WEBVTT

NOTE duration: ”00:43:02.000”

NOTE Confidence: 0.887178

00:00:00.399 --> 00:00:02.159 That's important that is important

NOTE Confidence: 0.887178

00:00:02.159 --> 00:00:03.220 in this application

NOTE Confidence: 0.97782373

00:00:03.840 --> 00:00:05.859 because there are no untreated

NOTE Confidence: 0.87642187

00:00:06.399 --> 00:00:09.059 outcome data in humans or

NOTE Confidence: 0.87642187

00:00:09.200 --> 00:00:11.039 alpha desperate that is the

NOTE Confidence: 0.87642187

00:00:11.039 --> 00:00:12.240 treatment that I will be

NOTE Confidence: 0.87642187

00:00:12.240 --> 00:00:13.139 talking about.

NOTE Confidence: 0.8365413

00:00:13.505 --> 00:00:15.425 Because alpha despa is still

NOTE Confidence: 0.8365413

00:00:15.425 --> 00:00:16.485 in its preclinical

NOTE Confidence: 0.91785073

00:00:16.864 --> 00:00:17.364 phase.

NOTE Confidence: 0.956595

00:00:17.665 --> 00:00:18.945 It has been tried out

NOTE Confidence: 0.956595

00:00:18.945 --> 00:00:20.704 in mice. It works really

NOTE Confidence: 0.956595

00:00:20.704 --> 00:00:22.305 well in mice, and it

NOTE Confidence: 0.956595

00:00:22.305 --> 00:00:23.904 has also been tried out

NOTE Confidence: 0.956595

00:00:23.904 --> 00:00:26.165 on petri dishes, these little

NOTE Confidence: 0.93178463

00:00:26.850 --> 00:00:28.370 plastic thingies that they mess

NOTE Confidence: 0.93178463

00:00:28.370 --> 00:00:29.670 around with in the lab,

NOTE Confidence: 0.93178463

00:00:29.810 --> 00:00:31.670 works very well there too.

NOTE Confidence: 0.93178463

00:00:31.730 --> 00:00:33.190 But there is no authorization

NOTE Confidence: 0.94887656

00:00:34.530 --> 00:00:35.890 to use it in humans

NOTE Confidence: 0.94887656

00:00:35.890 --> 00:00:38.130 yet. So we cannot measure

NOTE Confidence: 0.94887656

00:00:38.130 --> 00:00:39.890 our own treatment outcome data

NOTE Confidence: 0.94887656

00:00:39.890 --> 00:00:40.390 yet.

NOTE Confidence: 0.9771531

00:00:40.905 --> 00:00:41.965 We can, however,

NOTE Confidence: 0.83527374

00:00:42.745 --> 00:00:44.045 think that hopefully

NOTE Confidence: 0.87183696

00:00:44.825 --> 00:00:47.065 the the alpha despa has

NOTE Confidence: 0.87183696

00:00:47.065 --> 00:00:48.985 a certain effect on what

NOTE Confidence: 0.87183696

00:00:48.985 --> 00:00:49.645 are called

NOTE Confidence: 0.74376416

00:00:50.265 --> 00:00:51.325 desperate positive

NOTE Confidence: 0.8377837

00:00:51.784 --> 00:00:53.085 neutrophil meds.

NOTE Confidence: 0.99427444

00:00:53.545 --> 00:00:54.765 And from that

NOTE Confidence: 0.8236861

00:00:55.220 --> 00:00:57.160 effect on desperate positive

NOTE Confidence: 0.9931059

00:00:57.780 --> 00:01:00.020 neutrophil meds, we hope to

NOTE Confidence: 0.9931059

00:01:00.020 --> 00:01:02.100 be able to estimate an

NOTE Confidence: 0.9931059

00:01:02.100 --> 00:01:03.080 indirect effect

NOTE Confidence: 0.97960067

00:01:03.860 --> 00:01:05.400 on the final outcome.

NOTE Confidence: 0.897495

00:01:05.700 --> 00:01:07.080 And that's caused a mediation

NOTE Confidence: 0.897495

00:01:07.220 --> 00:01:09.060 analysis for you, but then

NOTE Confidence: 0.897495

00:01:09.060 --> 00:01:11.295 without splitting up an effect,

NOTE Confidence: 0.897495

00:01:11.354 --> 00:01:12.814 but focusing only

NOTE Confidence: 0.9919214

00:01:13.194 --> 00:01:14.814 on an indirect effect.

NOTE Confidence: 0.9378633

00:01:15.674 --> 00:01:17.274 Why is that important? Because

NOTE Confidence: 0.9378633

00:01:17.274 --> 00:01:19.115 we don't know how Alpha

NOTE Confidence: 0.9378633

00:01:19.115 --> 00:01:20.814 Dashboard will work in humans,

NOTE Confidence: 0.9378633

00:01:20.954 --> 00:01:22.155 and we wanna get a

NOTE Confidence: 0.9378633

00:01:22.155 --> 00:01:23.854 sense of how it works

NOTE Confidence: 0.97566336

00:01:24.230 --> 00:01:25.850 and what we can expect

NOTE Confidence: 0.97566336

00:01:25.910 --> 00:01:27.830 of alphadespir once it will

NOTE Confidence: 0.97566336

00:01:27.830 --> 00:01:29.130 be used in humans,

NOTE Confidence: 0.9944311

00:01:29.750 --> 00:01:31.590 supposing that the only effect

NOTE Confidence: 0.9944311

00:01:31.590 --> 00:01:32.410 that alphadespir

NOTE Confidence: 0.9804544

00:01:32.790 --> 00:01:33.290 has

NOTE Confidence: 0.85517323

00:01:33.750 --> 00:01:35.850 is through those desperate positive

NOTE Confidence: 0.72037035

00:01:36.230 --> 00:01:37.370 neutrophil nets

NOTE Confidence: 0.90245813

00:01:37.685 --> 00:01:39.444 that are actually the target

NOTE Confidence: 0.90245813

00:01:39.444 --> 00:01:40.665 of alpha despa.

NOTE Confidence: 0.95519567

00:01:40.965 --> 00:01:42.005 So what I am going

NOTE Confidence: 0.95519567

00:01:42.005 --> 00:01:43.865 to estimate is the targeted

NOTE Confidence: 0.95519567

00:01:44.085 --> 00:01:46.005 effect, the effect of what

NOTE Confidence: 0.95519567

00:01:46.005 --> 00:01:48.085 the treatment is targeting. It's

NOTE Confidence: 0.95519567

00:01:48.085 --> 00:01:50.345 targeting desperate and positive neutrophil

NOTE Confidence: 0.95519567

00:01:50.405 --> 00:01:51.845 meds, so we are going

NOTE Confidence: 0.95519567

00:01:51.845 --> 00:01:53.630 to look at the effect

NOTE Confidence: 0.95519567

00:01:53.690 --> 00:01:54.910 through the targeted

NOTE Confidence: 0.76144713

00:01:56.010 --> 00:01:56.510 biopsy.

NOTE Confidence: 0.98798263

00:01:59.050 --> 00:02:00.190 Okay. So

NOTE Confidence: 0.89820653

00:02:00.730 --> 00:02:02.350 my talk is causal mediation

NOTE Confidence: 0.89820653

00:02:02.410 --> 00:02:04.010 analysis and the promise of

NOTE Confidence: 0.89820653

00:02:04.010 --> 00:02:04.510 alpha

NOTE Confidence: 0.6846969

00:02:04.985 --> 00:02:05.645 for a preclinical

NOTE Confidence: 0.9944566

00:02:06.105 --> 00:02:08.345 potential COVID nineteen treatment in

NOTE Confidence: 0.9944566

00:02:08.345 --> 00:02:09.085 the ICU.

NOTE Confidence: 0.8932427

00:02:09.465 --> 00:02:11.005 This is an actual treatment

NOTE Confidence: 0.8932427

00:02:11.145 --> 00:02:12.264 except it has not been

NOTE Confidence: 0.8932427

00:02:12.264 --> 00:02:13.325 tried in humans.

NOTE Confidence: 0.940658

00:02:16.880 --> 00:02:17.780 So typically,

NOTE Confidence: 0.87699246

00:02:18.320 --> 00:02:20.240 direct and indirect effects are

NOTE Confidence: 0.87699246

00:02:20.240 --> 00:02:22.660 used to separate a total

NOTE Confidence: 0.87699246

00:02:22.720 --> 00:02:24.000 effect. And so I let

NOTE Confidence: 0.87699246

00:02:24.000 --> 00:02:25.680 let me first introduce that

NOTE Confidence: 0.87699246

00:02:25.680 --> 00:02:27.760 to you. It's used because

NOTE Confidence: 0.87699246

00:02:27.760 --> 00:02:30.080 the mediation analysis separates the

NOTE Confidence: 0.87699246

00:02:30.080 --> 00:02:30.580 effect

NOTE Confidence: 0.99741924

00:02:31.065 --> 00:02:31.565 into

NOTE Confidence: 0.94329226

00:02:31.944 --> 00:02:33.224 a part that is oh,

NOTE Confidence: 0.94329226

00:02:33.224 --> 00:02:34.745 this doesn't work. A part

NOTE Confidence: 0.94329226

00:02:34.745 --> 00:02:36.525 that is mediated through covariant

NOTE Confidence: 0.94329226

00:02:36.665 --> 00:02:38.444 m, that's the indirect effect,

NOTE Confidence: 0.9471901

00:02:38.825 --> 00:02:40.185 and the part that is

NOTE Confidence: 0.9471901

00:02:40.185 --> 00:02:41.465 not, and that is the

NOTE Confidence: 0.9471901

00:02:41.465 --> 00:02:43.065 direct effect. It works through

NOTE Confidence: 0.9471901

00:02:43.065 --> 00:02:43.965 other pathways.

NOTE Confidence: 0.9748714

00:02:44.720 --> 00:02:46.319 For example, the treatment could

NOTE Confidence: 0.9748714

00:02:46.319 --> 00:02:48.180 be a blood pressure lowering

NOTE Confidence: 0.9748714

00:02:48.239 --> 00:02:48.739 medication.

NOTE Confidence: 0.95259726

00:02:49.439 --> 00:02:50.879 The outcome could be heart

NOTE Confidence: 0.95259726

00:02:50.879 --> 00:02:52.319 attack, yes or no, maybe

NOTE Confidence: 0.95259726

00:02:52.319 --> 00:02:54.099 within five years or so.

NOTE Confidence: 0.986728

00:02:54.400 --> 00:02:55.939 And then we can think

NOTE Confidence: 0.97279245

00:02:56.239 --> 00:02:57.360 how much of the effect

NOTE Confidence: 0.97279245

00:02:57.360 --> 00:02:58.720 of the blood pressure lowering

NOTE Confidence: 0.97279245

00:02:58.720 --> 00:03:01.275 medication a is mediated by

NOTE Confidence: 0.97279245

00:03:01.275 --> 00:03:02.395 the effect it has on

NOTE Confidence: 0.97279245

00:03:02.395 --> 00:03:03.775 blood pressure m

NOTE Confidence: 0.948232

00:03:04.075 --> 00:03:05.055 and how much

NOTE Confidence: 0.766178

00:03:05.435 --> 00:03:05.935 works,

NOTE Confidence: 0.9602837

00:03:06.315 --> 00:03:07.915 if any, works through other

NOTE Confidence: 0.9602837

00:03:07.915 --> 00:03:08.415 pathways.

NOTE Confidence: 0.9715753

00:03:09.035 --> 00:03:10.394 So also in this case,

NOTE Confidence: 0.9715753

00:03:10.394 --> 00:03:11.834 you see that there is

NOTE Confidence: 0.9715753

00:03:11.834 --> 00:03:13.935 an intended effect, a targeted

NOTE Confidence: 0.9715753

00:03:14.075 --> 00:03:14.575 effect

NOTE Confidence: 0.9946483

00:03:14.950 --> 00:03:16.150 that is the effect of

NOTE Confidence: 0.9946483

00:03:16.150 --> 00:03:16.969 blood pressure

NOTE Confidence: 0.87637156

00:03:17.430 --> 00:03:19.590 lowering medications working through blood

NOTE Confidence: 0.87637156

00:03:19.590 --> 00:03:20.090 pressure,

NOTE Confidence: 0.9945072

00:03:20.469 --> 00:03:21.909 but there may also be

NOTE Confidence: 0.9945072

00:03:21.909 --> 00:03:22.650 other effects.

NOTE Confidence: 0.98019713

00:03:25.269 --> 00:03:27.209 And here is my example

NOTE Confidence: 0.98019713

00:03:27.349 --> 00:03:28.889 that is also my application

NOTE Confidence: 0.6469846

00:03:29.655 --> 00:03:30.555 Alpha desperate,

NOTE Confidence: 0.8563763

00:03:30.855 --> 00:03:31.594 the preclinical

NOTE Confidence: 0.8889384

00:03:31.894 --> 00:03:34.715 pro potential COVID nineteen treatment

NOTE Confidence: 0.8889384

00:03:34.855 --> 00:03:35.834 in the ICU

NOTE Confidence: 0.9964898

00:03:36.295 --> 00:03:38.155 has been shown to eliminate

NOTE Confidence: 0.592269

00:03:38.534 --> 00:03:39.515 desperate positive

NOTE Confidence: 0.8145683

00:03:40.055 --> 00:03:41.194 neutrophil meds

NOTE Confidence: 0.9946681

00:03:41.495 --> 00:03:42.234 in rats

NOTE Confidence: 0.9405752

00:03:42.620 --> 00:03:43.980 and in petri dishes. Actually,

NOTE Confidence: 0.9405752

00:03:43.980 --> 00:03:44.939 I'm not sure it's rats

NOTE Confidence: 0.9405752

00:03:44.939 --> 00:03:45.819 or mice. I have on

NOTE Confidence: 0.9405752

00:03:45.819 --> 00:03:46.540 my list of to do

NOTE Confidence: 0.9405752

00:03:46.540 --> 00:03:47.500 things to figure it out,

NOTE Confidence: 0.9405752

00:03:47.500 --> 00:03:48.859 but these little small animals

NOTE Confidence: 0.9405752

00:03:48.859 --> 00:03:49.659 that we don't like in

NOTE Confidence: 0.9405752

00:03:49.659 --> 00:03:50.239 our house.

NOTE Confidence: 0.9344506

00:03:50.780 --> 00:03:53.260 So if alpha despera also

NOTE Confidence: 0.9344506

00:03:53.260 --> 00:03:55.659 eliminate despera positive neutrophil meds

NOTE Confidence: 0.9344506

00:03:55.659 --> 00:03:56.400 in humans,

NOTE Confidence: 0.86259824

00:03:56.815 --> 00:03:58.755 What is its indirect effect

NOTE Confidence: 0.86259824

00:03:58.815 --> 00:04:00.915 on the SOFA score ICU

NOTE Confidence: 0.7544953

00:04:01.295 --> 00:04:03.235 discharge and it's her outcome

NOTE Confidence: 0.7544953

00:04:03.295 --> 00:04:03.795 y

NOTE Confidence: 0.9446165

00:04:04.095 --> 00:04:05.075 that is mediated

NOTE Confidence: 0.98715943

00:04:05.535 --> 00:04:06.995 through Desperative Neutrofel

NOTE Confidence: 0.75279814

00:04:07.775 --> 00:04:08.275 NETs?

NOTE Confidence: 0.9946782

00:04:09.090 --> 00:04:10.210 So we have here an

NOTE Confidence: 0.9946782

00:04:10.210 --> 00:04:11.650 outcome that is measured at

NOTE Confidence: 0.9946782

00:04:11.650 --> 00:04:12.790 the end of the study.

NOTE Confidence: 0.9946782

00:04:12.850 --> 00:04:14.150 They also assign

NOTE Confidence: 0.7299846

00:04:14.850 --> 00:04:16.070 a SOFA score,

NOTE Confidence: 0.9704025

00:04:16.850 --> 00:04:18.450 if a person is not

NOTE Confidence: 0.9704025

00:04:18.450 --> 00:04:20.550 discharged alive. So if people

NOTE Confidence: 0.9704025

00:04:20.610 --> 00:04:22.050 die in the hospital, that

NOTE Confidence: 0.9704025

00:04:22.050 --> 00:04:23.845 happens when we're talking about

NOTE Confidence: 0.9704025

00:04:23.904 --> 00:04:24.965 ICU data,

NOTE Confidence: 0.8455013

00:04:25.345 --> 00:04:27.105 and then assign a score

NOTE Confidence: 0.8455013

00:04:27.105 --> 00:04:28.225 to people who died as

NOTE Confidence: 0.8455013

00:04:28.225 --> 00:04:28.725 well.

NOTE Confidence: 0.96018916

00:04:31.985 --> 00:04:33.505 Another application I have been

NOTE Confidence: 0.96018916

00:04:33.505 --> 00:04:35.400 working on also is,

NOTE Confidence: 0.96104133

00:04:36.120 --> 00:04:38.220 there are several potential preclinical

NOTE Confidence: 0.96485347

00:04:38.680 --> 00:04:39.180 HIV

NOTE Confidence: 0.87031525

00:04:39.639 --> 00:04:40.460 cure treatments,

NOTE Confidence: 0.94086075

00:04:41.240 --> 00:04:43.160 and they typically target the

NOTE Confidence: 0.94086075

00:04:43.160 --> 00:04:44.300 HIV HIV

NOTE Confidence: 0.8426853

00:04:44.680 --> 00:04:45.180 reservoir.

NOTE Confidence: 0.97482806

00:04:45.720 --> 00:04:47.080 And there are several measures

NOTE Confidence: 0.97482806

00:04:47.080 --> 00:04:48.520 of the HIV reservoir that

NOTE Confidence: 0.97482806

00:04:48.520 --> 00:04:49.500 they may target,

NOTE Confidence: 0.99471736

00:04:49.835 --> 00:04:50.795 and we can try to

NOTE Confidence: 0.99471736

00:04:50.795 --> 00:04:52.475 figure out what is the

NOTE Confidence: 0.99471736

00:04:52.475 --> 00:04:53.535 indirect effect

NOTE Confidence: 0.9334991

00:04:53.995 --> 00:04:56.714 of HIV curative treatment on

NOTE Confidence: 0.9334991

00:04:56.714 --> 00:04:57.855 long term outcomes

NOTE Confidence: 0.9876859

00:04:58.714 --> 00:05:00.335 mediated by their

NOTE Confidence: 0.93198085

00:05:00.635 --> 00:05:02.955 the HIV reservoir. And also

NOTE Confidence: 0.93198085

00:05:02.955 --> 00:05:04.235 here you see it's the

NOTE Confidence: 0.93198085

00:05:04.235 --> 00:05:06.000 the effect that is targeted.

NOTE Confidence: 0.9012529

00:05:06.699 --> 00:05:07.979 And you see often in

NOTE Confidence: 0.9012529

00:05:07.979 --> 00:05:10.240 causal mediation analysis that that

NOTE Confidence: 0.9012529

00:05:10.539 --> 00:05:12.060 indirect effect that goes to

NOTE Confidence: 0.9012529

00:05:12.060 --> 00:05:12.800 that pathway

NOTE Confidence: 0.9468116

00:05:14.139 --> 00:05:15.199 treatment to mediator

NOTE Confidence: 0.49709845

00:05:15.900 --> 00:05:16.400 treatment

NOTE Confidence: 0.97655547

00:05:16.939 --> 00:05:18.719 to mediator through outcome

NOTE Confidence: 0.99922323

00:05:19.264 --> 00:05:20.805 that is often the intended

NOTE Confidence: 0.99958426

00:05:21.105 --> 00:05:21.605 pathway

NOTE Confidence: 0.99108285

00:05:21.985 --> 00:05:23.345 for which the drug is

NOTE Confidence: 0.99108285

00:05:23.345 --> 00:05:23.845 designed.

NOTE Confidence: 0.93169767

00:05:25.345 --> 00:05:26.305 So what is the effect

NOTE Confidence: 0.93169767

00:05:26.305 --> 00:05:28.005 of an HIV curative treatment

NOTE Confidence: 0.93169767

00:05:28.225 --> 00:05:30.145 a on viral rebound? Why

NOTE Confidence: 0.93169767

00:05:30.145 --> 00:05:31.745 viral rebound is how good

NOTE Confidence: 0.93169767

00:05:31.745 --> 00:05:33.445 the treatment works long term

NOTE Confidence: 0.9260532

00:05:34.130 --> 00:05:36.389 mediated through the HIV repertoire.

NOTE Confidence: 0.9918596

00:05:38.210 --> 00:05:39.990 That's not my application today.

NOTE Confidence: 0.95977354

00:05:41.889 --> 00:05:43.669 The seminal article on mediation

NOTE Confidence: 0.95977354

00:05:43.810 --> 00:05:45.669 analysis that has been cited,

NOTE Confidence: 0.9591214

00:05:46.504 --> 00:05:47.865 a zillion times, not a

NOTE Confidence: 0.9591214

00:05:47.865 --> 00:05:50.125 zillion, one hundred thirty nine

NOTE Confidence: 0.9591214

00:05:50.345 --> 00:05:51.724 thousand something yesterday,

NOTE Confidence: 0.95875746

00:05:52.745 --> 00:05:54.345 in Google Scholar, and many

NOTE Confidence: 0.95875746

00:05:54.345 --> 00:05:55.305 of these are from the

NOTE Confidence: 0.95875746

00:05:55.305 --> 00:05:56.585 last ten years. So calls

NOTE Confidence: 0.95875746

00:05:56.585 --> 00:05:58.264 to mediation analysis has been

NOTE Confidence: 0.95875746

00:05:58.264 --> 00:06:00.060 boy booming. Maybe I shouldn't

NOTE Confidence: 0.95875746

00:06:00.139 --> 00:06:02.460 say causal mediation analysis. Maybe

NOTE Confidence: 0.95875746

00:06:02.460 --> 00:06:04.240 I should say mediation analysis

NOTE Confidence: 0.8807015

00:06:04.620 --> 00:06:06.220 because Baron and Kenny did

NOTE Confidence: 0.8807015

00:06:06.220 --> 00:06:06.960 not exactly

NOTE Confidence: 0.9324047

00:06:07.339 --> 00:06:09.900 popularize causal mediation analysis, but

NOTE Confidence: 0.9324047

00:06:09.900 --> 00:06:11.440 just look at half its.

NOTE Confidence: 0.997218

00:06:12.635 --> 00:06:14.635 Mediation analysis is very important

NOTE Confidence: 0.997218

00:06:14.635 --> 00:06:16.575 in the health sciences, psychology,

NOTE Confidence: 0.9643355

00:06:17.035 --> 00:06:17.535 epidemiology,

NOTE Confidence: 0.95782113

00:06:18.475 --> 00:06:20.555 space places like that. And

NOTE Confidence: 0.95782113

00:06:20.555 --> 00:06:21.915 it is very important to

NOTE Confidence: 0.95782113

00:06:21.915 --> 00:06:23.295 know the kinds of assumptions

NOTE Confidence: 0.95782113

00:06:23.355 --> 00:06:24.635 that we're making when this,

NOTE Confidence: 0.95782113

00:06:24.955 --> 00:06:26.255 when we do these conclusions.

NOTE Confidence: 0.8960657

00:06:26.800 --> 00:06:28.180 And I like this citation

NOTE Confidence: 0.8960657

00:06:28.320 --> 00:06:29.460 from Jamie Robinson,

NOTE Confidence: 0.93606997

00:06:29.840 --> 00:06:30.820 Thomas Richardson.

NOTE Confidence: 0.8500652

00:06:31.200 --> 00:06:32.480 They are much my senior,

NOTE Confidence: 0.8500652

00:06:32.480 --> 00:06:33.600 so they can say this.

NOTE Confidence: 0.8500652

00:06:33.600 --> 00:06:34.960 I can't, although I do

NOTE Confidence: 0.8500652

00:06:34.960 --> 00:06:36.400 happen to this happen to

NOTE Confidence: 0.8500652

00:06:36.400 --> 00:06:37.300 agree with them.

NOTE Confidence: 0.9541054

00:06:37.760 --> 00:06:39.220 The nature of the relationship

NOTE Confidence: 0.9541054

00:06:39.280 --> 00:06:41.200 between the senses expressing these

NOTE Confidence: 0.9541054

00:06:41.200 --> 00:06:42.260 causal conclusions

NOTE Confidence: 0.99312335

00:06:42.714 --> 00:06:44.895 and the statistical computer calculations

NOTE Confidence: 0.9972315

00:06:45.354 --> 00:06:46.955 performed on the string of

NOTE Confidence: 0.9972315

00:06:46.955 --> 00:06:47.455 numbers

NOTE Confidence: 0.9926922

00:06:47.995 --> 00:06:49.455 has been obscure.

NOTE Confidence: 0.9908656

00:06:50.315 --> 00:06:52.495 In other words, causal mediation

NOTE Confidence: 0.9908656

00:06:52.634 --> 00:06:55.134 analysis is much more disputed

NOTE Confidence: 0.99895

00:06:55.914 --> 00:06:56.815 than other

NOTE Confidence: 0.98911524

00:06:57.300 --> 00:06:59.080 types of causal inference

NOTE Confidence: 0.9302368

00:06:59.620 --> 00:07:00.900 and I will tell you

NOTE Confidence: 0.9302368

00:07:00.900 --> 00:07:01.720 why later.

NOTE Confidence: 0.9616972

00:07:03.300 --> 00:07:04.500 There are quite a number

NOTE Confidence: 0.9616972

00:07:04.500 --> 00:07:06.200 of people who like causal

NOTE Confidence: 0.9616972

00:07:06.339 --> 00:07:07.860 inference but who don't want

NOTE Confidence: 0.9616972

00:07:07.860 --> 00:07:09.540 to do causal mediation analysis.

NOTE Confidence: 0.9616972

00:07:09.540 --> 00:07:10.840 You may have met them.

NOTE Confidence: 0.93511313

00:07:12.205 --> 00:07:13.405 So the setting and the

NOTE Confidence: 0.93511313

00:07:13.405 --> 00:07:15.645 notation, randomized treatment a, that

NOTE Confidence: 0.93511313

00:07:15.645 --> 00:07:17.005 can be relaxed, but that

NOTE Confidence: 0.93511313

00:07:17.005 --> 00:07:18.125 is not the subject of

NOTE Confidence: 0.93511313

00:07:18.125 --> 00:07:18.865 this talk.

NOTE Confidence: 0.9425094

00:07:19.885 --> 00:07:21.965 Pre treatment common causes of

NOTE Confidence: 0.9425094

00:07:21.965 --> 00:07:23.645 the mediator m and the

NOTE Confidence: 0.9425094

00:07:23.645 --> 00:07:26.125 outcome y. I'm assuming here

NOTE Confidence: 0.9425094

00:07:26.125 --> 00:07:27.510 we have them all and

NOTE Confidence: 0.9425094

00:07:27.590 --> 00:07:29.190 I call them c for

NOTE Confidence: 0.9425094

00:07:29.190 --> 00:07:30.090 common causes.

NOTE Confidence: 0.9479746

00:07:30.950 --> 00:07:31.990 And I'm assuming that there

NOTE Confidence: 0.9479746

00:07:31.990 --> 00:07:33.590 are no cross treatment common

NOTE Confidence: 0.9479746

00:07:33.590 --> 00:07:34.810 causes of the mediator

NOTE Confidence: 0.8760707

00:07:35.110 --> 00:07:36.810 m and the outcome y.

NOTE Confidence: 0.89630264

00:07:37.350 --> 00:07:38.550 And the reason is that

NOTE Confidence: 0.89630264

00:07:38.550 --> 00:07:40.230 things get complicated in that

NOTE Confidence: 0.89630264

00:07:40.230 --> 00:07:41.565 case. I have some work

NOTE Confidence: 0.89630264

00:07:41.565 --> 00:07:42.685 on it, but that needs

NOTE Confidence: 0.89630264

00:07:42.685 --> 00:07:44.205 to do data sample reports

NOTE Confidence: 0.89630264

00:07:44.205 --> 00:07:45.345 with Ohio Tech.

NOTE Confidence: 0.8867707

00:07:47.485 --> 00:07:49.085 I use as usual a

NOTE Confidence: 0.8867707

00:07:49.085 --> 00:07:51.245 superscript zero to say without

NOTE Confidence: 0.8867707

00:07:51.245 --> 00:07:52.845 treatment. So zero is no

NOTE Confidence: 0.8867707

00:07:52.845 --> 00:07:55.805 treatment. Superscript one indicates under

NOTE Confidence: 0.8867707

00:07:55.805 --> 00:07:56.305 treatment.

NOTE Confidence: 0.9831438

00:07:59.610 --> 00:08:00.650 So then we have the

NOTE Confidence: 0.9831438

00:08:00.650 --> 00:08:02.349 following causal diagram.

NOTE Confidence: 0.92497736

00:08:03.210 --> 00:08:04.410 Wouldn't call it that bad

NOTE Confidence: 0.92497736

00:08:04.410 --> 00:08:05.289 because and then they get

NOTE Confidence: 0.92497736

00:08:05.289 --> 00:08:06.669 in trouble with some people.

NOTE Confidence: 0.92497736

00:08:06.810 --> 00:08:07.849 So we have here the

NOTE Confidence: 0.92497736

00:08:07.849 --> 00:08:08.349 treatment.

NOTE Confidence: 0.9853528

00:08:08.729 --> 00:08:10.430 It may affect the mediator,

NOTE Confidence: 0.9830483

00:08:11.134 --> 00:08:12.895 which in turn may affect

NOTE Confidence: 0.9830483

00:08:12.895 --> 00:08:13.634 the outcome.

NOTE Confidence: 0.9770897

00:08:14.014 --> 00:08:15.775 So this path from a

NOTE Confidence: 0.9770897

00:08:15.775 --> 00:08:17.215 to m to y, that

NOTE Confidence: 0.9770897

00:08:17.215 --> 00:08:18.835 is the indirect effect.

NOTE Confidence: 0.9366891

00:08:19.294 --> 00:08:20.735 And there could be effects

NOTE Confidence: 0.9366891

00:08:20.735 --> 00:08:22.975 through other pathways. Those go

NOTE Confidence: 0.9366891

00:08:22.975 --> 00:08:24.115 around the mediator,

NOTE Confidence: 0.9383279

00:08:24.495 --> 00:08:25.935 and the that is called

NOTE Confidence: 0.9383279

00:08:25.935 --> 00:08:27.000 the direct effect.

NOTE Confidence: 0.85981077

00:08:31.000 --> 00:08:32.459 Effect. And my recurring

NOTE Confidence: 0.83843434

00:08:33.080 --> 00:08:33.580 example,

NOTE Confidence: 0.5861872

00:08:34.040 --> 00:08:34.940 alpha despora,

NOTE Confidence: 0.9860977

00:08:35.720 --> 00:08:37.559 that is the treatment that

NOTE Confidence: 0.9860977

00:08:37.559 --> 00:08:38.860 I'm interested in.

NOTE Confidence: 0.9484486

00:08:39.240 --> 00:08:40.440 And I, that is the

NOTE Confidence: 0.9484486

00:08:40.440 --> 00:08:42.200 mediator that I'm interested in.

NOTE Confidence: 0.9484486

00:08:42.200 --> 00:08:43.605 In this case, it's desperate

NOTE Confidence: 0.9484486

00:08:43.605 --> 00:08:45.445 positive neutrophil nets. It's a

NOTE Confidence: 0.9484486

00:08:45.445 --> 00:08:46.965 mouthful, but they're really pretty.

NOTE Confidence: 0.9484486

00:08:46.965 --> 00:08:48.645 They make really pretty pictures

NOTE Confidence: 0.9484486

00:08:48.645 --> 00:08:50.245 of these nets, and then

NOTE Confidence: 0.9484486

00:08:50.245 --> 00:08:51.365 they are able to count

NOTE Confidence: 0.9484486

00:08:51.365 --> 00:08:53.045 them. And it's a whole

NOTE Confidence: 0.9484486

00:08:53.045 --> 00:08:53.865 big process.

NOTE Confidence: 0.96296036

00:08:54.165 --> 00:08:55.605 So the datasets that I'm

NOTE Confidence: 0.96296036

00:08:55.605 --> 00:08:56.880 using in this project are

NOTE Confidence: 0.96296036

00:08:57.040 --> 00:08:58.480 small. There are like thirty

NOTE Confidence: 0.96296036

00:08:58.480 --> 00:09:00.500 four patients or thirty five.

NOTE Confidence: 0.96296036

00:09:00.559 --> 00:09:01.760 There are few because it

NOTE Confidence: 0.96296036

00:09:01.760 --> 00:09:02.880 takes a ton of time

NOTE Confidence: 0.96296036

00:09:02.880 --> 00:09:04.400 to make these beautiful pictures

NOTE Confidence: 0.96296036

00:09:04.400 --> 00:09:05.600 and then to count all

NOTE Confidence: 0.96296036

00:09:05.600 --> 00:09:06.340 these nets.

NOTE Confidence: 0.9251132

00:09:08.400 --> 00:09:10.100 Final outcome is the SOWFA

NOTE Confidence: 0.9251132

00:09:10.240 --> 00:09:11.300 score and ICU

NOTE Confidence: 0.971427

00:09:11.855 --> 00:09:13.615 discharge. It's a measure of

NOTE Confidence: 0.971427

00:09:13.615 --> 00:09:15.235 multi organ failure

NOTE Confidence: 0.9939427

00:09:15.615 --> 00:09:17.135 that is typically used in

NOTE Confidence: 0.9939427

00:09:17.135 --> 00:09:17.955 the ICU

NOTE Confidence: 0.89873904

00:09:18.575 --> 00:09:20.415 and again, they also assign

NOTE Confidence: 0.89873904

00:09:20.415 --> 00:09:22.175 a score if a patient

NOTE Confidence: 0.89873904

00:09:22.175 --> 00:09:22.675 dies.

NOTE Confidence: 0.9820816

00:09:23.535 --> 00:09:24.575 And then there is a

NOTE Confidence: 0.9820816

00:09:24.575 --> 00:09:26.515 common cause of the mediator

NOTE Confidence: 0.9350586

00:09:26.970 --> 00:09:28.170 and the outcome. So the

NOTE Confidence: 0.9350586

00:09:28.170 --> 00:09:29.610 mediator is the desperate positive

NOTE Confidence: 0.9350586

00:09:29.610 --> 00:09:31.129 neutrophil nets. The outcome is

NOTE Confidence: 0.9350586

00:09:31.129 --> 00:09:32.990 the SOWFA score at ICU

NOTE Confidence: 0.9350586

00:09:33.129 --> 00:09:33.629 discharge.

NOTE Confidence: 0.9549018

00:09:34.089 --> 00:09:35.610 And this common cause that

NOTE Confidence: 0.9549018

00:09:35.610 --> 00:09:37.069 we have been using

NOTE Confidence: 0.9822201

00:09:37.689 --> 00:09:39.850 is the SOWFA score at

NOTE Confidence: 0.9822201

00:09:39.850 --> 00:09:41.610 ICU admission or close to

NOTE Confidence: 0.9822201

00:09:41.610 --> 00:09:42.589 ICU admission.

NOTE Confidence: 0.9974765

00:09:43.184 --> 00:09:44.625 It is a measure of

NOTE Confidence: 0.9974765

00:09:44.625 --> 00:09:46.225 how well a person is

NOTE Confidence: 0.9974765

00:09:46.225 --> 00:09:47.665 doing when they enter the

NOTE Confidence: 0.9974765

00:09:47.665 --> 00:09:48.165 ICU.

NOTE Confidence: 0.90415967

00:09:48.705 --> 00:09:50.705 It's also, again, the the

NOTE Confidence: 0.90415967

00:09:50.705 --> 00:09:52.885 score of multi organ failure.

NOTE Confidence: 0.9134832

00:09:55.880 --> 00:09:57.480 So what I'm interested in

NOTE Confidence: 0.9134832

00:09:57.480 --> 00:09:59.080 especially is the effect of

NOTE Confidence: 0.9134832

00:09:59.080 --> 00:09:59.980 alpha desprud

NOTE Confidence: 0.91349334

00:10:00.520 --> 00:10:02.780 that affects the desprud positive

NOTE Confidence: 0.91349334

00:10:02.840 --> 00:10:04.200 neutral film that's in turn

NOTE Confidence: 0.91349334

00:10:04.200 --> 00:10:05.480 the SOWFA score. So I'm

NOTE Confidence: 0.91349334

00:10:05.480 --> 00:10:07.000 mainly going to estimate the

NOTE Confidence: 0.91349334

00:10:07.000 --> 00:10:08.059 indirect effect

NOTE Confidence: 0.9139881

00:10:08.465 --> 00:10:09.825 because it turns out I

NOTE Confidence: 0.9139881

00:10:09.825 --> 00:10:11.445 cannot do the direct effect.

NOTE Confidence: 0.8606627

00:10:15.345 --> 00:10:16.785 I like Baron and Kanesho.

NOTE Confidence: 0.8606627

00:10:16.785 --> 00:10:17.905 I wanted to put that

NOTE Confidence: 0.8606627

00:10:17.905 --> 00:10:18.804 up also.

NOTE Confidence: 0.9694705

00:10:19.505 --> 00:10:20.785 Suppose the model for m

NOTE Confidence: 0.9694705

00:10:20.785 --> 00:10:22.065 given a is a linear

NOTE Confidence: 0.9694705

00:10:22.065 --> 00:10:23.890 model where the mean of

NOTE Confidence: 0.9694705

00:10:23.890 --> 00:10:25.410 the mediator given the outcome

NOTE Confidence: 0.9694705

00:10:25.410 --> 00:10:26.690 is just, you have two

NOTE Confidence: 0.9694705

00:10:26.690 --> 00:10:28.370 different means, one for treated

NOTE Confidence: 0.9694705

00:10:28.370 --> 00:10:29.510 and one for untreated.

NOTE Confidence: 0.9944382

00:10:30.209 --> 00:10:31.410 And then the model for

NOTE Confidence: 0.9944382

00:10:31.410 --> 00:10:33.429 the outcome given the mediator

NOTE Confidence: 0.9522619

00:10:33.809 --> 00:10:35.029 and the treatment

NOTE Confidence: 0.9487771

00:10:35.730 --> 00:10:37.510 is also a linear model,

NOTE Confidence: 0.9256068

00:10:37.934 --> 00:10:39.215 can depend on the treatment

NOTE Confidence: 0.9256068

00:10:39.215 --> 00:10:40.095 and it can depend on

NOTE Confidence: 0.9256068

00:10:40.095 --> 00:10:40.755 the mediator.

NOTE Confidence: 0.87899995

00:10:41.295 --> 00:10:43.054 And then what, Baron and

NOTE Confidence: 0.87899995

00:10:43.054 --> 00:10:44.735 Kenny say is that the

NOTE Confidence: 0.87899995

00:10:44.735 --> 00:10:45.235 effect

NOTE Confidence: 0.99429685

00:10:45.934 --> 00:10:46.995 that is mediated

NOTE Confidence: 0.9412404

00:10:47.535 --> 00:10:49.455 is first alpha one so

NOTE Confidence: 0.9412404

00:10:49.455 --> 00:10:50.735 that you get the different

NOTE Confidence: 0.9412404

00:10:50.735 --> 00:10:51.235 mediator.

NOTE Confidence: 0.94878906

00:10:51.695 --> 00:10:52.860 And then in the next,

NOTE Confidence: 0.94878906

00:10:53.019 --> 00:10:54.220 you see that the different

NOTE Confidence: 0.94878906

00:10:54.220 --> 00:10:56.559 mediator causes beta two alpha

NOTE Confidence: 0.94878906

00:10:56.620 --> 00:10:57.920 one on average.

NOTE Confidence: 0.9968815

00:10:58.459 --> 00:11:00.079 So that's how they motivate

NOTE Confidence: 0.98923737

00:11:00.700 --> 00:11:03.040 their alpha one beta two.

NOTE Confidence: 0.98923737

00:11:03.339 --> 00:11:05.920 They don't use causal mediation

NOTE Confidence: 0.98923737

00:11:06.140 --> 00:11:07.279 analysis notation

NOTE Confidence: 0.8125508

00:11:07.660 --> 00:11:08.480 with counterfactual

NOTE Confidence: 0.94263583

00:11:09.235 --> 00:11:10.695 outcomes, or even maybe,

NOTE Confidence: 0.80720854

00:11:11.315 --> 00:11:11.815 crossroads

NOTE Confidence: 0.86272544

00:11:12.195 --> 00:11:12.695 counterfactuals.

NOTE Confidence: 0.9431246

00:11:13.235 --> 00:11:14.915 Nothing of that. They just

NOTE Confidence: 0.9431246

00:11:14.915 --> 00:11:16.115 say, look, we had this

NOTE Confidence: 0.9431246

00:11:16.115 --> 00:11:17.635 mediator goes and it makes

NOTE Confidence: 0.9431246

00:11:17.635 --> 00:11:19.015 it alpha one bigger.

NOTE Confidence: 0.91293806

00:11:19.475 --> 00:11:20.835 The treatment goes, makes the

NOTE Confidence: 0.91293806

00:11:20.835 --> 00:11:22.515 mediator alpha one bigger, and

NOTE Confidence: 0.91293806

00:11:22.515 --> 00:11:23.635 then look at this model

NOTE Confidence: 0.91293806

00:11:23.635 --> 00:11:24.890 that causes is beta two

NOTE Confidence: 0.91293806

00:11:24.890 --> 00:11:26.190 times alpha one.

NOTE Confidence: 0.96723497

00:11:27.930 --> 00:11:28.890 And then when they say

NOTE Confidence: 0.96723497

00:11:28.890 --> 00:11:30.330 the direct effect is whatever

NOTE Confidence: 0.96723497

00:11:30.330 --> 00:11:31.610 is left, and you can

NOTE Confidence: 0.96723497

00:11:31.610 --> 00:11:33.290 show in these models that

NOTE Confidence: 0.96723497

00:11:33.290 --> 00:11:34.750 that is just beta one.

NOTE Confidence: 0.9394755

00:11:35.130 --> 00:11:36.570 That's the difference between the

NOTE Confidence: 0.9394755

00:11:36.570 --> 00:11:37.470 total effect

NOTE Confidence: 0.9130378

00:11:37.930 --> 00:11:39.130 you can also get from

NOTE Confidence: 0.9130378

00:11:39.130 --> 00:11:39.870 these things

NOTE Confidence: 0.9718628

00:11:40.235 --> 00:11:42.095 and the indirect effect.

NOTE Confidence: 0.9974597

00:11:44.554 --> 00:11:46.654 Most applications of causal mediation

NOTE Confidence: 0.9974597

00:11:46.954 --> 00:11:47.454 analysis

NOTE Confidence: 0.99505234

00:11:47.755 --> 00:11:48.975 estimate natural

NOTE Confidence: 0.9933635

00:11:49.434 --> 00:11:51.514 indirect effects. Those have really

NOTE Confidence: 0.9933635

00:11:51.514 --> 00:11:52.334 been booming.

NOTE Confidence: 0.9798791

00:11:52.800 --> 00:11:54.080 You see that there is

NOTE Confidence: 0.9798791

00:11:54.080 --> 00:11:55.620 not that many applications

NOTE Confidence: 0.9930803

00:11:56.000 --> 00:11:58.000 of other approaches to causal

NOTE Confidence: 0.9930803

00:11:58.000 --> 00:11:59.220 mediation analysis.

NOTE Confidence: 0.86693746

00:12:00.080 --> 00:12:00.960 Well, they will go on

NOTE Confidence: 0.86693746

00:12:00.960 --> 00:12:03.540 to apply causal mediation analysis,

NOTE Confidence: 0.9316864

00:12:04.080 --> 00:12:06.080 find a package online, and

NOTE Confidence: 0.9316864

00:12:06.080 --> 00:12:08.115 typically say, I want the

NOTE Confidence: 0.9316864

00:12:08.115 --> 00:12:10.295 natural indirect and direct effects.

NOTE Confidence: 0.9845338

00:12:10.755 --> 00:12:12.035 And I will argue that

NOTE Confidence: 0.9845338

00:12:12.035 --> 00:12:13.075 that is not always the

NOTE Confidence: 0.9845338

00:12:13.075 --> 00:12:14.515 way to go, but,

NOTE Confidence: 0.9777985

00:12:15.075 --> 00:12:16.695 let's let's see why.

NOTE Confidence: 0.9709065

00:12:17.555 --> 00:12:19.895 The building blocks for natural

NOTE Confidence: 0.9709065

00:12:19.955 --> 00:12:21.335 direct and indirect effects

NOTE Confidence: 0.88289404

00:12:21.660 --> 00:12:22.559 are the outcome,

NOTE Confidence: 0.8658166

00:12:23.339 --> 00:12:24.559 but under treatment,

NOTE Confidence: 0.8631961

00:12:25.100 --> 00:12:26.940 be the mediator set to

NOTE Confidence: 0.8631961

00:12:26.940 --> 00:12:28.559 its failure without treatment.

NOTE Confidence: 0.90399206

00:12:31.420 --> 00:12:33.179 Okay? So is the outcome

NOTE Confidence: 0.90399206

00:12:33.179 --> 00:12:34.720 under treatment had the mediator

NOTE Confidence: 0.9057329

00:12:35.245 --> 00:12:36.785 been set to its value

NOTE Confidence: 0.9057329

00:12:36.925 --> 00:12:37.985 without treatment.

NOTE Confidence: 0.9394941

00:12:40.365 --> 00:12:42.045 And then the natural direct

NOTE Confidence: 0.9394941

00:12:42.045 --> 00:12:44.285 effect you see here maybe

NOTE Confidence: 0.9394941

00:12:44.285 --> 00:12:45.325 I should stand here so

NOTE Confidence: 0.9394941

00:12:45.325 --> 00:12:46.684 that the people online can

NOTE Confidence: 0.9394941

00:12:46.684 --> 00:12:48.285 also see what I point

NOTE Confidence: 0.9394941

00:12:48.285 --> 00:12:48.785 to.

NOTE Confidence: 0.9411102

00:12:49.900 --> 00:12:51.020 So here you have the

NOTE Confidence: 0.9411102

00:12:51.020 --> 00:12:52.800 mediator under no treatment.

NOTE Confidence: 0.9281443

00:12:53.340 --> 00:12:54.460 Here you also have the

NOTE Confidence: 0.9281443

00:12:54.460 --> 00:12:56.059 mediator under no treatment. Right?

NOTE Confidence: 0.9281443

00:12:56.059 --> 00:12:57.740 Because these are untreated people.

NOTE Confidence: 0.9281443

00:12:57.740 --> 00:12:58.940 They don't know are not

NOTE Confidence: 0.9281443

00:12:58.940 --> 00:13:00.720 messing with their mediator specifically.

NOTE Confidence: 0.98053515

00:13:01.434 --> 00:13:03.115 So it's mediator under no

NOTE Confidence: 0.98053515

00:13:03.115 --> 00:13:05.194 treatment versus mediator under no

NOTE Confidence: 0.98053515

00:13:05.194 --> 00:13:05.694 treatment,

NOTE Confidence: 0.9740573

00:13:06.074 --> 00:13:08.074 but treated versus untreated. So

NOTE Confidence: 0.9740573

00:13:08.074 --> 00:13:09.434 that's the direct effect that

NOTE Confidence: 0.9740573

00:13:09.434 --> 00:13:11.274 works to other pathways that

NOTE Confidence: 0.9740573

00:13:11.274 --> 00:13:12.254 are not n.

NOTE Confidence: 0.9282253

00:13:13.670 --> 00:13:15.190 And here we have the

NOTE Confidence: 0.9282253

00:13:15.190 --> 00:13:17.029 outcome here. The mediator is

NOTE Confidence: 0.9282253

00:13:17.029 --> 00:13:18.949 mediator under treatment because we're

NOTE Confidence: 0.9282253

00:13:18.949 --> 00:13:19.990 not messing with it and

NOTE Confidence: 0.9282253

00:13:19.990 --> 00:13:21.029 we are treating these people.

NOTE Confidence: 0.9282253

00:13:21.029 --> 00:13:22.730 So it's mediator under treatment

NOTE Confidence: 0.9731852

00:13:23.429 --> 00:13:25.769 versus mediator under no treatment.

NOTE Confidence: 0.9623919

00:13:26.865 --> 00:13:28.565 All these people are treated,

NOTE Confidence: 0.9623919

00:13:28.705 --> 00:13:30.145 both these ones are treated

NOTE Confidence: 0.9623919

00:13:30.145 --> 00:13:31.345 and these ones are treated,

NOTE Confidence: 0.9623919

00:13:31.345 --> 00:13:32.804 but it's m one

NOTE Confidence: 0.9452975

00:13:33.345 --> 00:13:34.725 versus m zero.

NOTE Confidence: 0.98721546

00:13:35.184 --> 00:13:36.965 So this is the indirect

NOTE Confidence: 0.98721546

00:13:37.025 --> 00:13:38.625 effect. This goes through the

NOTE Confidence: 0.98721546

00:13:38.625 --> 00:13:40.085 pathway through the mediator.

NOTE Confidence: 0.9977031

00:13:41.730 --> 00:13:42.929 And that's the kind of

NOTE Confidence: 0.9977031

00:13:42.929 --> 00:13:45.250 mediation analysis that most people

NOTE Confidence: 0.9977031

00:13:45.250 --> 00:13:46.070 are applying.

NOTE Confidence: 0.9923567

00:13:46.610 --> 00:13:47.750 It's maybe not

NOTE Confidence: 0.92131585

00:13:48.210 --> 00:13:50.390 the mediation causal mediation analysis

NOTE Confidence: 0.92131585

00:13:50.450 --> 00:13:51.490 that you see the most

NOTE Confidence: 0.92131585

00:13:51.490 --> 00:13:52.870 theory papers on.

NOTE Confidence: 0.7993048

00:13:55.825 --> 00:13:57.525 So suppose treatment is randomized,

NOTE Confidence: 0.96457

00:13:57.905 --> 00:13:59.684 then estimation of the expectation

NOTE Confidence: 0.96457

00:13:59.825 --> 00:14:01.425 of the outcome under treatment

NOTE Confidence: 0.96457

00:14:01.425 --> 00:14:02.625 is very easy. You just

NOTE Confidence: 0.96457

00:14:02.625 --> 00:14:04.065 did the average in the

NOTE Confidence: 0.96457

00:14:04.065 --> 00:14:05.045 treated group.

NOTE Confidence: 0.87067366

00:14:05.745 --> 00:14:06.945 So then you need to

NOTE Confidence: 0.87067366

00:14:06.945 --> 00:14:07.770 still for,

NOTE Confidence: 0.8606105

00:14:08.250 --> 00:14:09.690 an indirect and direct effect

NOTE Confidence: 0.8606105

00:14:09.690 --> 00:14:11.210 because, look, they are based

NOTE Confidence: 0.8606105

00:14:11.210 --> 00:14:11.950 on this

NOTE Confidence: 0.91106606

00:14:12.730 --> 00:14:14.809 on this expectation of y

NOTE Confidence: 0.91106606

00:14:14.809 --> 00:14:16.030 one and zero.

NOTE Confidence: 0.9323642

00:14:16.410 --> 00:14:17.950 We still need to

NOTE Confidence: 0.98915344

00:14:18.410 --> 00:14:18.910 estimate

NOTE Confidence: 0.9574483

00:14:19.450 --> 00:14:21.790 the expected outcome under treatment

NOTE Confidence: 0.9574483

00:14:21.850 --> 00:14:23.450 with the mediator set to

NOTE Confidence: 0.9574483

00:14:23.450 --> 00:14:25.045 its value without treatment.

NOTE Confidence: 0.9065102

00:14:25.665 --> 00:14:26.385 And there,

NOTE Confidence: 0.8725094

00:14:26.865 --> 00:14:28.385 is a, what is called

NOTE Confidence: 0.8725094

00:14:28.385 --> 00:14:29.125 the mediation

NOTE Confidence: 0.91292524

00:14:29.665 --> 00:14:30.165 formula.

NOTE Confidence: 0.8556484

00:14:31.265 --> 00:14:32.725 So that says first,

NOTE Confidence: 0.99738103

00:14:33.505 --> 00:14:34.005 the

NOTE Confidence: 0.9275577

00:14:34.865 --> 00:14:36.565 common causes come about.

NOTE Confidence: 0.9382108

00:14:37.430 --> 00:14:39.430 Then the mediator comes about

NOTE Confidence: 0.9382108

00:14:39.430 --> 00:14:40.730 given the common causes

NOTE Confidence: 0.97649527

00:14:41.350 --> 00:14:43.510 according to its distribution under,

NOTE Confidence: 0.9868593

00:14:43.910 --> 00:14:45.029 under a is equal to

NOTE Confidence: 0.9868593

00:14:45.029 --> 00:14:46.490 zero, which makes sense.

NOTE Confidence: 0.9913445

00:14:47.510 --> 00:14:48.790 And then after that, you

NOTE Confidence: 0.9913445

00:14:48.790 --> 00:14:49.690 get the expected

NOTE Confidence: 0.9994179

00:14:50.070 --> 00:14:50.570 outcome

NOTE Confidence: 0.9304815

00:14:51.084 --> 00:14:52.605 given that common calls and

NOTE Confidence: 0.9304815

00:14:52.605 --> 00:14:53.964 given the mediator that we

NOTE Confidence: 0.9304815

00:14:53.964 --> 00:14:55.485 just had had had the

NOTE Confidence: 0.9304815

00:14:55.485 --> 00:14:57.404 distribution of, but they come

NOTE Confidence: 0.9304815

00:14:57.404 --> 00:14:58.765 about under a is equal

NOTE Confidence: 0.9304815

00:14:58.765 --> 00:15:00.285 to one, which also makes

NOTE Confidence: 0.9304815

00:15:00.285 --> 00:15:01.644 sense because you see a

NOTE Confidence: 0.9304815

00:15:01.644 --> 00:15:02.385 one there.

NOTE Confidence: 0.95383203

00:15:03.160 --> 00:15:04.360 So when the first time

NOTE Confidence: 0.95383203

00:15:04.360 --> 00:15:05.720 when I saw this mediation

NOTE Confidence: 0.95383203

00:15:05.720 --> 00:15:06.920 formula, I was like, okay,

NOTE Confidence: 0.95383203

00:15:06.920 --> 00:15:08.280 that's cool. I understand that.

NOTE Confidence: 0.95383203

00:15:08.280 --> 00:15:09.880 That seems nice. And then

NOTE Confidence: 0.95383203

00:15:09.880 --> 00:15:11.160 I was told, well, actually

NOTE Confidence: 0.95383203

00:15:11.160 --> 00:15:13.160 to prove that, you need

NOTE Confidence: 0.95383203

00:15:13.160 --> 00:15:15.000 a lot of assumptions and

NOTE Confidence: 0.95383203

00:15:15.000 --> 00:15:16.440 there's a lot of mess

NOTE Confidence: 0.95383203

00:15:16.440 --> 00:15:18.585 going around behind the scenes.

NOTE Confidence: 0.9831361

00:15:20.505 --> 00:15:21.945 So I will tell you

NOTE Confidence: 0.9831361

00:15:21.945 --> 00:15:22.745 a little bit of that

NOTE Confidence: 0.9831361

00:15:22.745 --> 00:15:24.265 mess that comes around behind

NOTE Confidence: 0.9831361

00:15:24.265 --> 00:15:25.945 the scenes, but not until

NOTE Confidence: 0.9831361

00:15:25.945 --> 00:15:27.945 I say, well, actually, if

NOTE Confidence: 0.9831361

00:15:27.945 --> 00:15:30.205 there is no treatment mediator

NOTE Confidence: 0.9723762

00:15:30.585 --> 00:15:32.425 interaction in the outcome model,

NOTE Confidence: 0.9723762

00:15:32.425 --> 00:15:33.865 so this outcome model, the

NOTE Confidence: 0.9723762

00:15:33.865 --> 00:15:34.365 expectation

NOTE Confidence: 0.95926726

00:15:34.960 --> 00:15:35.540 of y

NOTE Confidence: 0.9340968

00:15:35.840 --> 00:15:37.760 given m and a doesn't

NOTE Confidence: 0.9340968

00:15:37.760 --> 00:15:38.260 have

NOTE Confidence: 0.9311896

00:15:38.880 --> 00:15:40.820 some kind of parameter times

NOTE Confidence: 0.9311896

00:15:40.880 --> 00:15:43.380 a times m. It's just

NOTE Confidence: 0.9311896

00:15:43.520 --> 00:15:46.080 a, parameter times m plus

NOTE Confidence: 0.9311896

00:15:46.080 --> 00:15:47.865 other term parameters times

NOTE Confidence: 0.9535558

00:15:48.345 --> 00:15:48.845 a,

NOTE Confidence: 0.9870092

00:15:49.145 --> 00:15:50.205 then the resulting,

NOTE Confidence: 0.9741113

00:15:52.105 --> 00:15:53.084 indirect effect

NOTE Confidence: 0.909503

00:15:53.385 --> 00:15:54.985 is actually the same as

NOTE Confidence: 0.909503

00:15:54.985 --> 00:15:56.285 the one that was proposed

NOTE Confidence: 0.909503

00:15:56.345 --> 00:15:57.565 by Varun and Kemi.

NOTE Confidence: 0.9649508

00:15:58.505 --> 00:15:59.625 It turns out if there

NOTE Confidence: 0.9649508

00:15:59.625 --> 00:16:02.310 is an interaction between treatment

NOTE Confidence: 0.9649508

00:16:02.310 --> 00:16:03.910 and the mediator in that

NOTE Confidence: 0.9649508

00:16:03.910 --> 00:16:04.970 outcome model,

NOTE Confidence: 0.9696639

00:16:05.350 --> 00:16:07.029 that there there is a

NOTE Confidence: 0.9696639

00:16:07.029 --> 00:16:08.730 difference between the two approaches.

NOTE Confidence: 0.9608584

00:16:09.269 --> 00:16:10.709 And this has actually been

NOTE Confidence: 0.9608584

00:16:10.709 --> 00:16:12.550 used by causal inference people

NOTE Confidence: 0.9608584

00:16:12.550 --> 00:16:13.990 to say that Baron and

NOTE Confidence: 0.9608584

00:16:13.990 --> 00:16:15.290 Kenny got it wrong.

NOTE Confidence: 0.9917541

00:16:16.095 --> 00:16:17.295 And this is something with

NOTE Confidence: 0.9917541

00:16:17.295 --> 00:16:19.074 which I personally completely

NOTE Confidence: 0.9638684

00:16:19.375 --> 00:16:20.975 disagree with because I do

NOTE Confidence: 0.9638684

00:16:20.975 --> 00:16:22.095 not think I got it

NOTE Confidence: 0.9638684

00:16:22.095 --> 00:16:22.595 wrong.

NOTE Confidence: 0.9964021

00:16:22.975 --> 00:16:24.014 I think we have to

NOTE Confidence: 0.9964021

00:16:24.014 --> 00:16:24.915 think carefully

NOTE Confidence: 0.96506894

00:16:25.375 --> 00:16:26.755 about what we want.

NOTE Confidence: 0.93703794

00:16:27.295 --> 00:16:29.139 And, there I mean, do

NOTE Confidence: 0.93703794

00:16:29.139 --> 00:16:30.500 we want to set the

NOTE Confidence: 0.93703794

00:16:30.500 --> 00:16:32.440 mediator to its value without

NOTE Confidence: 0.93703794

00:16:32.500 --> 00:16:33.000 treatment,

NOTE Confidence: 0.9953283

00:16:33.620 --> 00:16:34.980 or do we want to

NOTE Confidence: 0.9953283

00:16:34.980 --> 00:16:36.500 set the mediator to its

NOTE Confidence: 0.9953283

00:16:36.500 --> 00:16:37.800 value with treatment?

NOTE Confidence: 0.9831163

00:16:38.500 --> 00:16:40.279 And depending on the application,

NOTE Confidence: 0.9831163

00:16:40.579 --> 00:16:41.800 the one is of interest

NOTE Confidence: 0.9831163

00:16:41.940 --> 00:16:43.060 or the other is of

NOTE Confidence: 0.9831163

00:16:43.060 --> 00:16:43.560 interest.

NOTE Confidence: 0.9619624

00:16:45.185 --> 00:16:46.645 If we set the mediator

NOTE Confidence: 0.9619624

00:16:46.705 --> 00:16:48.645 to its value with treatment,

NOTE Confidence: 0.8182268

00:16:50.225 --> 00:16:51.525 suddenly get it right.

NOTE Confidence: 0.98786575

00:16:52.145 --> 00:16:53.265 In other words, if we

NOTE Confidence: 0.98786575

00:16:53.265 --> 00:16:54.705 start missing out with what

NOTE Confidence: 0.98786575

00:16:54.705 --> 00:16:55.985 we call treatment and what

NOTE Confidence: 0.98786575

00:16:55.985 --> 00:16:57.205 we call control,

NOTE Confidence: 0.9125261

00:16:57.770 --> 00:16:59.450 then sometimes Baron and Kenny

NOTE Confidence: 0.9125261

00:16:59.450 --> 00:17:00.890 get it right and sometimes

NOTE Confidence: 0.9125261

00:17:00.890 --> 00:17:02.030 they get it wrong.

NOTE Confidence: 0.9652316

00:17:02.570 --> 00:17:04.350 In other ways, they are

NOTE Confidence: 0.9652316

00:17:04.410 --> 00:17:04.910 after

NOTE Confidence: 0.92020065

00:17:05.369 --> 00:17:05.869 both

NOTE Confidence: 0.93274325

00:17:07.290 --> 00:17:09.210 by causal inference people have

NOTE Confidence: 0.93274325

00:17:09.210 --> 00:17:11.710 been called the pure indirect

NOTE Confidence: 0.93274325

00:17:11.850 --> 00:17:12.350 effect.

NOTE Confidence: 0.94869095

00:17:12.805 --> 00:17:13.845 And then you look at

NOTE Confidence: 0.94869095

00:17:13.845 --> 00:17:14.345 their

NOTE Confidence: 0.9967997

00:17:15.845 --> 00:17:16.345 interpretation

NOTE Confidence: 0.9713153

00:17:16.645 --> 00:17:18.105 that I just showed you,

NOTE Confidence: 0.9713153

00:17:18.165 --> 00:17:19.525 that is also more in

NOTE Confidence: 0.9713153

00:17:19.525 --> 00:17:21.305 line with the pure indirect

NOTE Confidence: 0.9713153

00:17:21.365 --> 00:17:21.865 effect

NOTE Confidence: 0.9441386

00:17:22.165 --> 00:17:23.045 than it is with a

NOTE Confidence: 0.9441386

00:17:23.045 --> 00:17:24.585 natural indirect effect.

NOTE Confidence: 0.99614096

00:17:26.609 --> 00:17:27.750 Okay. So

NOTE Confidence: 0.91642493

00:17:28.050 --> 00:17:30.150 under certain conditions, strong parametric

NOTE Confidence: 0.91642493

00:17:30.290 --> 00:17:32.290 assumptions, linear models, and no

NOTE Confidence: 0.91642493

00:17:32.290 --> 00:17:34.930 exposure mediator indirection, they do

NOTE Confidence: 0.91642493

00:17:34.930 --> 00:17:36.210 get the same as Baron

NOTE Confidence: 0.91642493

00:17:36.210 --> 00:17:37.730 and Kenny. And so they

NOTE Confidence: 0.91642493

00:17:37.730 --> 00:17:39.109 add a causal interpretation

NOTE Confidence: 0.9404726

00:17:39.490 --> 00:17:40.230 to that,

NOTE Confidence: 0.98526543

00:17:40.835 --> 00:17:42.435 line of research, which is

NOTE Confidence: 0.98526543

00:17:42.435 --> 00:17:43.255 very important

NOTE Confidence: 0.86158776

00:17:43.795 --> 00:17:45.335 because you saw how many

NOTE Confidence: 0.86158776

00:17:45.395 --> 00:17:46.695 citations that got.

NOTE Confidence: 0.98085153

00:17:47.875 --> 00:17:49.715 It's important to underpin that

NOTE Confidence: 0.98085153

00:17:49.715 --> 00:17:51.255 also from a causal perspective.

NOTE Confidence: 0.89636785

00:17:52.035 --> 00:17:54.135 Most methods need many quantifiable

NOTE Confidence: 0.84611815

00:17:54.515 --> 00:17:56.609 outcomes. They use the come

NOTE Confidence: 0.84611815

00:17:56.609 --> 00:17:57.890 on their treatment with the

NOTE Confidence: 0.84611815

00:17:57.890 --> 00:17:59.570 mediator set which value without

NOTE Confidence: 0.84611815

00:17:59.570 --> 00:18:00.070 treatment,

NOTE Confidence: 0.9768573

00:18:00.530 --> 00:18:02.050 and I don't haven't seen

NOTE Confidence: 0.9768573

00:18:02.050 --> 00:18:03.910 many causal inference approaches

NOTE Confidence: 0.9692797

00:18:04.530 --> 00:18:06.130 that don't also talk about

NOTE Confidence: 0.9692797

00:18:06.130 --> 00:18:06.869 the outcome

NOTE Confidence: 0.78918546

00:18:07.650 --> 00:18:08.550 on their treatment

NOTE Confidence: 0.87729764

00:18:08.945 --> 00:18:10.705 where the mediator sets to

NOTE Confidence: 0.87729764

00:18:10.705 --> 00:18:11.845 any very particular

NOTE Confidence: 0.97875416

00:18:12.304 --> 00:18:14.565 value of the mediator.

NOTE Confidence: 0.998058

00:18:15.505 --> 00:18:16.804 And this requires

NOTE Confidence: 0.9722643

00:18:17.105 --> 00:18:18.304 that you can set the

NOTE Confidence: 0.9722643

00:18:18.304 --> 00:18:18.804 mediator,

NOTE Confidence: 0.9274699

00:18:19.825 --> 00:18:21.105 which you can sometimes do

NOTE Confidence: 0.9274699

00:18:21.105 --> 00:18:22.565 but sometimes also not.

NOTE Confidence: 0.99602747

00:18:24.930 --> 00:18:26.770 So the first thing is,

NOTE Confidence: 0.9534458

00:18:27.330 --> 00:18:28.369 so when we talk about

NOTE Confidence: 0.9534458

00:18:28.369 --> 00:18:29.350 these counterfactual

NOTE Confidence: 0.917762

00:18:29.650 --> 00:18:31.490 outcomes, they are called cross

NOTE Confidence: 0.917762

00:18:31.490 --> 00:18:31.990 rules

NOTE Confidence: 0.96551526

00:18:32.369 --> 00:18:32.869 counterfactuals

NOTE Confidence: 0.90259874

00:18:33.330 --> 00:18:34.609 because we are talking out

NOTE Confidence: 0.90259874

00:18:34.609 --> 00:18:36.050 about the mediator that is

NOTE Confidence: 0.90259874

00:18:36.050 --> 00:18:37.410 set to its value without

NOTE Confidence: 0.90259874

00:18:37.410 --> 00:18:37.910 treatment

NOTE Confidence: 0.96502924

00:18:38.369 --> 00:18:40.125 while a person is treated.

NOTE Confidence: 0.9704189

00:18:40.505 --> 00:18:41.545 So even if we could

NOTE Confidence: 0.9704189

00:18:41.545 --> 00:18:42.905 set the mediator, we don't

NOTE Confidence: 0.9704189

00:18:42.905 --> 00:18:44.424 typically know how to set

NOTE Confidence: 0.9704189

00:18:44.424 --> 00:18:45.804 it or where to set

NOTE Confidence: 0.9704189

00:18:46.025 --> 00:18:47.465 it because we don't if

NOTE Confidence: 0.9704189

00:18:47.465 --> 00:18:48.665 we treat the person, we

NOTE Confidence: 0.9704189

00:18:48.665 --> 00:18:50.525 don't observe their mediator under

NOTE Confidence: 0.9704189

00:18:50.744 --> 00:18:51.960 under no treatment, so we

NOTE Confidence: 0.9704189

00:18:51.960 --> 00:18:53.640 don't know where to set

NOTE Confidence: 0.9704189

00:18:53.640 --> 00:18:54.600 it. And

NOTE Confidence: 0.9027667

00:18:55.320 --> 00:18:56.280 but this is this is

NOTE Confidence: 0.9027667

00:18:56.280 --> 00:18:57.640 what has been generally in

NOTE Confidence: 0.9027667

00:18:57.640 --> 00:18:59.100 the postural inference literature

NOTE Confidence: 0.7162745

00:18:59.960 --> 00:19:00.780 being attacked

NOTE Confidence: 0.99017406

00:19:01.400 --> 00:19:02.060 to the

NOTE Confidence: 0.938619

00:19:02.440 --> 00:19:03.260 to the,

NOTE Confidence: 0.98889893

00:19:04.440 --> 00:19:06.380 natural indirect effect approach.

NOTE Confidence: 0.9663227

00:19:07.135 --> 00:19:08.575 But what I find actually

NOTE Confidence: 0.9663227

00:19:08.575 --> 00:19:09.475 more bothersome

NOTE Confidence: 0.9710886

00:19:10.174 --> 00:19:11.455 is that in many cases,

NOTE Confidence: 0.9710886

00:19:11.455 --> 00:19:13.234 we cannot set a mediator.

NOTE Confidence: 0.9508658

00:19:13.775 --> 00:19:15.054 When you look at the

NOTE Confidence: 0.9508658

00:19:15.054 --> 00:19:17.455 first paper that Judea Pearl

NOTE Confidence: 0.9508658

00:19:17.455 --> 00:19:19.794 published on causal mediation analysis,

NOTE Confidence: 0.87338525

00:19:20.414 --> 00:19:22.500 his example is a mediator

NOTE Confidence: 0.78862983

00:19:22.900 --> 00:19:23.400 aspirin

NOTE Confidence: 0.8328457

00:19:24.580 --> 00:19:26.440 and aspirin use was more

NOTE Confidence: 0.99908245

00:19:26.980 --> 00:19:27.480 common

NOTE Confidence: 0.86616117

00:19:28.180 --> 00:19:30.020 under treatment than under no

NOTE Confidence: 0.86616117

00:19:30.020 --> 00:19:31.859 treatment because aspirin use was

NOTE Confidence: 0.86616117

00:19:31.859 --> 00:19:33.400 you, aspirin was used

NOTE Confidence: 0.9965971

00:19:33.780 --> 00:19:34.280 to

NOTE Confidence: 0.930034

00:19:35.385 --> 00:19:36.505 make sure that the side

NOTE Confidence: 0.930034

00:19:36.505 --> 00:19:37.945 effects of the treatment were

NOTE Confidence: 0.930034

00:19:37.945 --> 00:19:39.625 not too heavy because the

NOTE Confidence: 0.930034

00:19:39.625 --> 00:19:40.905 treatment treatment con

NOTE Confidence: 0.811078

00:19:42.025 --> 00:19:43.405 resulted in headaches,

NOTE Confidence: 0.95943147

00:19:44.265 --> 00:19:45.625 and so the aspirin was

NOTE Confidence: 0.95943147

00:19:45.625 --> 00:19:47.005 used to treat the headaches.

NOTE Confidence: 0.95212775

00:19:47.770 --> 00:19:48.970 About then, the effect of

NOTE Confidence: 0.95212775

00:19:48.970 --> 00:19:51.150 the treatment was mediated through

NOTE Confidence: 0.91678256

00:19:51.609 --> 00:19:53.369 the aspirin dose, which was

NOTE Confidence: 0.91678256

00:19:53.369 --> 00:19:53.869 helpful,

NOTE Confidence: 0.97036386

00:19:54.410 --> 00:19:56.170 but was not the was

NOTE Confidence: 0.97036386

00:19:56.170 --> 00:19:57.850 not really the intended effect

NOTE Confidence: 0.97036386

00:19:57.850 --> 00:19:58.670 of the treatment.

NOTE Confidence: 0.9443103

00:19:59.290 --> 00:20:00.410 So they wanted to figure

NOTE Confidence: 0.9443103

00:20:00.410 --> 00:20:01.369 out how much of the

NOTE Confidence: 0.9443103

00:20:01.369 --> 00:20:03.115 effect of the original treatment

NOTE Confidence: 0.9443103

00:20:03.115 --> 00:20:04.715 will work through the aspirin

NOTE Confidence: 0.9443103

00:20:04.715 --> 00:20:06.234 use and how much of

NOTE Confidence: 0.9443103

00:20:06.234 --> 00:20:07.994 the treatment effect works through

NOTE Confidence: 0.9443103

00:20:07.994 --> 00:20:08.815 our pathways.

NOTE Confidence: 0.82026404

00:20:09.835 --> 00:20:11.355 But our pathways were in

NOTE Confidence: 0.82026404

00:20:11.355 --> 00:20:12.895 this case actually the intended

NOTE Confidence: 0.82026404

00:20:12.955 --> 00:20:13.455 effect.

NOTE Confidence: 0.9463766

00:20:14.520 --> 00:20:16.140 But there are other settings,

NOTE Confidence: 0.9632918

00:20:16.440 --> 00:20:18.619 and that includes my HIV

NOTE Confidence: 0.9632918

00:20:18.840 --> 00:20:19.340 example,

NOTE Confidence: 0.89416575

00:20:19.960 --> 00:20:20.780 where the,

NOTE Confidence: 0.99238145

00:20:21.400 --> 00:20:22.220 where the

NOTE Confidence: 0.9240511

00:20:22.520 --> 00:20:24.940 mediator is the HIV reservoir.

NOTE Confidence: 0.9304819

00:20:25.640 --> 00:20:26.840 Now if you were able

NOTE Confidence: 0.9304819

00:20:26.840 --> 00:20:28.140 to set the HIV

NOTE Confidence: 0.9983347

00:20:28.440 --> 00:20:28.940 reservoir,

NOTE Confidence: 0.6584892

00:20:29.994 --> 00:20:32.494 HIV research would be down

NOTE Confidence: 0.94040936

00:20:33.115 --> 00:20:35.355 there. We're we're ready because

NOTE Confidence: 0.94040936

00:20:35.355 --> 00:20:36.794 if we can set the

NOTE Confidence: 0.94040936

00:20:36.794 --> 00:20:37.934 HIV reservoir,

NOTE Confidence: 0.9547038

00:20:38.554 --> 00:20:39.914 we're going to set it

NOTE Confidence: 0.9547038

00:20:39.914 --> 00:20:40.734 to zero,

NOTE Confidence: 0.9820157

00:20:41.434 --> 00:20:42.955 and all these patients are

NOTE Confidence: 0.9820157

00:20:42.955 --> 00:20:44.815 suddenly cured of HIV.

NOTE Confidence: 0.54639745

00:20:46.020 --> 00:20:46.520 And,

NOTE Confidence: 0.98442984

00:20:48.260 --> 00:20:48.760 hypothetically,

NOTE Confidence: 0.94594306

00:20:49.140 --> 00:20:50.740 this is awesome. In practice,

NOTE Confidence: 0.94594306

00:20:50.740 --> 00:20:52.340 it doesn't doesn't work because

NOTE Confidence: 0.94594306

00:20:52.340 --> 00:20:54.100 there are no treatments that

NOTE Confidence: 0.94594306

00:20:54.100 --> 00:20:55.800 set the HIV reservoir.

NOTE Confidence: 0.97994274

00:20:56.260 --> 00:20:58.260 People are really trying very

NOTE Confidence: 0.97994274

00:20:58.260 --> 00:20:59.960 hard to reduce it.

NOTE Confidence: 0.98601407

00:21:00.285 --> 00:21:01.405 But even if they can

NOTE Confidence: 0.98601407

00:21:01.405 --> 00:21:03.005 reduce it, they can probably

NOTE Confidence: 0.98601407

00:21:03.005 --> 00:21:04.365 not set it to any

NOTE Confidence: 0.98601407

00:21:04.365 --> 00:21:06.125 particular value. They'll be able

NOTE Confidence: 0.98601407

00:21:06.125 --> 00:21:07.665 to change the distribution,

NOTE Confidence: 0.96180314

00:21:08.285 --> 00:21:09.244 but they are not able

NOTE Confidence: 0.96180314

00:21:09.244 --> 00:21:10.045 to set it to a

NOTE Confidence: 0.96180314

00:21:10.045 --> 00:21:11.265 particular value.

NOTE Confidence: 0.99643785

00:21:11.565 --> 00:21:13.505 So I I don't usually

NOTE Confidence: 0.99643785

00:21:13.645 --> 00:21:14.145 know

NOTE Confidence: 0.9640797

00:21:14.445 --> 00:21:16.040 how to set that mediator,

NOTE Confidence: 0.9640797

00:21:16.180 --> 00:21:18.280 how to how to internalize

NOTE Confidence: 0.97980976

00:21:18.580 --> 00:21:19.080 that.

NOTE Confidence: 0.94543856

00:21:19.860 --> 00:21:20.820 So how to set the

NOTE Confidence: 0.94543856

00:21:20.820 --> 00:21:22.680 mediator is usually left unanswered.

NOTE Confidence: 0.9127228

00:21:22.980 --> 00:21:24.820 Outcomes are undefined in many

NOTE Confidence: 0.9127228

00:21:24.820 --> 00:21:26.600 many practical situations.

NOTE Confidence: 0.8614793

00:21:27.525 --> 00:21:29.625 Colin Frankakis provide an illustrative

NOTE Confidence: 0.8614793

00:21:29.845 --> 00:21:30.345 example.

NOTE Confidence: 0.993794

00:21:30.885 --> 00:21:32.505 There are many competing

NOTE Confidence: 0.9502901

00:21:32.805 --> 00:21:35.065 ways to assign hypothetically

NOTE Confidence: 0.95995635

00:21:35.445 --> 00:21:36.645 a body mass index of

NOTE Confidence: 0.95995635

00:21:36.645 --> 00:21:38.565 twenty five kilograms per square

NOTE Confidence: 0.95995635

00:21:38.565 --> 00:21:40.265 meter to an individual,

NOTE Confidence: 0.9746034

00:21:40.565 --> 00:21:41.685 and each of them may

NOTE Confidence: 0.9746034

00:21:41.685 --> 00:21:43.590 have a different effect, causal

NOTE Confidence: 0.9746034

00:21:43.590 --> 00:21:44.090 effect

NOTE Confidence: 0.7285105

00:21:44.470 --> 00:21:45.290 on me.

NOTE Confidence: 0.9909403

00:21:47.109 --> 00:21:48.310 You can think of very

NOTE Confidence: 0.9909403

00:21:48.310 --> 00:21:49.369 extreme ways

NOTE Confidence: 0.9354474

00:21:50.310 --> 00:21:51.750 to reduce their body mass

NOTE Confidence: 0.9354474

00:21:51.750 --> 00:21:52.250 index.

NOTE Confidence: 0.8960686

00:21:56.645 --> 00:21:57.925 So people have been trying

NOTE Confidence: 0.8960686

00:21:57.925 --> 00:21:59.925 to get around these couch

NOTE Confidence: 0.8960686

00:22:00.165 --> 00:22:02.105 the these crossroads counterfactuals.

NOTE Confidence: 0.97842896

00:22:02.805 --> 00:22:04.645 I haven't seen many approaches

NOTE Confidence: 0.97842896

00:22:04.645 --> 00:22:06.025 that also try to

NOTE Confidence: 0.9943816

00:22:06.325 --> 00:22:07.705 get out of,

NOTE Confidence: 0.9895127

00:22:08.085 --> 00:22:09.465 out of these ones.

NOTE Confidence: 0.9376178

00:22:09.980 --> 00:22:11.180 My approach also tries to

NOTE Confidence: 0.9376178

00:22:11.180 --> 00:22:12.220 get out of these ones

NOTE Confidence: 0.9376178

00:22:12.220 --> 00:22:13.900 because I want to apply

NOTE Confidence: 0.9376178

00:22:13.900 --> 00:22:16.300 to these HIV examples, to

NOTE Confidence: 0.9376178

00:22:16.300 --> 00:22:17.900 the COVID nineteen example where

NOTE Confidence: 0.9376178

00:22:17.900 --> 00:22:19.340 we cannot set them in

NOTE Confidence: 0.9376178

00:22:19.340 --> 00:22:19.840 use.

NOTE Confidence: 0.8754529

00:22:21.740 --> 00:22:23.280 So I have been proposing

NOTE Confidence: 0.8754529

00:22:23.340 --> 00:22:24.940 organic direct and indirect effects

NOTE Confidence: 0.8754529

00:22:24.940 --> 00:22:25.994 that I will tell you

NOTE Confidence: 0.8754529

00:22:25.994 --> 00:22:26.494 about.

NOTE Confidence: 0.8874739

00:22:27.035 --> 00:22:28.155 It can be shown that

NOTE Confidence: 0.8874739

00:22:28.155 --> 00:22:29.215 they are a generalization

NOTE Confidence: 0.9691717

00:22:29.835 --> 00:22:31.755 of randomized direct and indirect

NOTE Confidence: 0.9691717

00:22:31.755 --> 00:22:32.255 effects.

NOTE Confidence: 0.981221

00:22:33.835 --> 00:22:34.975 And they're also

NOTE Confidence: 0.88409483

00:22:35.355 --> 00:22:36.875 most likely, I have the

NOTE Confidence: 0.88409483

00:22:36.875 --> 00:22:37.915 proof for that, but not

NOTE Confidence: 0.88409483

00:22:37.915 --> 00:22:38.415 published.

NOTE Confidence: 0.80722207

00:22:38.960 --> 00:22:40.500 There are also a generalization

NOTE Confidence: 0.94027203

00:22:40.880 --> 00:22:42.820 of separable, direct, and indirect

NOTE Confidence: 0.94027203

00:22:42.880 --> 00:22:44.160 effects that are also around

NOTE Confidence: 0.94027203

00:22:44.160 --> 00:22:44.820 the literature.

NOTE Confidence: 0.95847553

00:22:45.119 --> 00:22:46.080 So I will tell you

NOTE Confidence: 0.95847553

00:22:46.080 --> 00:22:47.700 what those are, the organic

NOTE Confidence: 0.95847553

00:22:47.760 --> 00:22:49.140 indirect and direct effects.

NOTE Confidence: 0.92353886

00:22:50.160 --> 00:22:51.700 So I as an intervention

NOTE Confidence: 0.92353886

00:22:51.760 --> 00:22:53.280 on the mediator that is

NOTE Confidence: 0.92353886

00:22:53.280 --> 00:22:55.274 not that doesn't affect the

NOTE Confidence: 0.92353886

00:22:55.274 --> 00:22:57.115 pretreatment common causes of the

NOTE Confidence: 0.92353886

00:22:57.115 --> 00:22:59.375 mediator m and the outcome

NOTE Confidence: 0.92353886

00:22:59.514 --> 00:23:00.014 y.

NOTE Confidence: 0.997572

00:23:00.635 --> 00:23:01.755 And then I'm going to

NOTE Confidence: 0.997572

00:23:01.755 --> 00:23:02.815 talk about

NOTE Confidence: 0.9950923

00:23:03.274 --> 00:23:04.014 the mediator

NOTE Confidence: 0.89508814

00:23:04.635 --> 00:23:05.994 under no treatment but with

NOTE Confidence: 0.89508814

00:23:05.994 --> 00:23:06.575 the intervention

NOTE Confidence: 0.967677

00:23:07.519 --> 00:23:09.119 and the outcome under no

NOTE Confidence: 0.967677

00:23:09.119 --> 00:23:10.659 treatment but with the intervention.

NOTE Confidence: 0.835336

00:23:12.559 --> 00:23:13.760 It's an intervention on the

NOTE Confidence: 0.835336

00:23:13.760 --> 00:23:14.260 mediator.

NOTE Confidence: 0.9897228

00:23:16.960 --> 00:23:18.960 And then I define something

NOTE Confidence: 0.9897228

00:23:18.960 --> 00:23:20.580 as an organic intervention

NOTE Confidence: 0.98649

00:23:21.175 --> 00:23:22.635 If under the intervention,

NOTE Confidence: 0.9985799

00:23:22.935 --> 00:23:24.455 the mediator has the same

NOTE Confidence: 0.9985799

00:23:24.455 --> 00:23:26.455 distribution as the mediator under

NOTE Confidence: 0.9985799

00:23:26.455 --> 00:23:27.115 the treatment

NOTE Confidence: 0.89434534

00:23:28.535 --> 00:23:29.975 given the common causes, you

NOTE Confidence: 0.89434534

00:23:29.975 --> 00:23:31.415 have to always respect the

NOTE Confidence: 0.89434534

00:23:31.415 --> 00:23:32.234 common causes.

NOTE Confidence: 0.9967147

00:23:33.600 --> 00:23:35.700 And then the other condition

NOTE Confidence: 0.9967147

00:23:35.920 --> 00:23:37.299 for an organic intervention

NOTE Confidence: 0.99570525

00:23:38.000 --> 00:23:40.020 is that once the mediator

NOTE Confidence: 0.99570525

00:23:40.240 --> 00:23:42.580 comes about under the intervention,

NOTE Confidence: 0.99603766

00:23:44.240 --> 00:23:46.320 then it doesn't matter how

NOTE Confidence: 0.99603766

00:23:46.320 --> 00:23:46.815 that

NOTE Confidence: 0.9910181

00:23:47.134 --> 00:23:48.894 mediator comes about under the

NOTE Confidence: 0.9910181

00:23:48.894 --> 00:23:49.394 intervention.

NOTE Confidence: 0.93327516

00:23:50.095 --> 00:23:51.554 After this, the outcomes

NOTE Confidence: 0.95320696

00:23:52.494 --> 00:23:54.734 follow their natural course as

NOTE Confidence: 0.95320696

00:23:54.734 --> 00:23:56.994 though that mediator equals m

NOTE Confidence: 0.95320696

00:23:57.215 --> 00:23:59.455 came about naturally under no

NOTE Confidence: 0.95320696

00:23:59.455 --> 00:23:59.955 treatment.

NOTE Confidence: 0.9984248

00:24:02.070 --> 00:24:03.750 So after the mediator comes

NOTE Confidence: 0.9984248

00:24:03.750 --> 00:24:05.210 about under the intervention,

NOTE Confidence: 0.9515843

00:24:06.390 --> 00:24:08.010 the system follow its natural

NOTE Confidence: 0.9515843

00:24:08.070 --> 00:24:09.690 course as though the mediator

NOTE Confidence: 0.9515843

00:24:09.750 --> 00:24:10.570 came about

NOTE Confidence: 0.9053537

00:24:10.950 --> 00:24:12.789 without treatment. The expected outcome

NOTE Confidence: 0.9053537

00:24:12.789 --> 00:24:13.830 is the same. I have,

NOTE Confidence: 0.9053537

00:24:13.830 --> 00:24:15.029 in the past, sometimes even

NOTE Confidence: 0.9053537

00:24:15.029 --> 00:24:16.230 have a vaguely sign language,

NOTE Confidence: 0.9053537

00:24:16.230 --> 00:24:17.049 but the distribution

NOTE Confidence: 0.9705877

00:24:17.429 --> 00:24:19.085 is the same. The only

NOTE Confidence: 0.9705877

00:24:19.085 --> 00:24:20.125 thing that you really need

NOTE Confidence: 0.9705877

00:24:20.125 --> 00:24:21.244 is the expected value that's

NOTE Confidence: 0.9705877

00:24:21.244 --> 00:24:21.905 the same.

NOTE Confidence: 0.87846476

00:24:22.525 --> 00:24:24.205 So after I effects the

NOTE Confidence: 0.87846476

00:24:24.205 --> 00:24:24.705 mediator,

NOTE Confidence: 0.9456038

00:24:25.725 --> 00:24:27.244 the system follows its natural

NOTE Confidence: 0.9456038

00:24:27.244 --> 00:24:28.465 course as though the mediator

NOTE Confidence: 0.9456038

00:24:28.525 --> 00:24:30.280 value came about with no

NOTE Confidence: 0.9456038

00:24:30.280 --> 00:24:31.560 treatment a is equal to

NOTE Confidence: 0.9456038

00:24:31.560 --> 00:24:33.080 zero. And for the system

NOTE Confidence: 0.9456038

00:24:33.080 --> 00:24:34.119 to know where it has

NOTE Confidence: 0.9456038

00:24:34.119 --> 00:24:34.940 to go,

NOTE Confidence: 0.9552631

00:24:35.480 --> 00:24:37.240 you need to condition on

NOTE Confidence: 0.9552631

00:24:37.240 --> 00:24:38.300 the common causes

NOTE Confidence: 0.89995795

00:24:39.080 --> 00:24:40.760 because otherwise the system will

NOTE Confidence: 0.89995795

00:24:40.760 --> 00:24:42.140 go wherever it will ignore

NOTE Confidence: 0.89995795

00:24:42.280 --> 00:24:43.560 common causes and then you

NOTE Confidence: 0.89995795

00:24:43.560 --> 00:24:44.920 don't really truly know where

NOTE Confidence: 0.89995795

00:24:44.920 --> 00:24:45.855 it wants to go.

NOTE Confidence: 0.987376

00:24:47.934 --> 00:24:49.215 For example, a is equal

NOTE Confidence: 0.987376

00:24:49.215 --> 00:24:50.015 to one is the blood

NOTE Confidence: 0.987376

00:24:50.015 --> 00:24:51.234 pressure lowering medication

NOTE Confidence: 0.9507847

00:24:51.775 --> 00:24:53.215 and blood pressure by the

NOTE Confidence: 0.9507847

00:24:53.215 --> 00:24:54.755 occurrence of a heart attack.

NOTE Confidence: 0.9253554

00:24:55.215 --> 00:24:56.415 Does a is one have

NOTE Confidence: 0.9253554

00:24:56.415 --> 00:24:57.775 a direct havoc on heart

NOTE Confidence: 0.9253554

00:24:57.775 --> 00:24:58.275 attacks?

NOTE Confidence: 0.94912934

00:24:58.600 --> 00:25:00.119 Well, for example, blood pressure

NOTE Confidence: 0.94912934

00:25:00.119 --> 00:25:01.559 lowering medication, so this could

NOTE Confidence: 0.94912934

00:25:01.559 --> 00:25:02.679 be the distribution of the

NOTE Confidence: 0.94912934

00:25:02.679 --> 00:25:03.419 blood pressure,

NOTE Confidence: 0.9619068

00:25:03.799 --> 00:25:05.159 then maybe it's just a

NOTE Confidence: 0.9619068

00:25:05.159 --> 00:25:06.619 shift of the blood pressure

NOTE Confidence: 0.8789659

00:25:07.720 --> 00:25:08.619 distribution, the treatment.

NOTE Confidence: 0.9942959

00:25:09.000 --> 00:25:10.759 So the intervention also has

NOTE Confidence: 0.9942959

00:25:10.759 --> 00:25:12.440 to be a shift in

NOTE Confidence: 0.9942959

00:25:12.440 --> 00:25:13.019 the distribution

NOTE Confidence: 0.9065266

00:25:13.320 --> 00:25:15.305 of the blood pressure and

NOTE Confidence: 0.9065266

00:25:15.305 --> 00:25:16.125 maybe we could

NOTE Confidence: 0.95529795

00:25:16.744 --> 00:25:18.585 think of this as, as

NOTE Confidence: 0.95529795

00:25:18.585 --> 00:25:20.185 a salt reduction because that

NOTE Confidence: 0.95529795

00:25:20.185 --> 00:25:22.025 also changes the blood pressure

NOTE Confidence: 0.95529795

00:25:22.025 --> 00:25:22.525 distribution.

NOTE Confidence: 0.99804634

00:25:23.545 --> 00:25:24.285 And then

NOTE Confidence: 0.96538067

00:25:24.585 --> 00:25:25.945 after that, it has to

NOTE Confidence: 0.96538067

00:25:25.945 --> 00:25:26.765 be that,

NOTE Confidence: 0.96482164

00:25:29.049 --> 00:25:30.570 the heart attacks follow their

NOTE Confidence: 0.96482164

00:25:30.570 --> 00:25:32.090 course as though that reduced

NOTE Confidence: 0.96482164

00:25:32.090 --> 00:25:34.190 blood pressure came about without

NOTE Confidence: 0.7573718

00:25:35.770 --> 00:25:37.309 the treatment or without

NOTE Confidence: 0.83099794

00:25:37.770 --> 00:25:38.510 the Schult.

NOTE Confidence: 0.944451

00:25:41.455 --> 00:25:42.734 And it turns out that

NOTE Confidence: 0.944451

00:25:42.734 --> 00:25:44.414 Schult is believed to have

NOTE Confidence: 0.944451

00:25:44.414 --> 00:25:46.174 an effect on on heart

NOTE Confidence: 0.944451

00:25:46.174 --> 00:25:47.855 attacks only through its effects

NOTE Confidence: 0.944451

00:25:47.855 --> 00:25:49.455 on blood pressure. You can

NOTE Confidence: 0.944451

00:25:49.455 --> 00:25:50.255 look it up in the

NOTE Confidence: 0.944451

00:25:50.255 --> 00:25:51.315 CDC website.

NOTE Confidence: 0.8393913

00:25:51.934 --> 00:25:53.294 And so maybe we can

NOTE Confidence: 0.8393913

00:25:53.294 --> 00:25:54.655 affect and we can we

NOTE Confidence: 0.8393913

00:25:54.655 --> 00:25:55.395 can think

NOTE Confidence: 0.98336625

00:25:55.710 --> 00:25:57.330 that once the blood pressure

NOTE Confidence: 0.98336625

00:25:57.390 --> 00:25:59.309 has been lowered by the

NOTE Confidence: 0.98336625

00:25:59.309 --> 00:26:00.130 salt reduction,

NOTE Confidence: 0.96317726

00:26:00.590 --> 00:26:01.789 that after that, it is

NOTE Confidence: 0.96317726

00:26:01.789 --> 00:26:03.390 just as though the blood

NOTE Confidence: 0.96317726

00:26:03.390 --> 00:26:04.830 pressure came about without the

NOTE Confidence: 0.96317726

00:26:04.830 --> 00:26:05.570 salt reduction.

NOTE Confidence: 0.981804

00:26:07.230 --> 00:26:08.684 So what does salt reduction

NOTE Confidence: 0.981804

00:26:08.684 --> 00:26:09.965 do? It has no direct

NOTE Confidence: 0.981804

00:26:09.965 --> 00:26:11.484 effect on heart attacks according

NOTE Confidence: 0.981804

00:26:11.484 --> 00:26:12.304 to the CDC.

NOTE Confidence: 0.93768793

00:26:12.605 --> 00:26:14.125 It affects blood pressure and

NOTE Confidence: 0.93768793

00:26:14.125 --> 00:26:15.244 the same as a is

NOTE Confidence: 0.93768793

00:26:15.244 --> 00:26:16.765 equal to one does. So

NOTE Confidence: 0.93768793

00:26:16.765 --> 00:26:17.885 its effect should be the

NOTE Confidence: 0.93768793

00:26:17.885 --> 00:26:19.165 effect of a is equal

NOTE Confidence: 0.93768793

00:26:19.165 --> 00:26:20.684 to one mediated through the

NOTE Confidence: 0.93768793

00:26:20.684 --> 00:26:22.649 blood pressure. So that's the

NOTE Confidence: 0.93768793

00:26:22.649 --> 00:26:24.750 idea of an organic intervention.

NOTE Confidence: 0.93768793

00:26:24.889 --> 00:26:25.629 It affects

NOTE Confidence: 0.982284

00:26:26.169 --> 00:26:27.529 the mediator the same way

NOTE Confidence: 0.982284

00:26:27.529 --> 00:26:29.210 as the treatment does, but

NOTE Confidence: 0.982284

00:26:29.210 --> 00:26:30.649 after that, the system follows

NOTE Confidence: 0.982284

00:26:30.649 --> 00:26:32.029 its natural course

NOTE Confidence: 0.9878668

00:26:32.330 --> 00:26:34.169 as though that mediator came

NOTE Confidence: 0.9878668

00:26:34.169 --> 00:26:35.389 about without treatment.

NOTE Confidence: 0.97192955

00:26:38.855 --> 00:26:40.475 And then you can define

NOTE Confidence: 0.97192955

00:26:40.535 --> 00:26:42.375 the indirect effect. So here

NOTE Confidence: 0.97192955

00:26:42.375 --> 00:26:44.554 we have the mediator distribution

NOTE Confidence: 0.90508354

00:26:45.015 --> 00:26:46.615 is the distribution of m

NOTE Confidence: 0.90508354

00:26:46.615 --> 00:26:47.994 one under the intervention.

NOTE Confidence: 0.9644077

00:26:48.455 --> 00:26:49.815 Here we have m zero

NOTE Confidence: 0.9644077

00:26:49.815 --> 00:26:51.175 itself. So this is the

NOTE Confidence: 0.9644077

00:26:51.175 --> 00:26:52.315 mediated effect.

NOTE Confidence: 0.9444896

00:26:52.980 --> 00:26:54.520 And here we have the

NOTE Confidence: 0.9899176

00:26:55.060 --> 00:26:56.359 mediator distribution

NOTE Confidence: 0.9814436

00:26:56.900 --> 00:26:58.760 is m one. The mediator

NOTE Confidence: 0.9814436

00:26:58.820 --> 00:26:59.320 distribution

NOTE Confidence: 0.95596313

00:26:59.700 --> 00:27:01.460 is m one, but with

NOTE Confidence: 0.95596313

00:27:01.460 --> 00:27:02.820 or without treatment, so that

NOTE Confidence: 0.95596313

00:27:02.820 --> 00:27:04.119 is the direct effect.

NOTE Confidence: 0.9821231

00:27:04.420 --> 00:27:05.540 And then maybe what you

NOTE Confidence: 0.9821231

00:27:05.540 --> 00:27:06.740 can think of is that

NOTE Confidence: 0.9821231

00:27:06.740 --> 00:27:08.185 maybe this is not a

NOTE Confidence: 0.9821231

00:27:08.185 --> 00:27:08.965 good definition

NOTE Confidence: 0.9650242

00:27:09.505 --> 00:27:10.865 because we are doing it

NOTE Confidence: 0.9650242

00:27:10.865 --> 00:27:12.485 relative to c.

NOTE Confidence: 0.99664706

00:27:13.585 --> 00:27:15.045 But you can show

NOTE Confidence: 0.9784279

00:27:16.625 --> 00:27:17.125 so

NOTE Confidence: 0.9312259

00:27:17.825 --> 00:27:18.945 and so I can my

NOTE Confidence: 0.9312259

00:27:18.945 --> 00:27:20.130 first is, I can be

NOTE Confidence: 0.9312259

00:27:20.130 --> 00:27:21.910 seen as a hypothetical intervention

NOTE Confidence: 0.9312259

00:27:21.970 --> 00:27:23.330 to phrase the question, what

NOTE Confidence: 0.9312259

00:27:23.330 --> 00:27:25.430 if the mediator distribution changes

NOTE Confidence: 0.9312259

00:27:25.490 --> 00:27:26.770 according to treatment a is

NOTE Confidence: 0.9312259

00:27:26.770 --> 00:27:28.369 equal to one? And after

NOTE Confidence: 0.9312259

00:27:28.369 --> 00:27:30.050 that, the system follow its

NOTE Confidence: 0.9312259

00:27:30.050 --> 00:27:31.109 natural course

NOTE Confidence: 0.96095383

00:27:31.410 --> 00:27:32.470 as though the mediator

NOTE Confidence: 0.96604395

00:27:32.770 --> 00:27:34.790 value came about without treatment.

NOTE Confidence: 0.93518466

00:27:36.825 --> 00:27:38.185 And then there's another this

NOTE Confidence: 0.93518466

00:27:38.185 --> 00:27:39.785 is the consistency assumption. When

NOTE Confidence: 0.93518466

00:27:39.785 --> 00:27:41.225 we treat someone, we measure

NOTE Confidence: 0.93518466

00:27:41.225 --> 00:27:43.065 their treatment treated outcome and

NOTE Confidence: 0.93518466

00:27:43.065 --> 00:27:43.565 mediator,

NOTE Confidence: 0.93350756

00:27:44.025 --> 00:27:45.545 and under no treatment, we

NOTE Confidence: 0.93350756

00:27:45.545 --> 00:27:47.625 measure the untreated mediator and

NOTE Confidence: 0.93350756

00:27:47.625 --> 00:27:50.049 outcome. And only under that,

NOTE Confidence: 0.93350756

00:27:50.049 --> 00:27:51.429 so now all these assumptions

NOTE Confidence: 0.93350756

00:27:51.570 --> 00:27:53.409 that natural indirect effects are

NOTE Confidence: 0.93350756

00:27:53.409 --> 00:27:55.090 based on, you own you

NOTE Confidence: 0.93350756

00:27:55.090 --> 00:27:56.609 you need nothing more than

NOTE Confidence: 0.93350756

00:27:56.609 --> 00:27:58.710 the definition of organic intervention

NOTE Confidence: 0.9707317

00:27:59.010 --> 00:28:00.070 and this consistency

NOTE Confidence: 0.99670887

00:28:00.529 --> 00:28:01.029 assumption

NOTE Confidence: 0.90924215

00:28:01.490 --> 00:28:03.350 to write down the mediation.

NOTE Confidence: 0.99611396

00:28:04.585 --> 00:28:05.644 If you're interested,

NOTE Confidence: 0.9939423

00:28:06.105 --> 00:28:06.664 at the end of the

NOTE Confidence: 0.9939423

00:28:06.664 --> 00:28:07.865 talk, I can give you

NOTE Confidence: 0.9939423

00:28:07.865 --> 00:28:08.924 the proof. It's

NOTE Confidence: 0.9935221

00:28:09.725 --> 00:28:10.225 very

NOTE Confidence: 0.84408283

00:28:11.024 --> 00:28:11.524 short.

NOTE Confidence: 0.9211246

00:28:13.625 --> 00:28:15.325 So it's and and and

NOTE Confidence: 0.9498044

00:28:16.530 --> 00:28:17.730 what I try to do

NOTE Confidence: 0.9498044

00:28:17.730 --> 00:28:19.350 here with this organic intervention

NOTE Confidence: 0.9371157

00:28:19.810 --> 00:28:21.010 is read off the results

NOTE Confidence: 0.9371157

00:28:21.010 --> 00:28:22.450 from the mediation formula to

NOTE Confidence: 0.9371157

00:28:22.450 --> 00:28:23.490 get a sense of what

NOTE Confidence: 0.9371157

00:28:23.490 --> 00:28:24.530 we want and also to

NOTE Confidence: 0.9371157

00:28:24.530 --> 00:28:25.830 follow Baron and Kenny

NOTE Confidence: 0.8679969

00:28:26.210 --> 00:28:27.990 before because first, the mediator

NOTE Confidence: 0.969377

00:28:28.530 --> 00:28:30.455 comes about according to its

NOTE Confidence: 0.969377

00:28:30.455 --> 00:28:32.055 distribution under treatment. That's my

NOTE Confidence: 0.969377

00:28:32.055 --> 00:28:33.994 first condition for organic intervention.

NOTE Confidence: 0.979054

00:28:35.015 --> 00:28:36.535 And then the outcome comes

NOTE Confidence: 0.979054

00:28:36.535 --> 00:28:37.755 about under treatment.

NOTE Confidence: 0.9340041

00:28:38.455 --> 00:28:39.355 It's the second

NOTE Confidence: 0.8958319

00:28:39.975 --> 00:28:41.895 condition of organic intervention. So

NOTE Confidence: 0.8958319

00:28:41.895 --> 00:28:42.855 it's just read off of

NOTE Confidence: 0.8958319

00:28:42.855 --> 00:28:43.595 the mediation

NOTE Confidence: 0.6848637

00:28:44.135 --> 00:28:44.635 formula

NOTE Confidence: 0.9306829

00:28:44.935 --> 00:28:45.870 because the the first time

NOTE Confidence: 0.9306829

00:28:45.870 --> 00:28:47.030 I saw the mediation formula,

NOTE Confidence: 0.9306829

00:28:47.030 --> 00:28:48.030 I was like, that is

NOTE Confidence: 0.9306829

00:28:48.030 --> 00:28:48.850 really cool.

NOTE Confidence: 0.9972974

00:28:49.230 --> 00:28:50.850 So I wanted that formula

NOTE Confidence: 0.8593459

00:28:51.310 --> 00:28:53.090 but without those extra assumption.

NOTE Confidence: 0.9847054

00:28:55.790 --> 00:28:57.630 So without common including common

NOTE Confidence: 0.9847054

00:28:57.630 --> 00:28:59.070 causes, the system doesn't know

NOTE Confidence: 0.9847054

00:28:59.070 --> 00:29:00.030 where it can where it

NOTE Confidence: 0.9847054

00:29:00.030 --> 00:29:01.010 has to go.

NOTE Confidence: 0.9817772

00:29:01.395 --> 00:29:03.555 I have proven that if

NOTE Confidence: 0.9817772

00:29:03.555 --> 00:29:05.395 you include all common causes

NOTE Confidence: 0.9817772

00:29:05.395 --> 00:29:06.915 of the mediator and the

NOTE Confidence: 0.9817772

00:29:06.915 --> 00:29:07.415 outcome,

NOTE Confidence: 0.9134724

00:29:07.715 --> 00:29:09.875 then these organic indirect indirect

NOTE Confidence: 0.9134724

00:29:09.875 --> 00:29:11.815 effects are uniquely defined.

NOTE Confidence: 0.95320743

00:29:13.830 --> 00:29:15.049 And this is a definition

NOTE Confidence: 0.95320743

00:29:15.190 --> 00:29:16.470 and stuff. So what I

NOTE Confidence: 0.95320743

00:29:16.470 --> 00:29:18.010 want to do now is

NOTE Confidence: 0.9988644

00:29:18.390 --> 00:29:20.010 apply this idea

NOTE Confidence: 0.9883946

00:29:20.549 --> 00:29:21.030 to,

NOTE Confidence: 0.8778353

00:29:21.429 --> 00:29:22.250 alpha despa.

NOTE Confidence: 0.9964899

00:29:22.710 --> 00:29:23.210 So,

NOTE Confidence: 0.946953

00:29:23.910 --> 00:29:26.105 the organic indirect effects can

NOTE Confidence: 0.946953

00:29:26.105 --> 00:29:27.725 be estimated with the distribution

NOTE Confidence: 0.946953

00:29:27.785 --> 00:29:28.985 of the mediator on the

NOTE Confidence: 0.946953

00:29:28.985 --> 00:29:29.485 treatment

NOTE Confidence: 0.90929615

00:29:29.945 --> 00:29:31.165 and under no treatment,

NOTE Confidence: 0.986258

00:29:31.545 --> 00:29:32.985 and the expectation of the

NOTE Confidence: 0.986258

00:29:32.985 --> 00:29:34.745 outcome given the mediator and

NOTE Confidence: 0.986258

00:29:34.745 --> 00:29:35.885 pretreatment covariates

NOTE Confidence: 0.9704034

00:29:36.585 --> 00:29:38.365 only under no treatment.

NOTE Confidence: 0.91063786

00:29:39.340 --> 00:29:40.620 And that comes from the

NOTE Confidence: 0.91063786

00:29:40.620 --> 00:29:42.380 mediation formula. If you can

NOTE Confidence: 0.91063786

00:29:42.380 --> 00:29:43.580 go back to the mediation

NOTE Confidence: 0.91063786

00:29:43.580 --> 00:29:44.080 formula.

NOTE Confidence: 0.96571743

00:29:44.620 --> 00:29:46.780 Look. The indirect effect is

NOTE Confidence: 0.96571743

00:29:46.780 --> 00:29:48.060 going to be this one

NOTE Confidence: 0.96571743

00:29:48.060 --> 00:29:49.820 minus the expectation of the

NOTE Confidence: 0.96571743

00:29:49.820 --> 00:29:50.320 untreated

NOTE Confidence: 0.9898303

00:29:52.154 --> 00:29:52.654 outcome.

NOTE Confidence: 0.8913333

00:29:53.674 --> 00:29:55.514 The untreated outcome, I can

NOTE Confidence: 0.8913333

00:29:55.514 --> 00:29:56.955 estimate the mean without on

NOTE Confidence: 0.8913333

00:29:56.955 --> 00:29:58.475 treat without outcome beta because

NOTE Confidence: 0.8913333

00:29:58.475 --> 00:30:00.394 it's the untreated outcome. And

NOTE Confidence: 0.8913333

00:30:00.394 --> 00:30:01.615 look at this formula.

NOTE Confidence: 0.98817253

00:30:01.995 --> 00:30:04.154 It has only expectation of

NOTE Confidence: 0.98817253

00:30:04.154 --> 00:30:05.355 y given a is equal

NOTE Confidence: 0.98817253

00:30:05.355 --> 00:30:07.660 to zero. There's no treated

NOTE Confidence: 0.98817253

00:30:07.720 --> 00:30:09.100 outcomes in this formula.

NOTE Confidence: 0.9752945

00:30:09.559 --> 00:30:10.540 People typically

NOTE Confidence: 0.9742586

00:30:11.000 --> 00:30:11.500 model

NOTE Confidence: 0.90720475

00:30:11.880 --> 00:30:13.900 the outcome given the mediator

NOTE Confidence: 0.90720475

00:30:14.120 --> 00:30:15.100 and the treatment,

NOTE Confidence: 0.9782887

00:30:15.880 --> 00:30:17.240 but there's no need to

NOTE Confidence: 0.9782887

00:30:17.240 --> 00:30:18.200 do that. It would be

NOTE Confidence: 0.9782887

00:30:18.200 --> 00:30:19.340 borrowing strength

NOTE Confidence: 0.9954357

00:30:19.915 --> 00:30:21.215 from treated outcomes

NOTE Confidence: 0.9946591

00:30:21.835 --> 00:30:24.015 to make more precision happen

NOTE Confidence: 0.9402935

00:30:24.395 --> 00:30:25.615 under more assumptions.

NOTE Confidence: 0.9744253

00:30:26.235 --> 00:30:27.855 But if you only have

NOTE Confidence: 0.9744253

00:30:27.995 --> 00:30:28.495 untreated

NOTE Confidence: 0.9236224

00:30:28.955 --> 00:30:31.275 outcome data, that's enough to

NOTE Confidence: 0.9236224

00:30:31.275 --> 00:30:32.715 use the negation formula in

NOTE Confidence: 0.9236224

00:30:32.715 --> 00:30:34.230 this case. And that is

NOTE Confidence: 0.9236224

00:30:34.230 --> 00:30:36.470 because I've been working with

NOTE Confidence: 0.9236224

00:30:36.470 --> 00:30:38.470 the outcome under no treatment

NOTE Confidence: 0.9236224

00:30:38.470 --> 00:30:39.910 but an intervention on the

NOTE Confidence: 0.9236224

00:30:39.910 --> 00:30:42.010 mediator instead of the outcome

NOTE Confidence: 0.9236224

00:30:42.070 --> 00:30:42.890 under treatment

NOTE Confidence: 0.99569935

00:30:43.270 --> 00:30:44.630 with an intervention on the

NOTE Confidence: 0.99569935

00:30:44.630 --> 00:30:45.130 mediator.

NOTE Confidence: 0.9158735

00:30:45.664 --> 00:30:46.784 So this is the an

NOTE Confidence: 0.9158735

00:30:47.105 --> 00:30:49.044 analog of a pure indirect

NOTE Confidence: 0.9158735

00:30:49.184 --> 00:30:49.684 effect

NOTE Confidence: 0.9444539

00:30:49.985 --> 00:30:51.365 where I look at untreated

NOTE Confidence: 0.9444539

00:30:51.585 --> 00:30:52.085 mediator

NOTE Confidence: 0.7574687

00:30:52.625 --> 00:30:53.445 under treatment

NOTE Confidence: 0.9038129

00:30:54.544 --> 00:30:56.164 instead of treated

NOTE Confidence: 0.8407062

00:30:56.544 --> 00:30:57.044 and

NOTE Confidence: 0.9976915

00:30:57.585 --> 00:30:58.725 untreated mediator.

NOTE Confidence: 0.98386467

00:31:01.590 --> 00:31:02.090 Okay.

NOTE Confidence: 0.99723685

00:31:02.790 --> 00:31:04.170 So if we do that,

NOTE Confidence: 0.9382351

00:31:04.950 --> 00:31:06.490 we don't need treated outcomes

NOTE Confidence: 0.94172364

00:31:07.270 --> 00:31:09.130 to estimate an indirect effect.

NOTE Confidence: 0.99436766

00:31:11.190 --> 00:31:12.309 And I will show you

NOTE Confidence: 0.99436766

00:31:12.309 --> 00:31:13.590 how that helps in a

NOTE Confidence: 0.99436766

00:31:13.590 --> 00:31:14.090 preclinical

NOTE Confidence: 0.99655616

00:31:14.390 --> 00:31:14.890 stage.

NOTE Confidence: 0.9991724

00:31:15.715 --> 00:31:16.995 So this is the

NOTE Confidence: 0.96154183

00:31:17.394 --> 00:31:18.674 oh, let's take this out

NOTE Confidence: 0.96154183

00:31:18.674 --> 00:31:19.414 of the way.

NOTE Confidence: 0.9860192

00:31:20.034 --> 00:31:20.995 Yeah. So,

NOTE Confidence: 0.99933326

00:31:21.475 --> 00:31:22.215 this is

NOTE Confidence: 0.9067221

00:31:23.235 --> 00:31:25.335 the graph that my clinical

NOTE Confidence: 0.9067221

00:31:25.394 --> 00:31:25.894 collaborators

NOTE Confidence: 0.8535923

00:31:26.195 --> 00:31:27.475 came me first time I

NOTE Confidence: 0.8535923

00:31:27.475 --> 00:31:28.215 met them.

NOTE Confidence: 0.9761206

00:31:28.580 --> 00:31:30.660 They wanted causal mediation analysis,

NOTE Confidence: 0.9761206

00:31:30.660 --> 00:31:31.620 and they had been told

NOTE Confidence: 0.9761206

00:31:31.620 --> 00:31:32.900 by the NIH and by

NOTE Confidence: 0.9761206

00:31:32.900 --> 00:31:34.440 the reviewers of their paper,

NOTE Confidence: 0.98720616

00:31:34.820 --> 00:31:36.520 you need a statistician.

NOTE Confidence: 0.94929814

00:31:37.620 --> 00:31:38.980 And so when they went

NOTE Confidence: 0.94929814

00:31:38.980 --> 00:31:40.500 on the BU website, who

NOTE Confidence: 0.94929814

00:31:40.500 --> 00:31:41.240 is a statistician

NOTE Confidence: 0.93748343

00:31:41.620 --> 00:31:42.740 at BU who knows about

NOTE Confidence: 0.93748343

00:31:42.740 --> 00:31:44.280 causal mediation analysis,

NOTE Confidence: 0.6814629

00:31:45.035 --> 00:31:45.855 There's not.

NOTE Confidence: 0.941206

00:31:46.715 --> 00:31:47.835 So they ended up with

NOTE Confidence: 0.941206

00:31:47.835 --> 00:31:49.115 me, and they were like,

NOTE Confidence: 0.941206

00:31:49.115 --> 00:31:50.235 we want to do causal

NOTE Confidence: 0.941206

00:31:50.235 --> 00:31:51.995 mediation analysis, and this is

NOTE Confidence: 0.941206

00:31:51.995 --> 00:31:53.215 what we want to do.

NOTE Confidence: 0.941206

00:31:53.434 --> 00:31:55.455 The effect of SOFA one

NOTE Confidence: 0.5791946

00:31:56.315 --> 00:31:57.695 mediated by positive

NOTE Confidence: 0.8251659

00:31:58.315 --> 00:31:59.455 neutrophil nets

NOTE Confidence: 0.8586983

00:31:59.830 --> 00:32:01.350 on the SOFA score at

NOTE Confidence: 0.8586983

00:32:01.350 --> 00:32:02.490 ICU discharge.

NOTE Confidence: 0.92011553

00:32:03.510 --> 00:32:04.630 And it took me a

NOTE Confidence: 0.92011553

00:32:04.630 --> 00:32:06.410 while before I could interpret

NOTE Confidence: 0.92011553

00:32:06.630 --> 00:32:08.410 that SOFA score at baseline

NOTE Confidence: 0.92011553

00:32:08.550 --> 00:32:09.990 as a treatment because for

NOTE Confidence: 0.92011553

00:32:09.990 --> 00:32:11.690 me that was a conveyor

NOTE Confidence: 0.92011553

00:32:11.750 --> 00:32:12.570 not a treatment.

NOTE Confidence: 0.9949245

00:32:12.885 --> 00:32:14.325 But they see it as

NOTE Confidence: 0.9949245

00:32:14.325 --> 00:32:16.105 a measure of how much

NOTE Confidence: 0.9949245

00:32:16.245 --> 00:32:16.745 badness

NOTE Confidence: 0.9989427

00:32:17.605 --> 00:32:20.025 each patient has been exposed

NOTE Confidence: 0.9976143

00:32:20.325 --> 00:32:20.825 to.

NOTE Confidence: 0.98371613

00:32:21.445 --> 00:32:23.045 So for them, it's a

NOTE Confidence: 0.98371613

00:32:23.045 --> 00:32:24.345 measure of exposure.

NOTE Confidence: 0.96437037

00:32:25.285 --> 00:32:26.965 How much badness has this

NOTE Confidence: 0.96437037

00:32:26.965 --> 00:32:28.185 patient been exposed?

NOTE Confidence: 0.95330733

00:32:28.780 --> 00:32:29.980 And they wanted this, and

NOTE Confidence: 0.95330733

00:32:29.980 --> 00:32:31.180 I gave them this. It's

NOTE Confidence: 0.95330733

00:32:31.180 --> 00:32:32.720 a multi it's a continuous

NOTE Confidence: 0.95330733

00:32:32.860 --> 00:32:33.980 exposure, so it's a little

NOTE Confidence: 0.95330733

00:32:33.980 --> 00:32:34.720 bit complicated,

NOTE Confidence: 0.9751286

00:32:35.100 --> 00:32:36.480 but you can do it.

NOTE Confidence: 0.9751286

00:32:36.620 --> 00:32:38.220 But after two or three

NOTE Confidence: 0.9751286

00:32:38.220 --> 00:32:39.820 meetings, I was like, I'm

NOTE Confidence: 0.9751286

00:32:39.820 --> 00:32:40.320 fine.

NOTE Confidence: 0.7970737

00:32:40.780 --> 00:32:41.280 Why?

NOTE Confidence: 0.9985798

00:32:41.820 --> 00:32:43.360 Why do you want this?

NOTE Confidence: 0.9345461

00:32:44.945 --> 00:32:45.985 And it turned out what

NOTE Confidence: 0.9345461

00:32:45.985 --> 00:32:48.245 they wanted actually was, well,

NOTE Confidence: 0.9345461

00:32:48.305 --> 00:32:49.985 if we have this and

NOTE Confidence: 0.9345461

00:32:49.985 --> 00:32:50.885 it's mediated,

NOTE Confidence: 0.99314374

00:32:51.585 --> 00:32:52.965 then that's a measure

NOTE Confidence: 0.83235043

00:32:53.345 --> 00:32:55.665 that also alpha desperate, that's

NOTE Confidence: 0.83235043

00:32:55.665 --> 00:32:56.885 our treatment, our

NOTE Confidence: 0.92402524

00:32:57.230 --> 00:32:59.070 prekinable treatment that we hope

NOTE Confidence: 0.92402524

00:32:59.070 --> 00:33:00.190 to bring on the market

NOTE Confidence: 0.92402524

00:33:00.190 --> 00:33:02.290 someday, that actually affects

NOTE Confidence: 0.997837

00:33:02.750 --> 00:33:03.250 the

NOTE Confidence: 0.8240293

00:33:03.790 --> 00:33:06.050 the despa positive neutrophil nets.

NOTE Confidence: 0.8240293

00:33:06.350 --> 00:33:07.550 And if it me if

NOTE Confidence: 0.8240293

00:33:07.550 --> 00:33:09.890 the despa positive neutrophils fit,

NOTE Confidence: 0.7395333

00:33:10.445 --> 00:33:11.585 neutrophil mediate

NOTE Confidence: 0.88847035

00:33:12.205 --> 00:33:14.225 so far so far too,

NOTE Confidence: 0.88847035

00:33:14.285 --> 00:33:15.645 then that's an indication that

NOTE Confidence: 0.88847035

00:33:15.645 --> 00:33:17.345 maybe our treatment does something.

NOTE Confidence: 0.88847035

00:33:17.485 --> 00:33:18.705 And then I was like,

NOTE Confidence: 0.91802746

00:33:19.405 --> 00:33:20.285 ah, but I know a

NOTE Confidence: 0.91802746

00:33:20.285 --> 00:33:21.325 thing or two about false

NOTE Confidence: 0.91802746

00:33:21.325 --> 00:33:22.545 remediation analysis.

NOTE Confidence: 0.9934427

00:33:22.925 --> 00:33:23.965 So why don't we look

NOTE Confidence: 0.9934427

00:33:23.965 --> 00:33:24.945 at this graph?

NOTE Confidence: 0.9293339

00:33:27.130 --> 00:33:28.250 And they were like, can

NOTE Confidence: 0.9293339

00:33:28.250 --> 00:33:28.750 we?

NOTE Confidence: 0.9433559

00:33:30.410 --> 00:33:32.170 Yeah, we can. I published

NOTE Confidence: 0.9433559

00:33:32.170 --> 00:33:33.390 something on this

NOTE Confidence: 0.8021559

00:33:34.010 --> 00:33:34.510 similar

NOTE Confidence: 0.95784646

00:33:34.810 --> 00:33:36.810 for HIV curative treatment in

NOTE Confidence: 0.95784646

00:33:36.810 --> 00:33:38.890 epidemiology in twenty twenty one

NOTE Confidence: 0.95784646

00:33:38.890 --> 00:33:40.645 together with a collaborator and

NOTE Confidence: 0.95784646

00:33:40.645 --> 00:33:41.945 we looked at hypothetical,

NOTE Confidence: 0.9808096

00:33:43.525 --> 00:33:45.785 interventions on the HIV reservoir,

NOTE Confidence: 0.9808096

00:33:46.005 --> 00:33:46.505 hypothetical

NOTE Confidence: 0.99700063

00:33:46.885 --> 00:33:47.385 reductions

NOTE Confidence: 0.9775335

00:33:48.005 --> 00:33:49.225 of the HIV reservoir.

NOTE Confidence: 0.9570215

00:33:50.085 --> 00:33:51.285 But in your case, it's

NOTE Confidence: 0.9570215

00:33:51.285 --> 00:33:52.345 not even hypothetical,

NOTE Confidence: 0.88828516

00:33:54.539 --> 00:33:56.620 effects on the on the

NOTE Confidence: 0.88828516

00:33:56.620 --> 00:33:58.220 desperate positive movement from that.

NOTE Confidence: 0.88828516

00:33:58.220 --> 00:33:59.659 You actually have done this

NOTE Confidence: 0.88828516

00:33:59.659 --> 00:34:01.500 in animal studies and feathery

NOTE Confidence: 0.88828516

00:34:01.500 --> 00:34:03.419 dishes, so you have a

NOTE Confidence: 0.88828516

00:34:03.419 --> 00:34:05.260 clear hope for what that

NOTE Confidence: 0.88828516

00:34:05.260 --> 00:34:06.620 effect on the mediator is

NOTE Confidence: 0.88828516

00:34:06.620 --> 00:34:07.440 gonna be.

NOTE Confidence: 0.8578916

00:34:07.894 --> 00:34:08.855 So yes, we can do

NOTE Confidence: 0.8578916

00:34:08.855 --> 00:34:09.575 causal mediation

NOTE Confidence: 0.79667187

00:34:10.055 --> 00:34:11.594 causal mediation analysis

NOTE Confidence: 0.8885535

00:34:12.055 --> 00:34:14.234 really for alpha desperate itself

NOTE Confidence: 0.8885535

00:34:14.454 --> 00:34:15.815 as well and that got

NOTE Confidence: 0.8885535

00:34:15.815 --> 00:34:17.494 them excited so we added

NOTE Confidence: 0.8885535

00:34:17.494 --> 00:34:18.714 this to their paper.

NOTE Confidence: 0.903582

00:34:19.015 --> 00:34:20.635 So we have alpha desperate,

NOTE Confidence: 0.903582

00:34:20.694 --> 00:34:22.980 it affects desperate positive neutrophil

NOTE Confidence: 0.903582

00:34:23.040 --> 00:34:24.880 nets in turn, hopefully, the

NOTE Confidence: 0.903582

00:34:24.880 --> 00:34:27.460 SOWFA score and ICU discharge.

NOTE Confidence: 0.9479927

00:34:28.239 --> 00:34:29.600 Now this made it very

NOTE Confidence: 0.9479927

00:34:29.600 --> 00:34:30.640 easy to come up with

NOTE Confidence: 0.9479927

00:34:30.640 --> 00:34:32.100 a common cause because,

NOTE Confidence: 0.8291284

00:34:32.880 --> 00:34:33.380 look,

NOTE Confidence: 0.9169476

00:34:33.905 --> 00:34:35.025 there is a common cause

NOTE Confidence: 0.9169476

00:34:35.025 --> 00:34:36.545 of MMI. You see that?

NOTE Confidence: 0.9169476

00:34:36.545 --> 00:34:37.825 It's it's so far one.

NOTE Confidence: 0.9169476

00:34:37.825 --> 00:34:39.025 It now becomes a common

NOTE Confidence: 0.9169476

00:34:39.025 --> 00:34:39.525 cause.

NOTE Confidence: 0.9289044

00:34:39.905 --> 00:34:41.425 Not a treatment anymore. It

NOTE Confidence: 0.9289044

00:34:41.425 --> 00:34:42.545 becomes a common cause. So

NOTE Confidence: 0.9289044

00:34:42.545 --> 00:34:43.585 we need that common cause

NOTE Confidence: 0.9289044

00:34:43.585 --> 00:34:44.885 because that's what they started.

NOTE Confidence: 0.96216124

00:34:46.960 --> 00:34:49.040 Okay. So the indirect effect

NOTE Confidence: 0.96216124

00:34:49.040 --> 00:34:49.780 is here,

NOTE Confidence: 0.98614377

00:34:50.719 --> 00:34:52.080 and the direct effect is

NOTE Confidence: 0.98614377

00:34:52.080 --> 00:34:53.360 something that I cannot get

NOTE Confidence: 0.98614377

00:34:53.360 --> 00:34:54.800 my hands on until they

NOTE Confidence: 0.98614377

00:34:54.800 --> 00:34:56.640 get permission to actually try

NOTE Confidence: 0.98614377

00:34:56.640 --> 00:34:58.160 this treatment out in human

NOTE Confidence: 0.98614377

00:34:58.160 --> 00:34:58.660 beings.

NOTE Confidence: 0.92901474

00:35:01.895 --> 00:35:03.494 So we investigated the progress

NOTE Confidence: 0.92901474

00:35:03.494 --> 00:35:05.355 of alpha despa by estimating

NOTE Confidence: 0.92901474

00:35:05.415 --> 00:35:07.194 its indirect effect mediated

NOTE Confidence: 0.8616532

00:35:07.494 --> 00:35:09.915 by despa positive neutrophil nets,

NOTE Confidence: 0.7618933

00:35:10.535 --> 00:35:11.035 assuming,

NOTE Confidence: 0.92319924

00:35:11.655 --> 00:35:13.255 as was shown in animal

NOTE Confidence: 0.92319924

00:35:13.255 --> 00:35:15.114 studies and peckerly dishes,

NOTE Confidence: 0.96679544

00:35:15.415 --> 00:35:16.795 that alpha despa

NOTE Confidence: 0.99627966

00:35:17.570 --> 00:35:18.070 eliminates

NOTE Confidence: 0.5564742

00:35:18.370 --> 00:35:19.190 this propositive

NOTE Confidence: 0.61627954

00:35:19.570 --> 00:35:21.670 looping terms. Completely invented.

NOTE Confidence: 0.815749

00:35:22.290 --> 00:35:23.410 We can do it otherwise.

NOTE Confidence: 0.815749

00:35:23.410 --> 00:35:24.690 We can say it has

NOTE Confidence: 0.815749

00:35:24.690 --> 00:35:25.890 or whatever kind of stuff,

NOTE Confidence: 0.815749

00:35:25.890 --> 00:35:26.850 but I really think it

NOTE Confidence: 0.815749

00:35:26.850 --> 00:35:28.390 will eliminate, so we will.

NOTE Confidence: 0.71227634

00:35:30.875 --> 00:35:32.234 So what can we expect

NOTE Confidence: 0.71227634

00:35:32.234 --> 00:35:34.075 if alpha desperate eliminates this

NOTE Confidence: 0.71227634

00:35:34.075 --> 00:35:36.234 positive neutral film nets and

NOTE Confidence: 0.71227634

00:35:36.234 --> 00:35:37.454 after that the body

NOTE Confidence: 0.94242525

00:35:37.755 --> 00:35:40.015 system follows its natural course

NOTE Confidence: 0.9832567

00:35:40.474 --> 00:35:42.315 as though alpha desperate was

NOTE Confidence: 0.9832567

00:35:42.315 --> 00:35:43.550 not the cause

NOTE Confidence: 0.89258415

00:35:44.010 --> 00:35:46.110 of the absence of desperate

NOTE Confidence: 0.89258415

00:35:46.250 --> 00:35:48.110 positive neutrophil mats.

NOTE Confidence: 0.97938013

00:35:48.650 --> 00:35:49.770 And this is something that

NOTE Confidence: 0.97938013

00:35:49.770 --> 00:35:50.590 we can estimate.

NOTE Confidence: 0.99223894

00:35:52.489 --> 00:35:53.870 And this was published

NOTE Confidence: 0.8971655

00:35:54.330 --> 00:35:54.830 in,

NOTE Confidence: 0.9280328

00:35:55.855 --> 00:35:57.614 in in, in a paper

NOTE Confidence: 0.9280328

00:35:57.614 --> 00:35:58.575 together with,

NOTE Confidence: 0.7313034

00:35:59.055 --> 00:36:00.355 in my clinical collaborate.

NOTE Confidence: 0.879666

00:36:02.575 --> 00:36:03.935 So we don't have alpha

NOTE Confidence: 0.879666

00:36:03.935 --> 00:36:05.555 and s for outcome measures

NOTE Confidence: 0.879666

00:36:05.614 --> 00:36:06.114 net

NOTE Confidence: 0.9190912

00:36:06.975 --> 00:36:07.475 yet.

NOTE Confidence: 0.8381216

00:36:08.580 --> 00:36:10.120 So what we did is

NOTE Confidence: 0.8381216

00:36:10.260 --> 00:36:11.540 just use the core the

NOTE Confidence: 0.8381216

00:36:11.540 --> 00:36:12.600 mediation formula.

NOTE Confidence: 0.9867163

00:36:13.219 --> 00:36:15.000 We get the expected

NOTE Confidence: 0.91947466

00:36:15.380 --> 00:36:16.980 outcome with it. So we

NOTE Confidence: 0.91947466

00:36:16.980 --> 00:36:18.420 get the expected out the

NOTE Confidence: 0.91947466

00:36:18.420 --> 00:36:20.260 mediation for maybe oh, we

NOTE Confidence: 0.91947466

00:36:20.260 --> 00:36:21.960 don't have one. So

NOTE Confidence: 0.9297314

00:36:23.015 --> 00:36:24.455 let's go back to mediation

NOTE Confidence: 0.9297314

00:36:24.455 --> 00:36:24.955 form.

NOTE Confidence: 0.909317

00:36:27.415 --> 00:36:28.375 So we need to do

NOTE Confidence: 0.909317

00:36:28.375 --> 00:36:30.135 this. So first, the common

NOTE Confidence: 0.909317

00:36:30.135 --> 00:36:31.094 goal is that it's the

NOTE Confidence: 0.909317

00:36:31.094 --> 00:36:32.475 SOFA score. Right?

NOTE Confidence: 0.9872552

00:36:32.935 --> 00:36:33.895 And then we need the

NOTE Confidence: 0.9872552

00:36:33.895 --> 00:36:35.355 distribution of the mediator

NOTE Confidence: 0.8732033

00:36:35.735 --> 00:36:36.235 under,

NOTE Confidence: 0.8679013

00:36:36.969 --> 00:36:39.050 under alpha dash prop zero

NOTE Confidence: 0.8679013

00:36:39.050 --> 00:36:40.270 zero zero

NOTE Confidence: 0.9339717

00:36:40.570 --> 00:36:42.250 zero zero. So that's that's

NOTE Confidence: 0.9339717

00:36:42.250 --> 00:36:43.370 fine. It's a it's a

NOTE Confidence: 0.9339717

00:36:43.370 --> 00:36:44.110 point mass.

NOTE Confidence: 0.8691501

00:36:44.410 --> 00:36:45.450 And then we get the

NOTE Confidence: 0.8691501

00:36:45.450 --> 00:36:45.950 outcome,

NOTE Confidence: 0.8707777

00:36:46.489 --> 00:36:48.090 the SOFA score given that

NOTE Confidence: 0.8707777

00:36:48.090 --> 00:36:49.530 there is no that's proper

NOTE Confidence: 0.8707777

00:36:49.530 --> 00:36:51.494 positive filter fill nets, given

NOTE Confidence: 0.8707777

00:36:51.494 --> 00:36:53.894 the SOFA score and under

NOTE Confidence: 0.8707777

00:36:53.894 --> 00:36:55.015 a is equal to zero,

NOTE Confidence: 0.8707777

00:36:55.015 --> 00:36:56.295 then we do have outcome

NOTE Confidence: 0.8707777

00:36:56.295 --> 00:36:56.854 data under a is equal

NOTE Confidence: 0.8707777

00:36:56.854 --> 00:36:57.434 to zero. It

NOTE Confidence: 0.6928203

00:37:00.855 --> 00:37:01.355 back.

NOTE Confidence: 0.9387511

00:37:05.590 --> 00:37:07.270 So the outcome under no

NOTE Confidence: 0.9387511

00:37:07.270 --> 00:37:08.630 treatment, that's just their outcome

NOTE Confidence: 0.9387511

00:37:08.630 --> 00:37:09.930 because they don't have treatment.

NOTE Confidence: 0.9853046

00:37:10.710 --> 00:37:12.550 And the other one, we

NOTE Confidence: 0.9853046

00:37:12.550 --> 00:37:13.050 need

NOTE Confidence: 0.99930656

00:37:13.510 --> 00:37:14.010 to

NOTE Confidence: 0.9120138

00:37:14.310 --> 00:37:16.010 do average over the distribution

NOTE Confidence: 0.9120138

00:37:16.150 --> 00:37:16.950 of the c. So we

NOTE Confidence: 0.9120138

00:37:16.950 --> 00:37:18.230 just get mass one over

NOTE Confidence: 0.9120138

00:37:18.230 --> 00:37:19.005 m to each of the

NOTE Confidence: 0.9120138

00:37:19.085 --> 00:37:19.585 c's.

NOTE Confidence: 0.8040385

00:37:20.364 --> 00:37:21.724 And so that is the

NOTE Confidence: 0.8040385

00:37:21.724 --> 00:37:22.224 empirical

NOTE Confidence: 0.8157404

00:37:22.765 --> 00:37:24.364 distribution function of the c's.

NOTE Confidence: 0.8157404

00:37:24.364 --> 00:37:25.964 Just get mass one over

NOTE Confidence: 0.8157404

00:37:25.964 --> 00:37:27.025 m to each of them.

NOTE Confidence: 0.8157404

00:37:27.164 --> 00:37:28.125 They have to do given

NOTE Confidence: 0.8157404

00:37:28.125 --> 00:37:29.644 the mediator is zero because

NOTE Confidence: 0.8157404

00:37:29.644 --> 00:37:31.325 everything what alpha desperate will

NOTE Confidence: 0.8157404

00:37:31.325 --> 00:37:32.684 do, that's a point mass

NOTE Confidence: 0.8157404

00:37:32.684 --> 00:37:33.505 at zero,

NOTE Confidence: 0.92127895

00:37:33.890 --> 00:37:35.350 and we get the expected

NOTE Confidence: 0.92127895

00:37:35.489 --> 00:37:36.290 outcome on,

NOTE Confidence: 0.86618465

00:37:37.010 --> 00:37:38.530 expanded so far two score

NOTE Confidence: 0.86618465

00:37:38.530 --> 00:37:39.650 under m is equal to

NOTE Confidence: 0.86618465

00:37:39.650 --> 00:37:41.090 zero, c is equal to

NOTE Confidence: 0.86618465

00:37:41.090 --> 00:37:42.050 c, and a I is

NOTE Confidence: 0.86618465

00:37:42.050 --> 00:37:43.410 equal to zero. So what

NOTE Confidence: 0.86618465

00:37:43.410 --> 00:37:44.870 we still need to do

NOTE Confidence: 0.91094416

00:37:45.330 --> 00:37:46.310 is make,

NOTE Confidence: 0.93044347

00:37:47.065 --> 00:37:49.005 outcome model under no treatment.

NOTE Confidence: 0.93044347

00:37:49.145 --> 00:37:50.985 But we have outcomes under

NOTE Confidence: 0.93044347

00:37:50.985 --> 00:37:52.105 no treatment so that we

NOTE Confidence: 0.93044347

00:37:52.105 --> 00:37:52.605 can

NOTE Confidence: 0.8244959

00:37:56.425 --> 00:37:57.864 we we took a regression

NOTE Confidence: 0.8244959

00:37:57.864 --> 00:37:59.805 model for that, simple regression

NOTE Confidence: 0.8244959

00:37:59.864 --> 00:38:00.364 model.

NOTE Confidence: 0.9667862

00:38:02.099 --> 00:38:03.719 And here is the correlations,

NOTE Confidence: 0.9995882

00:38:05.219 --> 00:38:06.440 and here is

NOTE Confidence: 0.9837811

00:38:06.819 --> 00:38:07.400 the fit.

NOTE Confidence: 0.8714971

00:38:07.700 --> 00:38:09.960 They wanted the interaction between

NOTE Confidence: 0.8714971

00:38:10.180 --> 00:38:12.339 the SOFA score and the

NOTE Confidence: 0.8714971

00:38:12.339 --> 00:38:13.160 best proposal.

NOTE Confidence: 0.86298233

00:38:13.779 --> 00:38:15.140 They thought it was important,

NOTE Confidence: 0.86298233

00:38:15.140 --> 00:38:15.880 so I included.

NOTE Confidence: 0.80847365

00:38:17.285 --> 00:38:18.325 And they were right. You

NOTE Confidence: 0.80847365

00:38:18.325 --> 00:38:19.525 see that the PBL is

NOTE Confidence: 0.80847365

00:38:19.525 --> 00:38:19.605 quite

NOTE Confidence: 0.5282904

00:38:22.165 --> 00:38:23.065 standard residuals

NOTE Confidence: 0.97020745

00:38:23.445 --> 00:38:24.485 looked a little bit all

NOTE Confidence: 0.97020745

00:38:24.485 --> 00:38:25.845 over the place, so we

NOTE Confidence: 0.97020745

00:38:25.845 --> 00:38:27.205 decided to not go with

NOTE Confidence: 0.97020745

00:38:27.205 --> 00:38:28.345 parametric models.

NOTE Confidence: 0.9633082

00:38:28.739 --> 00:38:30.660 Parametric semi parametric models where

NOTE Confidence: 0.9633082

00:38:30.660 --> 00:38:31.700 we don't want to assume

NOTE Confidence: 0.9633082

00:38:31.700 --> 00:38:33.060 that the distribution of these

NOTE Confidence: 0.9633082

00:38:33.060 --> 00:38:33.960 things is normal

NOTE Confidence: 0.8959383

00:38:35.060 --> 00:38:36.920 because there's only thirty four

NOTE Confidence: 0.9469222

00:38:37.300 --> 00:38:38.820 observations and three fall out

NOTE Confidence: 0.9469222

00:38:38.820 --> 00:38:39.560 of the boundary.

NOTE Confidence: 0.9477841

00:38:41.205 --> 00:38:42.665 So here's my zeros.

NOTE Confidence: 0.90895444

00:38:43.364 --> 00:38:44.325 I made sure I had

NOTE Confidence: 0.90895444

00:38:44.325 --> 00:38:45.364 enough of them. I needed

NOTE Confidence: 0.90895444

00:38:45.364 --> 00:38:46.405 enough of them, so I

NOTE Confidence: 0.90895444

00:38:46.405 --> 00:38:48.005 counted them. And so you

NOTE Confidence: 0.90895444

00:38:48.005 --> 00:38:49.285 see they they have the

NOTE Confidence: 0.90895444

00:38:49.445 --> 00:38:50.565 we have the model. There's

NOTE Confidence: 0.90895444

00:38:50.565 --> 00:38:52.565 the model. Here. Yeah. Yeah.

NOTE Confidence: 0.90895444

00:38:52.565 --> 00:38:54.505 Here's the model sofa score,

NOTE Confidence: 0.82226676

00:38:55.700 --> 00:38:57.059 and then the t one

NOTE Confidence: 0.82226676

00:38:57.059 --> 00:38:58.420 sofa that is the predictor

NOTE Confidence: 0.82226676

00:38:58.420 --> 00:38:59.539 and then the post it

NOTE Confidence: 0.82226676

00:38:59.539 --> 00:39:01.319 both. And the there's prepulsive

NOTE Confidence: 0.82226676

00:39:01.460 --> 00:39:03.160 neutrophil nets and the interaction.

NOTE Confidence: 0.95511353

00:39:04.500 --> 00:39:05.960 So we need to,

NOTE Confidence: 0.89321023

00:39:07.539 --> 00:39:08.440 do the predicted

NOTE Confidence: 0.8897585

00:39:08.739 --> 00:39:09.239 values

NOTE Confidence: 0.99844694

00:39:10.180 --> 00:39:10.760 of that

NOTE Confidence: 0.57197225

00:39:11.285 --> 00:39:11.785 model,

NOTE Confidence: 0.9376311

00:39:12.965 --> 00:39:14.425 but with the new data.

NOTE Confidence: 0.9376311

00:39:14.565 --> 00:39:16.085 And the new data have

NOTE Confidence: 0.9376311

00:39:16.085 --> 00:39:17.864 all the positive the positive

NOTE Confidence: 0.86469334

00:39:18.405 --> 00:39:19.364 the all the desperate and

NOTE Confidence: 0.86469334

00:39:19.364 --> 00:39:20.885 positive neutrophil nets equal to

NOTE Confidence: 0.86469334

00:39:20.885 --> 00:39:22.165 zero. That's that m zero

NOTE Confidence: 0.86469334

00:39:22.165 --> 00:39:23.125 that I have there, all

NOTE Confidence: 0.86469334

00:39:23.125 --> 00:39:23.625 zeros.

NOTE Confidence: 0.98764354

00:39:24.420 --> 00:39:25.460 So we can just do

NOTE Confidence: 0.98764354

00:39:25.460 --> 00:39:27.400 this, and we find

NOTE Confidence: 0.9690324

00:39:28.339 --> 00:39:30.579 a pure indirect effect or

NOTE Confidence: 0.9690324

00:39:30.579 --> 00:39:32.420 an organic indirect effect relative

NOTE Confidence: 0.9690324

00:39:32.420 --> 00:39:33.460 to a is equal to

NOTE Confidence: 0.9690324

00:39:33.460 --> 00:39:33.960 zero,

NOTE Confidence: 0.94231254

00:39:34.260 --> 00:39:35.780 a decrease in time to

NOTE Confidence: 0.94231254

00:39:35.780 --> 00:39:37.700 SOWFA score of zero point

NOTE Confidence: 0.94231254

00:39:37.700 --> 00:39:39.174 seventy one. They were a

NOTE Confidence: 0.94231254

00:39:39.174 --> 00:39:40.775 little bit bit disappointed, the

NOTE Confidence: 0.94231254

00:39:40.775 --> 00:39:41.895 doctors, and then they were

NOTE Confidence: 0.94231254

00:39:41.895 --> 00:39:43.575 like, ah, but there are

NOTE Confidence: 0.94231254

00:39:43.575 --> 00:39:45.734 people actually that we don't

NOTE Confidence: 0.94231254

00:39:45.734 --> 00:39:46.234 expect

NOTE Confidence: 0.9980401

00:39:47.015 --> 00:39:49.035 to have a big effect

NOTE Confidence: 0.9601111

00:39:49.494 --> 00:39:50.855 because they already have a

NOTE Confidence: 0.9601111

00:39:50.855 --> 00:39:52.694 pretty good SOWFA score once

NOTE Confidence: 0.9601111

00:39:52.694 --> 00:39:54.150 they come in. So we

NOTE Confidence: 0.9601111

00:39:54.150 --> 00:39:55.910 cannot expect a much of,

NOTE Confidence: 0.9601111

00:39:56.309 --> 00:39:57.589 of an effect in those

NOTE Confidence: 0.9601111

00:39:57.589 --> 00:39:59.190 people because they're already pretty

NOTE Confidence: 0.9601111

00:39:59.190 --> 00:39:59.690 healthy.

NOTE Confidence: 0.9562811

00:40:00.150 --> 00:40:01.510 So they said, let's also

NOTE Confidence: 0.9562811

00:40:01.510 --> 00:40:02.549 figure out how it is

NOTE Confidence: 0.9562811

00:40:02.549 --> 00:40:03.910 in people who come into

NOTE Confidence: 0.9562811

00:40:03.910 --> 00:40:04.730 the ICU

NOTE Confidence: 0.8796067

00:40:05.030 --> 00:40:06.230 with the score with the

NOTE Confidence: 0.8796067

00:40:06.230 --> 00:40:06.730 SOFA

NOTE Confidence: 0.9158799

00:40:07.244 --> 00:40:08.464 score below two.

NOTE Confidence: 0.9491076

00:40:08.924 --> 00:40:10.364 And there we found an

NOTE Confidence: 0.9491076

00:40:10.364 --> 00:40:12.125 indirect effect of zero point

NOTE Confidence: 0.9491076

00:40:12.125 --> 00:40:13.025 ninety eight.

NOTE Confidence: 0.9799568

00:40:13.404 --> 00:40:14.924 And the ICU doctors told

NOTE Confidence: 0.9799568

00:40:14.924 --> 00:40:16.704 me that's a meaningful clinically

NOTE Confidence: 0.9799568

00:40:16.844 --> 00:40:17.344 meaningful,

NOTE Confidence: 0.7666223

00:40:18.844 --> 00:40:19.344 difference.

NOTE Confidence: 0.9812094

00:40:20.829 --> 00:40:22.450 A clinically meaningful defect.

NOTE Confidence: 0.8832876

00:40:23.950 --> 00:40:25.869 So normality and constant variance

NOTE Confidence: 0.8832876

00:40:25.869 --> 00:40:26.750 may not hold, so we

NOTE Confidence: 0.8832876

00:40:26.750 --> 00:40:27.950 use the bootstrap for the

NOTE Confidence: 0.8832876

00:40:27.950 --> 00:40:29.390 conference interval. You see that

NOTE Confidence: 0.8832876

00:40:29.390 --> 00:40:30.690 there we create a.

NOTE Confidence: 0.99743193

00:40:35.335 --> 00:40:35.835 Okay.

NOTE Confidence: 0.90497744

00:40:38.535 --> 00:40:39.974 So COVID nineteen in the

NOTE Confidence: 0.90497744

00:40:39.974 --> 00:40:41.335 ICU, the effect of SOWFA

NOTE Confidence: 0.90497744

00:40:41.335 --> 00:40:42.714 one of SOWFA two mediated

NOTE Confidence: 0.7730994

00:40:43.015 --> 00:40:44.550 through this proposal neutralness that

NOTE Confidence: 0.7730994

00:40:44.550 --> 00:40:45.750 was the question that came

NOTE Confidence: 0.7730994

00:40:45.750 --> 00:40:46.489 in first,

NOTE Confidence: 0.95463496

00:40:46.790 --> 00:40:48.150 but we can also use

NOTE Confidence: 0.95463496

00:40:48.150 --> 00:40:49.750 the same data to estimate

NOTE Confidence: 0.95463496

00:40:49.750 --> 00:40:51.430 the indirect effect of alpha

NOTE Confidence: 0.95463496

00:40:51.430 --> 00:40:51.930 desperate

NOTE Confidence: 0.9755795

00:40:52.790 --> 00:40:54.090 on SOFA two

NOTE Confidence: 0.77366

00:40:55.270 --> 00:40:57.510 mediated by this positive neutral

NOTE Confidence: 0.77366

00:40:57.510 --> 00:40:58.010 film

NOTE Confidence: 0.95732427

00:40:58.785 --> 00:41:00.944 without on treatment outcome data.

NOTE Confidence: 0.95732427

00:41:00.944 --> 00:41:02.625 And I have not seen

NOTE Confidence: 0.95732427

00:41:02.625 --> 00:41:03.605 other applications

NOTE Confidence: 0.95524406

00:41:04.464 --> 00:41:05.905 where people do that, that

NOTE Confidence: 0.95524406

00:41:05.905 --> 00:41:07.765 they estimate indirect effects

NOTE Confidence: 0.9331182

00:41:08.065 --> 00:41:10.165 without on treatment outcome data.

NOTE Confidence: 0.9331182

00:41:10.385 --> 00:41:11.585 It can be done. We

NOTE Confidence: 0.9331182

00:41:11.585 --> 00:41:12.625 did it. We get it.

NOTE Confidence: 0.9331182

00:41:12.625 --> 00:41:13.684 We call it public.

NOTE Confidence: 0.87493587

00:41:15.920 --> 00:41:16.799 I also looked at the

NOTE Confidence: 0.87493587

00:41:16.799 --> 00:41:18.079 effect of HIV cure for

NOTE Confidence: 0.87493587

00:41:18.079 --> 00:41:19.279 these treatments out in the

NOTE Confidence: 0.87493587

00:41:19.279 --> 00:41:21.039 HIV reservoir. There are several

NOTE Confidence: 0.87493587

00:41:21.039 --> 00:41:22.559 papers on that, and I

NOTE Confidence: 0.87493587

00:41:22.559 --> 00:41:24.799 looked at causal mediation and

NOTE Confidence: 0.87493587

00:41:24.799 --> 00:41:25.779 loss of neuroprotection

NOTE Confidence: 0.99306995

00:41:26.319 --> 00:41:26.775 of

NOTE Confidence: 0.79539764

00:41:27.174 --> 00:41:28.154 APO gene

NOTE Confidence: 0.9480605

00:41:28.454 --> 00:41:30.375 through lipid pathways. He wanted

NOTE Confidence: 0.9480605

00:41:30.375 --> 00:41:32.075 to do natural indirect effects.

NOTE Confidence: 0.91431046

00:41:32.375 --> 00:41:33.515 It can be done.

NOTE Confidence: 0.90497166

00:41:35.974 --> 00:41:37.994 I'm working on including measurement

NOTE Confidence: 0.90497166

00:41:38.214 --> 00:41:39.654 error in the mediator, not

NOTE Confidence: 0.90497166

00:41:39.654 --> 00:41:41.335 in these models because here

NOTE Confidence: 0.90497166

00:41:41.335 --> 00:41:43.010 we don't really model the

NOTE Confidence: 0.90497166

00:41:43.010 --> 00:41:44.930 mediator. We just may assume

NOTE Confidence: 0.90497166

00:41:44.930 --> 00:41:46.849 that the effects of alpha

NOTE Confidence: 0.90497166

00:41:46.849 --> 00:41:48.390 despais is making it zero.

NOTE Confidence: 0.9564624

00:41:48.690 --> 00:41:50.230 But in the HIV application,

NOTE Confidence: 0.9564624

00:41:50.450 --> 00:41:52.070 there is an HIV reservoir,

NOTE Confidence: 0.9564624

00:41:52.369 --> 00:41:53.650 and that is measured with

NOTE Confidence: 0.9564624

00:41:53.650 --> 00:41:54.150 error.

NOTE Confidence: 0.99380136

00:41:54.984 --> 00:41:56.505 I am also working on

NOTE Confidence: 0.99380136

00:41:56.505 --> 00:41:57.005 relating,

NOTE Confidence: 0.92015976

00:41:57.864 --> 00:42:00.285 causal mediation analysis on surrogate

NOTE Confidence: 0.92015976

00:42:00.425 --> 00:42:01.805 to surrogate markers

NOTE Confidence: 0.9638162

00:42:02.265 --> 00:42:03.464 because you can if you

NOTE Confidence: 0.9638162

00:42:03.464 --> 00:42:05.145 don't need on treatment outcome

NOTE Confidence: 0.9638162

00:42:05.145 --> 00:42:06.425 data, if you have the

NOTE Confidence: 0.9638162

00:42:06.425 --> 00:42:07.785 effect on a surrogate, you

NOTE Confidence: 0.9638162

00:42:07.785 --> 00:42:09.900 can estimate its indirect effect

NOTE Confidence: 0.9638162

00:42:09.900 --> 00:42:10.640 through the

NOTE Confidence: 0.8589035

00:42:11.260 --> 00:42:13.680 server without long term data.

NOTE Confidence: 0.9607283

00:42:15.340 --> 00:42:16.540 I've been looking at post

NOTE Confidence: 0.9607283

00:42:16.540 --> 00:42:18.460 including post treatment common causes

NOTE Confidence: 0.9607283

00:42:18.460 --> 00:42:20.000 of the mediator and outcome.

NOTE Confidence: 0.9607283

00:42:20.219 --> 00:42:21.405 If you have a good

NOTE Confidence: 0.9607283

00:42:21.485 --> 00:42:23.325 applied application and are interested

NOTE Confidence: 0.9607283

00:42:23.325 --> 00:42:24.605 in dealing with it because

NOTE Confidence: 0.9607283

00:42:24.605 --> 00:42:26.145 it's difficult to deal with,

NOTE Confidence: 0.9607283

00:42:26.285 --> 00:42:27.645 please send me an email

NOTE Confidence: 0.9607283

00:42:27.645 --> 00:42:28.925 because maybe we can make

NOTE Confidence: 0.9607283

00:42:28.925 --> 00:42:30.205 a team because I have

NOTE Confidence: 0.9607283

00:42:30.205 --> 00:42:30.705 theory

NOTE Confidence: 0.92133456

00:42:31.005 --> 00:42:32.445 but no good data example,

NOTE Confidence: 0.92133456

00:42:32.445 --> 00:42:33.565 and I don't wanna publish

NOTE Confidence: 0.92133456

00:42:33.565 --> 00:42:34.864 that without the good data.

NOTE Confidence: 0.92133456

00:42:34.925 --> 00:42:36.285 So if you have, please

NOTE Confidence: 0.92133456

00:42:36.285 --> 00:42:37.020 let me know.

NOTE Confidence: 0.9982098

00:42:37.580 --> 00:42:39.180 I am looking for other

NOTE Confidence: 0.9982098

00:42:39.180 --> 00:42:39.680 applications

NOTE Confidence: 0.5866393

00:42:40.140 --> 00:42:40.800 as well,

NOTE Confidence: 0.97175425

00:42:41.340 --> 00:42:42.719 and thank you so much.

NOTE Confidence: 0.81102246

00:42:51.844 --> 00:42:52.344 Question?

NOTE Confidence: 0.7118282

00:42:52.805 --> 00:42:54.085 Yeah. I have a question

NOTE Confidence: 0.7118282

00:42:54.085 --> 00:42:55.704 about the how you calculate

NOTE Confidence: 0.7118282

00:42:55.844 --> 00:42:57.145 your or any,

NOTE Confidence: 0.69485044

00:43:00.405 --> 00:43:02.000 Since based on your owner.