrightarrow 00:15:52.477$  where the dosing occurred in this.

NOTE Confidence: 0.853937831428571

 $00:15:52.480 \longrightarrow 00:15:54.635$  What's a typical though this

NOTE Confidence: 0.853937831428571

 $00:15:54.635 \rightarrow 00:15:56.790$  becoming familiar to this group

NOTE Confidence: 0.853937831428571

 $00:15:56.865 \rightarrow 00:15:59.138$  is that these dosing sessions are

NOTE Confidence: 0.853937831428571

 $00{:}15{:}59{.}138 \dashrightarrow 00{:}16{:}01{.}610$  administered in a slightly unusual

- NOTE Confidence: 0.853937831428571
- $00:16:01.610 \rightarrow 00:16:04.435$  environmental setting where you know,
- NOTE Confidence: 0.853937831428571
- $00:16:04.440 \longrightarrow 00:16:06.160$  as you can see in the picture here,
- NOTE Confidence: 0.853937831428571
- $00:16:06.160 \longrightarrow 00:16:07.600$  there is actually a couch.
- NOTE Confidence: 0.815448939230769
- $00:16:09.880 \rightarrow 00:16:12.197$  The room is set up to actually
- NOTE Confidence: 0.815448939230769
- 00:16:12.197 --> 00:16:16.680 looks to look like a ordinary room.
- NOTE Confidence: 0.815448939230769
- $00:16:16.680 \longrightarrow 00:16:18.390$  It's typically a little bit
- NOTE Confidence: 0.815448939230769
- $00:16:18.390 \rightarrow 00:16:19.633$  more aesthetically appealing
- NOTE Confidence: 0.815448939230769
- $00:16:19.633 \longrightarrow 00:16:22.398$  than a typical Med room.
- NOTE Confidence: 0.815448939230769
- $00{:}16{:}22{.}400 \dashrightarrow 00{:}16{:}25{.}208$  The other idea behind the setting
- NOTE Confidence: 0.815448939230769
- $00:16:25.208 \longrightarrow 00:16:27.751$  that it would facilitate A
- NOTE Confidence: 0.815448939230769
- $00:16:27.751 \rightarrow 00:16:30.103$  therapeutic alliance and between
- NOTE Confidence: 0.815448939230769
- $00:16:30.103 \rightarrow 00:16:32.132$  the facilitators and participants.
- NOTE Confidence: 0.815448939230769
- $00:16:32.132 \longrightarrow 00:16:35.114$  So you know this is what was
- NOTE Confidence: 0.815448939230769
- $00{:}16{:}35{.}114 \dashrightarrow 00{:}16{:}38{.}254$  taken into account during both the
- NOTE Confidence: 0.815448939230769
- $00:16:38.254 \rightarrow 00:16:40.879$  preparation as well as integration.
- NOTE Confidence: 0.815448939230769

 $00:16:40.880 \rightarrow 00:16:44.273$  This idea of using Satis setting

NOTE Confidence: 0.815448939230769

 $00{:}16{:}44.273 \dashrightarrow 00{:}16{:}46.870$  as a foundation for where a lot

NOTE Confidence: 0.815448939230769

 $00:16:46.944 \rightarrow 00:16:49.440$  of the conversations took place.

NOTE Confidence: 0.815448939230769

00:16:49.440 --> 00:16:51.000 So treatment sessions,

NOTE Confidence: 0.754274631666667

 $00:16:51.760 \longrightarrow 00:16:55.360$  so, so as Ben described this,

NOTE Confidence: 0.754274631666667

 $00:16:55.360 \rightarrow 00:16:59.568$  the idea of using the the integration,

NOTE Confidence: 0.7542746316666667

 $00{:}16{:}59{.}568 \dashrightarrow 00{:}17{:}02{.}816$  I'm sorry, the preparatory sessions to help

NOTE Confidence: 0.754274631666667

 $00:17:02.816 \rightarrow 00:17:05.857$  work on the set and the actual physical

NOTE Confidence: 0.754274631666667

 $00{:}17{:}05.857 \dashrightarrow 00{:}17{:}08.720$  setting was was very tightly controlled.

NOTE Confidence: 0.7542746316666667

 $00{:}17{:}08.720 \dashrightarrow 00{:}17{:}10.685$  During dosing sessions participants were

NOTE Confidence: 0.7542746316666667

00:17:10.685 --> 00:17:13.689 encouraged to wear eye shades and to listen

NOTE Confidence: 0.754274631666667

 $00{:}17{:}13.689 \dashrightarrow 00{:}17{:}15.639$  to a curated playlist with headphones.

NOTE Confidence: 0.754274631666667

 $00:17:15.640 \longrightarrow 00:17:17.796$  So this is again very tightly controlled.

NOTE Confidence: 0.7542746316666667

 $00{:}17{:}17{.}800 \dashrightarrow 00{:}17{:}20{.}611$  The setting the leaf facilitators

NOTE Confidence: 0.754274631666667

00:17:20.611 - 00:17:21.959 were all doctoral level,

NOTE Confidence: 0.754274631666667

 $00:17:21.960 \rightarrow 00:17:26.760$  either psychologists or physicians with

- NOTE Confidence: 0.754274631666667
- $00:17:26.760 \rightarrow 00:17:28.612$  treatment with depression treatment
- NOTE Confidence: 0.754274631666667
- $00{:}17{:}28.612 \dashrightarrow 00{:}17{:}30.927$  experience and the Co facilitators
- NOTE Confidence: 0.754274631666667
- 00:17:30.927 --> 00:17:32.980 held a minimum of a bachelor's degree
- NOTE Confidence: 0.754274631666667
- $00:17:32.980 \longrightarrow 00:17:34.960$  in a mental health related field.
- NOTE Confidence: 0.7542746316666667
- $00:17:34.960 \longrightarrow 00:17:36.175$  All facilitators completed
- NOTE Confidence: 0.754274631666667
- 00:17:36.175 --> 00:17:37.795 a study specific training.
- NOTE Confidence: 0.7542746316666667
- $00:17:37.800 \longrightarrow 00:17:40.222$  So this is clearly a case where
- NOTE Confidence: 0.754274631666667
- $00:17:40.222 \longrightarrow 00:17:42.464$  there was great effort taken to
- NOTE Confidence: 0.7542746316666667
- $00{:}17{:}42.464 \dashrightarrow 00{:}17{:}44.394$  make sure that the facilitating
- NOTE Confidence: 0.797341222
- 00:17:47.320 --> 00:17:49.560 study members were were providing
- NOTE Confidence: 0.797341222
- $00:17:49.560 \longrightarrow 00:17:52.413$  as much of the uniformed experience
- NOTE Confidence: 0.797341222
- $00{:}17{:}52{.}413 \dashrightarrow 00{:}17{:}55{.}478$  as possible in the study.
- NOTE Confidence: 0.797341222
- $00:17:55.480 \longrightarrow 00:17:57.088$  Here if we go through looking
- NOTE Confidence: 0.797341222
- $00{:}17{:}57{.}088 \dashrightarrow 00{:}17{:}58{.}160$  at the consort diagram.
- NOTE Confidence: 0.797341222
- $00{:}17{:}58.160 \dashrightarrow 00{:}18{:}00.768$  So this is one of the first interesting
- NOTE Confidence: 0.797341222

 $00:18:00.768 \longrightarrow 00:18:02.958$  things to see is that there were

NOTE Confidence: 0.97244084

00:18:05.200 --> 00:18:09.680 15129 people assessed by phone

NOTE Confidence: 0.97244084

 $00{:}18{:}09{.}680 \dashrightarrow 00{:}18{:}12{.}714$  screen with 1425 excluded.

NOTE Confidence: 0.97244084

 $00{:}18{:}12.714 \dashrightarrow 00{:}18{:}14.513$  So this is one of these studies

NOTE Confidence: 0.97244084

00:18:14.513 --> 00:18:16.002 where there was a lot of interest

NOTE Confidence: 0.97244084

 $00{:}18{:}16{.}002 \dashrightarrow 00{:}18{:}17{.}754$  and a lot of people that wanted to NOTE Confidence: 0.97244084

00:18:17.754 --> 00:18:19.516 take part in a study and we can

NOTE Confidence: 0.97244084

00:18:19.516 --> 00:18:20.902 talk about the pros and cons of

NOTE Confidence: 0.97244084

 $00{:}18{:}20{.}902 \dashrightarrow 00{:}18{:}22{.}302$  that that that that could either NOTE Confidence: 0.97244084

00:18:22.302 --> 00:18:23.979 work in your favour or that could

NOTE Confidence: 0.97244084

00:18:23.979 --> 00:18:25.395 work against you in some ways.

NOTE Confidence: 0.97244084

00:18:25.400 --> 00:18:26.412 But for this study,

NOTE Confidence: 0.97244084

 $00:18:26.412 \longrightarrow 00:18:28.305$  you can see that's a pretty large

NOTE Confidence: 0.97244084

 $00{:}18{:}28{.}305 \dashrightarrow 00{:}18{:}29{.}875$  number that was whittled down

NOTE Confidence: 0.860973454285714

 $00{:}18{:}32{.}640 \dashrightarrow 00{:}18{:}34{.}880$  to to a number.

NOTE Confidence: 0.860973454285714

 $00:18:34.880 \longrightarrow 00:18:37.610$  As you said, 11182 were excluded

- NOTE Confidence: 0.860973454285714
- $00:18:37.610 \longrightarrow 00:18:39.360$  just on the telephone screen.
- NOTE Confidence: 0.860973454285714
- $00:18:39.360 \rightarrow 00:18:41.600$  So just on those initial telephone screens,
- NOTE Confidence: 0.860973454285714
- $00:18:41.600 \rightarrow 00:18:44.140$  it was either the patient didn't meet
- NOTE Confidence: 0.860973454285714
- $00:18:44.140 \longrightarrow 00:18:46.310$  the depression or some of the patients
- NOTE Confidence: 0.860973454285714
- $00:18:46.310 \longrightarrow 00:18:48.835$  would call and didn't have depression at all.
- NOTE Confidence: 0.860973454285714
- 00:18:48.840 --> 00:18:52.000 They just wanted to try study,
- NOTE Confidence: 0.860973454285714
- $00{:}18{:}52{.}000 \dashrightarrow 00{:}18{:}53{.}752$  but others had other clear reasons
- NOTE Confidence: 0.860973454285714
- $00:18:53.752 \rightarrow 00:18:55.552$  where they may have had psychosis
- NOTE Confidence: 0.860973454285714
- 00:18:55.552 --> 00:18:57.274 or a family member had psychosis
- NOTE Confidence: 0.860973454285714
- $00:18:57.274 \rightarrow 00:18:59.039$  or for a variety of reasons.
- NOTE Confidence: 0.860973454285714
- $00:18:59.040 \rightarrow 00:19:01.155$  But then it got down to the point where
- NOTE Confidence: 0.860973454285714
- $00{:}19{:}01{.}160 \dashrightarrow 00{:}19{:}02{.}996$  240 were actually screened in person.
- NOTE Confidence: 0.860973454285714
- $00{:}19{:}03{.}000 \dashrightarrow 00{:}19{:}04.875$  And then there were additional
- NOTE Confidence: 0.860973454285714
- 00:19:04.875 --> 00:19:06.784 exclusions down to 104
- NOTE Confidence: 0.860973454285714
- $00:19:06.784 \rightarrow 00:19:09.920$  participants that were randomized,
- NOTE Confidence: 0.860973454285714

00:19:09.920 --> 00:19:13.118 51 randomized to receive the psilocybin

NOTE Confidence: 0.860973454285714

 $00{:}19{:}13.118 \dashrightarrow 00{:}19{:}16.680$  and 53 randomized to receive niac in.

NOTE Confidence: 0.860973454285714

00:19:16.680 --> 00:19:17.828 In fact, if we,

NOTE Confidence: 0.860973454285714

 $00:19:17.828 \rightarrow 00:19:19.263$  if you read the paper

NOTE Confidence: 0.860973454285714

 $00:19:19.263 \longrightarrow 00:19:20.920$  real quick real closely,

NOTE Confidence: 0.860973454285714

 $00:19:20.920 \longrightarrow 00:19:23.237$  it actually ended up that 50 people

NOTE Confidence: 0.860973454285714

 $00:19:23.240 \longrightarrow 00:19:26.252$  actually received the psilocybin and 54

NOTE Confidence: 0.860973454285714

00:19:26.252 --> 00:19:29.840 received niac<br/>in because one patient was

NOTE Confidence: 0.860973454285714

 $00:19:29.840 \longrightarrow 00:19:33.518$  by mistake given the wrong treatment.

NOTE Confidence: 0.860973454285714

 $00:19:33.520 \rightarrow 00:19:37.714$  So, so really ended up 50 to to 54

NOTE Confidence: 0.860973454285714

 $00:19:37.720 \longrightarrow 00:19:39.736$  which is actually not that uncommon

NOTE Confidence: 0.860973454285714

 $00{:}19{:}39{.}736 \dashrightarrow 00{:}19{:}41{.}794$  in in these studies that there's

NOTE Confidence: 0.860973454285714

 $00:19:41.794 \rightarrow 00:19:45.360$  one mistake in there somewhere.

NOTE Confidence: 0.860973454285714

 $00:19:45.360 \longrightarrow 00:19:47.754$  And then you can see the number

NOTE Confidence: 0.860973454285714

 $00:19:47.754 \longrightarrow 00:19:49.832$  that completed at the day 8

NOTE Confidence: 0.860973454285714

 $00:19:49.832 \longrightarrow 00:19:52.760$  assessment you had 51 of the of the

 $00{:}19{:}52{.}760 \dashrightarrow 00{:}19{:}55{.}080$ 51 patients completing the day at

NOTE Confidence: 0.860973454285714

 $00:19:55.080 \longrightarrow 00:19:57.525$  and actually 50 of the psilocybin.

NOTE Confidence: 0.860973454285714

 $00:19:57.525 \rightarrow 00:20:00.255$  Of the 51 psilocybin patients completing

NOTE Confidence: 0.860973454285714

 $00{:}20{:}00{.}255 \dashrightarrow 00{:}20{:}03{.}180$  the six week evaluation where for the

NOTE Confidence: 0.860973454285714

 $00{:}20{:}03.180 \dashrightarrow 00{:}20{:}06.292$ niacin you had 48 of the 53 make it

NOTE Confidence: 0.860973454285714

 $00:20:06.292 \rightarrow 00:20:09.360$  to day eight and only 42 of the 53

NOTE Confidence: 0.860973454285714

 $00{:}20{:}09{.}360 \dashrightarrow 00{:}20{:}12{.}118$  make it to the six week assessment.

NOTE Confidence: 0.860973454285714

 $00:20:12.120 \longrightarrow 00:20:13.896$  So you had nine people that

NOTE Confidence: 0.860973454285714

 $00:20:13.896 \longrightarrow 00:20:15.360$  did not make it on?

NOTE Confidence: 0.860973454285714

 $00:20:15.360 \longrightarrow 00:20:16.240$  And then on the right,

NOTE Confidence: 0.860973454285714

 $00:20:16.240 \longrightarrow 00:20:19.180$  you can actually see by the

NOTE Confidence: 0.860973454285714

 $00{:}20{:}19.180 \dashrightarrow 00{:}20{:}21.270$  individual sites how many people

NOTE Confidence: 0.860973454285714

 $00{:}20{:}21{.}270 \dashrightarrow 00{:}20{:}23{.}120$  were recruited at what percent.

NOTE Confidence: 0.860973454285714

 $00{:}20{:}23.120 \dashrightarrow 00{:}20{:}25.064$  This is the number of participants

NOTE Confidence: 0.860973454285714

 $00{:}20{:}25{.}064 \dashrightarrow 00{:}20{:}27{.}303$  that each site had and the percent

 $00:20:27.303 \longrightarrow 00:20:29.137$  of the total that they shared.

NOTE Confidence: 0.860973454285714

 $00:20:29.137 \rightarrow 00:20:32.153$  You can see although there was 11 sites,

NOTE Confidence: 0.860973454285714

00:20:32.160 --> 00:20:34.384 really the top five or six accounted for

NOTE Confidence: 0.860973454285714

 $00:20:34.384 \rightarrow 00:20:36.556$  the large majority of the patients run

NOTE Confidence: 0.767647362

 $00{:}20{:}39{.}480 \dashrightarrow 00{:}20{:}42{.}360$  Kathleen. At the patient characteristics

NOTE Confidence: 0.767647362

 $00{:}20{:}42{.}360 \dashrightarrow 00{:}20{:}44{.}467$  we can see that there was a

NOTE Confidence: 0.767647362

 $00:20:44.467 \longrightarrow 00:20:46.283$  pretty much an equal distribution

NOTE Confidence: 0.767647362

 $00:20:46.283 \rightarrow 00:20:48.935$  of men and women in this study.

NOTE Confidence: 0.767647362

 $00{:}20{:}48{.}935 \dashrightarrow 00{:}20{:}52{.}360$  The average age was about 41.

NOTE Confidence: 0.767647362

 $00:20:52.360 \longrightarrow 00:20:54.640$  Ethnicity was something

NOTE Confidence: 0.767647362

 $00{:}20{:}54.640 \dashrightarrow 00{:}20{:}57.680$  we'll talk about later.

NOTE Confidence: 0.767647362

 $00{:}20{:}57.680 \dashrightarrow 00{:}21{:}00.400$  There was about 94%

NOTE Confidence: 0.80088173125

 $00:21:04.000 \rightarrow 00:21:08.800$  white patients participants in the study

NOTE Confidence: 0.80088173125

 $00{:}21{:}08{.}800 \dashrightarrow 00{:}21{:}14{.}910$  and only less than 3% or about 3% black or

NOTE Confidence: 0.80088173125

00:21:14.910 --> 00:21:18.240 African American participating in this study.

NOTE Confidence: 0.80088173125

 $00:21:18.240 \rightarrow 00:21:23.022$  The other things of real interest is only

 $00{:}21{:}23{.}022 \dashrightarrow 00{:}21{:}27{.}234$  about 12% had treatment resistant depression.

NOTE Confidence: 0.80088173125

 $00{:}21{:}27{.}240 \dashrightarrow 00{:}21{:}29{.}656$  So this was primarily and the large majority

NOTE Confidence: 0.80088173125

 $00:21:29.656 \rightarrow 00:21:32.543$  of these patients were not meeting criteria

NOTE Confidence: 0.80088173125

 $00:21:32.543 \rightarrow 00:21:34.319$  for treatment resistant depression,

NOTE Confidence: 0.80088173125

 $00:21:34.320 \longrightarrow 00:21:36.427$  although there was no cap on the

NOTE Confidence: 0.80088173125

00:21:36.427 --> 00:21:37.920 number of treatment failures.

NOTE Confidence: 0.80088173125

 $00:21:37.920 \longrightarrow 00:21:40.656$  So, so there were people that could have

NOTE Confidence: 0.80088173125

 $00:21:40.656 \rightarrow 00:21:42.520$  had any number of treatment failures.

NOTE Confidence: 0.80088173125

 $00:21:42.520 \longrightarrow 00:21:44.280$  It was really about 12,

NOTE Confidence: 0.80088173125

 $00:21:44.280 \longrightarrow 00:21:46.499 1/2\%$  that would have met the criteria

NOTE Confidence: 0.80088173125

 $00:21:46.499 \rightarrow 00:21:48.080$  for treatment resistant depression.

NOTE Confidence: 0.80088173125

00:21:48.080 $\operatorname{-->}$ 00:21:50.026 And you can see the number that

NOTE Confidence: 0.80088173125

 $00:21:50.026 \rightarrow 00:21:51.920$  actually went through a medication taper

NOTE Confidence: 0.80088173125

 $00{:}21{:}51{.}920 \dashrightarrow 00{:}21{:}53{.}703$  both for psilocybin and for niacin.

NOTE Confidence: 0.80088173125

 $00{:}21{:}53.703 \dashrightarrow 00{:}21{:}56.240$  But in general it was about one out of

 $00:21:56.240 \rightarrow 00:21:58.196$  five people required a medication taper,

NOTE Confidence: 0.80088173125

 $00{:}21{:}58{.}200 \dashrightarrow 00{:}22{:}03{.}000$  meaning that about 80% of the patients or

NOTE Confidence: 0.80088173125

 $00:22:03.000 \longrightarrow 00:22:05.160$  75% of the patients didn't require a taper.

NOTE Confidence: 0.80088173125

 $00:22:05.160 \rightarrow 00:22:07.578$  They were not on an antidepressant

NOTE Confidence: 0.80088173125

 $00:22:07.578 \rightarrow 00:22:10.839$  at the time of entering the study.

NOTE Confidence: 0.80088173125

00:22:10.840 --> 00:22:11.524 Baseline mattress,

NOTE Confidence: 0.80088173125

 $00{:}22{:}11.524 \dashrightarrow 00{:}22{:}14.809$  as I said the cut off was was actually

NOTE Confidence: 0.80088173125

 $00:22:14.809 \rightarrow 00:22:17.080$  pretty high for the study of 28.

NOTE Confidence: 0.80088173125

 $00{:}22{:}17.080 \dashrightarrow 00{:}22{:}19.866$  So the the baseline mattress of 35

NOTE Confidence: 0.80088173125

00:22:19.866 --> 00:22:25.300 is is a pretty high average level

NOTE Confidence: 0.80088173125

 $00:22:25.300 \longrightarrow 00:22:27.200$  of severity for a study.

NOTE Confidence: 0.80088173125

00:22:27.200 --> 00:22:28.936 The SDS scores of,

NOTE Confidence: 0.80088173125

00:22:28.936 --> 00:22:32.061 you know somewhere around seven was actually

NOTE Confidence: 0.80088173125

 $00:22:32.061 \rightarrow 00:22:34.968$  a little bit lower then you would expect.

NOTE Confidence: 0.80088173125

 $00{:}22{:}34{.}968 \dashrightarrow 00{:}22{:}36{.}720$  So a lower level that's the

NOTE Confidence: 0.80088173125

 $00:22:36.779 \longrightarrow 00:22:38.240$  Sheehan disability scale,

 $00:22:38.240 \longrightarrow 00:22:40.832$  a little bit lower level of disability than

NOTE Confidence: 0.80088173125

 $00{:}22{:}40.832 \dashrightarrow 00{:}22{:}43.639$  you see in most other depression studies.

NOTE Confidence: 0.80088173125

 $00:22:43.640 \rightarrow 00:22:46.336$  And then you can see the average length of

NOTE Confidence: 0.80088173125

 $00:22:46.336 \rightarrow 00:22:49.706$  depression and number of previous episodes.

NOTE Confidence: 0.80088173125

00:22:49.706 --> 00:22:50.559 Jerry,

NOTE Confidence: 0.84663695

 $00{:}22{:}50{.}560 \dashrightarrow 00{:}22{:}52{.}296$  what do you make of that observation

NOTE Confidence: 0.84663695

 $00:22:52.296 \longrightarrow 00:22:54.137$  that the the Madras is on the high

NOTE Confidence: 0.84663695

 $00{:}22{:}54{.}137 \dashrightarrow 00{:}22{:}56{.}040$  side but the SDS is on the low side?

NOTE Confidence: 0.84663695

 $00{:}22{:}56{.}040 \dashrightarrow 00{:}22{:}57{.}951$  Is that because so many other possible

NOTE Confidence: 0.84663695

 $00:22:57.951 \rightarrow 00:22:59.598$  sources of disability are screened out?

NOTE Confidence: 0.688186763333333

 $00{:}23{:}00{.}000 \dashrightarrow 00{:}23{:}02{.}408$  I I think that's a a large possibility.

NOTE Confidence: 0.688186763333333

00:23:02.408 --> 00:23:04.840 The way the way the Sheen is collected

NOTE Confidence: 0.688186763333333

00:23:04.900 --> 00:23:06.285 may give you some artificial

NOTE Confidence: 0.688186763333333

 $00{:}23{:}06{.}285 \dashrightarrow 00{:}23{:}08{.}320$  ratings with that too a little bit.

NOTE Confidence: 0.688186763333333

 $00{:}23{:}08{.}320 \dashrightarrow 00{:}23{:}09{.}792$  But I also think and we'll talk about

 $00:23:09.792 \rightarrow 00:23:11.519$  when we talk about the generalizability,

NOTE Confidence: 0.688186763333333

 $00{:}23{:}11{.}520 \dashrightarrow 00{:}23{:}13{.}116$  this is kind of a unique population,

NOTE Confidence: 0.688186763333333

 $00:23:13.120 \longrightarrow 00:23:14.203$  very highly educated,

NOTE Confidence: 0.688186763333333

 $00:23:14.203 \longrightarrow 00:23:18.176$  more so than you would see in a lot of

NOTE Confidence: 0.688186763333333

 $00:23:18.176 \longrightarrow 00:23:20.000$  other typical antidepressant trials.

NOTE Confidence: 0.688186763333333

00:23:20.000 --> 00:23:21.300 And that I think probably

NOTE Confidence: 0.688186763333333

 $00:23:21.300 \longrightarrow 00:23:22.800$  attributes to some of that. There

NOTE Confidence: 0.69829368111111

 $00:23:22.800 \longrightarrow 00:23:25.110$  is buffer. There are various

NOTE Confidence: 0.698293681111111

 $00{:}23{:}25{.}110 \dashrightarrow 00{:}23{:}26{.}496$  characteristics that buffer

NOTE Confidence: 0.698293681111111

 $00:23:26.496 \rightarrow 00:23:27.680$  disability in this population.

NOTE Confidence: 0.709693466363636

 $00:23:28.360 \longrightarrow 00:23:30.866$  Yeah, they have a lot of other

NOTE Confidence: 0.709693466363636

00:23:30.866 - 00:23:32.982 buffers to to prevent it.

NOTE Confidence: 0.709693466363636

 $00:23:32.982 \longrightarrow 00:23:35.274$  All right. So here's the data.

NOTE Confidence: 0.709693466363636

 $00:23:35.280 \longrightarrow 00:23:37.086$  I mean, there's the data is the

NOTE Confidence: 0.709693466363636

 $00{:}23{:}37.086 \dashrightarrow 00{:}23{:}38.799$  real easy thing to present here.

NOTE Confidence: 0.709693466363636

 $00:23:38.800 \rightarrow 00:23:41.560$  This is pretty, pretty clear.
- NOTE Confidence: 0.709693466363636
- $00{:}23{:}41{.}560 \dashrightarrow 00{:}23{:}45{.}124$  So that, yeah, that there was no doubt in

 $00:23:45.124 \rightarrow 00:23:48.673$  the significance there with AP of 001.001.

NOTE Confidence: 0.709693466363636

00:23:48.673 -> 00:23:52.066 The mean difference was the 12.3 points

NOTE Confidence: 0.709693466363636

 $00:23:52.066 \rightarrow 00:23:54.957$  on a mattress which is quite large,

NOTE Confidence: 0.709693466363636

 $00:23:54.960 \longrightarrow 00:23:58.360$  you know very large.

NOTE Confidence: 0.709693466363636

 $00:23:58.360 \longrightarrow 00:24:00.369$  So this is really standing out in

NOTE Confidence: 0.709693466363636

 $00:24:00.369 \rightarrow 00:24:02.358$  in many ways as a very strong.

NOTE Confidence: 0.709693466363636

 $00:24:02.360 \longrightarrow 00:24:03.920$  Remember the the primary end

NOTE Confidence: 0.709693466363636

 $00:24:03.920 \longrightarrow 00:24:05.480$  point here is day 43,

NOTE Confidence: 0.709693466363636

 $00:24:05.480 \longrightarrow 00:24:07.436$  so it's this last time point.

NOTE Confidence: 0.709693466363636

 $00:24:07.440 \longrightarrow 00:24:09.360$  If you look look at it other ways,

NOTE Confidence: 0.709693466363636

 $00{:}24{:}09{.}360 \dashrightarrow 00{:}24{:}11{.}448$  this is actually my new favorite

NOTE Confidence: 0.709693466363636

 $00{:}24{:}11{.}448 \dashrightarrow 00{:}24{:}12{.}840$  way to present data.

NOTE Confidence: 0.709693466363636

 $00{:}24{:}12{.}840 \dashrightarrow 00{:}24{:}14{.}472$  It's called the waterfall

NOTE Confidence: 0.709693466363636

 $00:24:14.472 \rightarrow 00:24:16.026$  plot where you actually,

 $00:24:16.026 \rightarrow 00:24:18.250$  you can see the the mattress

NOTE Confidence: 0.709693466363636

00:24:18.250 --> 00:24:19.975 score that the patients start

NOTE Confidence: 0.709693466363636

00:24:19.975 --> 00:24:23.745 with or the participants and

NOTE Confidence: 0.709693466363636

 $00:24:23.745 \longrightarrow 00:24:25.880$  then how far they drop or rise.

NOTE Confidence: 0.709693466363636

 $00:24:25.880 \rightarrow 00:24:28.120$  For the few people that actually got worse,

NOTE Confidence: 0.709693466363636

 $00{:}24{:}28{.}120 \dashrightarrow 00{:}24{:}30{.}880$  you can see here that there's an increase.

NOTE Confidence: 0.709693466363636

 $00:24:30.880 \longrightarrow 00:24:32.800$  So you can see the group,

NOTE Confidence: 0.709693466363636

 $00:24:32.800 \rightarrow 00:24:35.764$  the orange represents the psilocybin and

NOTE Confidence: 0.709693466363636

 $00:24:35.764 \rightarrow 00:24:38.640$  the blue representing the the niacin.

NOTE Confidence: 0.709693466363636

 $00:24:38.640 \rightarrow 00:24:40.474$  You can see that the large majority

NOTE Confidence: 0.709693466363636

 $00{:}24{:}40{.}474 \dashrightarrow 00{:}24{:}42{.}072$  of people getting psilocybin

NOTE Confidence: 0.709693466363636

 $00:24:42.072 \longrightarrow 00:24:43.680$  had significant drops,

NOTE Confidence: 0.709693466363636

 $00:24:43.680 \longrightarrow 00:24:45.384$  very few that did a little

NOTE Confidence: 0.709693466363636

 $00:24:45.384 \rightarrow 00:24:47.119$  bit worse and in fact no,

NOTE Confidence: 0.709693466363636

 $00:24:47.120 \longrightarrow 00:24:48.920$  no more doing worse than

NOTE Confidence: 0.709693466363636

 $00:24:48.920 \longrightarrow 00:24:50.457$  the people getting niacin.

- NOTE Confidence: 0.709693466363636
- 00:24:50.457 --> 00:24:53.656 So it's really nice way of looking
- NOTE Confidence: 0.709693466363636
- $00:24:53.656 \longrightarrow 00:24:56.118$  at individual patient data here.
- NOTE Confidence: 0.709693466363636
- $00:24:56.120 \longrightarrow 00:24:58.164$  And then you can see the change
- NOTE Confidence: 0.709693466363636
- $00:24:58.164 \rightarrow 00:25:00.319$  in Madras from baseline to day 43,
- NOTE Confidence: 0.709693466363636
- $00:25:00.320 \longrightarrow 00:25:02.635$  which was the primary outcome
- NOTE Confidence: 0.709693466363636
- $00{:}25{:}02.635 \dashrightarrow 00{:}25{:}04.487$  measure very clearly hitting
- NOTE Confidence: 0.709693466363636
- 00:25:04.487 --> 00:25:05.880 statistical significance.
- NOTE Confidence: 0.709693466363636
- $00{:}25{:}05{.}880 \dashrightarrow 00{:}25{:}08{.}323$  So this data for the primary outcome
- NOTE Confidence: 0.709693466363636
- $00{:}25{:}08{.}323 \dashrightarrow 00{:}25{:}11{.}119$  I don't think could be more promising.
- NOTE Confidence: 0.709693466363636
- 00:25:11.120 --> 00:25:13.352 I don't think you could have
- NOTE Confidence: 0.709693466363636
- $00:25:13.352 \longrightarrow 00:25:14.840$  asked for much more.
- NOTE Confidence: 0.709693466363636
- $00:25:14.840 \longrightarrow 00:25:16.544$  Also for secondary measures,
- NOTE Confidence: 0.709693466363636
- $00:25:16.544 \rightarrow 00:25:18.674$  the data were very strong.
- NOTE Confidence: 0.709693466363636
- 00:25:18.680 --> 00:25:20.498 So here's looking at the Madras
- NOTE Confidence: 0.709693466363636
- $00:25:20.498 \longrightarrow 00:25:22.000$  scores throughout the different days.
- NOTE Confidence: 0.709693466363636

00:25:22.000 -> 00:25:23.540 You can see pretty much

NOTE Confidence: 0.709693466363636

 $00:25:23.540 \rightarrow 00:25:25.080$  significance all the way through.

NOTE Confidence: 0.709693466363636

 $00:25:25.080 \longrightarrow 00:25:26.052$  Even the sheehan,

NOTE Confidence: 0.709693466363636

 $00:25:26.052 \rightarrow 00:25:27.861$  even though I said the the

NOTE Confidence: 0.709693466363636

00:25:27.861 - > 00:25:29.037 baseline levels of disability

NOTE Confidence: 0.709693466363636

 $00{:}25{:}29{.}037 \dashrightarrow 00{:}25{:}31{.}098$  weren't may be as high as you may

NOTE Confidence: 0.709693466363636

 $00:25:31.098 \rightarrow 00:25:32.438$  expect in some other studies,

NOTE Confidence: 0.709693466363636

 $00:25:32.440 \rightarrow 00:25:35.824$  they still showed high levels of change

NOTE Confidence: 0.709693466363636

 $00:25:35.824 \rightarrow 00:25:38.960$  significance compared to niacin.

NOTE Confidence: 0.709693466363636

 $00{:}25{:}38{.}960 \dashrightarrow 00{:}25{:}42{.}656$  And if you looked at the sustained

NOTE Confidence: 0.709693466363636

 $00:25:42.656 \rightarrow 00:25:45.240$  depressive response at the six week point,

NOTE Confidence: 0.709693466363636

00:25:45.240 --> 00:25:47.480 highly statistically significant remission

NOTE Confidence: 0.709693466363636

 $00{:}25{:}47{.}480 \dashrightarrow 00{:}25{:}50{.}280$ didn't quite hit statistical significance,

NOTE Confidence: 0.709693466363636

 $00:25:50.280 \rightarrow 00:25:51.528$  but pretty darn close.

NOTE Confidence: 0.709693466363636

 $00{:}25{:}51{.}528 \dashrightarrow 00{:}25{:}53{.}827$  And you can actually see here sometimes

NOTE Confidence: 0.709693466363636

 $00:25:53.827 \rightarrow 00:25:56.396$  visually it's just a little bit better.

 $00:25:56.400 \rightarrow 00:25:58.234$  This is looking at the response rates.

NOTE Confidence: 0.709693466363636

 $00{:}25{:}58{.}240 \dashrightarrow 00{:}26{:}00{.}814$  So we had 20 of 48 in psilocybin 5

NOTE Confidence: 0.709693466363636

 $00{:}26{:}00{.}814 \dashrightarrow 00{:}26{:}03{.}439$  and 44 in Niacin meeting response,

NOTE Confidence: 0.709693466363636

 $00:26:03.440 \longrightarrow 00:26:05.660$  which was a 50% improvement on

NOTE Confidence: 0.709693466363636

 $00:26:05.660 \longrightarrow 00:26:08.240$  the Madras and an odds ratio

NOTE Confidence: 0.709693466363636

 $00:26:08.240 \longrightarrow 00:26:10.502$  of response of about 5.6.

NOTE Confidence: 0.709693466363636

00:26:10.502 --> 00:26:13.034 If you look at sustained remission,

NOTE Confidence: 0.709693466363636

 $00:26:13.040 \longrightarrow 00:26:15.504$  there was 12 of 48 meaning that

NOTE Confidence: 0.709693466363636

 $00:26:15.504 \rightarrow 00:26:18.990$  they had a Madras less than 10 for

NOTE Confidence: 0.709693466363636

 $00{:}26{:}18.990 \dashrightarrow 00{:}26{:}22.346$  psilocybin and only about I think it

NOTE Confidence: 0.709693466363636

 $00:26:22.346 \longrightarrow 00:26:25.675$  was about 11 percent or so for for

NOTE Confidence: 0.709693466363636

 $00{:}26{:}25.675 \dashrightarrow 00{:}26{:}29.155$  Niacin with an odd ratio of over three.

NOTE Confidence: 0.709693466363636

00:26:29.160 --> 00:26:31.561 So again very strong data and remember

NOTE Confidence: 0.709693466363636

 $00{:}26{:}31{.}561 \dashrightarrow 00{:}26{:}33{.}834$  this is different than some of the

NOTE Confidence: 0.709693466363636

 $00:26:33.834 \rightarrow 00:26:36.074$  other studies that you may have seen

 $00:26:36.074 \rightarrow 00:26:38.119$  where there's been repeated dosing.

NOTE Confidence: 0.709693466363636

 $00{:}26{:}38{.}120 \dashrightarrow 00{:}26{:}40{.}070$  This is just that one single

NOTE Confidence: 0.709693466363636

 $00{:}26{:}40.070 \dashrightarrow 00{:}26{:}41.370$  dose and then these

NOTE Confidence: 0.907544118461538

 $00:26:41.446 \rightarrow 00:26:45.538$  measures are made day 43 out other

NOTE Confidence: 0.907544118461538

 $00{:}26{:}45{.}538 \dashrightarrow 00{:}26{:}47{.}210$  secondary measures pretty much

NOTE Confidence: 0.907544118461538

 $00{:}26{:}47{.}210$  -->  $00{:}26{:}50{.}156$  across the board you you can look at

NOTE Confidence: 0.907544118461538

 $00:26:50.156 \rightarrow 00:26:51.920$  and see how they were carried out.

NOTE Confidence: 0.907544118461538

 $00:26:51.920 \longrightarrow 00:26:54.557$  I did forget to say early on that these

NOTE Confidence: 0.907544118461538

 $00{:}26{:}54{.}557 \dashrightarrow 00{:}26{:}56{.}918$  ratings are all done by central Raiders.

NOTE Confidence: 0.907544118461538

 $00{:}26{:}56{.}920 \dashrightarrow 00{:}26{:}59{.}680$  So in order to address the

NOTE Confidence: 0.907544118461538

 $00:26:59.680 \longrightarrow 00:27:03.240$  the unblinding of the Raider,

NOTE Confidence: 0.907544118461538

 $00:27:03.240 \longrightarrow 00:27:05.298$  all these ratings were done by

NOTE Confidence: 0.907544118461538

 $00:27:05.298 \longrightarrow 00:27:06.920$  somebody off site calling in.

NOTE Confidence: 0.907544118461538

 $00:27:06.920 \longrightarrow 00:27:10.591$  And it was very rigorous that the

NOTE Confidence: 0.907544118461538

00:27:10.591 --> 00:27:12.697 the person doing the raid and

NOTE Confidence: 0.907544118461538

00:27:12.697 - 00:27:15.198 did not even know at what point

- NOTE Confidence: 0.907544118461538
- $00:27:15.200 \longrightarrow 00:27:17.078$  the person was in the study.
- NOTE Confidence: 0.907544118461538
- $00:27:17.080 \longrightarrow 00:27:19.408$  So they didn't know if this was a
- NOTE Confidence: 0.907544118461538
- $00{:}27{:}19{.}408 \dashrightarrow 00{:}27{:}21{.}325$  baseline rating this is the end of
- NOTE Confidence: 0.907544118461538
- $00:27:21.325 \longrightarrow 00:27:23.080$  study rating if this was a week,
- NOTE Confidence: 0.907544118461538
- 00:27:23.080 --> 00:27:25.320 Week 2 rating, a week 1 rating.
- NOTE Confidence: 0.907544118461538
- $00:27:25.320 \longrightarrow 00:27:26.760$  So they really didn't know
- NOTE Confidence: 0.907544118461538
- $00:27:26.760 \dashrightarrow 00:27:28.200$  everybody was treated the same.
- NOTE Confidence: 0.907544118461538
- $00{:}27{:}28{.}200 \dashrightarrow 00{:}27{:}30{.}096$  So these these data are pretty
- NOTE Confidence: 0.907544118461538
- $00:27:30.096 \rightarrow 00:27:31.360$  strong from that perspective.
- NOTE Confidence: 0.907544118461538
- 00:27:31.360 --> 00:27:31.440 So
- NOTE Confidence: 0.7371139666666667
- $00:27:31.520 \longrightarrow 00:27:33.560$  it wasn't the same rater consistent,
- NOTE Confidence: 0.7371139666666667
- $00{:}27{:}33.560 \dashrightarrow 00{:}27{:}35.650$  it was not the same rater
- NOTE Confidence: 0.7371139666666667
- 00:27:35.650 00:27:36.800 consistently which is you know
- NOTE Confidence: 0.903351388571428
- $00{:}27{:}36{.}800 \dashrightarrow 00{:}27{:}38{.}655$  when you design studies that's
- NOTE Confidence: 0.903351388571428
- $00{:}27{:}38.655 \dashrightarrow 00{:}27{:}41.960$  something you usually do want to have.
- NOTE Confidence: 0.903351388571428

 $00:27:41.960 \longrightarrow 00:27:45.200$  But in this case to try to prevent

NOTE Confidence: 0.903351388571428

 $00:27:45.200 \longrightarrow 00:27:48.200$  the functional on blinding of

NOTE Confidence: 0.903351388571428

 $00:27:48.200 \longrightarrow 00:27:50.432$  the of the rater that was a

NOTE Confidence: 0.903351388571428

 $00:27:50.432 \rightarrow 00:27:52.280$  precaution that was put in place was

NOTE Confidence: 0.850431003076923

 $00:27:52.280 \longrightarrow 00:27:53.750$  there any formal assessment of blind

NOTE Confidence: 0.850431003076923

 $00{:}27{:}53.750 \dashrightarrow 00{:}27{:}55.319$  for either the subject or the rater.

NOTE Confidence: 0.86438697

 $00{:}27{:}55{.}440 \dashrightarrow 00{:}27{:}56{.}830$  So that we'll we'll talk

NOTE Confidence: 0.86438697

 $00:27:56.830 \longrightarrow 00:27:58.641$  about that's one of the major

NOTE Confidence: 0.86438697

 $00:27:58.641 \longrightarrow 00:28:00.077$  limitations of the study.

NOTE Confidence: 0.86438697

 $00{:}28{:}00{.}080 \dashrightarrow 00{:}28{:}01{.}480$  So there there was not

NOTE Confidence: 0.768518528571428

 $00{:}28{:}03.640 \dashrightarrow 00{:}28{:}05.953$  the other I I I think the the flip

NOTE Confidence: 0.768518528571428

 $00{:}28{:}05{.}953 \dashrightarrow 00{:}28{:}08{.}000$  side the real important data from

NOTE Confidence: 0.768518528571428

 $00{:}28{:}08{.}000 \dashrightarrow 00{:}28{:}10{.}120$  the study of the safety data.

NOTE Confidence: 0.768518528571428

 $00:28:10.120 \longrightarrow 00:28:14.274$  So here you can see that 88% or

NOTE Confidence: 0.768518528571428

 $00:28:14.274 \longrightarrow 00:28:16.896$  44 or 50 other participants in

NOTE Confidence: 0.768518528571428

00:28:16.896 --> 00:28:19.848 psilocybin and 33 or out of 54 or

 $00:28:19.848 \longrightarrow 00:28:22.088 61\%$  receiving niacin reported at

NOTE Confidence: 0.768518528571428

 $00{:}28{:}22.088 \dashrightarrow 00{:}28{:}24.878$  least one AE through throughout the

NOTE Confidence: 0.768518528571428

 $00:28:24.878 \longrightarrow 00:28:28.840$  end of the 43 day follow up.

NOTE Confidence: 0.768518528571428

 $00:28:28.840 \longrightarrow 00:28:32.072$  But I think a little bit more important

NOTE Confidence: 0.768518528571428

 $00:28:32.072 \rightarrow 00:28:34.598$  is what would be considered drug related.

NOTE Confidence: 0.768518528571428

 $00{:}28{:}34.600 \dashrightarrow 00{:}28{:}36.749$  So the investigator at least said it's

NOTE Confidence: 0.768518528571428

 $00{:}28{:}36{.}749 \dashrightarrow 00{:}28{:}38{.}591$  possible that that these side effects

NOTE Confidence: 0.768518528571428

 $00{:}28{:}38{.}591 \dashrightarrow 00{:}28{:}40{.}889$  were related to the drug and you can

NOTE Confidence: 0.768518528571428

 $00:28:40.889 \longrightarrow 00:28:43.902$  say here that it was 41 of the 50 or

NOTE Confidence: 0.768518528571428

 $00{:}28{:}43{.}902 \dashrightarrow 00{:}28{:}47{.}918$  82% of the patients in the psilocybin group.

NOTE Confidence: 0.768518528571428

 $00:28:47.920 \longrightarrow 00:28:51.196$  And you can see it was 24 of the

NOTE Confidence: 0.768518528571428

00:28:51.196 --> 00:28:54.800 54 or 44% in the niac<br/>in group

NOTE Confidence: 0.768518528571428

 $00{:}28{:}54.800 \dashrightarrow 00{:}28{:}57.299$  experienced at least an AE that was

NOTE Confidence: 0.768518528571428

 $00{:}28{:}57{.}299 \dashrightarrow 00{:}28{:}59{.}399$  thought to be drug related.

NOTE Confidence: 0.768518528571428

 $00:28:59.400 \longrightarrow 00:29:01.633$  And then even bumping it up a

 $00:29:01.633 \longrightarrow 00:29:03.806$  little bit more in importance is

NOTE Confidence: 0.768518528571428

 $00{:}29{:}03.806 \dashrightarrow 00{:}29{:}06.080$  more of the severe related AES.

NOTE Confidence: 0.768518528571428

 $00:29:06.080 \rightarrow 00:29:09.120$  And this is through the first week really.

NOTE Confidence: 0.768518528571428

 $00:29:09.120 \longrightarrow 00:29:12.312$  I reported four out of the 50

NOTE Confidence: 0.768518528571428

00:29:12.312 --> 00:29:14.120 participants receiving psilocybin or 8%

NOTE Confidence: 0.768518528571428

 $00:29:14.120 \longrightarrow 00:29:16.796$  of those that consisted of migraines,

NOTE Confidence: 0.768518528571428

00:29:16.800 --> 00:29:21.280 headaches, illusions, panic attacks,

NOTE Confidence: 0.768518528571428

00:29:21.280 --> 00:29:22.400 paranoia.

NOTE Confidence: 0.768518528571428

00:29:22.400 --> 00:29:25.557 There were none in the Niacin group,

NOTE Confidence: 0.768518528571428

 $00:29:25.560 \rightarrow 00:29:27.800$  but I I'm bumping it up one more

NOTE Confidence: 0.768518528571428

 $00{:}29{:}27{.}800 \dashrightarrow 00{:}29{:}29{.}820$  in level of importance and this

NOTE Confidence: 0.768518528571428

 $00{:}29{:}29{.}820 \dashrightarrow 00{:}29{:}31.070$  is obviously the most important

NOTE Confidence: 0.768518528571428

 $00{:}29{:}31{.}070 \dashrightarrow 00{:}29{:}33{.}193$  all of these there were no serious

NOTE Confidence: 0.768518528571428

 $00:29:33.193 \rightarrow 00:29:34.513$  treatment emergent adverse events.

NOTE Confidence: 0.768518528571428

 $00:29:34.520 \longrightarrow 00:29:36.221$  So for those of you that aren't

NOTE Confidence: 0.768518528571428

 $00:29:36.221 \rightarrow 00:29:37.320$  familiar with clinical trials,

- NOTE Confidence: 0.768518528571428
- $00:29:37.320 \rightarrow 00:29:40.145$  a serious adverse event basically
- NOTE Confidence: 0.768518528571428
- 00:29:40.145 --> 00:29:41.275 means hospitalization,
- NOTE Confidence: 0.768518528571428
- 00:29:41.280 --> 00:29:47.088 risk of death or some other long
- NOTE Confidence: 0.768518528571428
- $00:29:47.088 \rightarrow 00:29:49.640$  term impairment that results from it.
- NOTE Confidence: 0.768518528571428
- $00:29:49.640 \rightarrow 00:29:52.358$  So nothing along those lines occurred,
- NOTE Confidence: 0.578699218888889
- $00:29:52.920 \longrightarrow 00:29:54.908$  Jerry. Yeah, that difference
- NOTE Confidence: 0.578699218888889
- $00:29:54.908 \longrightarrow 00:29:57.393$  between in in severe aids.
- NOTE Confidence: 0.578699218888889
- $00:29:57.400 \longrightarrow 00:29:58.672$  Well, in both categories,
- NOTE Confidence: 0.578699218888889
- 00:29:58.672 --> 00:29:59.944 I guess you're lumping
- NOTE Confidence: 0.578699218888889
- $00:29:59.944 \rightarrow 00:30:01.360$  together days one through 9,
- NOTE Confidence: 0.578699218888889
- $00:30:01.360 \longrightarrow 00:30:03.544$  but we expect a lot of
- NOTE Confidence: 0.578699218888889
- $00:30:03.544 \dashrightarrow 00:30:05.000$  psychological effects during dosing.
- NOTE Confidence: 0.578699218888889
- $00:30:05.000 \dashrightarrow 00:30:06.708$  So I'd be interested in the differences
- NOTE Confidence: 0.578699218888889
- 00:30:06.708 --> 00:30:08.548 on days two through 9 because like
- NOTE Confidence: 0.578699218888889
- $00{:}30{:}08{.}548 \dashrightarrow 00{:}30{:}10{.}200$  how much of that difference was,
- NOTE Confidence: 0.578699218888889

00:30:10.200 --> 00:30:12.216 you know, panic attack on day one during

NOTE Confidence: 0.578699218888889

 $00:30:12.216 \rightarrow 00:30:13.958$  dosing means something very different.

NOTE Confidence: 0.578699218888889

00:30:13.960 --> 00:30:15.640 So many attacks four days later,

NOTE Confidence: 0.8739576575

 $00:30:15.920 \longrightarrow 00:30:17.920$  so many were here we can go through.

NOTE Confidence: 0.8739576575

 $00{:}30{:}17{.}920 \dashrightarrow 00{:}30{:}19{.}360$  We'll talk a little bit about some of

NOTE Confidence: 0.8739576575

00:30:19.360 --> 00:30:20.746 the more persistent ones or outside

NOTE Confidence: 0.8739576575

 $00{:}30{:}20{.}746 \dashrightarrow 00{:}30{:}22{.}222$  ones because those are obviously the

NOTE Confidence: 0.8739576575

 $00:30:22.269 \rightarrow 00:30:23.679$  ones that everybody's worried about.

NOTE Confidence: 0.8739576575

 $00{:}30{:}23.680 \dashrightarrow 00{:}30{:}26.640$  Yeah, good question.

NOTE Confidence: 0.8739576575

 $00:30:26.640 \longrightarrow 00:30:28.159$  Yeah, they'll come up a little bit.

NOTE Confidence: 0.772907803076923

 $00{:}30{:}29{.}120 \dashrightarrow 00{:}30{:}30{.}513$  I'm also, I'm a little surprised it's

NOTE Confidence: 0.772907803076923

00:30:30.513 - 00:30:32.022 reported as day one through 9, yeah.

NOTE Confidence: 0.772907803076923

00:30:32.022 --> 00:30:34.314 Yeah, As opposed to day one, yeah.

NOTE Confidence: 0.772907803076923

 $00:30:34.314 \dashrightarrow 00:30:35.920$  And then day two through nine. Well,

NOTE Confidence: 0.90480678625

 $00:30:35.920 \rightarrow 00:30:38.320$  I think that people were worried about that,

NOTE Confidence: 0.90480678625

 $00:30:38.320 \longrightarrow 00:30:40.400$  that total time frame,

 $00:30:40.400 \rightarrow 00:30:45.800$  people meeting the regulatory agencies, OK,

NOTE Confidence: 0.90480678625

 $00{:}30{:}45{.}800 \dashrightarrow 00{:}30{:}48{.}194$  when it came to solicited adverse events.

NOTE Confidence: 0.90480678625

 $00{:}30{:}48{.}200 \dashrightarrow 00{:}30{:}50{.}384$  So ones that were adverse events of

NOTE Confidence: 0.90480678625

 $00:30:50.384 \rightarrow 00:30:52.327$  interest that was specifically asked

NOTE Confidence: 0.90480678625

 $00:30:52.327 \rightarrow 00:30:54.880$  about the most common were headache,

NOTE Confidence: 0.90480678625

 $00{:}30{:}54{.}880 \dashrightarrow 00{:}30{:}59{.}920$  nausea and visual perceptual effects,

NOTE Confidence: 0.90480678625

 $00:30:59.920 \longrightarrow 00:31:02.928$  which was not so surprising I think and

NOTE Confidence: 0.90480678625

 $00:31:02.928 \longrightarrow 00:31:06.316$  you can see the relative ratios of them.

NOTE Confidence: 0.90480678625

 $00{:}31{:}06{.}320 \dashrightarrow 00{:}31{:}08{.}948$  The one that may be a little bit more

NOTE Confidence: 0.90480678625

 $00:31:08.948 \rightarrow 00:31:10.823$  concerning with the visual and perceptual

NOTE Confidence: 0.90480678625

 $00:31:10.823 \longrightarrow 00:31:13.177$  effects is 3 of the 50 patients

NOTE Confidence: 0.90480678625

00:31:13.177 --> 00:31:15.530 receiving psilocybin or 6% actually

NOTE Confidence: 0.90480678625

 $00:31:15.530 \longrightarrow 00:31:19.580$  reported some visual or perceptual

NOTE Confidence: 0.90480678625

 $00:31:19.580 \longrightarrow 00:31:22.272$  effects occurring after that first day.

NOTE Confidence: 0.90480678625

 $00{:}31{:}22{.}272 \dashrightarrow 00{:}31{:}25{.}092$  So this is getting a little bit more of what

00:31:25.092 --> 00:31:27.340 you're talking about S 6% smaller number,

NOTE Confidence: 0.90480678625

 $00{:}31{:}27{.}340 \dashrightarrow 00{:}31{:}30{.}296$  but still a number that I I think

NOTE Confidence: 0.90480678625

 $00:31:30.296 \longrightarrow 00:31:32.714$  it's important to pay attention to.

NOTE Confidence: 0.90480678625

 $00:31:32.720 \longrightarrow 00:31:33.830$  And and they all did resolve

NOTE Confidence: 0.90480678625

 $00:31:33.830 \longrightarrow 00:31:34.840$  by the end of this.

NOTE Confidence: 0.90480678625

 $00{:}31{:}34{.}840 \dashrightarrow 00{:}31{:}34{.}960$  Well

NOTE Confidence: 0.829558628666667

 $00:31:34.960 \longrightarrow 00:31:36.850$  what was the severity of those Because

NOTE Confidence: 0.829558628666667

 $00:31:36.850 \rightarrow 00:31:38.839$  if that's a little flickering on day

NOTE Confidence: 0.8295586286666667

00:31:38.839 --> 00:31:40.608 2 versus well formed hallucinations

NOTE Confidence: 0.8295586286666667

 $00:31:40.608 \rightarrow 00:31:42.840$  of pink elephants on day 20,

NOTE Confidence: 0.8295586286666667

 $00:31:42.840 \longrightarrow 00:31:43.880$  those are very different.

NOTE Confidence: 0.829558628666667

 $00{:}31{:}43.880 \dashrightarrow 00{:}31{:}45.160$  You know, so remember there were

NOTE Confidence: 0.838822982352941

 $00{:}31{:}45.160 \dashrightarrow 00{:}31{:}46.861$  no SAES, so nothing reaching the level

NOTE Confidence: 0.838822982352941

 $00{:}31{:}46.861 \dashrightarrow 00{:}31{:}49.160$  of an SAE and I don't think any of them,

NOTE Confidence: 0.838822982352941

00:31:49.160 --> 00:31:50.875 I I I can't say for sure,

NOTE Confidence: 0.838822982352941

 $00{:}31{:}50{.}880 \dashrightarrow 00{:}31{:}52{.}410$  but I don't think any of them even met

- NOTE Confidence: 0.838822982352941
- $00:31:52.410 \dashrightarrow 00:31:53.839$  the level of severe adverse event.
- NOTE Confidence: 0.787474428571428
- $00{:}31{:}54{.}640 \dashrightarrow 00{:}31{:}56{.}856$  I I I would have to look at
- NOTE Confidence: 0.787474428571428
- $00{:}31{:}56.856 \dashrightarrow 00{:}31{:}58.839$  the details but I don't recall.
- NOTE Confidence: 0.787474428571428
- $00:31:58.840 \longrightarrow 00:32:01.560$  I would have to agree.
- NOTE Confidence: 0.787474428571428
- $00:32:01.560 \longrightarrow 00:32:05.172$  And these out of those three,
- NOTE Confidence: 0.787474428571428
- $00:32:05.172 \longrightarrow 00:32:07.491$  I think it it's possible we worked
- NOTE Confidence: 0.787474428571428
- $00:32:07.491 \rightarrow 00:32:09.504$  with one of them and you're right,
- NOTE Confidence: 0.787474428571428
- 00:32:09.504 --> 00:32:12.180 it was more flickering and it was,
- NOTE Confidence: 0.787474428571428
- $00:32:12.180 \longrightarrow 00:32:14.400$  but it was not sustained or
- NOTE Confidence: 0.787474428571428
- $00:32:14.400 \rightarrow 00:32:16.546$  there was no overt hallucinate,
- NOTE Confidence: 0.787474428571428
- 00:32:16.546 --> 00:32:17.638 frank hallucinations,
- NOTE Confidence: 0.64446776
- $00:32:19.200 \longrightarrow 00:32:20.480$  no more kind of illusions.
- NOTE Confidence: 0.925418549090909
- 00:32:21.600 --> 00:32:26.037 And I think other good news is in terms
- NOTE Confidence: 0.925418549090909
- $00:32:26.037 \dashrightarrow 00:32:29.424$  of any suicidal ideation or behavior,
- NOTE Confidence: 0.925418549090909
- $00:32:29.424 \longrightarrow 00:32:31.040$  they're really the main
- NOTE Confidence: 0.925418549090909

 $00:32:31.040 \rightarrow 00:32:32.240$  thing is right on the bottom,

NOTE Confidence: 0.925418549090909

 $00:32:32.240 \rightarrow 00:32:35.150$  there was no real clinically significant

NOTE Confidence: 0.925418549090909

 $00{:}32{:}35{.}150 \dashrightarrow 00{:}32{:}37{.}919$  increases in suicidal ideation or behavior

NOTE Confidence: 0.925418549090909

 $00:32:37.920 \longrightarrow 00:32:39.798$  associated with the study, if any.

NOTE Confidence: 0.925418549090909

00:32:39.800 --> 00:32:42.194 If you look at any patients that

NOTE Confidence: 0.925418549090909

 $00:32:42.194 \longrightarrow 00:32:44.124$  even had some level of increase

NOTE Confidence: 0.925418549090909

 $00:32:44.124 \rightarrow 00:32:46.400$  throughout the main part of the study,

NOTE Confidence: 0.925418549090909

 $00:32:46.400 \rightarrow 00:32:48.300$  there were numerically more

NOTE Confidence: 0.925418549090909

 $00:32:48.300 \longrightarrow 00:32:50.200$  in the niacin group,

NOTE Confidence: 0.925418549090909

 $00:32:50.200 \longrightarrow 00:32:52.318$  about 10% compared to about 2%.

NOTE Confidence: 0.925418549090909

 $00:32:52.320 \rightarrow 00:32:54.870$  There are just five people versus

NOTE Confidence: 0.925418549090909

 $00:32:54.870 \longrightarrow 00:32:58.188$  one person that showed some increase

NOTE Confidence: 0.925418549090909

 $00:32:58.188 \rightarrow 00:33:01.273$  in suicidality or suicidal ideation.

NOTE Confidence: 0.925418549090909

 $00:33:01.280 \longrightarrow 00:33:04.271$  This I I think is becoming more

NOTE Confidence: 0.925418549090909

 $00:33:04.271 \longrightarrow 00:33:05.897$  important as we realize how to

NOTE Confidence: 0.925418549090909

 $00:33:05.897 \rightarrow 00:33:07.480$  move forward with these studies.

- NOTE Confidence: 0.925418549090909
- 00:33:07.480 --> 00:33:08.915 At least for me running these studies,
- NOTE Confidence: 0.925418549090909
- $00:33:08.920 \longrightarrow 00:33:10.426$  I worry less about the people
- NOTE Confidence: 0.925418549090909
- $00:33:10.426 \longrightarrow 00:33:11.961$  getting the active drug than the
- NOTE Confidence: 0.925418549090909
- 00:33:11.961 -> 00:33:13.160 people being randomized,
- NOTE Confidence: 0.925418549090909
- $00:33:13.160 \longrightarrow 00:33:14.924$  especially if there's functional
- NOTE Confidence: 0.925418549090909
- $00:33:14.924 \longrightarrow 00:33:16.868$  on blinding for the patient that
- NOTE Confidence: 0.925418549090909
- 00:33:16.868 --> 00:33:18.753 you really have to worry about
- NOTE Confidence: 0.925418549090909
- $00:33:18.753 \rightarrow 00:33:20.463$  how they're going to react to
- NOTE Confidence: 0.925418549090909
- $00:33:20.463 \dashrightarrow 00:33:22.239$  feeling they didn't get treatment.
- NOTE Confidence: 0.925418549090909
- $00:33:22.240 \longrightarrow 00:33:23.912$  So now if we just talk about the
- NOTE Confidence: 0.925418549090909
- $00:33:23.912 \rightarrow 00:33:25.398$  limitations of the study quickly and then
- NOTE Confidence: 0.925418549090909
- $00{:}33{:}25{.}398 \dashrightarrow 00{:}33{:}27{.}015$  we'll be able to go into discussions
- NOTE Confidence: 0.925418549090909
- $00:33:27.015 \rightarrow 00:33:28.919$  because I think that's the main thing.
- NOTE Confidence: 0.925418549090909
- 00:33:28.920 --> 00:33:30.976 So one of the biggest limitations and we
- NOTE Confidence: 0.925418549090909
- 00:33:30.976 --> 00:33:32.760 mentioned it one or two times already,
- NOTE Confidence: 0.925418549090909

 $00:33:32.760 \longrightarrow 00:33:35.388$  was this study was conducted between

NOTE Confidence: 0.925418549090909

 $00:33:35.388 \longrightarrow 00:33:38.165$  December of 2019 and June of 2022.

NOTE Confidence: 0.925418549090909

00:33:38.165 --> 00:33:40.595 Here is just the death rate

NOTE Confidence: 0.925418549090909

 $00:33:40.600 \rightarrow 00:33:42.358$  due to COVID during that time.

NOTE Confidence: 0.925418549090909

 $00{:}33{:}42{.}360 \dashrightarrow 00{:}33{:}44{.}826$  I mean this was smack, we started it.

NOTE Confidence: 0.925418549090909

00:33:44.826 --> 00:33:47.220 I think we were ready to run

NOTE Confidence: 0.925418549090909

00:33:47.301 --> 00:33:49.953 our first patient in like March

NOTE Confidence: 0.925418549090909

 $00:33:49.953 \dashrightarrow 00:33:52.920$  just as everything was hidden.

NOTE Confidence: 0.925418549090909

 $00:33:52.920 \rightarrow 00:33:56.280$  So this study was thrown on its head.

NOTE Confidence: 0.925418549090909

 $00:33:56.280 \longrightarrow 00:33:57.360$  That being said,

NOTE Confidence: 0.925418549090909

 $00{:}33{:}57{.}360 \dashrightarrow 00{:}33{:}59{.}160$  it's a limitation because the

NOTE Confidence: 0.925418549090909

00:33:59.160 --> 00:34:01.038 study was run during COVID.

NOTE Confidence: 0.925418549090909

00:34:01.040 --> 00:34:03.420 Almost most studies run during

NOTE Confidence: 0.925418549090909

 $00:34:03.420 \longrightarrow 00:34:06.600$  this time has had major problems

NOTE Confidence: 0.925418549090909

 $00:34:06.600 \rightarrow 00:34:08.205$  because the placebo response rates

NOTE Confidence: 0.925418549090909

 $00{:}34{:}08{.}205 \dashrightarrow 00{:}34{:}10{.}140$  have been astronomical and most of

- NOTE Confidence: 0.925418549090909
- $00:34:10.140 \longrightarrow 00:34:11.520$  these studies run during COVID.
- NOTE Confidence: 0.925418549090909
- $00:34:11.520 \longrightarrow 00:34:13.400$  And we're not quite sure why that is.
- NOTE Confidence: 0.925418549090909
- $00:34:13.400 \longrightarrow 00:34:15.500$  But many of the studies run in
- NOTE Confidence: 0.925418549090909
- $00:34:15.500 \rightarrow 00:34:17.108$  depression during the summer has
- NOTE Confidence: 0.925418549090909
- $00:34:17.108 \longrightarrow 00:34:18.810$  had very abnormal elevated and
- NOTE Confidence: 0.925418549090909
- $00:34:18.810 \longrightarrow 00:34:20.635$  it may be the people.
- NOTE Confidence: 0.925418549090909
- $00:34:20.640 \longrightarrow 00:34:22.754$  Some of the hypothesis that's been put
- NOTE Confidence: 0.925418549090909
- $00:34:22.754 \longrightarrow 00:34:25.400$  out is that people are really more
- NOTE Confidence: 0.925418549090909
- $00{:}34{:}25{.}400 \dashrightarrow 00{:}34{:}27{.}440$  starved for socialization and just
- NOTE Confidence: 0.925418549090909
- $00:34:27.513 \rightarrow 00:34:29.816$  the fact of getting out was actually
- NOTE Confidence: 0.925418549090909
- 00:34:29.816 --> 00:34:32.360 working a lot you know in their favor
- NOTE Confidence: 0.925418549090909
- $00:34:32.360 \dashrightarrow 00:34:34.640$  but against the study drugs favor.
- NOTE Confidence: 0.925418549090909
- $00:34:34.640 \longrightarrow 00:34:36.440$  And in this case if anything
- NOTE Confidence: 0.925418549090909
- $00:34:36.440 \longrightarrow 00:34:37.702$  this would be something.
- NOTE Confidence: 0.925418549090909
- $00:34:37.702 \longrightarrow 00:34:39.688$  The fact that we did see
- NOTE Confidence: 0.925418549090909

 $00:34:39.688 \rightarrow 00:34:41.488$  such a big effect is,

NOTE Confidence: 0.925418549090909

 $00:34:41.488 \longrightarrow 00:34:43.456$  is probably not a major limitation

NOTE Confidence: 0.925418549090909

 $00:34:43.456 \longrightarrow 00:34:45.892$  that we would use that we would

NOTE Confidence: 0.925418549090909

 $00:34:45.892 \rightarrow 00:34:47.280$  worry about going forward.

NOTE Confidence: 0.925418549090909

 $00{:}34{:}47{.}280 \dashrightarrow 00{:}34{:}49{.}576$  But there are some other limitations and

NOTE Confidence: 0.925418549090909

00:34:49.576 --> 00:34:53.080 and I think maybe the the biggest one

NOTE Confidence: 0.925418549090909

 $00:34:53.080 \rightarrow 00:34:55.600$  moving forward is the generalizability.

NOTE Confidence: 0.925418549090909

00:34:55.600 -> 00:34:57.000 So as I mentioned this,

NOTE Confidence: 0.925418549090909

 $00{:}34{:}57{.}000 \dashrightarrow 00{:}34{:}58{.}701$  you know ways that this differs than

NOTE Confidence: 0.925418549090909

 $00:34:58.701 \rightarrow 00:35:00.340$  many of the other depression trials

NOTE Confidence: 0.925418549090909

 $00{:}35{:}00{.}340 \dashrightarrow 00{:}35{:}02{.}328$  is that the male to female ratio

NOTE Confidence: 0.925418549090909

 $00:35:02.383 \rightarrow 00:35:04.159$  is different than we typically see.

NOTE Confidence: 0.925418549090909

 $00:35:04.160 \longrightarrow 00:35:06.400$  We typically see a one to two

NOTE Confidence: 0.925418549090909

 $00{:}35{:}06{.}400 \dashrightarrow 00{:}35{:}07{.}880$  male to female ratio.

NOTE Confidence: 0.925418549090909

 $00:35:07.880 \longrightarrow 00:35:09.800$  This was pretty much a one to one.

NOTE Confidence: 0.925418549090909

 $00:35:09.800 \rightarrow 00:35:12.088$  The age was a little bit younger in

- NOTE Confidence: 0.925418549090909
- $00:35:12.088 \rightarrow 00:35:14.192$  this group and typically in trials
- NOTE Confidence: 0.925418549090909
- 00:35:14.192 --> 00:35:16.394 of antidepressants the age is about
- NOTE Confidence: 0.859233582962963
- $00:35:16.458 \longrightarrow 00:35:18.194$  45 and here it was about 41.
- NOTE Confidence: 0.859233582962963
- 00:35:18.200 --> 00:35:20.120 I don't know if that's going
- NOTE Confidence: 0.859233582962963
- $00:35:20.120 \longrightarrow 00:35:22.240$  to make any major difference,
- NOTE Confidence: 0.859233582962963
- $00:35:22.240 \longrightarrow 00:35:26.386$  but there really was a failure to
- NOTE Confidence: 0.859233582962963
- $00:35:26.386 \rightarrow 00:35:28.864$  have adequate representation of the US
- NOTE Confidence: 0.859233582962963
- $00:35:28.864 \rightarrow 00:35:31.197$  population in general in this study,
- NOTE Confidence: 0.859233582962963
- $00:35:31.200 \longrightarrow 00:35:33.375$  mainly in terms of race
- NOTE Confidence: 0.859233582962963
- $00:35:33.375 \rightarrow 00:35:35.115$  and even in ethnicity.
- NOTE Confidence: 0.859233582962963
- $00:35:35.120 \longrightarrow 00:35:36.578 89\%$  were white,
- NOTE Confidence: 0.859233582962963
- $00{:}35{:}36{.}578 \dashrightarrow 00{:}35{:}39{.}080$  with only 3% black in the study.
- NOTE Confidence: 0.922497596363636
- 00:35:41.280 --> 00:35:43.776 And even if you broke it down during
- NOTE Confidence: 0.922497596363636
- $00{:}35{:}43.776 \dashrightarrow 00{:}35{:}45.932$  other things like other demographic
- NOTE Confidence: 0.922497596363636
- $00{:}35{:}45{.}932 \dashrightarrow 00{:}35{:}48{.}980$  and social demographic factors in
- NOTE Confidence: 0.922497596363636

00:35:48.980 --> 00:35:52.080 terms of income, education level,

NOTE Confidence: 0.922497596363636

 $00{:}35{:}52{.}080 \dashrightarrow 00{:}35{:}53{.}990$  this probably wasn't as representative

NOTE Confidence: 0.922497596363636

 $00:35:53.990 \rightarrow 00:35:56.680$  of the population as we'd like to see.

NOTE Confidence: 0.922497596363636

 $00:35:56.680 \rightarrow 00:35:58.588$  And and I think ultimately regulators

NOTE Confidence: 0.922497596363636

 $00:35:58.588 \longrightarrow 00:36:00.916$  would like to say that this,

NOTE Confidence: 0.922497596363636

 $00:36:00.920 \longrightarrow 00:36:03.062$  this is a treatment if approved

NOTE Confidence: 0.922497596363636

 $00:36:03.062 \rightarrow 00:36:05.402$  would work in the large majority

NOTE Confidence: 0.922497596363636

 $00:36:05.402 \rightarrow 00:36:08.190$  or would the data they would have

NOTE Confidence: 0.922497596363636

 $00{:}36{:}08{.}190 \dashrightarrow 00{:}36{:}10{.}557$  would be representative of the large

NOTE Confidence: 0.922497596363636

 $00:36:10.557 \rightarrow 00:36:12.916$  majority of of people in the US.

NOTE Confidence: 0.922497596363636

 $00:36:12.920 \longrightarrow 00:36:14.672$  The other point was that the

NOTE Confidence: 0.922497596363636

 $00:36:14.672 \rightarrow 00:36:16.588$  majority of these people were not

NOTE Confidence: 0.922497596363636

 $00{:}36{:}16.588 \dashrightarrow 00{:}36{:}18.318$  taking antidepressants at the time.

NOTE Confidence: 0.922497596363636

 $00{:}36{:}18{.}320 \dashrightarrow 00{:}36{:}21{.}016$  So you're really looking at a group of

NOTE Confidence: 0.922497596363636

 $00:36:21.016 \rightarrow 00:36:22.770$  either antidepressant naive patients

NOTE Confidence: 0.922497596363636

 $00:36:22.770 \longrightarrow 00:36:25.824$  or at least patients that weren't at

- NOTE Confidence: 0.922497596363636
- $00:36:25.824 \rightarrow 00:36:28.288$  the level of severity that they were
- NOTE Confidence: 0.922497596363636
- $00{:}36{:}28.288 \dashrightarrow 00{:}36{:}30.240$  seeking treatment in some of the way.
- NOTE Confidence: 0.922497596363636
- $00{:}36{:}30{.}240 \dashrightarrow 00{:}36{:}30{.}360$  And
- NOTE Confidence: 0.811201895
- $00{:}36{:}32.600 \dashrightarrow 00{:}36{:}34.595$  then there were also patients are able
- NOTE Confidence: 0.811201895
- $00{:}36{:}34{.}595 \dashrightarrow 00{:}36{:}36{.}760$  to remain free of both medication and
- NOTE Confidence: 0.811201895
- $00{:}36{:}36{.}760 \dashrightarrow 00{:}36{:}38{.}632$  free of contact with the the rapist.
- NOTE Confidence: 0.811201895
- $00{:}36{:}38{.}640 \dashrightarrow 00{:}36{:}40{.}624$  So these are all issues that in the
- NOTE Confidence: 0.811201895
- $00{:}36{:}40.624 \dashrightarrow 00{:}36{:}42.290$  future we're going to have to either
- NOTE Confidence: 0.811201895
- $00:36:42.290 \longrightarrow 00:36:44.320$  determine if we're going to limit it
- NOTE Confidence: 0.811201895
- $00:36:44.320 \longrightarrow 00:36:46.840$  to that or we're going to broaden the
- NOTE Confidence: 0.811201895
- $00:36:46.840 \rightarrow 00:36:49.125$  categories and and figure out other ways
- NOTE Confidence: 0.811201895
- $00:36:49.125 \longrightarrow 00:36:51.393$  of managing the risk associated with that.
- NOTE Confidence: 0.811201895
- $00:36:51.400 \longrightarrow 00:36:53.080$  As I said, the baseline SES was
- NOTE Confidence: 0.811201895
- $00:36:53.080 \dashrightarrow 00:36:54.550$  slightly lower and that that could
- NOTE Confidence: 0.811201895
- $00:36:54.550 \rightarrow 00:36:55.954$  be for a variety of reasons.
- NOTE Confidence: 0.811201895

00:36:55.960 --> 00:36:57.717 I wouldn't worry too much about that.

NOTE Confidence: 0.811201895

 $00{:}36{:}57{.}720 \dashrightarrow 00{:}37{:}00{.}184$  And the other main limitation is this

NOTE Confidence: 0.811201895

 $00:37{:}00.184 \dashrightarrow 00{:}37{:}02.342$  was probably over represented for the

NOTE Confidence: 0.811201895

 $00{:}37{:}02{.}342 \dashrightarrow 00{:}37{:}05{.}331$  age group and the number of people that

NOTE Confidence: 0.811201895

 $00:37:05.331 \dashrightarrow 00:37:07.836$  have had previous psychedelic experiences.

NOTE Confidence: 0.811201895

 $00:37{:}07.840 \dashrightarrow 00{:}37{:}09.840$  And as we know this can have a major impact.

NOTE Confidence: 0.811201895

 $00:37:09.840 \rightarrow 00:37:13.040$  I've been a major impact on the validity

NOTE Confidence: 0.811201895

 $00{:}37{:}13.040 \dashrightarrow 00{:}37{:}16.039$  of some of these measures that those

NOTE Confidence: 0.811201895

00:37:16.039 --> 00:37:17.992 first things I said were more related

NOTE Confidence: 0.811201895

 $00{:}37{:}17{.}992 \dashrightarrow 00{:}37{:}20{.}039$  to the ecological validity of the

NOTE Confidence: 0.811201895

 $00:37:20.039 \dashrightarrow 00:37:23.277$  study which we can fix by study design.

NOTE Confidence: 0.811201895

 $00{:}37{:}23.280 \dashrightarrow 00{:}37{:}25.443$  And some of these future ones I'll

NOTE Confidence: 0.811201895

 $00{:}37{:}25{.}443 \dashrightarrow 00{:}37{:}27{.}822$  talk about is related to really the

NOTE Confidence: 0.811201895

 $00:37:27.822 \dashrightarrow 00:37:29.677$  the interpretive validity of study

NOTE Confidence: 0.811201895

00:37:29.677 - 00:37:32.345 is you know is this due to the drug

NOTE Confidence: 0.811201895

 $00:37:32.345 \longrightarrow 00:37:34.319$  or some of the other effects.

- NOTE Confidence: 0.811201895
- $00:37:34.320 \longrightarrow 00:37:36.336$  And one of the major ones that
- NOTE Confidence: 0.811201895
- $00:37:36.336 \longrightarrow 00:37:37.200$  continues to the
- NOTE Confidence: 0.8433125866666667
- $00:37:39.400 \longrightarrow 00:37:41.848$  be dealt with or or the to be
- NOTE Confidence: 0.8433125866666667
- $00:37:41.848 \rightarrow 00:37:44.892$  difficult to deal with is the struggle
- NOTE Confidence: 0.8433125866666667
- $00:37:44.892 \longrightarrow 00:37:47.712$  around blinding or or unmasking
- NOTE Confidence: 0.8433125866666667
- 00:37:47.712 --> 00:37:51.480 of allocation, group allocation.
- NOTE Confidence: 0.8433125866666667
- $00:37:51.480 \longrightarrow 00:37:53.447$  You know it's really hard when you
- NOTE Confidence: 0.8433125866666667
- $00{:}37{:}53.447 \dashrightarrow 00{:}37{:}56.832$  have a drug that has very prominent
- NOTE Confidence: 0.8433125866666667
- $00{:}37{:}56{.}832 \dashrightarrow 00{:}37{:}59{.}096$  and acute psychoactive effects
- NOTE Confidence: 0.8433125866666667
- $00:37:59.096 \rightarrow 00:38:01.036$  in comparing it to something.
- NOTE Confidence: 0.8433125866666667
- $00:38:01.040 \longrightarrow 00:38:03.077$  So Niacin was used as an attempt.
- NOTE Confidence: 0.8433125866666667
- $00:38:03.080 \longrightarrow 00:38:04.040$  But as Chris mentioned,
- NOTE Confidence: 0.8433125866666667
- 00:38:04.040 --> 00:38:05.960 you know if you really ask somebody,
- NOTE Confidence: 0.8433125866666667
- 00:38:05.960 --> 00:38:07.920 I don't know I I can say now
- NOTE Confidence: 0.8433125866666667
- $00:38:07.920 \longrightarrow 00:38:09.517$  the study's over at our site.
- NOTE Confidence: 0.843312586666667

 $00:38:09.520 \rightarrow 00:38:12.024$  I think we may have had one person

NOTE Confidence: 0.8433125866666667

 $00{:}38{:}12.024 \dashrightarrow 00{:}38{:}14.540$  in each group that I think it's fair

NOTE Confidence: 0.8433125866666667

 $00{:}38{:}14{.}540 \dashrightarrow 00{:}38{:}17{.}108$  to say that we had one person that I

NOTE Confidence: 0.8433125866666667

 $00:38:17.108 \rightarrow 00:38:18.568$  think the staff would have guessed,

NOTE Confidence: 0.8433125866666667

 $00{:}38{:}18.568 \dashrightarrow 00{:}38{:}19.840$  got it and didn't get it.

NOTE Confidence: 0.8433125866666667

00:38:19.840 $\operatorname{-->}$ 00:38:21.136 And I think there was one person who

NOTE Confidence: 0.843312586666667

00:38:21.136 --> 00:38:22.599 got it and staff would have guessed,

NOTE Confidence: 0.8433125866666667

 $00:38:22.600 \longrightarrow 00:38:23.080$  didn't get

NOTE Confidence: 0.831229068

 $00{:}38{:}23.080 \dashrightarrow 00{:}38{:}25.920$  it. It was only one exactly.

NOTE Confidence: 0.47046827

00:38:25.920 --> 00:38:27.146 So probably many one on

NOTE Confidence: 0.47046827

00:38:27.146 --> 00:38:27.876 each time. What, I don't

NOTE Confidence: 0.549498885

 $00:38:28.000 \rightarrow 00:38:30.120$  know how many time I need to deal with 15.

NOTE Confidence: 0.645553602857143

00:38:30.120 --> 00:38:32.717 Yeah, I think 1350, I can't remember.

NOTE Confidence: 0.645553602857143

 $00{:}38{:}32{.}720 \dashrightarrow 00{:}38{:}35{.}078$  Yeah. So I mean there are,

NOTE Confidence: 0.645553602857143

 $00:38:35.080 \longrightarrow 00:38:36.040$  there are cases of it,

NOTE Confidence: 0.645553602857143

 $00:38:36.040 \rightarrow 00:38:38.960$  but I think the large majority of people,

 $00:38:38.960 \rightarrow 00:38:43.240$  both participants and site members,

NOTE Confidence: 0.645553602857143

 $00:38:43.240 \rightarrow 00:38:44.610$  staff members would would guess

NOTE Confidence: 0.645553602857143

 $00:38:44.610 \rightarrow 00:38:46.280$  for the majority of the point

NOTE Confidence: 0.645553602857143

 $00:38:46.280 \dashrightarrow 00:38:48.170$  And just an idea of how important

NOTE Confidence: 0.645553602857143

 $00:38:48.170 \longrightarrow 00:38:50.040$  some of this unmasking can be.

NOTE Confidence: 0.645553602857143

 $00:38:50.040 \longrightarrow 00:38:51.612$  There was a recent paper that

NOTE Confidence: 0.645553602857143

 $00:38:51.612 \rightarrow 00:38:53.689$  some of you may have seen that

NOTE Confidence: 0.645553602857143

 $00{:}38{:}53.689 \dashrightarrow 00{:}38{:}55.615$  came out of Stanford Boris Boris

NOTE Confidence: 0.645553602857143

00:38:55.615 --> 00:38:57.696 Heifetz paper where he was getting

NOTE Confidence: 0.645553602857143

 $00{:}38{:}57{.}696 \dashrightarrow 00{:}38{:}59{.}924$  ketamine under adequate blinding

NOTE Confidence: 0.645553602857143

 $00:38:59.924 \dashrightarrow 00:39:02.436$  because they're under anaesthesia.

NOTE Confidence: 0.645553602857143

 $00{:}39{:}02{.}440 \dashrightarrow 00{:}39{:}04{.}384$  So he actually these are people

NOTE Confidence: 0.645553602857143

 $00{:}39{:}04{.}384 \dashrightarrow 00{:}39{:}05{.}680$  going for surgical procedures

NOTE Confidence: 0.645553602857143

 $00{:}39{:}05{.}738 \dashrightarrow 00{:}39{:}07{.}703$  where they were getting general

NOTE Confidence: 0.645553602857143

 $00{:}39{:}07{.}703 \dashrightarrow 00{:}39{:}09{.}275$  anaes<br/>thesia during their anaes<br/>thesia

00:39:09.275 --> 00:39:11.068 given .5 milligrams per kilogram

NOTE Confidence: 0.645553602857143

00:39:11.068 --> 00:39:12.743 ketamine over 40 minutes during

NOTE Confidence: 0.645553602857143

 $00:39{:}12.743 \dashrightarrow 00{:}39{:}14.688$  that time with the idea of seeing

NOTE Confidence: 0.645553602857143

 $00:39:14.688 \rightarrow 00:39:16.926$  one of the questions is how much

NOTE Confidence: 0.645553602857143

 $00:39:16.926 \rightarrow 00:39:18.398$  does that psychological experience,

NOTE Confidence: 0.645553602857143

 $00:39:18.400 \dashrightarrow 00:39:20.822$  how necessary is that for ketamine but NOTE Confidence: 0.645553602857143

00:39:20.822 --> 00:39:23.758 also if it's blinded will it still work.

NOTE Confidence: 0.645553602857143

 $00{:}39{:}23.760 \dashrightarrow 00{:}39{:}26.385$  And I think that the results were

NOTE Confidence: 0.645553602857143

 $00:39:26.385 \rightarrow 00:39:28.526$  actually shocking to to some people

NOTE Confidence: 0.645553602857143

 $00{:}39{:}28{.}526 \dashrightarrow 00{:}39{:}31{.}360$  was and this is like a rush of

NOTE Confidence: 0.645553602857143

 $00{:}39{:}31{.}360 \dashrightarrow 00{:}39{:}33{.}358$  test on itself what people see

NOTE Confidence: 0.645553602857143

 $00:39:33.358 \rightarrow 00:39:35.194$  here and the date is small,

NOTE Confidence: 0.645553602857143

00:39:35.200 -> 00:39:36.380 so you may not see anything here.

NOTE Confidence: 0.645553602857143

00:39:36.380 --> 00:39:37.930 But I can tell you,

NOTE Confidence: 0.645553602857143

 $00{:}39{:}37{.}930 \dashrightarrow 00{:}39{:}41{.}760$  I can tell you what is here is you know

NOTE Confidence: 0.645553602857143

 $00:39:41.760 \rightarrow 00:39:45.648$  there was over 50% response at day

- NOTE Confidence: 0.645553602857143
- $00:39:45.648 \rightarrow 00:39:47.880$  one to the group that got ketamine,
- NOTE Confidence: 0.645553602857143
- $00{:}39{:}47{.}880 \dashrightarrow 00{:}39{:}49{.}886$  but there was nearly 50% to
- NOTE Confidence: 0.645553602857143
- $00:39:49.886 \rightarrow 00:39:51.316$  the group that got placebo.
- NOTE Confidence: 0.645553602857143
- $00:39:51.320 \longrightarrow 00:39:54.155$  So there was just a huge placebo
- NOTE Confidence: 0.645553602857143
- $00:39:54.160 \longrightarrow 00:39:56.176$  response rate in this in in in
- NOTE Confidence: 0.645553602857143
- $00:39:56.176 \rightarrow 00:39:58.320$  terms of their depression ratings.
- NOTE Confidence: 0.645553602857143
- $00:39:58.320 \rightarrow 00:40:00.133$  We we published sort of the commentary
- NOTE Confidence: 0.645553602857143
- $00{:}40{:}00{.}133 \dashrightarrow 00{:}40{:}02{.}359$  on this and there are a lot of
- NOTE Confidence: 0.645553602857143
- $00:40:02.359 \rightarrow 00:40:03.475$  problems with the interpretation
- NOTE Confidence: 0.645553602857143
- $00:40:03.475 \rightarrow 00:40:05.481$  of this study and we can go through
- NOTE Confidence: 0.645553602857143
- $00:40:05.481 \rightarrow 00:40:06.696$  that from the mechanistic side,
- NOTE Confidence: 0.645553602857143
- $00:40:06.696 \rightarrow 00:40:08.680$  but that's not the main point of it.
- NOTE Confidence: 0.645553602857143
- $00{:}40{:}08{.}680 \dashrightarrow 00{:}40{:}11{.}245$  I think the main point of it is to
- NOTE Confidence: 0.645553602857143
- $00:40:11.245 \rightarrow 00:40:12.893$  realize how important expectations
- NOTE Confidence: 0.645553602857143
- $00:40:12.893 \rightarrow 00:40:15.371$  and especially if you have unmasking
- NOTE Confidence: 0.645553602857143

- $00:40:15.371 \longrightarrow 00:40:16.880$  going on can be.
- NOTE Confidence: 0.645553602857143
- 00:40:16.880 --> 00:40:19.080 So if you look at the HEIFET study,
- NOTE Confidence: 0.645553602857143
- $00:40:19.080 \longrightarrow 00:40:21.680$  if you look at the 19 patients that
- NOTE Confidence: 0.645553602857143
- $00:40:21.680 \longrightarrow 00:40:24.367$  got ketamine and 19 patients that got
- NOTE Confidence: 0.645553602857143
- $00:40:24.367 \longrightarrow 00:40:27.080$  the placebo during their surgical procedure.
- NOTE Confidence: 0.645553602857143
- $00:40:27.080 \longrightarrow 00:40:28.640$  Really no difference in their
- NOTE Confidence: 0.645553602857143
- $00:40:28.640 \longrightarrow 00:40:30.600$  their Madras score at two weeks.
- NOTE Confidence: 0.645553602857143
- 00:40:30.600 --> 00:40:31.452 But if you add,
- NOTE Confidence: 0.645553602857143
- $00{:}40{:}31.452 \dashrightarrow 00{:}40{:}33.324$  but when they went back and asked the
- NOTE Confidence: 0.645553602857143
- $00:40:33.324 \rightarrow 00:40:34.956$  people what they thought they got,
- NOTE Confidence: 0.645553602857143
- $00:40:34.960 \longrightarrow 00:40:36.360$  then you can see dramatic.
- NOTE Confidence: 0.645553602857143
- $00:40:36.360 \rightarrow 00:40:37.886$  So the people that thought they got
- NOTE Confidence: 0.645553602857143
- $00:40:37.886 \longrightarrow 00:40:39.818$  it on average had a remission and the
- NOTE Confidence: 0.645553602857143
- $00:40:39.818 \rightarrow 00:40:41.292$  people that thought they didn't get
- NOTE Confidence: 0.645553602857143
- $00:40:41.292 \rightarrow 00:40:42.876$  it or didn't know didn't do so well.
- NOTE Confidence: 0.645553602857143
- $00:40:42.880 \longrightarrow 00:40:45.176$  So this idea of you know what you

- NOTE Confidence: 0.645553602857143
- $00:40:45.176 \rightarrow 00:40:47.176$  think you got an expectancy really
- NOTE Confidence: 0.645553602857143
- $00{:}40{:}47.176 \dashrightarrow 00{:}40{:}50.480$  plays a big role although that
- NOTE Confidence: 0.81315615
- $00:40:50.480 \longrightarrow 00:40:51.400$  it could work either way.
- NOTE Confidence: 0.81315615
- $00:40:51.400 \longrightarrow 00:40:52.708$  It could be that they thought
- NOTE Confidence: 0.81315615
- 00:40:52.708 --> 00:40:53.884 they didn't get ketamine because
- NOTE Confidence: 0.81315615
- $00:40:53.884 \rightarrow 00:40:54.920$  they didn't stay better.
- NOTE Confidence: 0.85909678
- $00:40:54.920 \longrightarrow 00:40:57.320$  So one, one of the big problems with
- NOTE Confidence: 0.85909678
- $00{:}40{:}57{.}320 \dashrightarrow 00{:}40{:}59{.}741$  this study and several of the other
- NOTE Confidence: 0.85909678
- $00:40:59.741 \longrightarrow 00:41:01.818$  studies including the next one I'll
- NOTE Confidence: 0.85909678
- $00:41:01.818 \longrightarrow 00:41:03.860$  show you is the asking post hoc
- NOTE Confidence: 0.85909678
- $00{:}41{:}03.860 \dashrightarrow 00{:}41{:}06.240$  asking you really have to ask these.
- NOTE Confidence: 0.85909678
- 00:41:06.240 --> 00:41:08.538 And that's some of the questions
- NOTE Confidence: 0.85909678
- $00{:}41{:}08{.}538 \dashrightarrow 00{:}41{:}10{.}493$  moving forward that we're trying
- NOTE Confidence: 0.85909678
- 00:41:10.493 --> 00:41:12.985 to really do is to assess both
- NOTE Confidence: 0.85909678
- $00{:}41{:}12.985 \dashrightarrow 00{:}41{:}14.759$  expectations and and preference.
- NOTE Confidence: 0.85909678

00:41:14.760 --> 00:41:17.216 And also what you think you got much

NOTE Confidence: 0.85909678

 $00{:}41{:}17{.}216 \dashrightarrow 00{:}41{:}19{.}511$  closer to the time because this is

NOTE Confidence: 0.85909678

00:41:19.511 -> 00:41:22.319 this is very flawed doing it this way.

NOTE Confidence: 0.85909678

 $00:41:22.320 \longrightarrow 00:41:23.320$  Was there any

NOTE Confidence: 0.809475735

 $00{:}41{:}24.000 \dashrightarrow 00{:}41{:}25.715$  Cyril asked this question in the chat

NOTE Confidence: 0.809475735

 $00{:}41{:}25.715 \dashrightarrow 00{:}41{:}27.848$  earlier, was there any assessment

NOTE Confidence: 0.809475735

 $00:41:27.848 \longrightarrow 00:41:30.680$  of expectation in the Usona study?

NOTE Confidence: 0.730384885

00:41:30.960 --> 00:41:33.000 No, no, no, no.

NOTE Confidence: 0.567767144

 $00{:}41{:}35{.}080 \dashrightarrow 00{:}41{:}37{.}211$  So and this is another, this is actually

NOTE Confidence: 0.567767144

 $00:41:37.211 \rightarrow 00:41:38.993$  a study that we recently completed.

NOTE Confidence: 0.567767144

 $00{:}41{:}39{.}000 \dashrightarrow 00{:}41{:}42{.}486$  This was the study funded by Pecorie

NOTE Confidence: 0.567767144

00:41:42.486 --> 00:41:45.560 which was ECT versus IV Ketamine,

NOTE Confidence: 0.567767144

 $00:41:45.560 \longrightarrow 00:41:47.320$  a 400 person study,

NOTE Confidence: 0.567767144

00:41:47.320 --> 00:41:49.080 actually a little bit more than 400 people,

NOTE Confidence: 0.567767144

00:41:49.080 --> 00:41:52.440 200 approximately 200 randomized C CHARM.

NOTE Confidence: 0.567767144

 $00:41:52.440 \rightarrow 00:41:55.548$  You can see where there's really not

 $00{:}41{:}55{.}548 \dashrightarrow 00{:}41{:}57{.}912$  the dramatic difference between the two.

NOTE Confidence: 0.567767144

 $00{:}41{:}57{.}912 \dashrightarrow 00{:}41{:}59{.}654$  Actually. Numerically ketamine looked

NOTE Confidence: 0.567767144

00:41:59.654 --> 00:42:03.639 like it did a little bit better than ECT,

NOTE Confidence: 0.567767144

 $00:42:03.640 \rightarrow 00:42:05.754$  but this was a non inferiority study.

NOTE Confidence: 0.567767144

 $00:42:05.760 \longrightarrow 00:42:07.937$  So all we can say with confidence

NOTE Confidence: 0.567767144

 $00{:}42{:}07{.}937 \dashrightarrow 00{:}42{:}09{.}872$  is that ketamine was non inferior

NOTE Confidence: 0.567767144

 $00:42:09.872 \rightarrow 00:42:11.512$  to ECT in this study.

NOTE Confidence: 0.567767144

 $00:42:11.520 \longrightarrow 00:42:14.428$  But the main point here was when we

NOTE Confidence: 0.567767144

 $00{:}42{:}14.428 \dashrightarrow 00{:}42{:}16.612$  went back to look at how preference.

NOTE Confidence: 0.567767144

 $00:42:16.612 \longrightarrow 00:42:18.754$  So the idea of what they wanted

NOTE Confidence: 0.567767144

 $00:42:18.754 \longrightarrow 00:42:20.440$  and impacted how they did.

NOTE Confidence: 0.567767144

00:42:20.440 --> 00:42:22.448 And again, this is limited by the fact

NOTE Confidence: 0.567767144

 $00{:}42{:}22{.}448 \dashrightarrow 00{:}42{:}24{.}478$  that we asked the preference after,

NOTE Confidence: 0.567767144

 $00:42:24.480 \longrightarrow 00:42:28.560$  not before. But if you look here,

NOTE Confidence: 0.567767144

 $00{:}42{:}28.560 \dashrightarrow 00{:}42{:}32.976$  you know the the percent, I'm sorry,

 $00:42:32.976 \rightarrow 00:42:36.420$  the percent of responders who preferred

NOTE Confidence: 0.567767144

 $00:42:36.514 \rightarrow 00:42:40.154$  ECT but got ketamine was only about 20%.

NOTE Confidence: 0.567767144

 $00{:}42{:}40{.}160 \dashrightarrow 00{:}42{:}41{.}972$  But the ones that preferred ketamine

NOTE Confidence: 0.567767144

 $00:42:41.972 \rightarrow 00:42:43.875$  and got ketamine was nearly 60%.

NOTE Confidence: 0.567767144

 $00:42:43.875 \longrightarrow 00:42:44.820$  So the how,

NOTE Confidence: 0.567767144

 $00:42:44.820 \longrightarrow 00:42:47.150$  how the impact of preference may play

NOTE Confidence: 0.567767144

 $00{:}42{:}47.150 \dashrightarrow 00{:}42{:}49.358$  on how well somebody actually does.

NOTE Confidence: 0.567767144

 $00:42:49.360 \longrightarrow 00:42:51.160$  So these are all things when

NOTE Confidence: 0.567767144

00:42:51.160 --> 00:42:52.631 we're designing these studies we

NOTE Confidence: 0.567767144

 $00:42:52.631 \longrightarrow 00:42:53.915$  just can't be blind to it.

NOTE Confidence: 0.567767144

 $00{:}42{:}53{.}920 \dashrightarrow 00{:}42{:}56{.}652$  And again these are very flawed analysis

NOTE Confidence: 0.567767144

 $00{:}42{:}56.652 \dashrightarrow 00{:}42{:}58.560$  because they were done post doc as it is.

NOTE Confidence: 0.567767144

 $00:42:58.560 \longrightarrow 00:43:01.272$  So the first thing is to make sure

NOTE Confidence: 0.567767144

00:43:01.272 --> 00:43:03.360 you're doing it earlier on and

NOTE Confidence: 0.567767144

 $00:43:03.360 \longrightarrow 00:43:05.760$  it's not just how it complicates,

NOTE Confidence: 0.567767144

 $00:43:05.760 \longrightarrow 00:43:06.935$  well maybe they wanted it

 $00{:}43{:}06{.}935 \dashrightarrow 00{:}43{:}07{.}875$  and they got better.

NOTE Confidence: 0.567767144

 $00:43:07.880 \longrightarrow 00:43:09.524$  It's really important if you have

NOTE Confidence: 0.567767144

 $00{:}43{:}09{.}524 \dashrightarrow 00{:}43{:}11{.}177$  differential drop out and in this

NOTE Confidence: 0.567767144

00:43:11.177 --> 00:43:12.934 case I did mention there was some

NOTE Confidence: 0.567767144

 $00{:}43{:}12{.}934 \dashrightarrow 00{:}43{:}14{.}196$  differential drop out the people

NOTE Confidence: 0.567767144

 $00{:}43{:}14.196 \dashrightarrow 00{:}43{:}16.092$  that really yeah they these people

NOTE Confidence: 0.567767144

 $00:43:16.092 \rightarrow 00:43:18.315$  came in my guess is the majority

NOTE Confidence: 0.567767144

00:43:18.315 --> 00:43:20.812 really one and we didn't ask but I

NOTE Confidence: 0.567767144

 $00{:}43{:}20{.}812 \dashrightarrow 00{:}43{:}23{.}008$  think the probably very likely they NOTE Confidence: 0.567767144

 $00{:}43{:}23.008 \dashrightarrow 00{:}43{:}25.594$  were very much looking forward to NOTE Confidence: 0.567767144

 $00{:}43{:}25{.}594 \dashrightarrow 00{:}43{:}27{.}344$  getting psilocybin when they didn't.

NOTE Confidence: 0.567767144

00:43:27.344 --> 00:43:29.679 There was some evidence of a little

NOTE Confidence: 0.567767144

00:43:29.679 --> 00:43:31.279 bit of a differential dropout

NOTE Confidence: 0.567767144

 $00{:}43{:}31{.}279 \dashrightarrow 00{:}43{:}33{.}478$  because when you do look at day 48,

NOTE Confidence: 0.567767144

 $00{:}43{:}33{.}480 \dashrightarrow 00{:}43{:}35{.}258$  there was only one of the psilocybin

 $00:43:35.258 \longrightarrow 00:43:36.743$  patients at day 43 that didn't

NOTE Confidence: 0.567767144

00:43:36.743 --> 00:43:37.635 make it that far,

NOTE Confidence: 0.567767144

 $00{:}43{:}37{.}640 \dashrightarrow 00{:}43{:}39{.}464$  but nine of the niac in and that remember

NOTE Confidence: 0.567767144

 $00:43:39.464 \rightarrow 00:43:41.277$  that was the primary outcome measure.

NOTE Confidence: 0.567767144

 $00{:}43{:}41{.}280 \dashrightarrow 00{:}43{:}43{.}666$  So now you have to impute their data.

NOTE Confidence: 0.567767144

 $00{:}43{:}43.666 \dashrightarrow 00{:}43{:}45.904$  So it really makes these trials

NOTE Confidence: 0.567767144

 $00:43:45.904 \rightarrow 00:43:48.398$  complicated that when when you don't have

NOTE Confidence: 0.567767144

 $00:43:48.398 \rightarrow 00:43:50.640$  data on everybody starting at the end.

NOTE Confidence: 0.567767144

 $00:43:50.640 \longrightarrow 00:43:51.166$  So yeah,

NOTE Confidence: 0.567767144

00:43:51.166 - 00:43:52.481 to manage those preferences is

NOTE Confidence: 0.567767144

 $00:43:52.481 \longrightarrow 00:43:54.199$  going to be really important.

NOTE Confidence: 0.84524183

 $00{:}43{:}54{.}320 \dashrightarrow 00{:}43{:}56{.}540$  There was no opportunity for

NOTE Confidence: 0.84524183

 $00:43:56.540 \longrightarrow 00:43:58.760$  open label follow up and

NOTE Confidence: 0.762519378

 $00:43:56.960 \rightarrow 00:43:59.680$  there was no open label. Yeah, I

NOTE Confidence: 0.801699842

 $00:43:58.760 \rightarrow 00:43:59.680$  know the answer to that. Yeah,

NOTE Confidence: 0.67909231

 $00:43:59.680 \longrightarrow 00:44:00.760$  there was, there was no.
- NOTE Confidence: 0.67909231
- $00{:}44{:}00.760 \dashrightarrow 00{:}44{:}02.629$  So that's why these things are so

 $00{:}44{:}02.629 \dashrightarrow 00{:}44{:}04.227$  important in the clinical trial design

NOTE Confidence: 0.67909231

 $00{:}44{:}04{.}227 \dashrightarrow 00{:}44{:}07{.}000$  is to do what you can to make sure you're

NOTE Confidence: 0.67909231

 $00:44:07.000 \rightarrow 00:44:08.992$  not getting this differential drop out.

NOTE Confidence: 0.67909231

 $00{:}44{:}09{.}000 \dashrightarrow 00{:}44{:}12{.}492$  And then lastly there there was

NOTE Confidence: 0.67909231

 $00{:}44{:}12{.}492 \dashrightarrow 00{:}44{:}14{.}696$  some questions or concerns about

NOTE Confidence: 0.67909231

 $00{:}44{:}14.696 \dashrightarrow 00{:}44{:}16.716$  the onset of antidepressant action.

NOTE Confidence: 0.67909231

00:44:16.720 --> 00:44:18.904 So I don't know if you, I can flip back,

NOTE Confidence: 0.67909231

 $00:44:18.904 \rightarrow 00:44:22.072$  but take my word for it on day one,

NOTE Confidence: 0.67909231

 $00:44:22.072 \longrightarrow 00:44:24.077$  day two, one day after,

NOTE Confidence: 0.67909231

 $00{:}44{:}24.077 \dashrightarrow 00{:}44{:}25.872$  there really wasn't a big

NOTE Confidence: 0.67909231

 $00{:}44{:}25.872 \dashrightarrow 00{:}44{:}27.274$  antidepressant response to either

NOTE Confidence: 0.67909231

 $00:44:27.274 \longrightarrow 00:44:28.834$  the niac in or the psilocybin.

NOTE Confidence: 0.67909231

 $00{:}44{:}28{.}840 \dashrightarrow 00{:}44{:}31{.}048$  And people were questioning how come

NOTE Confidence: 0.67909231

 $00{:}44{:}31.048 \dashrightarrow 00{:}44{:}33.335$  most of these other studies showed

 $00:44:33.335 \longrightarrow 00:44:35.555$  a more rapid onset of benefit.

NOTE Confidence: 0.67909231

 $00:44:35.560 \longrightarrow 00:44:36.484$  And it's difficult.

NOTE Confidence: 0.67909231

 $00:44:36.484 \rightarrow 00:44:39.640$  We don't know 100% why that happened here.

NOTE Confidence: 0.67909231

 $00:44:39.640 \longrightarrow 00:44:41.734$  But I think it's quite likely that

NOTE Confidence: 0.67909231

 $00{:}44{:}41.734 \dashrightarrow 00{:}44{:}43.839$  one of the main contributors to that

NOTE Confidence: 0.67909231

 $00:44:43.839 \rightarrow 00:44:46.680$  finding was the way that study was designed.

NOTE Confidence: 0.67909231

00:44:46.680 --> 00:44:48.448 I I mentioned in in order to try

NOTE Confidence: 0.67909231

 $00{:}44{:}48{.}448 \dashrightarrow 00{:}44{:}50{.}017$  to preserve the blinding of the

NOTE Confidence: 0.67909231

 $00{:}44{:}50{.}017 \dashrightarrow 00{:}44{:}51{.}357$  Raiders as much as possible.

NOTE Confidence: 0.67909231

 $00{:}44{:}51{.}360 \dashrightarrow 00{:}44{:}53{.}754$  These were remote Raiders done off site.

NOTE Confidence: 0.67909231

00:44:53.760 --> 00:44:55.794 They didn't know at what point

NOTE Confidence: 0.67909231

 $00:44:55.794 \longrightarrow 00:44:57.520$  in their assessments they were.

NOTE Confidence: 0.67909231

 $00:44:57.520 \longrightarrow 00:44:59.417$  They were at one point in their

NOTE Confidence: 0.67909231

 $00:44:59.417 \rightarrow 00:45:01.079$  treatment they were assessing them.

NOTE Confidence: 0.67909231

 $00{:}45{:}01{.}080 \dashrightarrow 00{:}45{:}05{.}800$  So they asked very carefully and very

NOTE Confidence: 0.67909231

00:45:05.800 --> 00:45:08.386 rigorous about saying tell me how

- NOTE Confidence: 0.67909231
- $00:45:08.386 \rightarrow 00:45:11.760$  you've been doing for the last seven days.
- NOTE Confidence: 0.67909231
- 00:45:11.760 --> 00:45:13.224 But so if they only received
- NOTE Confidence: 0.67909231
- $00:45:13.224 \rightarrow 00:45:14.640$  the drug one day before,
- NOTE Confidence: 0.67909231
- $00:45:14.640 \longrightarrow 00:45:16.096$  you know six of those seven days
- NOTE Confidence: 0.67909231
- $00:45:16.096 \rightarrow 00:45:17.319$  were before they got the drug.
- NOTE Confidence: 0.67909231
- $00:45:17.320 \longrightarrow 00:45:19.920$  So that may account for part of it.
- NOTE Confidence: 0.67909231
- $00:45:19.920 \longrightarrow 00:45:21.495$  So it's so when but when was
- NOTE Confidence: 0.67909231
- $00:45:21.495 \longrightarrow 00:45:23.720$  the integration session,
- NOTE Confidence: 0.67909231
- $00{:}45{:}23.720 \dashrightarrow 00{:}45{:}25.160$  the integration session was right,
- NOTE Confidence: 0.67909231
- $00:45:25.160 \longrightarrow 00:45:27.320$  was after this right after.
- NOTE Confidence: 0.67909231
- $00:45:27.320 \longrightarrow 00:45:27.840$  Yeah.
- NOTE Confidence: 0.67909231
- $00:45:27.840 \longrightarrow 00:45:29.118$  Question the 1st
- NOTE Confidence: 0.816027681333333
- $00{:}45{:}29{.}680 \dashrightarrow 00{:}45{:}31{.}732$  in your, I mean in my experience when you
- NOTE Confidence: 0.816027681333333
- $00{:}45{:}31.732 \dashrightarrow 00{:}45{:}33.790$  ask patients about seven days they use
- NOTE Confidence: 0.816027681333333
- $00{:}45{:}33.790 \dashrightarrow 00{:}45{:}35.722$  pecan heuristic but you know they talk
- NOTE Confidence: 0.816027681333333

 $00{:}45{:}35{.}722 \dashrightarrow 00{:}45{:}37{.}678$  about how they are now and yeah so I I

NOTE Confidence: 0.4780106025

00:45:38.400 --> 00:45:40.240 don't get incredibly powerful

NOTE Confidence: 0.6024981166666667

 $00:45:40.240 \longrightarrow 00:45:42.316$  effect made accurately across the week.

NOTE Confidence: 0.72090336625

 $00:45:42.400 \longrightarrow 00:45:44.885$  Yeah no that I mean that's why

NOTE Confidence: 0.72090336625

 $00:45:44.885 \longrightarrow 00:45:46.950$  these type of measures like the

NOTE Confidence: 0.72090336625

 $00:45:46.950 \rightarrow 00:45:50.120$  mattress says serious limitations.

NOTE Confidence: 0.72090336625

 $00{:}45{:}50{.}120 \dashrightarrow 00{:}45{:}53{.}160$  So I think this contributes part to it.

NOTE Confidence: 0.72090336625

 $00{:}45{:}53.160 \dashrightarrow 00{:}45{:}55.136$  I I'm not sure what some some of

NOTE Confidence: 0.72090336625

 $00{:}45{:}55{.}136 \dashrightarrow 00{:}45{:}57{.}159$  the other reason could just be that

NOTE Confidence: 0.72090336625

 $00{:}45{:}57{.}160 \dashrightarrow 00{:}45{:}58{.}870$  by really blinding the Raiders

NOTE Confidence: 0.72090336625

 $00{:}45{:}58.870 \dashrightarrow 00{:}46{:}02.200$  you do have some effect that way.

NOTE Confidence: 0.72090336625

 $00:46:02.200 \longrightarrow 00:46:03.244$  We don't know that,

NOTE Confidence: 0.72090336625

 $00:46:03.244 \rightarrow 00:46:05.143$  but it's one of the things moving

NOTE Confidence: 0.72090336625

 $00:46:05.143 \longrightarrow 00:46:07.075$  forward that we have to look at.

NOTE Confidence: 0.72090336625

 $00:46:07.080 \rightarrow 00:46:09.312$  And then the last thing that I I just

NOTE Confidence: 0.72090336625

 $00:46:09.312 \rightarrow 00:46:11.592$  put in here is to put it in perspective

- NOTE Confidence: 0.72090336625
- $00{:}46{:}11.592 \dashrightarrow 00{:}46{:}16.280$  a way or or to give some context to it,

 $00{:}46{:}16.280 \dashrightarrow 00{:}46{:}18.638$  'cause these results are pretty amazing.

NOTE Confidence: 0.72090336625

 $00:46:18.640 \rightarrow 00:46:21.040$  I mean there's there's you would be hard

NOTE Confidence: 0.72090336625

 $00:46:21.040 \rightarrow 00:46:23.360$  pressed to say these aren't impressive.

NOTE Confidence: 0.72090336625

 $00:46:23.360 \longrightarrow 00:46:25.004$  These are they're they're

NOTE Confidence: 0.72090336625

 $00:46:25.004 \rightarrow 00:46:26.237$  pretty big findings.

NOTE Confidence: 0.72090336625

 $00:46:26.240 \longrightarrow 00:46:27.671$  But I I did want to put them in

NOTE Confidence: 0.72090336625

 $00:46:27.671 \rightarrow 00:46:28.677$  perspective to some of the others.

NOTE Confidence: 0.72090336625

 $00{:}46{:}28.680 \dashrightarrow 00{:}46{:}31.767$  So this is to one of the ASPIRE studies

NOTE Confidence: 0.72090336625

 $00{:}46{:}31.767 \dashrightarrow 00{:}46{:}34.179$  done with S ketamine looking at treatment,

NOTE Confidence: 0.72090336625

 $00:46:34.179 \longrightarrow 00:46:35.817$  the green line here I have

NOTE Confidence: 0.72090336625

 $00{:}46{:}35{.}817 \dashrightarrow 00{:}46{:}37{.}277$  it faded out so you can,

NOTE Confidence: 0.72090336625

 $00:46:37.280 \longrightarrow 00:46:39.520$  I can superimpose them over.

NOTE Confidence: 0.72090336625

00:46:39.520 --> 00:46:42.250 But you can see that the response

NOTE Confidence: 0.72090336625

00:46:42.250 --> 00:46:44.388 to ketamine over S ketamine

 $00:46:44.388 \rightarrow 00:46:46.690$  sporvato over that time and going

NOTE Confidence: 0.72090336625

 $00:46:46.690 \longrightarrow 00:46:48.280$  out over the same time period,

NOTE Confidence: 0.72090336625

 $00:46:48.280 \longrightarrow 00:46:49.440$  that's on the graph here

NOTE Confidence: 0.857619112307692

 $00:46:52.280 \longrightarrow 00:46:54.933$  with with the extra going on for

NOTE Confidence: 0.857619112307692

 $00:46:54.933 \longrightarrow 00:46:57.118$  for the psilocybin in the study.

NOTE Confidence: 0.857619112307692

00:46:57.120 --> 00:46:58.236 But you can see, you know,

NOTE Confidence: 0.857619112307692

 $00{:}46{:}58{.}240 \dashrightarrow 00{:}47{:}00{.}438$  really on par with what we're seeing.

NOTE Confidence: 0.857619112307692

 $00:47:00.440 \longrightarrow 00:47:02.470$  And remember this is just a single

NOTE Confidence: 0.857619112307692

00:47:02.470 --> 00:47:05.040 dose of psilocybin witnesses

NOTE Confidence: 0.857619112307692

 $00{:}47{:}05{.}040 \dashrightarrow 00{:}47{:}08{.}840$ 8 doses of esketamine here.

NOTE Confidence: 0.857619112307692

 $00{:}47{:}08{.}840 \dashrightarrow 00{:}47{:}11{.}549$  But you know, one of the caveats is look

NOTE Confidence: 0.857619112307692

 $00{:}47{:}11.549 \dashrightarrow 00{:}47{:}14.720$  at where the standard of care treatment is.

NOTE Confidence: 0.857619112307692

 $00:47:14.720 \longrightarrow 00:47:16.452$  Yeah, which was another,

NOTE Confidence: 0.857619112307692

 $00{:}47{:}16.452 \dashrightarrow 00{:}47{:}19.048$  which was anti standard of

NOTE Confidence: 0.857619112307692

 $00{:}47{:}19.048 \dashrightarrow 00{:}47{:}20.766$  antidepressant treatments, big gap.

NOTE Confidence: 0.857619112307692

 $00:47:20.766 \longrightarrow 00:47:21.332$  The biggest,

- NOTE Confidence: 0.857619112307692
- $00:47:21.332 \longrightarrow 00:47:23.030$  the thing that stands alone here
- NOTE Confidence: 0.857619112307692
- $00:47:23.083 \longrightarrow 00:47:24.757$  is the psilocybin is the niacin,
- NOTE Confidence: 0.857619112307692
- $00:47:24.760 \longrightarrow 00:47:26.212$  not the psilocybin.
- NOTE Confidence: 0.857619112307692
- $00{:}47{:}26{.}212 \dashrightarrow 00{:}47{:}29{.}667$  So it's it's a lesson that for
- NOTE Confidence: 0.857619112307692
- $00:47:29.667 \rightarrow 00:47:31.855$  many trials in antidepressants
- NOTE Confidence: 0.857619112307692
- $00{:}47{:}31.855 \dashrightarrow 00{:}47{:}35.110$  what determines if a drug works
- NOTE Confidence: 0.857619112307692
- $00:47:35.110 \longrightarrow 00:47:37.235$  or not is the placebo.
- NOTE Confidence: 0.857619112307692
- $00{:}47{:}37{.}240 \dashrightarrow 00{:}47{:}39{.}580$  If you if if you get a large place bo
- NOTE Confidence: 0.857619112307692
- $00{:}47{:}39{.}580 \dashrightarrow 00{:}47{:}41{.}240$  response it's very difficult what
- NOTE Confidence: 0.855400474666667
- $00:47:41.240 \longrightarrow 00:47:42.570$  is the there are two lines there
- NOTE Confidence: 0.855400474666667
- $00:47:42.570 \longrightarrow 00:47:44.276$  is one of those placebo and one of
- NOTE Confidence: 0.880318715833333
- $00:47:44.280 \longrightarrow 00:47:46.275$  those. So one of these is the
- NOTE Confidence: 0.880318715833333
- $00:47:46.275 \longrightarrow 00:47:47.733$  actual esketamine is the green
- NOTE Confidence: 0.880318715833333
- $00{:}47{:}47{.}733 \dashrightarrow 00{:}47{:}49{.}644$  line and the blue line is actually
- NOTE Confidence: 0.880318715833333
- $00{:}47{:}49.644 \dashrightarrow 00{:}47{:}51.517$  the standard of care treatment.
- NOTE Confidence: 0.4693750766666667

 $00:47:52.720 \longrightarrow 00:47:54.196$  We what it mean well in

NOTE Confidence: 0.786984796

 $00:47:54.200 \longrightarrow 00:47:55.740$  in those esketamine studies they

NOTE Confidence: 0.786984796

 $00:47:55.740 \longrightarrow 00:47:57.280$  were allowed to have regulated.

NOTE Confidence: 0.786984796

 $00:47:57.280 \longrightarrow 00:47:59.080$  So a new antidepressant was

NOTE Confidence: 0.786984796

 $00{:}47{:}59{.}080 \dashrightarrow 00{:}48{:}01{.}000$  started, OK, so that that's

NOTE Confidence: 0.70193819

 $00{:}48{:}01{.}000 \dashrightarrow 00{:}48{:}03{.}920$  and they had intensive interventions

NOTE Confidence: 0.79561184

 $00:48:04.000 \rightarrow 00:48:05.998$  and they had very intensive interventions.

NOTE Confidence: 0.910782351428571

 $00:48:08.400 \rightarrow 00:48:12.216$  And this is just comparing it to one of the

NOTE Confidence: 0.910782351428571

00:48:12.216 --> 00:48:14.424 TRANSFORM studies with S ketamine seeing

NOTE Confidence: 0.910782351428571

 $00:48:14.424 \rightarrow 00:48:16.944$  here you don't see that rapid effects These

NOTE Confidence: 0.910782351428571

 $00:48:16.944 \rightarrow 00:48:18.954$  those other patients were hospitalized,

NOTE Confidence: 0.910782351428571

 $00{:}48{:}18{.}960 \dashrightarrow 00{:}48{:}21{.}840$  these patients weren't hospitalized.

NOTE Confidence: 0.910782351428571

00:48:21.840 --> 00:48:23.946 But again, you can see looking

NOTE Confidence: 0.910782351428571

 $00:48:23.946 \longrightarrow 00:48:26.200$  at that endpoint of four weeks,

NOTE Confidence: 0.910782351428571

 $00:48:26.200 \rightarrow 00:48:29.830$  you you can see where where it is overall

NOTE Confidence: 0.910782351428571

 $00:48:29.830 \longrightarrow 00:48:31.720$  compared to the effect with S ketamine.

 $00:48:31.720 \longrightarrow 00:48:32.860$  And again these are

NOTE Confidence: 0.910782351428571

 $00:48:32.860 \longrightarrow 00:48:34.000$  comparing apples and oranges.

NOTE Confidence: 0.910782351428571

00:48:34.000 --> 00:48:35.866 You have to be really careful

NOTE Confidence: 0.910782351428571

00:48:35.866 --> 00:48:36.799 comparing across studies.

NOTE Confidence: 0.910782351428571

 $00:48:36.800 \rightarrow 00:48:39.635$  This is just to give some level of context,

NOTE Confidence: 0.910782351428571

00:48:39.640 - 00:48:41.784 but again really to show where the big

NOTE Confidence: 0.910782351428571

 $00{:}48{:}41.784 \dashrightarrow 00{:}48{:}43.319$  difference lies is with the Niacin.

NOTE Confidence: 0.910782351428571

 $00:48:43.320 \longrightarrow 00:48:45.736$  So we really have to be careful you

NOTE Confidence: 0.910782351428571

 $00{:}48{:}45{.}736 \dashrightarrow 00{:}48{:}48{.}413$  know and moving forward not to get so

NOTE Confidence: 0.910782351428571

 $00{:}48{:}48{.}413 \dashrightarrow 00{:}48{:}50{.}434$  confident that these effects sizes are

NOTE Confidence: 0.910782351428571

 $00{:}48{:}50{.}434 \dashrightarrow 00{:}48{:}53{.}088$  going to hold up as you move forward.

NOTE Confidence: 0.910782351428571

 $00{:}48{:}53.088 \dashrightarrow 00{:}48{:}55.669$  There's there's a real trend in all

NOTE Confidence: 0.910782351428571

 $00{:}48{:}55.669 \dashrightarrow 00{:}48{:}58.027$  clinical trials work that going from

NOTE Confidence: 0.910782351428571

00:48:58.027 --> 00:49:00.800 phase two studies to phase three studies

NOTE Confidence: 0.910782351428571

 $00{:}49{:}00{.}800 \dashrightarrow 00{:}49{:}03{.}428$  that delta between the active and and

 $00{:}49{:}03{.}428$  -->  $00{:}49{:}05{.}516$  sham or place bo treatment narrows down.

NOTE Confidence: 0.910782351428571

 $00{:}49{:}05{.}520 \dashrightarrow 00{:}49{:}07{.}606$  So you really want to make sure

NOTE Confidence: 0.910782351428571

 $00:49:07.606 \rightarrow 00:49:09.600$  that's managed as much as possible.

NOTE Confidence: 0.910782351428571

00:49:09.600 --> 00:49:10.440 And then finally, Curtis,

NOTE Confidence: 0.828912814285714

 $00:49:10.480 \longrightarrow 00:49:12.106$  how would you interpret that the

NOTE Confidence: 0.828912814285714

 $00:49:12.106 \rightarrow 00:49:13.879$  fact that there's such a such a low,

NOTE Confidence: 0.828912814285714

 $00:49:13.880 \longrightarrow 00:49:15.959$  is that because of a nocebo effect,

NOTE Confidence: 0.828912814285714

 $00:49:15.960 \longrightarrow 00:49:17.920$  because of functional unblinding? Well

NOTE Confidence: 0.83094684

00:49:18.000 --> 00:49:20.184 I I mean I don't it's hard for

NOTE Confidence: 0.83094684

 $00:49:20.184 \rightarrow 00:49:22.480$  me to know for sure. I think

NOTE Confidence: 0.775509430909091

 $00{:}49{:}24.640 \dashrightarrow 00{:}49{:}27.210$  I I think functional unblinding

NOTE Confidence: 0.775509430909091

 $00:49:27.210 \longrightarrow 00:49:30.720$  probably plays a large role in it.

NOTE Confidence: 0.908663905882353

 $00:49:32.840 \longrightarrow 00:49:35.252$  So we don't really know but I think we

NOTE Confidence: 0.908663905882353

 $00{:}49{:}35{.}252 \dashrightarrow 00{:}49{:}37{.}634$  have to be careful as we move forward.

NOTE Confidence: 0.908663905882353

 $00:49:37.640 \longrightarrow 00:49:40.200$  I think expectations, functional

NOTE Confidence: 0.908663905882353

 $00:49:40.200 \longrightarrow 00:49:42.400$  unblinding play a large role and

- NOTE Confidence: 0.701243884285714
- $00:49:42.400 \longrightarrow 00:49:43.492$  lack of open labels.
- NOTE Confidence: 0.701243884285714
- $00:49:43.492 \longrightarrow 00:49:45.130$  So patients had really fun to
- NOTE Confidence: 0.701243884285714
- $00:49:45.193 \rightarrow 00:49:46.997$  because of functional unblinding,
- NOTE Confidence: 0.648720745625
- $00:49:47.000 \rightarrow 00:49:48.135$  that's going to increase the
- NOTE Confidence: 0.648720745625
- 00:49:48.135 --> 00:49:49.043 noce<br/>bo effect because there's
- NOTE Confidence: 0.648720745625
- $00:49:49.043 \longrightarrow 00:49:50.160$  going to be a sense of despair
- NOTE Confidence: 0.511063413333333
- $00:49:50.200 \rightarrow 00:49:53.838$  and betrayal. Yeah. So the questions yeah,
- NOTE Confidence: 0.7271092866666667
- $00:49:54.480 \longrightarrow 00:49:55.116$  I was going to ask you,
- NOTE Confidence: 0.7271092866666667
- $00:49:55.120 \rightarrow 00:49:57.060$  how do you feel as well about the psycho,
- NOTE Confidence: 0.7271092866666667
- 00:49:57.060 00:49:58.960 like the control psychotherapy?
- NOTE Confidence: 0.7271092866666667
- $00:49:58.960 \rightarrow 00:50:01.940$  Because there's recently being an editorial.
- NOTE Confidence: 0.7271092866666667
- $00{:}50{:}01{.}940 \dashrightarrow 00{:}50{:}03{.}520$  Right. Unless psychiatry on this.
- NOTE Confidence: 0.7271092866666667
- $00{:}50{:}03{.}520 \dashrightarrow 00{:}50{:}05{.}200$  And I think it's really valuable because
- NOTE Confidence: 0.9191937875
- $00{:}50{:}05{.}600 \dashrightarrow 00{:}50{:}07{.}230$  what the control condition is
- NOTE Confidence: 0.9191937875
- $00{:}50{:}07{.}230 \dashrightarrow 00{:}50{:}09{.}466$  given the patients is this form
- NOTE Confidence: 0.9191937875

00:50:09.466 - 00:50:11.096 of psychotherapy that has never

NOTE Confidence: 0.9191937875

00:50:11.096 --> 00:50:13.960 been tested for anything. So

NOTE Confidence: 0.8443720125

 $00:50:13.960 \longrightarrow 00:50:15.880$  it's it is truly nocebo

NOTE Confidence: 0.904478775

 $00:50:15.880 \longrightarrow 00:50:17.504$  in no way because it's not like

NOTE Confidence: 0.904478775

 $00:50:17.504 \longrightarrow 00:50:18.679$  we're giving them let's say

NOTE Confidence: 0.658188848333333

 $00:50:18.880 \rightarrow 00:50:22.480$  CBT active behavioral therapy you know

NOTE Confidence: 0.658188848333333

 $00{:}50{:}22.480 \dashrightarrow 00{:}50{:}24.398$  behavioral activation story and then

NOTE Confidence: 0.586092604

 $00:50:24.400 \rightarrow 00:50:25.420$  giving them you know you

NOTE Confidence: 0.586092604

 $00{:}50{:}25{.}420 \dashrightarrow 00{:}50{:}26{.}440$  know silos happened or not.

NOTE Confidence: 0.586092604

 $00:50:26.440 \longrightarrow 00:50:28.000$  I I wonder how you think you can

NOTE Confidence: 0.8445947

 $00{:}50{:}28.040 \dashrightarrow 00{:}50{:}29.816$  we can address that in the future if

NOTE Confidence: 0.8445947

 $00{:}50{:}29{.}816 \dashrightarrow 00{:}50{:}31{.}648$  there is room for that even because

NOTE Confidence: 0.8445947

 $00{:}50{:}31.648 \dashrightarrow 00{:}50{:}33.400$  I assume that user institute is

NOTE Confidence: 0.8445947

 $00:50:33.400 \rightarrow 00:50:35.220$  pushing forward that we test silo

NOTE Confidence: 0.8445947

 $00:50:35.220 \rightarrow 00:50:37.240$  cyber under that specific model.

NOTE Confidence: 0.674281812666667

 $00:50:37.720 \rightarrow 00:50:39.720$  So I've been maybe you want to answer

 $00:50:39.720 \rightarrow 00:50:42.006$  too I mean I'll stop by saying this

NOTE Confidence: 0.674281812666667

 $00:50:42.006 \rightarrow 00:50:43.962$  is a very complicated issue because

NOTE Confidence: 0.674281812666667

 $00:50:43.962 \rightarrow 00:50:45.989$  it actually comes to what's in your

NOTE Confidence: 0.6742818126666667

00:50:45.989 - 00:50:48.040 label when when you do get approved.

NOTE Confidence: 0.6742818126666667

 $00{:}50{:}48.040 \dashrightarrow 00{:}50{:}51.524$  So it it gets very complicated and has a

NOTE Confidence: 0.674281812666667

 $00{:}50{:}51{.}524 \dashrightarrow 00{:}50{:}55{.}044$  lot of legal and regulatory meanings to it.

NOTE Confidence: 0.6742818126666667

 $00:50:55.044 \rightarrow 00:50:56.984$  This study was really with

NOTE Confidence: 0.674281812666667

 $00:50:56.984 \rightarrow 00:50:57.760$  psychological assistance.

NOTE Confidence: 0.674281812666667

 $00{:}50{:}57{.}760 \dashrightarrow 00{:}51{:}01{.}560$  It it was not and very clearly not

NOTE Confidence: 0.6742818126666667

 $00:51:01.560 \longrightarrow 00:51:04.960$  done to augment a psychotherapy.

NOTE Confidence: 0.6742818126666667

00:51:04.960 --> 00:51:05.440 And Ben I

NOTE Confidence: 0.702470845

 $00{:}51{:}05{.}480 \dashrightarrow 00{:}51{:}07{.}181$  don't know if they used a model

NOTE Confidence: 0.702470845

 $00{:}51{:}07{.}181 \dashrightarrow 00{:}51{:}08{.}463$  that's called non directive

NOTE Confidence: 0.702470845

 $00{:}51{:}08{.}463 \dashrightarrow 00{:}51{:}10{.}320$  supportive the rapy which really does

NOTE Confidence: 0.702470845

 $00{:}51{:}10{.}320 \dashrightarrow 00{:}51{:}12{.}120$  not necessarily meet criteria of

 $00:51:12.120 \rightarrow 00:51:13.600$  structured targeted psychotherapy

NOTE Confidence: 0.702470845

 $00:51:13.600 \rightarrow 00:51:16.360$  that we would see conventionally.

NOTE Confidence: 0.702470845

00:51:16.360 --> 00:51:18.580 It still is a form of supportive

NOTE Confidence: 0.702470845

 $00:51:18.580 \longrightarrow 00:51:20.448$  therapy which really includes

NOTE Confidence: 0.702470845

00:51:20.448 --> 00:51:22.680 checking in during preparation,

NOTE Confidence: 0.702470845

 $00{:}51{:}22.680 \dashrightarrow 00{:}51{:}27.880$  building report and getting to become

NOTE Confidence: 0.702470845

 $00{:}51{:}27.880 \dashrightarrow 00{:}51{:}30.760$  familiar with the facilitators.

NOTE Confidence: 0.702470845

 $00{:}51{:}30.760 \dashrightarrow 00{:}51{:}34.036$  So it that's what non directive supportive

NOTE Confidence: 0.88329502944444

 $00{:}51{:}36{.}440 \dashrightarrow 00{:}51{:}38{.}784$  therapy is as opposed to in some other

NOTE Confidence: 0.88329502944444

 $00{:}51{:}38{.}784 \dashrightarrow 00{:}51{:}40{.}630$  studies where it's psilocybin assisted

NOTE Confidence: 0.883295029444444

00:51:40.630 - 00:51:42.635 psychotherapy which is much more

NOTE Confidence: 0.65621504

 $00:51:45.160 \rightarrow 00:51:47.764$  with kind of a conventional therapy

NOTE Confidence: 0.65621504

 $00:51:47.764 \rightarrow 00:51:49.678$  heavy as opposed to what was it here.

NOTE Confidence: 0.65621504

 $00:51:49.680 \longrightarrow 00:51:51.780$  So they try to actually use the

NOTE Confidence: 0.65621504

 $00:51:51.780 \longrightarrow 00:51:53.808$  the reason they use this non

NOTE Confidence: 0.65621504

 $00:51:53.808 \rightarrow 00:51:56.204$  directive approach is to minimize

 $00:51:56.204 \rightarrow 00:51:59.600$  the psychotherapy as a variable to

NOTE Confidence: 0.65621504

 $00{:}51{:}59{.}600 \dashrightarrow 00{:}52{:}01{.}960$  whatever as much as it's feasible.

NOTE Confidence: 0.65621504

 $00:52:01.960 \longrightarrow 00:52:06.517$  But it remains to be seen what

NOTE Confidence: 0.65621504

 $00{:}52{:}06{.}520 \dashrightarrow 00{:}52{:}08{.}776$  eventually how this will be packaged

NOTE Confidence: 0.65621504

 $00{:}52{:}08{.}776 \dashrightarrow 00{:}52{:}11{.}423$  in the label and how this what

NOTE Confidence: 0.65621504

 $00{:}52{:}11{.}423 \dashrightarrow 00{:}52{:}13{.}553$  sort of training will be required

NOTE Confidence: 0.65621504

 $00:52:13.553 \longrightarrow 00:52:15.984$  to say that you are certified to

NOTE Confidence: 0.65621504

 $00:52:15.984 \rightarrow 00:52:18.144$  actually deliver this treatment with

NOTE Confidence: 0.65621504

 $00{:}52{:}18{.}144 \dashrightarrow 00{:}52{:}20{.}320$  a non directive supported the rapy.

NOTE Confidence: 0.65621504

 $00{:}52{:}20{.}320 \dashrightarrow 00{:}52{:}24{.}478$  I that that remains to be seen

NOTE Confidence: 0.847678335833333

 $00{:}52{:}24{.}960 \dashrightarrow 00{:}52{:}27{.}616$  there there. I mean the first thing is

NOTE Confidence: 0.847678335833333

00:52:27.616 --> 00:52:30.120 let's just demonstrate that there is

NOTE Confidence: 0.847678335833333

 $00{:}52{:}30{.}120 \dashrightarrow 00{:}52{:}32{.}160$  efficacy in general safety and then

NOTE Confidence: 0.847678335833333

 $00{:}52{:}32{.}160 \dashrightarrow 00{:}52{:}34{.}880$  I think decomposing the treatments.

NOTE Confidence: 0.847678335833333

 $00{:}52{:}34{.}880 \dashrightarrow 00{:}52{:}37{.}193$  But as you see right down at the bottom

 $00:52:37.200 \rightarrow 00:52:38.838$  just very quickly things moving forward.

NOTE Confidence: 0.847678335833333

 $00{:}52{:}38{.}840 \dashrightarrow 00{:}52{:}40{.}905$  I think the field needs to address

NOTE Confidence: 0.847678335833333

 $00:52:40.905 \longrightarrow 00:52:42.344$  this to address the generalizability.

NOTE Confidence: 0.847678335833333

 $00:52:42.344 \dashrightarrow 00:52:44.358$  And I can tell you future studies

NOTE Confidence: 0.847678335833333

 $00{:}52{:}44{.}358 \dashrightarrow 00{:}52{:}46{.}052$  are working hard to make sure it's

NOTE Confidence: 0.847678335833333

 $00{:}52{:}46.052 \dashrightarrow 00{:}52{:}48.400$  a more representative sample of

NOTE Confidence: 0.847678335833333

 $00:52:48.400 \rightarrow 00:52:50.640$  participants address the safety.

NOTE Confidence: 0.847678335833333

 $00:52:50.640 \rightarrow 00:52:51.399$  And longer term,

NOTE Confidence: 0.847678335833333

 $00{:}52{:}51{.}399 \dashrightarrow 00{:}52{:}53{.}170$  you know if these are going to

NOTE Confidence: 0.847678335833333

 $00:52:53.230 \rightarrow 00:52:56.680$  move forward to approval,

NOTE Confidence: 0.847678335833333

 $00{:}52{:}56{.}680 \dashrightarrow 00{:}52{:}58{.}318$  the clinicians and the regulators are

NOTE Confidence: 0.847678335833333

 $00:52:58.318 \rightarrow 00:53:00.704$  going to want to have some more information

NOTE Confidence: 0.847678335833333

 $00:53:00.704 \rightarrow 00:53:02.558$  about what if the person relapses,

NOTE Confidence: 0.847678335833333

00:53:02.560 --> 00:53:04.220 can you do this again, how,

NOTE Confidence: 0.847678335833333

 $00:53:04.220 \longrightarrow 00:53:06.320$  how do you manage this?

NOTE Confidence: 0.847678335833333

 $00:53:06.320 \longrightarrow 00:53:07.545$  So that's more data that's

- NOTE Confidence: 0.847678335833333
- $00:53:07.545 \longrightarrow 00:53:09.360$  going to need to be collected,
- NOTE Confidence: 0.847678335833333
- $00{:}53{:}09{.}360 \dashrightarrow 00{:}53{:}10.685$  a better understanding of the
- NOTE Confidence: 0.847678335833333
- $00{:}53{:}10.685 \dashrightarrow 00{:}53{:}11.480$  dose response relationship,
- NOTE Confidence: 0.847678335833333
- $00:53:11.480 \longrightarrow 00:53:13.600$  that's only just one dose.
- NOTE Confidence: 0.847678335833333
- $00:53:13.600 \longrightarrow 00:53:14.656$  We're going to have to have
- NOTE Confidence: 0.847678335833333
- $00:53:14.656 \longrightarrow 00:53:15.360$  a better understanding is,
- NOTE Confidence: 0.847678335833333
- $00:53:15.360 \longrightarrow 00:53:18.640$  is that dose necessary.
- NOTE Confidence: 0.847678335833333
- $00{:}53{:}18.640 \dashrightarrow 00{:}53{:}21.066$  And then as I said,
- NOTE Confidence: 0.847678335833333
- $00:53:21.066 \rightarrow 00:53:22.340$  we're going to have to figure out
- NOTE Confidence: 0.847678335833333
- $00:53:22.385 \longrightarrow 00:53:23.743$  how to manage some of the trial
- NOTE Confidence: 0.847678335833333
- 00:53:23.743 > 00:53:25.118 design issues a little bit better,
- NOTE Confidence: 0.847678335833333
- $00:53:25.120 \rightarrow 00:53:27.100$  asking about expectations,
- NOTE Confidence: 0.847678335833333
- 00:53:27.100 --> 00:53:29.080 asking about preference,
- NOTE Confidence: 0.847678335833333
- $00:53:29.080 \dashrightarrow 00:53:32.540$  that guess of a study assignment,
- NOTE Confidence: 0.847678335833333
- $00:53:32.540 \longrightarrow 00:53:34.446$  those will all be studies.
- NOTE Confidence: 0.847678335833333

00:53:34.446 --> 00:53:36.276 And then really moving forward,

NOTE Confidence: 0.847678335833333

 $00{:}53{:}36{.}280 \dashrightarrow 00{:}53{:}38{.}180$  getting more to your question

NOTE Confidence: 0.847678335833333

 $00:53:38.180 \longrightarrow 00:53:40.520$  is you know how are we going to

NOTE Confidence: 0.847678335833333

 $00:53:40.520 \rightarrow 00:53:41.480$  address the cost effectiveness?

NOTE Confidence: 0.847678335833333

 $00:53:41.480 \longrightarrow 00:53:42.149$  You know how,

NOTE Confidence: 0.847678335833333

 $00:53:42.149 \longrightarrow 00:53:44.125$  how are we going to do this in a

NOTE Confidence: 0.847678335833333

00:53:44.125 --> 00:53:45.998 way that would increase access

NOTE Confidence: 0.847678335833333

 $00{:}53{:}45{.}998 \dashrightarrow 00{:}53{:}49{.}034$  and and reduce the overall cost.

NOTE Confidence: 0.847678335833333

 $00{:}53{:}49{.}040 \dashrightarrow 00{:}53{:}50{.}510$  And then a better understanding of

NOTE Confidence: 0.847678335833333

 $00:53:50.510 \rightarrow 00:53:51.774$  the mechanism, mechanistic actions.

NOTE Confidence: 0.847678335833333

 $00:53:51.774 \rightarrow 00:53:54.096$  And then a quick review of

NOTE Confidence: 0.847678335833333

 $00:53:54.096 \rightarrow 00:53:55.240$  everything just here.

NOTE Confidence: 0.847678335833333

 $00:53:55.240 \longrightarrow 00:53:56.120$  This is the main point.

NOTE Confidence: 0.847678335833333

 $00:53:56.120 \rightarrow 00:53:59.444$  It's a huge, that's a huge effect size.

NOTE Confidence: 0.847678335833333

 $00:53:59.444 \dashrightarrow 00:54:04.680$  I mean it the this is is encouraging.

NOTE Confidence: 0.847678335833333

 $00:54:04.680 \rightarrow 00:54:05.520$  Those of you that know me,

- NOTE Confidence: 0.847678335833333
- 00:54:05.520 --> 00:54:07.975 I'm quite sceptical coming into
- NOTE Confidence: 0.847678335833333
- $00{:}54{:}07{.}975 \dashrightarrow 00{:}54{:}10{.}680$  this and my scepticism share is
- NOTE Confidence: 0.847678335833333
- $00:54:10.680 \rightarrow 00:54:12.960$  across the board for everything.
- NOTE Confidence: 0.847678335833333
- $00:54:12.960 \rightarrow 00:54:14.647$  I think that's the way you should
- NOTE Confidence: 0.847678335833333
- $00{:}54{:}14.647 \dashrightarrow 00{:}54{:}16.200$  be running these clinical trials.
- NOTE Confidence: 0.847678335833333
- $00:54:16.200 \longrightarrow 00:54:18.416$  But I have to say this is quite
- NOTE Confidence: 0.847678335833333
- $00:54:18.416 \rightarrow 00:54:20.479$  encouraging that you know it's it's there.
- NOTE Confidence: 0.847678335833333
- $00:54:20.480 \longrightarrow 00:54:22.262$  I think there's very little doubt
- NOTE Confidence: 0.847678335833333
- $00:54:22.262 \longrightarrow 00:54:24.199$  that in this study design this,
- NOTE Confidence: 0.847678335833333
- $00:54:24.200 \rightarrow 00:54:27.432$  it's a very large effect and then
- NOTE Confidence: 0.847678335833333
- $00:54:27.432 \rightarrow 00:54:29.364$  really the support of so many people
- NOTE Confidence: 0.847678335833333
- $00:54:29.364 \rightarrow 00:54:31.064$  that just at this yell site just
- NOTE Confidence: 0.847678335833333
- $00:54:31.064 \rightarrow 00:54:33.327$  to give you a sense of how many
- NOTE Confidence: 0.847678335833333
- $00{:}54{:}33{.}327 \dashrightarrow 00{:}54{:}34{.}952$  people contribute to these studies.
- NOTE Confidence: 0.847678335833333
- $00:54:34.960 \longrightarrow 00:54:37.860$  So this is 11 sites doing this
- NOTE Confidence: 0.847678335833333

 $00:54:37.860 \longrightarrow 00:54:39.240$  and this is just an oversight.

NOTE Confidence: 0.847678335833333

 $00:54:39.240 \rightarrow 00:54:42.012$  So and really the patients participating

NOTE Confidence: 0.847678335833333

 $00:54:42.012 \longrightarrow 00:54:44.722$  in this especially during the pandemic

NOTE Confidence: 0.847678335833333

 $00:54:44.722 \rightarrow 00:54:46.600$  were were really troopers and and

NOTE Confidence: 0.847678335833333

 $00:54:46.600 \longrightarrow 00:54:48.394$  they all needed support systems that

NOTE Confidence: 0.847678335833333

 $00:54:48.394 \rightarrow 00:54:49.960$  would bring them back and forth.

NOTE Confidence: 0.847678335833333

 $00:54:49.960 \longrightarrow 00:54:51.544$  So really required a lot of

NOTE Confidence: 0.847678335833333

 $00{:}54{:}51{.}544 \dashrightarrow 00{:}54{:}53{.}005$  work both from the participants

NOTE Confidence: 0.847678335833333

 $00{:}54{:}53.005 \dashrightarrow 00{:}54{:}55.300$  and all the staff and faculty.

NOTE Confidence: 0.847678335833333

 $00:54:55.300 \rightarrow 00:54:57.400$  So I'll stop with that.

NOTE Confidence: 0.847678335833333

00:54:57.400 --> 00:55:00.079 All right, thanks.

NOTE Confidence: 0.847678335833333

 $00:55:00.080 \longrightarrow 00:55:00.810$  Any question?

NOTE Confidence: 0.847678335833333

 $00{:}55{:}00{.}810 \dashrightarrow 00{:}55{:}01{.}175$  Oh,

NOTE Confidence: 0.847678335833333

00:55:01.175 --> 00:55:02.635 I should probably go

NOTE Confidence: 0.6107969266666667

 $00:55:09.810 \longrightarrow 00:55:12.846$  kind of are there any questions,

NOTE Confidence: 0.6107969266666667

 $00:55:12.850 \rightarrow 00:55:13.588$  Terry, why don't you stop

 $00:55:13.588 \longrightarrow 00:55:14.698$  the share so we can see it?

NOTE Confidence: 0.6107969266666667

00:55:14.698 --> 00:55:15.930 Yeah, let me stop share

NOTE Confidence: 0.815341936111111

 $00:55:31.280 \rightarrow 00:55:33.278$  the questions about the blinding and

NOTE Confidence: 0.815341936111111

00:55:33.278 --> 00:55:35.425 expectancy that I think we've addressed

NOTE Confidence: 0.815341936111111

 $00{:}55{:}35{.}425 \dashrightarrow 00{:}55{:}37{.}675$  a question about modifying the Madras, NOTE Confidence: 0.815341936111111

 $00{:}55{:}37{.}680 \dashrightarrow 00{:}55{:}40{.}299$  the time frame of the Madras in order to

NOTE Confidence: 0.815341936111111

 $00{:}55{:}40{.}299 \dashrightarrow 00{:}55{:}43{.}920$  try to avoid that day two point but that

NOTE Confidence: 0.897001289285714

 $00:55:44.880 \rightarrow 00:55:48.723$  So I I think honestly if for these clinical

NOTE Confidence: 0.897001289285714

 $00:55:48.723 \rightarrow 00:55:51.560$  trials that are going through FDA,

NOTE Confidence: 0.897001289285714

 $00{:}55{:}51{.}560 \dashrightarrow 00{:}55{:}54{.}640$  the FDA doesn't care about day two,

NOTE Confidence: 0.897001289285714

 $00:55:54.640 \longrightarrow 00:55:56.060$  right. It's just not it.

NOTE Confidence: 0.897001289285714

 $00{:}55{:}56{.}060 \dashrightarrow 00{:}55{:}57{.}960$  You know they're much more

NOTE Confidence: 0.897001289285714

 $00{:}55{:}57{.}960 \dashrightarrow 00{:}55{:}59{.}480$  interested in this endpoint.

NOTE Confidence: 0.897001289285714

 $00:55:59.480 \longrightarrow 00:56:01.000$  So you can modify it if you want,

NOTE Confidence: 0.897001289285714

 $00{:}56{:}01.000 \dashrightarrow 00{:}56{:}03.072$  but it's always going to be a

 $00:56:03.072 \rightarrow 00:56:06.220$  secondary or an exploratory aim here

NOTE Confidence: 0.897001289285714

 $00{:}56{:}06{.}220 \dashrightarrow 00{:}56{:}09{.}175$  because the I don't think the FDA

NOTE Confidence: 0.897001289285714

 $00:56:09.175 \rightarrow 00:56:10.670$  is interested in giving approval

NOTE Confidence: 0.897001289285714

 $00:56:10.727 \rightarrow 00:56:12.343$  for rapid acting specifically

NOTE Confidence: 0.897001289285714

 $00:56:12.343 \rightarrow 00:56:14.363$  that's they're they're much more

NOTE Confidence: 0.897001289285714

 $00:56:14.363 \rightarrow 00:56:15.879$  interested in the longer term.

NOTE Confidence: 0.875681539285714

 $00{:}56{:}17.000 \dashrightarrow 00{:}56{:}18.456$  It was an early question I don't

NOTE Confidence: 0.875681539285714

 $00{:}56{:}18.456 \dashrightarrow 00{:}56{:}20.078$  think we talked about about the music.

NOTE Confidence: 0.875681539285714

 $00{:}56{:}20.080 \dashrightarrow 00{:}56{:}21.872$  I think you every one listens to the

NOTE Confidence: 0.875681539285714

 $00:56:21.872 \rightarrow 00:56:24.160$  same playlist in the same order. Yes.

NOTE Confidence: 0.875681539285714

 $00:56:24.160 \rightarrow 00:56:26.360$  And sequence which is an interesting,

NOTE Confidence: 0.875681539285714

 $00:56:26.360 \dashrightarrow 00:56:28.060$  I mean that's going to be more that's going

NOTE Confidence: 0.875681539285714

 $00:56:28.060 \longrightarrow 00:56:29.722$  to be a perfect fit for some people and

NOTE Confidence: 0.875681539285714

 $00{:}56{:}29{.}722 \dashrightarrow 00{:}56{:}31{.}360$  kind of weird for other people, right.

NOTE Confidence: 0.875681539285714

 $00:56:31.360 \rightarrow 00:56:35.250$  So that's some participants and that may

NOTE Confidence: 0.875681539285714

 $00:56:35.250 \rightarrow 00:56:36.800$  interact with ethnicity or cultural.

- NOTE Confidence: 0.875681539285714
- 00:56:36.800 --> 00:56:38.240 Absolutely. Yep.
- NOTE Confidence: 0.847593806
- $00:56:39.800 \longrightarrow 00:56:40.480$  And I think this is,
- NOTE Confidence: 0.847593806
- $00:56:40.480 \longrightarrow 00:56:41.960$  this is the general idea,
- NOTE Confidence: 0.847593806
- $00:56:41.960 \rightarrow 00:56:43.640$  the whole idea of generalizability.
- NOTE Confidence: 0.76980329
- $00{:}56{:}43{.}960 \dashrightarrow 00{:}56{:}44{.}840$  And and I think
- NOTE Confidence: 0.902346942857143
- $00:56:45.120 \longrightarrow 00:56:47.115$  one of the comments in the bottom,
- NOTE Confidence: 0.902346942857143
- 00:56:47.120 --> 00:56:48.560 Chris, if you don't mind scrolling,
- NOTE Confidence: 0.902346942857143
- 00:56:48.560 --> 00:56:51.670 Steve made a really good
- NOTE Confidence: 0.902346942857143
- $00:56:51.670 \rightarrow 00:56:55.954$  point which ties into, yeah,
- NOTE Confidence: 0.902346942857143
- $00:56:55.954 \rightarrow 00:56:58.078$  that's the one, ties into the
- NOTE Confidence: 0.664185198571429
- $00:57:00.920 \rightarrow 00:57:02.975$  functional unblinding potential
- NOTE Confidence: 0.664185198571429
- $00{:}57{:}02{.}975 \dashrightarrow 00{:}57{:}07{.}355$  NASEBO effect is that because of the
- NOTE Confidence: 0.664185198571429
- $00:57:07.355 \rightarrow 00:57:10.080$  uniqueness of the study designed
- NOTE Confidence: 0.664185198571429
- $00{:}57{:}10{.}080 \dashrightarrow 00{:}57{:}12{.}313$  patients who knew that they did not
- NOTE Confidence: 0.664185198571429
- $00:57:12.313 \rightarrow 00:57:14.225$  receive psilocybin and they had to stay
- NOTE Confidence: 0.664185198571429

 $00:57:14.225 \rightarrow 00:57:16.238$  in the study for a total of 6 weeks.

NOTE Confidence: 0.664185198571429

 $00:57:16.240 \rightarrow 00:57:18.360$  That was very challenging also on the staff,

NOTE Confidence: 0.664185198571429

 $00{:}57{:}18.360 \dashrightarrow 00{:}57{:}22.332$  both on the facilitators as well

NOTE Confidence: 0.664185198571429

 $00:57:22.332 \longrightarrow 00:57:24.896$  as research assistants who work

NOTE Confidence: 0.664185198571429

 $00:57:24.896 \rightarrow 00:57:26.885$  more closely with participants.

NOTE Confidence: 0.664185198571429

 $00{:}57{:}26.885 \dashrightarrow 00{:}57{:}30.275$  It was just a shared heartfelt

NOTE Confidence: 0.664185198571429

 $00:57:30.280 \longrightarrow 00:57:31.200$  experience. And

NOTE Confidence: 0.8450657375

 $00:57:31.440 \rightarrow 00:57:33.008$  when it's easy to imagine there being

NOTE Confidence: 0.8450657375

 $00{:}57{:}33.008 \dashrightarrow 00{:}57{:}34.240$  a feedback process that's right,

NOTE Confidence: 0.8450657375

 $00{:}57{:}34{.}240 \dashrightarrow 00{:}57{:}36{.}008$  the distress and the staff and the distress

NOTE Confidence: 0.8450657375

 $00{:}57{:}36.008 \dashrightarrow 00{:}57{:}37.798$  and the patient over that time period,

NOTE Confidence: 0.8450657375

 $00:57:37.800 \longrightarrow 00:57:39.150$  well that's the importance of

NOTE Confidence: 0.8450657375

 $00{:}57{:}39{.}150 \dashrightarrow 00{:}57{:}40{.}960$  the of the raters being blinded.

NOTE Confidence: 0.8450657375

 $00{:}57{:}40{.}960 \dashrightarrow 00{:}57{:}43{.}396$  But that's that could have been.

NOTE Confidence: 0.89831017375

 $00:57:44.040 \rightarrow 00:57:45.640$  So thank you Steve for bringing that up.

NOTE Confidence: 0.762250812

 $00:57:48.680 \rightarrow 00:57:51.080$  Any other questions or hi,

- NOTE Confidence: 0.762250812
- $00{:}57{:}51{.}080 \dashrightarrow 00{:}57{:}53{.}352$  I have a question.
- NOTE Confidence: 0.762250812
- $00{:}57{:}53{.}352 \dashrightarrow 00{:}57{.}57{.}568$  So in the paper there's mention of three
- NOTE Confidence: 0.762250812
- $00:57:57.568 \rightarrow 00:58:00.200$  people in both groups that started
- NOTE Confidence: 0.762250812
- $00:58:00.200 \rightarrow 00:58:02.520$  an antidepressant during the study.
- NOTE Confidence: 0.762250812
- 00:58:02.520 --> 00:58:06.158 To clarify, for any of the participants
- NOTE Confidence: 0.762250812
- $00:58:06.160 \longrightarrow 00:58:07.720$  that were on a medication,
- NOTE Confidence: 0.762250812
- $00:58:07.720 \longrightarrow 00:58:11.540$  did they restart or was it only patients
- NOTE Confidence: 0.762250812
- $00:58:11.540 \longrightarrow 00:58:14.600$  that had not been on a medication
- NOTE Confidence: 0.951262945
- $00:58:14.600 \rightarrow 00:58:15.600$  prior to the study?
- NOTE Confidence: 0.807810771818182
- $00:58:17.640 \longrightarrow 00:58:19.890$  So I I I can only I think we
- NOTE Confidence: 0.807810771818182
- $00:58:19.890 \longrightarrow 00:58:22.628$  had one at our site and I think
- NOTE Confidence: 0.807810771818182
- $00:58:22.628 \longrightarrow 00:58:24.520$  that patient was a restart.
- NOTE Confidence: 0.807810771818182
- 00:58:24.520 --> 00:58:26.256 I the other ones, I don't know
- NOTE Confidence: 0.807810771818182
- 00:58:26.256 --> 00:58:28.140 for sure, I can't answer.
- NOTE Confidence: 0.807810771818182
- $00:58:28.140 \rightarrow 00:58:31.088$  But these are people that you know
- NOTE Confidence: 0.807810771818182

 $00:58:31.088 \rightarrow 00:58:33.356$  the the way the protocol was written

NOTE Confidence: 0.807810771818182

00:58:33.356 - 00:58:35.780 was patients were supposed to

NOTE Confidence: 0.807810771818182

 $00:58:35.780 \longrightarrow 00:58:38.280$  remain off all oral antidepressant

NOTE Confidence: 0.807810771818182

 $00:58:38.280 \rightarrow 00:58:41.040$  medications or all types of medication

NOTE Confidence: 0.807810771818182

 $00{:}58{:}41.040 \dashrightarrow 00{:}58{:}44.958$  antidepressant treatments from

NOTE Confidence: 0.807810771818182

 $00{:}58{:}44{.}960 \dashrightarrow 00{:}58{:}47{.}678$  baseline through or at least be

NOTE Confidence: 0.807810771818182

 $00{:}58{:}47.678 \dashrightarrow 00{:}58{:}50.857$  at least five half lives prior to

NOTE Confidence: 0.807810771818182

 $00:58:50.857 \rightarrow 00:58:55.200$  dosing until the end of day 4243.

NOTE Confidence: 0.807810771818182

 $00{:}58{:}55{.}200 \dashrightarrow 00{:}58{:}57{.}528$  So that meant they were supposed

NOTE Confidence: 0.807810771818182

 $00:58:57.528 \longrightarrow 00:58:59.982$  to not have any contact with

NOTE Confidence: 0.807810771818182

 $00:58:59.982 \longrightarrow 00:59:02.237$  their therapist or to have

NOTE Confidence: 0.8380440016666667

 $00:59:04.440 \rightarrow 00:59:06.678$  any antidepressant used during that time.

NOTE Confidence: 0.838044001666667

 $00:59:06.680 \longrightarrow 00:59:08.060$  And some people just said

NOTE Confidence: 0.838044001666667

00:59:08.060 --> 00:59:09.440 they couldn't stay that long.

NOTE Confidence: 0.838044001666667

 $00:59:09.440 \rightarrow 00:59:11.960$  It's going six weeks without any treatment.

NOTE Confidence: 0.838044001666667

 $00:59:11.960 \longrightarrow 00:59:14.608$  So I I don't know to answer your

- NOTE Confidence: 0.838044001666667
- $00:59:14.608 \rightarrow 00:59:16.027$  question specifically if these
- NOTE Confidence: 0.838044001666667
- $00:59:16.027 \rightarrow 00:59:17.747$  are people that were restarting
- NOTE Confidence: 0.838044001666667
- $00{:}59{:}17.747 \dashrightarrow 00{:}59{:}19.639$  or starting new ones of fhand.
- NOTE Confidence: 0.838044001666667
- 00:59:19.640 --> 00:59:22.280 And do you, did
- NOTE Confidence: 0.970164023333333
- $00{:}59{:}22{.}280 \dashrightarrow 00{:}59{:}23{.}480$  you account for
- NOTE Confidence: 0.814345113333333
- $00{:}59{:}23.480 \dashrightarrow 00{:}59{:}26.226$  how starting or restarting a
- NOTE Confidence: 0.814345113333333
- $00:59:26.226 \rightarrow 00:59:29.520$  medication affected their outcomes
- NOTE Confidence: 0.8388164
- $00{:}59{:}29{.}520 \dashrightarrow 00{:}59{:}33{.}376$  in terms of how the Mitras was affected
- NOTE Confidence: 0.8388164
- $00:59:33.376 \rightarrow 00:59:36.440$  with those medications? We we do not,
- NOTE Confidence: 0.8388164
- $00:59:36.440 \rightarrow 00:59:38.360$  I I'm sure we can get that data.
- NOTE Confidence: 0.8388164
- $00:59:38.360 \longrightarrow 00:59:39.638$  We don't have that data offhand,
- NOTE Confidence: 0.8388164
- $00{:}59{:}39{.}640 \dashrightarrow 00{:}59{:}42{.}200$  but it's it's probably going to be difficult.
- NOTE Confidence: 0.8388164
- $00{:}59{:}42{.}200$  -->  $00{:}59{:}43{.}892$  I mean it's a small number of people and NOTE Confidence: 0.8388164
- $00:59:43.892 \rightarrow 00:59:46.664$  they, I think all of these people started the
- NOTE Confidence: 0.8388164
- $00:59:46.664 \rightarrow 00:59:48.839$  medication 'cause they weren't feeling well. NOTE Confidence: 0.8388164

- $00:59:48.840 \longrightarrow 00:59:50.864$  So you're going to have a lot of
- NOTE Confidence: 0.8388164
- $00{:}59{:}50{.}864 \dashrightarrow 00{:}59{:}52{.}745$  regression to the mean going on things
- NOTE Confidence: 0.8388164
- $00{:}59{:}52.745 \dashrightarrow 00{:}59{:}54.692$  that I don't think such a small number.
- NOTE Confidence: 0.8388164
- $00:59:54.692 \rightarrow 00:59:55.584$  It's probably not going
- NOTE Confidence: 0.8388164
- $00:59:55.584 \longrightarrow 00:59:56.840$  to be that informative.
- NOTE Confidence: 0.8388164
- $00{:}59{:}56{.}840 \dashrightarrow 00{:}59{:}59{.}960$  All right, thank you.
- NOTE Confidence: 0.8388164
- $00{:}59{:}59{.}960 \dashrightarrow 01{:}00{:}00{.}760$  Thank you.
- NOTE Confidence: 0.8388164
- 01:00:00.760 --> 01:00:02.200 Hey, Jerry, thanks.
- NOTE Confidence: 0.89939721
- $01{:}00{:}02.200 \dashrightarrow 01{:}00{:}04.140$  Thanks for the talk question
- NOTE Confidence: 0.89939721
- $01:00:04.140 \longrightarrow 01:00:07.638$  about the 22% who had previous
- NOTE Confidence: 0.89939721
- $01:00:07.638 \rightarrow 01:00:09.276$  experience with psychedelics.
- NOTE Confidence: 0.89939721
- $01{:}00{:}09{.}280 \dashrightarrow 01{:}00{:}11{.}464$  Was it sensitivity analysis conducted
- NOTE Confidence: 0.89939721
- $01:00:11.464 \rightarrow 01:00:14.840$  where if you took out those 22%, was there
- NOTE Confidence: 0.9693051766666667
- $01:00:14.840 \rightarrow 01:00:18.040$  any change in the responses?
- NOTE Confidence: 0.9693051766666667
- 01:00:18.040 --> 01:00:19.284 Great question.
- NOTE Confidence: 0.9693051766666667
- 01:00:19.284 --> 01:00:22.394 I don't remember seeing that,

- NOTE Confidence: 0.483684598
- $01:00:22.840 \longrightarrow 01:00:24.251$  Ben. I don't think so, no.
- NOTE Confidence: 0.483684598
- $01:00:24.251 \longrightarrow 01:00:26.106$  But that's a really good
- NOTE Confidence: 0.483684598
- $01{:}00{:}26.106 \dashrightarrow 01{:}00{:}28.355$  question to what because that's a
- NOTE Confidence: 0.483684598
- $01:00:28.355 \rightarrow 01:00:29.480$  disproportionately high number.
- NOTE Confidence: 0.483684598
- $01:00:29.480 \longrightarrow 01:00:31.280$  It's something it's above
- NOTE Confidence: 0.483684598
- 01:00:31.280 --> 01:00:33.360 general population as well. So,
- NOTE Confidence: 0.800592818333333
- $01:00:36.240 \longrightarrow 01:00:38.118$  and one would imagine that that
- NOTE Confidence: 0.800592818333333
- $01:00:38.120 \longrightarrow 01:00:40.960$  those 22% would have the highest
- NOTE Confidence: 0.8571466866666667
- $01{:}00{:}40.960 \dashrightarrow 01{:}00{:}43.608$  expectancies and that's why they've
- NOTE Confidence: 0.8571466866666667
- $01{:}00{:}43.608 \dashrightarrow 01{:}00{:}45.750$  taken part in the study and it would be
- NOTE Confidence: 0.8571466866666667
- $01:00:45.750 \rightarrow 01:00:48.413$  interesting to look at that. So go ahead.
- NOTE Confidence: 0.857146686666667
- 01:00:48.413 --> 01:00:50.480 No, I'll let you go first. Yeah.
- NOTE Confidence: 0.901413523
- $01{:}00{:}50.480 \dashrightarrow 01{:}00{:}54.764$  No, I think there's actually a bit of a
- NOTE Confidence: 0.901413523
- $01{:}00{:}54.764 \dashrightarrow 01{:}00{:}56.864$  paradox when it comes to think how we NOTE Confidence: 0.901413523
- $01:00:56.864 \rightarrow 01:00:59.890$  think about the participant participants NOTE Confidence: 0.901413523

 $01:00:59.890 \longrightarrow 01:01:02.853$  who had prior exposure to psilocybin

NOTE Confidence: 0.901413523

 $01:01:02.853 \rightarrow 01:01:04.518$  and psychedelics for that matter.

NOTE Confidence: 0.901413523

01:01:04.520 --> 01:01:08.194 Specifically what I'm getting at is those

NOTE Confidence: 0.901413523

 $01{:}01{:}08{.}194 \dashrightarrow 01{:}01{:}13{.}224$  who actually had prior exposure and ended

NOTE Confidence: 0.901413523

 $01:01:13.224 \rightarrow 01:01:17.360$  up getting either psilocybin or niacin,

NOTE Confidence: 0.901413523

 $01{:}01{:}17{.}360 \dashrightarrow 01{:}01{:}19{.}864$  they had less of AI should say it

NOTE Confidence: 0.901413523

 $01{:}01{:}19.864 \dashrightarrow 01{:}01{:}22.212$  called a disappointment or a let

NOTE Confidence: 0.901413523

 $01:01:22.212 \rightarrow 01:01:24.672$  down and they were less likely.

NOTE Confidence: 0.901413523

01:01:24.680 --> 01:01:27.340 Again, this is just based on my

NOTE Confidence: 0.901413523

 $01{:}01{:}27{.}340 \dashrightarrow 01{:}01{:}30{.}035$  general impression in the from the

NOTE Confidence: 0.901413523

01:01:30.035 --> 01:01:33.296 participants that we worked with to have

NOTE Confidence: 0.901413523

 $01:01:33.296 \rightarrow 01:01:35.612$  an exaggerated response because they

NOTE Confidence: 0.901413523

 $01{:}01{:}35.612 \dashrightarrow 01{:}01{:}39.000$  knew sort of they were already familiar

NOTE Confidence: 0.901413523

 $01{:}01{:}39.085 \dashrightarrow 01{:}01{:}41.900$  with the the effect of psilocybin.

NOTE Confidence: 0.901413523

 $01{:}01{:}41{.}900 \dashrightarrow 01{:}01{:}44{.}995$  So they actually based in this conversation,

NOTE Confidence: 0.901413523

 $01:01:44.995 \rightarrow 01:01:47.130$  they were much more realistic about what

 $01{:}01{:}47{.}184 \dashrightarrow 01{:}01{:}49{.}032$  to expect that they did not come into

NOTE Confidence: 0.901413523

 $01{:}01{:}49{.}032 \dashrightarrow 01{:}01{:}50{.}854$  the study thinking that this was going NOTE Confidence: 0.901413523

 $01{:}01{:}50.854 \dashrightarrow 01{:}01{:}52.582$  to be a Tennessee unlike participants NOTE Confidence: 0.901413523

01:01:52.582 --> 01:01:55.114 with no prior exposure to psilocybin,

NOTE Confidence: 0.901413523

 $01:01:55.120 \rightarrow 01:01:57.538$  their sense of expectancy was really NOTE Confidence: 0.901413523

 $01:01:57.538 \rightarrow 01:02:00.041$  through the roof and we struggled

NOTE Confidence: 0.901413523

 $01{:}02{:}00{.}041 \dashrightarrow 01{:}02{:}02{.}911$  to really bring down that sense of

NOTE Confidence: 0.901413523

 $01{:}02{:}02{.}911 \dashrightarrow 01{:}02{:}04.834$  expectancy which was really being

NOTE Confidence: 0.901413523

01:02:04.834 --> 01:02:07.673 enforced by you know as it's become

NOTE Confidence: 0.901413523

 $01{:}02{:}07.673 \dashrightarrow 01{:}02{:}11.038$  dubbed as the pollen effect.

NOTE Confidence: 0.901413523

 $01:02:11.040 \longrightarrow 01:02:13.536$  Michael Pollan that is.

NOTE Confidence: 0.901413523

01:02:13.536 --> 01:02:18.336 And so it's I think prior exposure

NOTE Confidence: 0.901413523

 $01{:}02{:}18.336 \dashrightarrow 01{:}02{:}22.443$  to psilocybin actually is going to

NOTE Confidence: 0.901413523

01:02:22.443 --> 01:02:24.448 give participants a more realistic

NOTE Confidence: 0.901413523

 $01{:}02{:}24.448 \dashrightarrow 01{:}02{:}26.527$  expectation rather than the ones who

01:02:26.527 --> 01:02:29.108 have not had any prior exposure who are

NOTE Confidence: 0.901413523

 $01{:}02{:}29{.}108 \dashrightarrow 01{:}02{:}31{.}558$  coming in really expecting a silver bullet.

NOTE Confidence: 0.901413523

 $01:02:31.560 \longrightarrow 01:02:33.931$  Like there really are just it's spelled

NOTE Confidence: 0.901413523

 $01:02:33.931 \longrightarrow 01:02:36.157$  silver bullet when they're coming in.

NOTE Confidence: 0.901413523

 $01{:}02{:}36{.}160 \dashrightarrow 01{:}02{:}38{.}998$  Yeah perhaps it perhaps it contributes

NOTE Confidence: 0.901413523

 $01{:}02{:}39{.}000 \dashrightarrow 01{:}02{:}42{.}439$  to lower side effects profile

NOTE Confidence: 0.877725054

 $01{:}02{:}43.040 \dashrightarrow 01{:}02{:}44.280$  because they've had some experience

NOTE Confidence: 0.868966675

 $01:02:44.280 \longrightarrow 01:02:46.000$  with it before it's

NOTE Confidence: 0.784048702857143

 $01{:}02{:}46.200 \dashrightarrow 01{:}02{:}49.035$  that's very likely. Yes I I absolutely.

NOTE Confidence: 0.71114726

01:02:49.720 --> 01:02:52.576 Yeah. So I I actually we've been

NOTE Confidence: 0.71114726

 $01{:}02{:}52{.}576 \dashrightarrow 01{:}02{:}53{.}824$  I hadn't really talked about this

NOTE Confidence: 0.71114726

 $01:02:53.824 \rightarrow 01:02:55.076$  before but I I I agree with Ben.

NOTE Confidence: 0.71114726

 $01{:}02{:}55{.}080 \dashrightarrow 01{:}02{:}57{.}752$  I think in general people came in with

NOTE Confidence: 0.71114726

 $01{:}02{:}57{.}752 \dashrightarrow 01{:}03{:}00{.}110$  such a high level of expectation that

NOTE Confidence: 0.71114726

 $01:03:00.110 \longrightarrow 01:03:02.617$  I'm not sure there was a big difference

NOTE Confidence: 0.71114726

 $01{:}03{:}02{.}617 \dashrightarrow 01{:}03{:}05{.}473$  between the previous exposed and the audit.

- NOTE Confidence: 0.71114726
- 01:03:05.480 --> 01:03:07.083 And if anything, they may have had

01:03:07.083 --> 01:03:08.680 a more realistic expectation. So,

NOTE Confidence: 0.441312625

01:03:12.360 --> 01:03:14.972 hey, Jerry, I have a question for you.

NOTE Confidence: 0.441312625

01:03:14.972 --> 01:03:16.860 You or Ben, You know,

NOTE Confidence: 0.441312625

 $01:03:16.860 \longrightarrow 01:03:18.910$  talking about the issues of

NOTE Confidence: 0.441312625

 $01:03:18.910 \longrightarrow 01:03:20.504$  generalizability and the fact that

NOTE Confidence: 0.441312625

 $01:03:20.504 \rightarrow 01:03:24.000 \text{ most of your population was Caucasian}$ 

NOTE Confidence: 0.441312625

 $01:03:24.000 \rightarrow 01:03:27.531$  what strategies you think may need to

NOTE Confidence: 0.441312625

 $01:03:27.531 \longrightarrow 01:03:30.016$  be done to actually improve on that?

NOTE Confidence: 0.441312625

01:03:30.016 --> 01:03:32.990 I mean is, are these like echoes of Tu<br/>skegee

NOTE Confidence: 0.441312625

 $01:03:32.990 \rightarrow 01:03:37.038$  or what are your thoughts about that?

NOTE Confidence: 0.441312625

 $01{:}03{:}37{.}040 \dashrightarrow 01{:}03{:}39{.}040$  Hey Gerard, first of all great great hearing.

NOTE Confidence: 0.666594638

01:03:41.160 --> 01:03:44.480 I I I think it's you know

NOTE Confidence: 0.666594638

 $01{:}03{:}44{.}480 \dashrightarrow 01{:}03{:}46{.}448$  it's a multi fold issue.

NOTE Confidence: 0.666594638

 $01{:}03{:}46{.}448 \dashrightarrow 01{:}03{:}49{.}616$  I mean it's always difficult getting

 $01:03:49.616 \rightarrow 01:03:51.676$  adequate representation from all

NOTE Confidence: 0.666594638

 $01:03:51.676 \rightarrow 01:03:54.434$  aspects of the you know the population.

NOTE Confidence: 0.666594638

01:03:54.440 --> 01:03:55.780 I think this study was

NOTE Confidence: 0.666594638

 $01:03:55.780 \longrightarrow 01:03:57.120$  unique in some ways that

NOTE Confidence: 0.8844757575

 $01{:}03{:}59{.}280 \dashrightarrow 01{:}04{:}02{.}705$  among certain groups this psyched elics

NOTE Confidence: 0.8844757575

 $01{:}04{:}02{.}705 \dashrightarrow 01{:}04{:}06{.}960$  is much more talked about and much

NOTE Confidence: 0.8844757575

 $01{:}04{:}06{.}960 \dashrightarrow 01{:}04{:}09{.}170$  more seen in a favourable light than

NOTE Confidence: 0.8844757575

 $01:04:09.170 \longrightarrow 01:04:11.439$  than in other groups in the population.

NOTE Confidence: 0.8844757575

01:04:11.440 --> 01:04:13.515 And I think that contributes

NOTE Confidence: 0.8844757575

 $01:04:13.515 \longrightarrow 01:04:14.760$  specifically to this.

NOTE Confidence: 0.8844757575

01:04:14.760 --> 01:04:15.640 But I think, you know,

NOTE Confidence: 0.8844757575

 $01:04:15.640 \rightarrow 01:04:17.832$  obviously having adequate representation

NOTE Confidence: 0.8844757575

 $01{:}04{:}17.832 \dashrightarrow 01{:}04{:}22.239$  is a struggle in in all of medicine.

NOTE Confidence: 0.8844757575

 $01:04:22.240 \longrightarrow 01:04:24.392$  How to how to improve that I I

NOTE Confidence: 0.8844757575

 $01:04:24.392 \rightarrow 01:04:26.318$  think is really to make sure

NOTE Confidence: 0.8677910656666667

 $01{:}04{:}28{.}560 \dashrightarrow 01{:}04{:}30{.}842$  the sites are chosen well that that

 $01:04:30.842 \rightarrow 01:04:32.188$  there's really adequate representation

NOTE Confidence: 0.8677910656666667

 $01{:}04{:}32.188 \dashrightarrow 01{:}04{:}34.924$  at each site and and I don't mean that's

NOTE Confidence: 0.8677910656666667

01:04:34.987 - > 01:04:36.979 going in and just going into an area

NOTE Confidence: 0.867791065666667

 $01{:}04{:}36{.}979 \dashrightarrow 01{:}04{:}39{.}185$  that has an over represented group of

NOTE Confidence: 0.867791065666667

01:04:39.185 --> 01:04:41.893 anywhere but trying to go into groups NOTE Confidence: 0.8677910656666667

 $01:04:41.893 \longrightarrow 01:04:44.238$  that have adequate broad representation.

NOTE Confidence: 0.689564852

 $01{:}04{:}46.880 \dashrightarrow 01{:}04{:}49.399$  And I and I think you know getting

NOTE Confidence: 0.689564852

01:04:49.399 --> 01:04:51.064 realistic information out and getting

NOTE Confidence: 0.689564852

01:04:51.064 --> 01:04:52.925 real patience I mean that I think NOTE Confidence: 0.689564852

 $01:04:52.925 \rightarrow 01:04:54.658$  is going to be that's the thing I've

NOTE Confidence: 0.689564852

01:04:54.658 --> 01:04:56.572 said over and over is you know we're

NOTE Confidence: 0.689564852

 $01{:}04{:}56{.}572 \dashrightarrow 01{:}04{:}58{.}434$  we're going to really need to get

NOTE Confidence: 0.689564852

 $01:04:58.440 \rightarrow 01:05:00.248$  active treatment seeking patients.

NOTE Confidence: 0.689564852

 $01{:}05{:}00{.}248 \dashrightarrow 01{:}05{:}02{.}508$  So people that are responding

NOTE Confidence: 0.689564852

 $01:05:02.508 \rightarrow 01:05:04.211$  specifically for a research study

01:05:04.211 --> 01:05:06.233 already are quite a unique group.

NOTE Confidence: 0.689564852

 $01{:}05{:}06{.}240 \dashrightarrow 01{:}05{:}07{.}452$  So you're going to really want

NOTE Confidence: 0.689564852

 $01:05:07.452 \longrightarrow 01:05:09.014$  to get people that are much more

NOTE Confidence: 0.689564852

 $01:05:09.014 \rightarrow 01:05:10.199$  coming out of clinical settings.

NOTE Confidence: 0.689564852

01:05:10.200 --> 01:05:11.320 So Ben, I don't know.

NOTE Confidence: 0.645885562857143

 $01{:}05{:}11{.}480 \dashrightarrow 01{:}05{:}15{.}297$  Yeah, no I I think Jerry you that covers it.

NOTE Confidence: 0.645885562857143

 $01:05:15.297 \rightarrow 01:05:17.353$  I don't think I have anything to add.

NOTE Confidence: 0.645885562857143

 $01:05:17.360 \longrightarrow 01:05:19.920$  There is actually in our group and I do not

NOTE Confidence: 0.645885562857143

 $01:05:19.920 \rightarrow 01:05:24.040$  want to single out that tan single amount.

NOTE Confidence: 0.645885562857143

 $01:05:24.040 \longrightarrow 01:05:25.885$  I'm going to single him up.

NOTE Confidence: 0.645885562857143

01:05:25.885 --> 01:05:28.810 But who has done a lot of work in

NOTE Confidence: 0.645885562857143

 $01{:}05{:}28.898 \dashrightarrow 01{:}05{:}31.138$  this area and to explore different

NOTE Confidence: 0.645885562857143

 $01{:}05{:}31{.}138 \dashrightarrow 01{:}05{:}34{.}237$  strategies and how is it that we can

NOTE Confidence: 0.645885562857143

01:05:34.237 --> 01:05:37.660 actually improve our recruitment,

NOTE Confidence: 0.645885562857143

 $01:05:37.660 \rightarrow 01:05:40.431$  diversify our recruitment and what sort

NOTE Confidence: 0.645885562857143

 $01{:}05{:}40{.}431 \dashrightarrow 01{:}05{:}42{.}813$  of outreach programs that have been
$01{:}05{:}42.813 \dashrightarrow 01{:}05{:}45.748$  more successful in achieving this goal

NOTE Confidence: 0.645885562857143

 $01{:}05{:}45{.}748 \dashrightarrow 01{:}05{:}48{.}124$  versus some that have been tried and

NOTE Confidence: 0.645885562857143

 $01:05:48.124 \rightarrow 01:05:50.560$  have proven not to be as successful.

NOTE Confidence: 0.645885562857143

 $01{:}05{:}50{.}560 \dashrightarrow 01{:}05{:}54{.}452$  And but you can most definitely look

NOTE Confidence: 0.645885562857143

 $01{:}05{:}54{.}452 \dashrightarrow 01{:}05{:}58{.}957$  up some of his work on Pub Med and

NOTE Confidence: 0.645885562857143

 $01:05:58.960 \longrightarrow 01:06:01.080$  and I think I'll leave it at that,

NOTE Confidence: 0.645885562857143

 $01{:}06{:}01{.}080 \dashrightarrow 01{:}06{:}03{.}600$  but I do not have anything else to add.

NOTE Confidence: 0.56885285

01:06:04.280 --> 01:06:05.318 What Jerry said,

NOTE Confidence: 0.833750174615385

01:06:06.960 --> 01:06:08.360 Jared, do you want to speak to

NOTE Confidence: 0.833750174615385

 $01:06:08.360 \longrightarrow 01:06:10.080$  that at all briefly or not today?

NOTE Confidence: 0.8471053

 $01:06:12.160 \longrightarrow 01:06:16.400$  Thank you for singling me out just really

NOTE Confidence: 0.911767558333333

 $01:06:16.400 \longrightarrow 01:06:20.115$  briefly. I think it is really it's

NOTE Confidence: 0.911767558333333

 $01{:}06{:}20.115 \dashrightarrow 01{:}06{:}23.160$  already so hard to run a clinical

NOTE Confidence: 0.911767558333333

 $01{:}06{:}23.160 \dashrightarrow 01{:}06{:}26.000$  trial navigating all of the regulatory

NOTE Confidence: 0.911767558333333

 $01:06:26.000 \rightarrow 01:06:28.200$  demands and everything on top of what

 $01:06:28.200 \rightarrow 01:06:30.260$  needs to be done in the study itself

NOTE Confidence: 0.911767558333333

 $01{:}06{:}30{.}260 \dashrightarrow 01{:}06{:}32{.}620$  that it requires tremendous effort.

NOTE Confidence: 0.911767558333333

 $01:06:32.620 \longrightarrow 01:06:35.740$  On top of all of that to conduct

NOTE Confidence: 0.911767558333333

01:06:35.740 --> 01:06:37.280 really intensive outreach

NOTE Confidence: 0.911767558333333

 $01{:}06{:}37{.}280 \dashrightarrow 01{:}06{:}40{.}542$  efforts to communities of color,

NOTE Confidence: 0.911767558333333

 $01:06:40.542 \rightarrow 01:06:42.186$  particularly the black and

NOTE Confidence: 0.911767558333333

 $01:06:42.186 \longrightarrow 01:06:44.320$  brown population in New Haven.

NOTE Confidence: 0.781737085

01:06:46.720 --> 01:06:48.190 You know, just really pointing to

NOTE Confidence: 0.781737085

 $01{:}06{:}48.190 \dashrightarrow 01{:}06{:}50.000$  the cultural ambass adors program.

NOTE Confidence: 0.781737085

 $01:06:50.000 \longrightarrow 01:06:54.000$  We've been in touch with them,

NOTE Confidence: 0.781737085

01:06:54.000 --> 01:06:55.916 Jordan, Jordan Slowshower is also

NOTE Confidence: 0.781737085

 $01{:}06{:}55{.}916 \dashrightarrow 01{:}06{:}57{.}862$  on this call and we've had a

NOTE Confidence: 0.781737085

 $01:06:57.862 \rightarrow 01:06:59.959$  couple of conversations with them.

NOTE Confidence: 0.781737085

 $01:06:59.960 \longrightarrow 01:07:01.120$  They've never done anything

NOTE Confidence: 0.781737085

 $01{:}07{:}01{.}120 \dashrightarrow 01{:}07{:}02{.}560$  psychedelic related.

NOTE Confidence: 0.781737085

 $01:07:02.560 \longrightarrow 01:07:04.056$  So it's all just going to

- NOTE Confidence: 0.781737085
- $01:07:04.056 \longrightarrow 01:07:05.996$  be new frontiers for us.
- NOTE Confidence: 0.781737085
- $01:07:06.000 \longrightarrow 01:07:08.198$  It's worth the effort,
- NOTE Confidence: 0.781737085
- $01:07:08.200 \longrightarrow 01:07:11.373$  but have haven't worked on an
- NOTE Confidence: 0.781737085
- 01:07:11.373 --> 01:07:14.438 MDMA trial looking to exclusively
- NOTE Confidence: 0.781737085
- $01:07:14.440 \longrightarrow 01:07:16.546$  recruit by POC participants.
- NOTE Confidence: 0.781737085
- 01:07:16.546 --> 01:07:18.678 I can say that
- NOTE Confidence: 0.8552270525
- $01:07:19.440 \longrightarrow 01:07:21.840$  it it really is a very
- NOTE Confidence: 0.8552270525
- $01:07:21.840 \longrightarrow 01:07:23.078$  tremendous effort that is
- NOTE Confidence: 0.60940523
- $01:07:23.080 \longrightarrow 01:07:24.559$  required to to
- NOTE Confidence: 0.952292257142857
- $01:07:24.560 \longrightarrow 01:07:27.710$  even bring people into the consent
- NOTE Confidence: 0.952292257142857
- $01:07:27.710 \longrightarrow 01:07:29.360$  call to run through screening
- NOTE Confidence: 0.952292257142857
- $01{:}07{:}29{.}360 \dashrightarrow 01{:}07{:}30{.}690$  procedures with them because
- NOTE Confidence: 0.952292257142857
- $01:07:30.690 \rightarrow 01:07:32.440$  there's just so many considerations
- NOTE Confidence: 0.9290262666666667
- $01{:}07{:}32{.}440 \dashrightarrow 01{:}07{:}33{.}358$  that people have
- NOTE Confidence: 0.959145885
- $01:07:33.880 \longrightarrow 01:07:36.640$  about completing the trial.
- NOTE Confidence: 0.959145885

 $01:07:36.640 \longrightarrow 01:07:38.760$  So all of these are worthwhile issues

NOTE Confidence: 0.9759234

 $01{:}07{:}38.760 \dashrightarrow 01{:}07{:}42.160$  to think about that I think you know

NOTE Confidence: 0.8412093166666667

 $01:07:42.200 \longrightarrow 01:07:44.396$  it. If the team is aligned

NOTE Confidence: 0.8865914566666667

 $01:07:44.960 \longrightarrow 01:07:45.758$  in making this

NOTE Confidence: 0.971988522

 $01{:}07{:}45.760 \dashrightarrow 01{:}07{:}48.728$  work, I think we can move the needle

NOTE Confidence: 0.971988522

 $01{:}07{:}48.728$  -->  $01{:}07{:}50.156$  on making sure that we have more

NOTE Confidence: 0.971988522

 $01{:}07{:}50{.}160 \dashrightarrow 01{:}07{:}51{.}640$  diverse samples moving forward.

NOTE Confidence: 0.6524430525

01:07:54.120 --> 01:07:56.739 Jerry, I had a Jerry and Ben I had

NOTE Confidence: 0.6524430525

 $01{:}07{:}56.739 \dashrightarrow 01{:}07{:}58.880$  a question about generalizability.

NOTE Confidence: 0.87500643

 $01{:}07{:}58.880 \dashrightarrow 01{:}07{:}59.712$  So all these patients

NOTE Confidence: 0.87500643

 $01{:}07{:}59{.}712 \dashrightarrow 01{:}08{:}01{.}160$  were off antidepressants.

NOTE Confidence: 0.937361836

 $01{:}08{:}01{.}600 \dashrightarrow 01{:}08{:}04{.}660$  How compelling is the data that

NOTE Confidence: 0.937361836

 $01:08:04.660 \rightarrow 01:08:06.430$  antidepressants would interfere

NOTE Confidence: 0.937361836

 $01:08:06.430 \longrightarrow 01:08:08.320$  with the effects of these drugs?

NOTE Confidence: 0.937361836

 $01{:}08{:}08{.}320 \dashrightarrow 01{:}08{:}11{.}296$  And in future trials is the

NOTE Confidence: 0.937361836

01:08:11.296 --> 01:08:13.000 FDA going to, you know,

01:08:13.400 --> 01:08:17.640 allow patients who are taking antidepressants

NOTE Confidence: 0.949613468

01:08:17.640 --> 01:08:20.226 participate in studies with with the

NOTE Confidence: 0.949613468

 $01:08:20.226 \rightarrow 01:08:21.680$  serotoninergic psych psychedelics?

NOTE Confidence: 0.6478982766666667

 $01:08:23.320 \longrightarrow 01:08:23.719$  It's a really

NOTE Confidence: 0.919367392

 $01{:}08{:}23.720 \dashrightarrow 01{:}08{:}27.363$  good question and I think there is some

NOTE Confidence: 0.919367392

 $01{:}08{:}27.363 \dashrightarrow 01{:}08{:}30.750$  work being done in this area to explore

NOTE Confidence: 0.919367392

 $01{:}08{:}30.750 \dashrightarrow 01{:}08{:}35.320$  the extent to which the presence of

NOTE Confidence: 0.919367392

 $01:08:35.320 \rightarrow 01:08:38.300$  antidepressants at the time of dosing

NOTE Confidence: 0.919367392

01:08:38.300 --> 01:08:42.834 versus a six week follow up versus 5

NOTE Confidence: 0.919367392

 $01:08:42.834 \rightarrow 01:08:46.224$  half life paper is impacting outcome.

NOTE Confidence: 0.919367392

 $01{:}08{:}46{.}224 \dashrightarrow 01{:}08{:}49{.}560$  I think in this particular study

NOTE Confidence: 0.919367392

01:08:49.658 --> 01:08:53.852 Particip I many participants did not.

NOTE Confidence: 0.919367392

 $01{:}08{:}53.852 \dashrightarrow 01{:}08{:}55.236$  We're not an antidepressants.

NOTE Confidence: 0.919367392

 $01{:}08{:}55{.}240 \dashrightarrow 01{:}08{:}57{.}354$  And the ones that were on antidepressants,

NOTE Confidence: 0.919367392

 $01:08:57.360 \rightarrow 01:09:00.741$  they were actually tapered and they had

- $01:09:00.741 \rightarrow 01:09:03.560$  to have been off of antidepressants,
- NOTE Confidence: 0.919367392
- 01:09:03.560 --> 01:09:08.600 fully tapered for six weeks prior to
- NOTE Confidence: 0.670358304
- $01:09:10.880 \longrightarrow 01:09:12.032$  baseline rating.
- NOTE Confidence: 0.670358304
- $01:09:12.032 \longrightarrow 01:09:14.510$  I believe it's five half lives.
- NOTE Confidence: 0.670358304
- $01:09:14.510 \longrightarrow 01:09:16.480$  Five half lives, five half lives.
- NOTE Confidence: 0.670358304
- $01{:}09{:}16{.}480 \dashrightarrow 01{:}09{:}19{.}626$  So, yeah, so there's basic and
- NOTE Confidence: 0.670358304
- $01:09:19.626 \rightarrow 01:09:22.356$  recently there's been a paper
- NOTE Confidence: 0.670358304
- $01:09:22.356 \rightarrow 01:09:25.186$  that has and more specifically,
- NOTE Confidence: 0.670358304
- $01{:}09{:}25.186 \dashrightarrow 01{:}09{:}28.724$  there is a a company that's received,
- NOTE Confidence: 0.670358304
- 01:09:28.724 --> 01:09:30.276 I believe mind Mendapatent,
- NOTE Confidence: 0.670358304
- $01:09:30.280 \longrightarrow 01:09:32.160$  where they actually are used
- NOTE Confidence: 0.670358304
- $01:09:32.160 \rightarrow 01:09:36.850$  using psilocybin with Lexapro to
- NOTE Confidence: 0.670358304
- $01:09:36.850 \longrightarrow 01:09:39.100$  enhance the effect of psilocybin
- NOTE Confidence: 0.670358304
- $01:09:39.100 \longrightarrow 01:09:41.600$  by minimizing its side effects.
- NOTE Confidence: 0.670358304
- $01:09:41.600 \rightarrow 01:09:43.520$  And so there is some preliminary
- NOTE Confidence: 0.670358304
- $01:09:43.520 \rightarrow 01:09:45.193$  data showing that the presence

- NOTE Confidence: 0.670358304
- 01:09:45.193 --> 01:09:48.505 of SSRI in fact might actually
- NOTE Confidence: 0.670358304
- 01:09:48.505 --> 01:09:52.089 enhance the effect of psilocybin by
- NOTE Confidence: 0.670358304
- $01:09:52.089 \rightarrow 01:09:54.760$  mitigating some of the side effects.
- NOTE Confidence: 0.670358304
- $01:09:54.760 \rightarrow 01:09:56.800$  But that is just very clear.
- NOTE Confidence: 0.670358304
- 01:09:56.800 --> 01:09:59.400 But it does go back to your question,
- NOTE Confidence: 0.670358304
- $01{:}09{:}59{.}400 \dashrightarrow 01{:}10{:}02{.}324$  Doctor Sousa and that is we do
- NOTE Confidence: 0.670358304
- $01:10:02.324 \rightarrow 01:10:04.256$  not to say that actually patients
- NOTE Confidence: 0.670358304
- $01:10:04.256 \longrightarrow 01:10:06.200$  should be off of SSR is to
- NOTE Confidence: 0.670358304
- $01:10:06.200 \longrightarrow 01:10:07.320$  participate in these studies.
- NOTE Confidence: 0.670358304
- $01{:}10{:}07{.}320 \dashrightarrow 01{:}10{:}13{.}072$  I think that is not any more supported.
- NOTE Confidence: 0.670358304
- 01:10:13.072 --> 01:10:15.358 And it's also the COMPASS
- NOTE Confidence: 0.670358304
- $01:10:15.360 \longrightarrow 01:10:17.000$  and the COMPASS open label.
- NOTE Confidence: 0.670358304
- 01:10:17.000 --> 01:10:17.630 That's right.
- NOTE Confidence: 0.670358304
- 01:10:17.630 $\operatorname{-->}$ 01:10:19.960 So there's been a couple of studies and
- NOTE Confidence: 0.758118894
- $01:10:20.440 \longrightarrow 01:10:21.260$  there are two different.
- NOTE Confidence: 0.758118894

01:10:21.260 --> 01:10:22.982 I mean you said that that having Lexapro

NOTE Confidence: 0.758118894

 $01{:}10{:}22{.}982 \dashrightarrow 01{:}10{:}24{.}758$  on board at the time may not interfere,

NOTE Confidence: 0.758118894

 $01{:}10{:}24.760 \dashrightarrow 01{:}10{:}26.794$  may actually enhance, but that's a

NOTE Confidence: 0.758118894

 $01{:}10{:}26.794 \dashrightarrow 01{:}10{:}28.640$  very different question from chronic.

NOTE Confidence: 0.758118894

 $01:10:28.640 \rightarrow 01:10:29.835$  There's evidence from animal studies NOTE Confidence: 0.758118894

 $01{:}10{:}29.835 \dashrightarrow 01{:}10{:}31.926$  and I think this is where some of the NOTE Confidence: 0.758118894

 $01:10:31.926 \rightarrow 01:10:33.465$  thinking came from that you need to NOTE Confidence: 0.758118894

 $01:10:33.465 \rightarrow 01:10:34.956$  be off is edited from animal studies.

NOTE Confidence: 0.758118894

 $01{:}10{:}34{.}960 \dashrightarrow 01{:}10{:}37{.}104$  The chronic SSRI use leads to a down NOTE Confidence: 0.758118894

 $01{:}10{:}37{.}104 \dashrightarrow 01{:}10{:}38{.}719$  regulation of the two a receptor.

NOTE Confidence: 0.758118894

01:10:38.720 --> 01:10:41.520 That's right. And so it may,

NOTE Confidence: 0.758118894

 $01:10:41.520 \rightarrow 01:10:43.440$  which is a different question from

NOTE Confidence: 0.758118894

 $01{:}10{:}43.440 \dashrightarrow 01{:}10{:}44.868$  what's the effect of having an SSRI

NOTE Confidence: 0.758118894

 $01:10:44.868 \rightarrow 01:10:46.360$  on board at the time of dosing.

NOTE Confidence: 0.758118894

 $01:10:46.360 \longrightarrow 01:10:48.208$  Yeah. So the five half lives is

NOTE Confidence: 0.758118894

 $01{:}10{:}48.208 \dashrightarrow 01{:}10{:}50.034$  calculated to make sure it's out of

- NOTE Confidence: 0.758118894
- $01:10:50.034 \rightarrow 01:10:51.780$  the system so that there's no SSRI

 $01{:}10{:}51{.}780 \dashrightarrow 01{:}10{:}53{.}040$  on board at the time of dosing.

NOTE Confidence: 0.758118894

 $01:10:53.040 \rightarrow 01:10:54.714$  But that may not be enough time to reverse

NOTE Confidence: 0.758118894

 $01:10:54.714 \rightarrow 01:10:56.517$  the down regulation of the two A receptors.

NOTE Confidence: 0.758118894

 $01:10:56.520 \longrightarrow 01:10:57.360$  So two different.

NOTE Confidence: 0.758118894

 $01{:}10{:}57.360 \dashrightarrow 01{:}10{:}59.040$  And then the third mechanistic concern

NOTE Confidence: 0.758118894

01:10:59.040 --> 01:11:00.455 I've heard is seroton<br/>in syndrome

NOTE Confidence: 0.758118894

01:11:00.455 - 01:11:02.081 as a risk of serotonin syndrome

NOTE Confidence: 0.758118894

 $01{:}11{:}02{.}129 \dashrightarrow 01{:}11{:}03{.}802$  that I think is overblown and I've

NOTE Confidence: 0.758118894

01:11:03.802 --> 01:11:05.660 seen that's right to suggest that,

NOTE Confidence: 0.758118894

 $01:11:05.660 \longrightarrow 01:11:07.160$  that's a realistic concern.

NOTE Confidence: 0.758118894

 $01{:}11{:}07{.}160 \dashrightarrow 01{:}11{:}08{.}680$  But those are kind of the three different.

NOTE Confidence: 0.611833374

01:11:08.720 --> 01:11:10.600 Yeah, I I mean, I

NOTE Confidence: 0.844377282

 $01:11:10.600 \longrightarrow 01:11:13.040$  think this is a major,

NOTE Confidence: 0.844377282

01:11:13.040 --> 01:11:14.760 I mean this is going to be a big issue

 $01:11:14.806 \rightarrow 01:11:16.112$  moving forward in implementation.

NOTE Confidence: 0.844377282

 $01:11:16.112 \longrightarrow 01:11:19.440$  This is going to be a big deal exactly

NOTE Confidence: 0.844377282

01:11:19.440 --> 01:11:21.720 in generalizability too. Yeah.

NOTE Confidence: 0.844377282

01:11:21.720 --> 01:11:24.052 Yeah, yeah, You know, I think this,

NOTE Confidence: 0.844377282

01:11:24.052 --> 01:11:27.790 I mean my take on it is, you know,

NOTE Confidence: 0.844377282

 $01{:}11{:}27.790 \dashrightarrow 01{:}11{:}29.995$  it's really the lore in the fields.

NOTE Confidence: 0.844377282

01:11:30.000 --> 01:11:31.152 I I think the studies will

NOTE Confidence: 0.844377282

 $01:11:31.152 \longrightarrow 01:11:32.479$  have to be done to test it.

NOTE Confidence: 0.844377282

 $01{:}11{:}32{.}480 \dashrightarrow 01{:}11{:}35{.}312$  There is the preclinical data that

NOTE Confidence: 0.844377282

01:11:35.312 --> 01:11:37.959 suggests that maybe but and now there's

NOTE Confidence: 0.844377282

01:11:37.960 --> 01:11:39.164 exactly companies are in an open label

NOTE Confidence: 0.844377282

01:11:39.164 --> 01:11:40.477 city where it didn't seem to make and

NOTE Confidence: 0.64826884625

 $01:11:40.560 \longrightarrow 01:11:42.320$  if it is a 2A down regulation issue,

NOTE Confidence: 0.64826884625

01:11:42.320 --> 01:11:44.110 it may just be an issue of dose, maybe you

NOTE Confidence: 0.64826884625

 $01:11:44.110 \longrightarrow 01:11:46.040$  need a slightly higher dose and that's

NOTE Confidence: 0.521396071

 $01{:}11{:}47.200 \dashrightarrow 01{:}11{:}50.688$  so the pre the preclinical date on down

- NOTE Confidence: 0.521396071
- 01:11:50.688 --> 01:11:53.480 regulation of 2A receptors preclinically
- NOTE Confidence: 0.521396071
- $01{:}11{:}53{.}480 \dashrightarrow 01{:}11{:}55{.}480$  is actually really quite spotty.
- NOTE Confidence: 0.521396071
- $01:11:55.480 \longrightarrow 01:11:58.740$  There's really and is down regulation
- NOTE Confidence: 0.521396071
- $01:11:58.740 \rightarrow 01:12:01.290$  really meaningful or are there alter
- NOTE Confidence: 0.521396071
- $01:12:01.369 \rightarrow 01:12:04.399$  other alterations in 2A receptor function?
- NOTE Confidence: 0.521396071
- 01:12:04.400 --> 01:12:06.650 I looked at, I looked at it once in a
- NOTE Confidence: 0.521396071
- $01{:}12{:}06.650 \dashrightarrow 01{:}12{:}08.692$  very small population of that's and
- NOTE Confidence: 0.521396071
- $01{:}12{:}08.692 \dashrightarrow 01{:}12{:}10.990$  I saw absolutely nothing with them
- NOTE Confidence: 0.521396071
- $01:12:11.060 \rightarrow 01:12:14.320$  getting reasonable exposures of an SSRI.
- NOTE Confidence: 0.521396071
- 01:12:14.320 --> 01:12:16.360 So it's, it's questionable I think.
- NOTE Confidence: 0.77581198
- 01:12:16.560 --> 01:12:17.436 Yeah. Thank you, Jerry.
- NOTE Confidence: 0.77581198
- 01:12:17.436 --> 01:12:18.750 It's like it's like 2 papers
- NOTE Confidence: 0.77581198
- 01:12:18.799 --> 01:12:20.080 from 20 years ago. Yeah, that's
- NOTE Confidence: 0.73265141375
- $01{:}12{:}21{.}320 \dashrightarrow 01{:}12{:}23{.}480$  right. I mean this is something I think
- NOTE Confidence: 0.73265141375
- $01:12:23.480 \longrightarrow 01:12:25.626$  that feels it's like all of all of,
- NOTE Confidence: 0.73265141375

01:12:25.626 --> 01:12:26.718 you know, biomedical science,

NOTE Confidence: 0.73265141375

 $01:12:26.720 \longrightarrow 01:12:28.560$  but especially in this area,

NOTE Confidence: 0.73265141375

 $01{:}12{:}28.560 \dashrightarrow 01{:}12{:}30.954$  there's a lot of war that's hard to overcome.

NOTE Confidence: 0.73265141375

01:12:30.960 --> 01:12:33.148 I mean this is things, you know,

NOTE Confidence: 0.73265141375

 $01{:}12{:}33.148 \dashrightarrow 01{:}12{:}35.512$  people have been doing this since

NOTE Confidence: 0.73265141375

 $01:12:35.512 \rightarrow 01:12:38.712$  the 1950s and to try to to try to

NOTE Confidence: 0.73265141375

 $01:12:38.712 \longrightarrow 01:12:40.936$  change that with data requires data.

NOTE Confidence: 0.73265141375

01:12:40.936 --> 01:12:44.200 So, and I I do respect that companies

NOTE Confidence: 0.73265141375

01:12:44.284 --> 01:12:47.374 being nervous about jumping right into

NOTE Confidence: 0.73265141375

 $01:12:47.374 \longrightarrow 01:12:50.480$  those studies first, first prove,

NOTE Confidence: 0.73265141375

 $01{:}12{:}50{.}480 \dashrightarrow 01{:}12{:}52{.}280$  you know, proof of concept under those

NOTE Confidence: 0.73265141375

 $01{:}12{:}52{.}280 \dashrightarrow 01{:}12{:}53{.}880$  conditions and then going forward.

NOTE Confidence: 0.73265141375

01:12:53.880 --> 01:12:55.750 But I agree with you.

NOTE Confidence: 0.73265141375

01:12:55.750 --> 01:12:57.160 Yeah, I think and

NOTE Confidence: 0.80547798

 $01{:}12{:}58{.}960 \dashrightarrow 01{:}13{:}03{.}400$  not too dissimilar from the REMS that

NOTE Confidence: 0.80547798

 $01:13:03.400 \rightarrow 01:13:06.396$  was eventually was attached to the label.

- NOTE Confidence: 0.80547798
- $01:13:06.400 \longrightarrow 01:13:08.308$  As for Avada, where if patients
- NOTE Confidence: 0.80547798
- 01:13:08.308 --> 01:13:11.443 did not at the time of dosing with
- NOTE Confidence: 0.80547798
- $01{:}13{:}11{.}443 \dashrightarrow 01{:}13{:}13{.}673$  Astravada were not on antidepressants,
- NOTE Confidence: 0.80547798
- $01:13:13.680 \rightarrow 01:13:17.238$  they had to start an antidepressant.
- NOTE Confidence: 0.80547798
- $01{:}13{:}17{.}240 \dashrightarrow 01{:}13{:}20{.}920$  And I would not be surprised to that if NOTE Confidence: 0.80547798
- $01{:}13{:}20{.}920 \dashrightarrow 01{:}13{:}24{.}404$  the data begins to show that the Pres
- NOTE Confidence: 0.80547798
- $01:13:24.404 \rightarrow 01:13:26.400$  adding an antidepressant before dosing,
- NOTE Confidence: 0.80547798
- $01:13:26.400 \longrightarrow 01:13:29.871$  whether it is for treatment issues
- NOTE Confidence: 0.80547798
- 01:13:29.871 --> 01:13:34.008 or to have something on board when
- NOTE Confidence: 0.80547798
- 01:13:34.008 --> 01:13:36.785 psilocybin wears off or to really
- NOTE Confidence: 0.80547798
- 01:13:36.785 --> 01:13:39.155 just minimize some of the adverse
- NOTE Confidence: 0.80547798
- $01{:}13{:}39{.}155 \dashrightarrow 01{:}13{:}41{.}640$  events associated with psilocybin.
- NOTE Confidence: 0.80547798
- 01:13:41.640 --> 01:13:44.144 I would not be surprised that we will
- NOTE Confidence: 0.80547798
- 01:13:44.144 $\operatorname{-->}$ 01:13:46.479 be seeing more of those studies in
- NOTE Confidence: 0.80547798
- $01:13:46.479 \rightarrow 01:13:48.922$  the next couple of years to really
- NOTE Confidence: 0.80547798

 $01:13:48.922 \rightarrow 01:13:50.772$  either optimize the treatment or

NOTE Confidence: 0.80547798

 $01:13:50.772 \rightarrow 01:13:54.354$  sort of provide an antidepressant

NOTE Confidence: 0.80547798

01:13:54.354 --> 01:13:57.198 on board as a safety mechanism.

NOTE Confidence: 0.882593879130435

01:14:00.680 --> 01:14:02.010 I do want to put in a plug to the

NOTE Confidence: 0.882593879130435

01:14:02.053 --> 01:14:03.183 issue of the regulatory framework

NOTE Confidence: 0.882593879130435

 $01:14:03.183 \rightarrow 01:14:04.880$  and what this is going to look like.

NOTE Confidence: 0.882593879130435

01:14:04.880 --> 01:14:06.672 Will there be a Rams and so forth

NOTE Confidence: 0.882593879130435

01:14:06.672 --> 01:14:08.373 has come up several times at

NOTE Confidence: 0.882593879130435

 $01:14:08.373 \rightarrow 01:14:10.038$  this seminar time in February.

NOTE Confidence: 0.882593879130435

 $01:14:10.040 \longrightarrow 01:14:12.400$  We're going to have a panel of folks

NOTE Confidence: 0.882593879130435

 $01{:}14{:}12{.}400 \dashrightarrow 01{:}14{:}13{.}969$  discussing precisely that issue including

NOTE Confidence: 0.882593879130435

01:14:13.969 --> 01:14:16.111 two folks whose names I don't remember

NOTE Confidence: 0.882593879130435

01:14:16.166 --> 01:14:18.122 off the top of my head, Sean Bulan.

NOTE Confidence: 0.882593879130435

 $01{:}14{:}18{.}122 \dashrightarrow 01{:}14{:}20{.}027$  But leaders from the Department

NOTE Confidence: 0.882593879130435

 $01:14:20.027 \rightarrow 01:14:22.239$  of Health and Human Services,

NOTE Confidence: 0.882593879130435

 $01:14:22.240 \longrightarrow 01:14:24.103$  who are the people who are going to be

 $01:14:24.103 \rightarrow 01:14:25.756$  running the process of developing this,

NOTE Confidence: 0.882593879130435

 $01:14:25.760 \rightarrow 01:14:28.256$  as well as Jerry and a couple other

NOTE Confidence: 0.882593879130435

 $01:14:28.256 \longrightarrow 01:14:30.146$  discussions from from a couple

NOTE Confidence: 0.882593879130435

 $01{:}14{:}30{.}146 \dashrightarrow 01{:}14{:}32{.}640$  universities across the country who are

NOTE Confidence: 0.882593879130435

 $01:14:32.640 \rightarrow 01:14:34.640$  thinking deeply about these issues.

NOTE Confidence: 0.882593879130435

 $01{:}14{:}34{.}640 \dashrightarrow 01{:}14{:}36{.}524$  There's a call for commentary open

NOTE Confidence: 0.882593879130435

 $01:14:36.524 \rightarrow 01:14:38.908$  right now from the Department of Health

NOTE Confidence: 0.882593879130435

01:14:38.908 --> 01:14:41.038 and Human Services asking for people

NOTE Confidence: 0.882593879130435

 $01:14:41.038 \longrightarrow 01:14:43.358$  in the field to put in information,

NOTE Confidence: 0.882593879130435

 $01:14:43.360 \rightarrow 01:14:45.760$  questions and concerns on these issues.

NOTE Confidence: 0.882593879130435

 $01:14:45.760 \longrightarrow 01:14:46.980$  And we've timed that round

NOTE Confidence: 0.882593879130435

01:14:46.980 --> 01:14:47.956 table discussion in February.

NOTE Confidence: 0.882593879130435

 $01:14:47.960 \longrightarrow 01:14:49.093$  So it'll be shortly before

NOTE Confidence: 0.882593879130435

01:14:49.093 --> 01:14:50.788 the close of that call.

NOTE Confidence: 0.882593879130435

 $01:14:50.788 \longrightarrow 01:14:53.000$  So there will be discussion of the,

 $01:14:53.000 \longrightarrow 01:14:54.519$  you know the the in the early.

NOTE Confidence: 0.882593879130435

 $01:14:54.520 \longrightarrow 01:14:56.506$  I think it's the first public

NOTE Confidence: 0.882593879130435

 $01:14:56.506 \rightarrow 01:14:57.904$  synthesis of the information that

NOTE Confidence: 0.882593879130435

 $01{:}14{:}57{.}904 \dashrightarrow 01{:}15{:}00{.}159$  has come in over the next two months.

NOTE Confidence: 0.882593879130435

 $01{:}15{:}00{.}160 \dashrightarrow 01{:}15{:}02{.}848$  And then after that there will be still

NOTE Confidence: 0.882593879130435

 $01{:}15{:}02.848 \dashrightarrow 01{:}15{:}05.648$  another week I think to where one can can,

NOTE Confidence: 0.882593879130435

 $01{:}15{:}05{.}648 \dashrightarrow 01{:}15{:}07{.}184$  where where folks can after hearing

NOTE Confidence: 0.882593879130435

 $01:15:07.184 \rightarrow 01:15:08.680$  that discussion continue to put

NOTE Confidence: 0.882593879130435

 $01:15:08.680 \longrightarrow 01:15:10.160$  in information on that call.

NOTE Confidence: 0.882593879130435

 $01:15:10.160 \rightarrow 01:15:11.600$  So I think it'll be and we're going

NOTE Confidence: 0.882593879130435

 $01:15:11.600 \longrightarrow 01:15:12.599$  to advertise this nationally.

NOTE Confidence: 0.882593879130435

 $01:15:12.600 \rightarrow 01:15:14.822$  I think it's going to be an important event.

NOTE Confidence: 0.882593879130435

 $01{:}15{:}14.822 \dashrightarrow 01{:}15{:}16.920$  So I just want to put in the plug for that.

NOTE Confidence: 0.882593879130435

 $01:15:16.920 \longrightarrow 01:15:18.355$  It'll be at the usual time the,

NOTE Confidence: 0.882593879130435

 $01{:}15{:}18.360 \dashrightarrow 01{:}15{:}21.797$  you know, the the third Friday in

NOTE Confidence: 0.882593879130435

01:15:21.797 --> 01:15:24.120 February publicity going out soon.

- NOTE Confidence: 0.882593879130435
- $01{:}15{:}24{.}120 \dashrightarrow 01{:}15{:}24{.}600$  OK, That's right.
- NOTE Confidence: 0.882593879130435
- $01:15:25.120 \longrightarrow 01:15:26.640$  Well,
- NOTE Confidence: 0.7285724916666667
- 01:15:26.640 --> 01:15:29.464 OK, just all right.
- NOTE Confidence: 0.7285724916666667
- $01:15:29.464 \rightarrow 01:15:32.839$  Any other any other questions?
- NOTE Confidence: 0.893077625714286
- $01{:}15{:}34{.}560 \dashrightarrow 01{:}15{:}36{.}648$  What's on the horizon for the
- NOTE Confidence: 0.893077625714286
- 01:15:36.648 --> 01:15:42.480 Yasona program? So. So I think
- NOTE Confidence: 0.839974988947368
- $01:15:44.880 \longrightarrow 01:15:46.856$  clearly it is a plan for a phase
- NOTE Confidence: 0.839974988947368
- $01:15:46.856 \rightarrow 01:15:48.365$  three study that hopefully will
- NOTE Confidence: 0.839974988947368
- $01:15:48.365 \longrightarrow 01:15:50.273$  be underway in the near future.
- NOTE Confidence: 0.8338018225
- $01{:}15{:}53{.}520 \dashrightarrow 01{:}15{:}56{.}480$  So the the goal is to move forward. Yeah.
- NOTE Confidence: 0.6366484
- 01:15:59.000 --> 01:16:01.626 OK. Chris, anything else?
- NOTE Confidence: 0.6366484
- 01:16:01.626 --> 01:16:02.520 Anything else? Yeah.
- NOTE Confidence: 0.677138975
- 01:16:02.800 --> 01:16:03.360 Thank you both. Thank
- NOTE Confidence: 0.677138975
- $01{:}16{:}03{.}360 \dashrightarrow 01{:}16{:}06{.}000$  you all. Thank you. By e.