

WEBVTT

NOTE duration: "00:44:58.239"

NOTE Confidence: 0.65077543

00:00:00.399 --> 00:00:00.900 Okay.

NOTE Confidence: 0.9175066

00:00:05.519 --> 00:00:07.040 This meeting is being recorded.

NOTE Confidence: 0.9175066

00:00:07.040 --> 00:00:08.240 So if you make comments,

NOTE Confidence: 0.9175066

00:00:08.240 --> 00:00:09.780 they would be here forever.

NOTE Confidence: 0.98204964

00:00:10.880 --> 00:00:11.380 So

NOTE Confidence: 0.85159075

00:00:11.759 --> 00:00:12.160 they are

NOTE Confidence: 0.63490623

00:00:13.965 --> 00:00:15.745 they'll study among statisticians

NOTE Confidence: 0.9737528

00:00:16.685 --> 00:00:18.945 and they're increasingly also applied

NOTE Confidence: 0.8243583

00:00:19.325 --> 00:00:21.165 in in public health and

NOTE Confidence: 0.8243583

00:00:21.165 --> 00:00:21.665 medical

NOTE Confidence: 0.97302675

00:00:23.085 --> 00:00:25.025 science. So the goal of

NOTE Confidence: 0.9375804

00:00:26.040 --> 00:00:27.720 of an adaptive design is

NOTE Confidence: 0.9375804

00:00:27.720 --> 00:00:29.180 to be able to modify

NOTE Confidence: 0.94568974

00:00:29.480 --> 00:00:31.000 and sometimes also stop a

NOTE Confidence: 0.94568974

00:00:31.000 --> 00:00:32.140 clinical trial
NOTE Confidence: 0.32672358
00:00:33.159 --> 00:00:33.659 after
NOTE Confidence: 0.4298812
00:00:34.280 --> 00:00:35.340 not in unplanned
NOTE Confidence: 0.7330773
00:00:35.800 --> 00:00:37.580 yeah even planned but unplanned.
NOTE Confidence: 0.8182855
00:00:38.120 --> 00:00:39.720 So the rules the rules
NOTE Confidence: 0.8182855
00:00:39.720 --> 00:00:40.220 to
NOTE Confidence: 0.6896683
00:00:40.825 --> 00:00:41.865 carry out in a depth
NOTE Confidence: 0.6896683
00:00:41.865 --> 00:00:42.845 of variable trial,
NOTE Confidence: 0.90344715
00:00:44.185 --> 00:00:45.565 they have to be specified
NOTE Confidence: 0.90344715
00:00:45.705 --> 00:00:47.145 in advance. The FDA is
NOTE Confidence: 0.90344715
00:00:47.145 --> 00:00:48.345 very clear about that if
NOTE Confidence: 0.90344715
00:00:48.345 --> 00:00:49.784 you won't register anything of
NOTE Confidence: 0.90344715
00:00:49.784 --> 00:00:50.925 your medicine
NOTE Confidence: 0.9219228
00:00:51.465 --> 00:00:52.745 with the FDA, you have
NOTE Confidence: 0.9219228
00:00:52.745 --> 00:00:54.205 to prepend everything.
NOTE Confidence: 0.9821498
00:00:54.780 --> 00:00:55.980 That doesn't mean that you

NOTE Confidence: 0.9821498

00:00:55.980 --> 00:00:57.580 have to keep the sample

NOTE Confidence: 0.9821498

00:00:57.580 --> 00:00:59.180 sizes the same and everything

NOTE Confidence: 0.9821498

00:00:59.180 --> 00:01:00.540 the same. It's just that

NOTE Confidence: 0.9821498

00:01:00.540 --> 00:01:01.740 you have to say how

NOTE Confidence: 0.9821498

00:01:01.740 --> 00:01:03.420 you will adapt it and

NOTE Confidence: 0.9821498

00:01:03.420 --> 00:01:04.860 you also, in those cases,

NOTE Confidence: 0.9821498

00:01:04.860 --> 00:01:06.220 you will probably have to,

NOTE Confidence: 0.9829514

00:01:06.860 --> 00:01:08.300 have a conversation with the

NOTE Confidence: 0.9829514

00:01:08.300 --> 00:01:09.520 FDA in advance

NOTE Confidence: 0.99547786

00:01:09.985 --> 00:01:11.524 of starting your study.

NOTE Confidence: 0.9505628

00:01:11.905 --> 00:01:13.265 So everything has to be

NOTE Confidence: 0.9505628

00:01:13.265 --> 00:01:15.125 pre planned when we adapt

NOTE Confidence: 0.9505628

00:01:15.185 --> 00:01:16.325 a clinical trial.

NOTE Confidence: 0.97422236

00:01:16.625 --> 00:01:18.965 Examples are sample size adjustments,

NOTE Confidence: 0.9253514

00:01:19.344 --> 00:01:21.584 removing treatment arms and changing

NOTE Confidence: 0.9253514

00:01:21.584 --> 00:01:22.804 the target population.
NOTE Confidence: 0.9351787

00:01:23.510 --> 00:01:25.050 But in public health intervention
NOTE Confidence: 0.9351787

00:01:25.270 --> 00:01:27.430 trials, sometimes there there there
NOTE Confidence: 0.9351787

00:01:27.430 --> 00:01:28.790 is more that people want
NOTE Confidence: 0.9351787

00:01:28.790 --> 00:01:29.450 to adapt.
NOTE Confidence: 0.6407297

00:01:31.110 --> 00:01:33.030 Let's try this out the
NOTE Confidence: 0.6407297

00:01:33.030 --> 00:01:33.530 notice.
NOTE Confidence: 0.8237438

00:01:46.705 --> 00:01:47.825 We have too much too
NOTE Confidence: 0.8237438

00:01:47.825 --> 00:01:49.185 much on the screen. And,
NOTE Confidence: 0.88661706

00:01:50.460 --> 00:01:51.580 so there is more that
NOTE Confidence: 0.88661706

00:01:51.580 --> 00:01:52.940 people want to want to
NOTE Confidence: 0.88661706

00:01:52.940 --> 00:01:54.780 adapt because in these large
NOTE Confidence: 0.88661706

00:01:54.780 --> 00:01:56.640 scale implementation trials,
NOTE Confidence: 0.9789347

00:01:56.940 --> 00:01:58.540 there's often more than one
NOTE Confidence: 0.9789347

00:01:58.540 --> 00:02:00.160 intervention. There could be
NOTE Confidence: 0.8428827

00:02:01.260 --> 00:02:02.540 a roll out of the

NOTE Confidence: 0.8428827
00:02:02.540 --> 00:02:03.040 intervention
NOTE Confidence: 0.92887384
00:02:03.340 --> 00:02:04.700 that may take one or
NOTE Confidence: 0.92887384
00:02:04.700 --> 00:02:06.375 may take three days. There
NOTE Confidence: 0.92887384
00:02:06.375 --> 00:02:08.455 could be coaching visits that
NOTE Confidence: 0.92887384
00:02:08.455 --> 00:02:09.815 that take place during over
NOTE Confidence: 0.92887384
00:02:09.815 --> 00:02:11.495 the course of time. And
NOTE Confidence: 0.92887384
00:02:11.495 --> 00:02:12.474 all these intervention
NOTE Confidence: 0.956024
00:02:12.775 --> 00:02:13.275 components,
NOTE Confidence: 0.938569
00:02:13.894 --> 00:02:14.935 if you would have to
NOTE Confidence: 0.938569
00:02:14.935 --> 00:02:17.095 specify exactly how many coaching
NOTE Confidence: 0.938569
00:02:17.095 --> 00:02:18.694 days, exactly all these things
NOTE Confidence: 0.938569
00:02:18.694 --> 00:02:19.995 and the of these intervention
NOTE Confidence: 0.938569
00:02:20.135 --> 00:02:20.635 components,
NOTE Confidence: 0.9199574
00:02:21.389 --> 00:02:22.510 that might just be too
NOTE Confidence: 0.9199574
00:02:22.510 --> 00:02:24.269 much to ask for. In
NOTE Confidence: 0.9199574

00:02:24.269 --> 00:02:25.310 in most of the trial,
NOTE Confidence: 0.9199574

00:02:25.310 --> 00:02:26.829 people typically have an idea
NOTE Confidence: 0.9199574

00:02:26.829 --> 00:02:27.950 about what would be the
NOTE Confidence: 0.9199574

00:02:27.950 --> 00:02:29.010 optimal intervention
NOTE Confidence: 0.7498332

00:02:29.389 --> 00:02:29.889 package,
NOTE Confidence: 0.89732337

00:02:30.349 --> 00:02:31.870 but then this this center
NOTE Confidence: 0.89732337

00:02:31.870 --> 00:02:33.230 does something else. This other
NOTE Confidence: 0.89732337

00:02:33.230 --> 00:02:34.750 thing sets about something else.
NOTE Confidence: 0.89732337

00:02:34.750 --> 00:02:35.870 And maybe over the course
NOTE Confidence: 0.89732337

00:02:35.870 --> 00:02:37.005 of time, it seems like
NOTE Confidence: 0.89732337

00:02:37.085 --> 00:02:37.905 one of the intervention
NOTE Confidence: 0.9883457

00:02:38.685 --> 00:02:40.065 components is more
NOTE Confidence: 0.9534372

00:02:40.525 --> 00:02:42.525 useful and people focus more
NOTE Confidence: 0.9534372

00:02:42.525 --> 00:02:44.945 on that. So what statisticians
NOTE Confidence: 0.73683023

00:02:45.325 --> 00:02:46.525 have often done is say,
NOTE Confidence: 0.73683023

00:02:46.525 --> 00:02:47.485 okay. If you're in an

NOTE Confidence: 0.73683023
00:02:47.485 --> 00:02:49.165 ethnic intervention about the trials
NOTE Confidence: 0.73683023
00:02:49.165 --> 00:02:49.665 ongoing,
NOTE Confidence: 0.98283213
00:02:50.285 --> 00:02:51.105 we don't wanna
NOTE Confidence: 0.97275555
00:02:51.419 --> 00:02:53.019 touch the data because that's
NOTE Confidence: 0.97275555
00:02:53.019 --> 00:02:54.379 not planned and there could
NOTE Confidence: 0.97275555
00:02:54.379 --> 00:02:55.659 be all kinds of issues
NOTE Confidence: 0.97275555
00:02:55.659 --> 00:02:56.319 with that.
NOTE Confidence: 0.9560954
00:02:57.099 --> 00:02:58.939 And Donna found out through
NOTE Confidence: 0.9560954
00:02:58.939 --> 00:02:59.439 her,
NOTE Confidence: 0.98564976
00:03:00.299 --> 00:03:02.700 sounding board people that it
NOTE Confidence: 0.98564976
00:03:02.700 --> 00:03:03.900 would be a good idea
NOTE Confidence: 0.98564976
00:03:03.900 --> 00:03:05.579 to also figure out if
NOTE Confidence: 0.98564976
00:03:05.579 --> 00:03:06.560 we can formalize
NOTE Confidence: 0.9991301
00:03:07.415 --> 00:03:09.755 this learning from prior data
NOTE Confidence: 0.87842315
00:03:10.135 --> 00:03:11.975 because that's what, LAGO is
NOTE Confidence: 0.87842315

00:03:11.975 --> 00:03:13.975 about. It's a at least
NOTE Confidence: 0.87842315

00:03:13.975 --> 00:03:15.275 two stage trial
NOTE Confidence: 0.53876835

00:03:15.735 --> 00:03:16.235 where
NOTE Confidence: 0.9227419

00:03:16.615 --> 00:03:18.135 the data from the first
NOTE Confidence: 0.9227419

00:03:18.135 --> 00:03:19.995 stage are in are analyzed,
NOTE Confidence: 0.90843946

00:03:20.790 --> 00:03:22.230 and they are used to
NOTE Confidence: 0.90843946

00:03:22.230 --> 00:03:23.430 figure out which would be
NOTE Confidence: 0.90843946

00:03:23.430 --> 00:03:25.110 a good intervention to do
NOTE Confidence: 0.90843946

00:03:25.110 --> 00:03:26.570 in the next step.
NOTE Confidence: 0.9285613

00:03:28.070 --> 00:03:29.430 So the intervention could be
NOTE Confidence: 0.9285613

00:03:29.430 --> 00:03:30.790 a treatment, a device, a
NOTE Confidence: 0.9285613

00:03:30.790 --> 00:03:32.550 new way to organize care
NOTE Confidence: 0.9285613

00:03:32.550 --> 00:03:34.150 or a combination of all
NOTE Confidence: 0.9285613

00:03:34.150 --> 00:03:34.650 that.
NOTE Confidence: 0.9994785

00:03:35.265 --> 00:03:35.765 And
NOTE Confidence: 0.89022577

00:03:36.784 --> 00:03:38.465 the Lago trial, an inherent

NOTE Confidence: 0.89022577
00:03:38.465 --> 00:03:39.745 part of a Lago trial
NOTE Confidence: 0.89022577
00:03:39.745 --> 00:03:41.584 is to optimize and prevent
NOTE Confidence: 0.89022577
00:03:41.584 --> 00:03:43.105 it. And that means maybe
NOTE Confidence: 0.89022577
00:03:43.105 --> 00:03:44.064 then you want to search
NOTE Confidence: 0.89022577
00:03:44.064 --> 00:03:45.424 an outcome or maybe you
NOTE Confidence: 0.89022577
00:03:45.424 --> 00:03:47.284 want a probability of success
NOTE Confidence: 0.89022577
00:03:47.345 --> 00:03:48.885 of at least ninety percent
NOTE Confidence: 0.8815239
00:03:49.424 --> 00:03:50.724 or maybe forty percent,
NOTE Confidence: 0.9566229
00:03:51.160 --> 00:03:52.440 Whatever but some kind of
NOTE Confidence: 0.9566229
00:03:52.440 --> 00:03:54.200 goal or maybe you want
NOTE Confidence: 0.9566229
00:03:54.200 --> 00:03:55.800 a mean blood pressure in
NOTE Confidence: 0.9566229
00:03:55.800 --> 00:03:57.660 those who have suffered from
NOTE Confidence: 0.89175004
00:03:58.600 --> 00:03:59.560 who have who have suffered
NOTE Confidence: 0.89175004
00:03:59.560 --> 00:04:00.780 from high blood pressure
NOTE Confidence: 0.75539637
00:04:01.160 --> 00:04:02.380 of say eighty
NOTE Confidence: 0.8640563

00:04:02.840 --> 00:04:03.980 or maybe nine
NOTE Confidence: 0.95135236

00:04:04.575 --> 00:04:06.895 depending on your aim. So
NOTE Confidence: 0.95135236

00:04:06.895 --> 00:04:07.855 maybe you have an idea
NOTE Confidence: 0.95135236

00:04:07.855 --> 00:04:08.895 about how you want to
NOTE Confidence: 0.95135236

00:04:08.895 --> 00:04:09.875 have the outcome
NOTE Confidence: 0.6832717

00:04:10.175 --> 00:04:11.155 and that an
NOTE Confidence: 0.9179021

00:04:11.455 --> 00:04:12.735 important part of a lab
NOTE Confidence: 0.9179021

00:04:12.735 --> 00:04:14.495 coat trial is to figure
NOTE Confidence: 0.9179021

00:04:14.495 --> 00:04:15.795 out what is the optimal
NOTE Confidence: 0.9179021

00:04:15.855 --> 00:04:17.875 way to achieve this goal
NOTE Confidence: 0.9179021

00:04:17.960 --> 00:04:19.960 where we not only look
NOTE Confidence: 0.9179021

00:04:19.960 --> 00:04:21.800 at efficacy, we also look
NOTE Confidence: 0.9179021

00:04:21.800 --> 00:04:22.540 at cost.
NOTE Confidence: 0.9332659

00:04:23.560 --> 00:04:24.060 Because,
NOTE Confidence: 0.9263064

00:04:24.440 --> 00:04:25.320 of course, if you look
NOTE Confidence: 0.9263064

00:04:25.320 --> 00:04:26.600 at efficacy, then you will

NOTE Confidence: 0.9263064
00:04:26.600 --> 00:04:27.880 just max out all the
NOTE Confidence: 0.9263064
00:04:27.880 --> 00:04:29.580 effect effective components,
NOTE Confidence: 0.93162596
00:04:30.305 --> 00:04:31.185 but then you may add
NOTE Confidence: 0.93162596
00:04:31.425 --> 00:04:33.045 end up with a implementation
NOTE Confidence: 0.99633574
00:04:33.425 --> 00:04:33.925 package
NOTE Confidence: 0.9944706
00:04:34.305 --> 00:04:35.605 that is very expensive
NOTE Confidence: 0.9684059
00:04:35.985 --> 00:04:37.425 and maybe also not very
NOTE Confidence: 0.9684059
00:04:37.425 --> 00:04:37.925 practical.
NOTE Confidence: 0.80402166
00:04:38.464 --> 00:04:39.825 So we also look at
NOTE Confidence: 0.80402166
00:04:39.825 --> 00:04:40.325 first
NOTE Confidence: 0.7822276
00:04:40.705 --> 00:04:42.464 to, to optimize here the
NOTE Confidence: 0.7822276
00:04:42.464 --> 00:04:42.964 batch.
NOTE Confidence: 0.7867554
00:04:47.480 --> 00:04:49.420 In the beta burst study,
NOTE Confidence: 0.9995533
00:04:49.880 --> 00:04:50.620 the intervention
NOTE Confidence: 0.9982069
00:04:50.920 --> 00:04:52.440 was the encouragement of the
NOTE Confidence: 0.9982069

00:04:52.440 --> 00:04:54.120 use of a checklist to
NOTE Confidence: 0.9982069

00:04:54.120 --> 00:04:54.620 improve
NOTE Confidence: 0.98883027

00:04:55.400 --> 00:04:56.920 safety of mother and the
NOTE Confidence: 0.98883027

00:04:56.920 --> 00:04:57.420 newborn
NOTE Confidence: 0.7525357

00:04:58.040 --> 00:04:59.675 child, and it goes to
NOTE Confidence: 0.7525357

00:04:59.675 --> 00:05:00.255 a WHO
NOTE Confidence: 0.9664621

00:05:00.555 --> 00:05:01.995 checklist of a lot of
NOTE Confidence: 0.9664621

00:05:01.995 --> 00:05:02.495 interventions
NOTE Confidence: 0.9855798

00:05:03.035 --> 00:05:04.654 that are known to help,
NOTE Confidence: 0.99960536

00:05:06.075 --> 00:05:06.575 prevent
NOTE Confidence: 0.93549865

00:05:07.115 --> 00:05:09.355 complications during birth, complications of
NOTE Confidence: 0.93549865

00:05:09.355 --> 00:05:11.515 the child and complications of
NOTE Confidence: 0.93549865

00:05:11.515 --> 00:05:12.175 the mother.
NOTE Confidence: 0.9854668

00:05:13.150 --> 00:05:14.690 And how they
NOTE Confidence: 0.89699847

00:05:15.310 --> 00:05:17.970 implemented this this this, enforcement
NOTE Confidence: 0.89699847

00:05:18.110 --> 00:05:19.550 of the checklist changed over

NOTE Confidence: 0.89699847
00:05:19.550 --> 00:05:21.070 a course of time. They
NOTE Confidence: 0.89699847
00:05:21.070 --> 00:05:22.510 first had a trial with
NOTE Confidence: 0.89699847
00:05:22.510 --> 00:05:23.950 with limited number of centers
NOTE Confidence: 0.89699847
00:05:23.950 --> 00:05:25.310 then then the next phase
NOTE Confidence: 0.89699847
00:05:25.310 --> 00:05:26.270 where they had they had
NOTE Confidence: 0.89699847
00:05:26.270 --> 00:05:27.884 another number of centers and
NOTE Confidence: 0.89699847
00:05:27.884 --> 00:05:29.245 then the big trial where
NOTE Confidence: 0.89699847
00:05:29.245 --> 00:05:31.264 they actually randomized the intervention.
NOTE Confidence: 0.930966
00:05:32.525 --> 00:05:34.125 The VEDAMAR study took place
NOTE Confidence: 0.930966
00:05:34.125 --> 00:05:36.065 in Uttar Pradesh in India
NOTE Confidence: 0.88588476
00:05:36.764 --> 00:05:37.985 and the outcomes,
NOTE Confidence: 0.9814645
00:05:38.764 --> 00:05:39.964 are the outcomes of a
NOTE Confidence: 0.9814645
00:05:39.964 --> 00:05:41.745 coaching based WHO
NOTE Confidence: 0.9004116
00:05:42.205 --> 00:05:44.060 safe burn safe childbirth
NOTE Confidence: 0.95523757
00:05:44.759 --> 00:05:45.259 checklist
NOTE Confidence: 0.99825567

00:05:45.560 --> 00:05:46.060 program
NOTE Confidence: 0.8795862
00:05:46.520 --> 00:05:47.259 in India.
NOTE Confidence: 0.9938348
00:05:47.720 --> 00:05:48.620 And this,
NOTE Confidence: 0.92631626
00:05:49.159 --> 00:05:50.439 this was published in the
NOTE Confidence: 0.92631626
00:05:50.439 --> 00:05:52.219 New England Journal of Medicine.
NOTE Confidence: 0.9362984
00:05:52.759 --> 00:05:53.879 One of the aspects of
NOTE Confidence: 0.9362984
00:05:53.879 --> 00:05:55.240 the better bird trial, it
NOTE Confidence: 0.9362984
00:05:55.240 --> 00:05:57.560 did provide useful information on
NOTE Confidence: 0.9362984
00:05:57.560 --> 00:05:58.620 how to improve
NOTE Confidence: 0.97550154
00:05:59.555 --> 00:06:00.695 process outcomes,
NOTE Confidence: 0.9970349
00:06:01.154 --> 00:06:02.675 but it failed to show
NOTE Confidence: 0.9970349
00:06:02.675 --> 00:06:04.775 a significant result on the
NOTE Confidence: 0.9970349
00:06:05.074 --> 00:06:06.695 on the primary outcome.
NOTE Confidence: 0.9276533
00:06:07.154 --> 00:06:08.514 So, technically, it was a
NOTE Confidence: 0.9276533
00:06:08.514 --> 00:06:10.455 failed trial, although still,
NOTE Confidence: 0.9750063
00:06:10.915 --> 00:06:13.175 they found effects on process

NOTE Confidence: 0.9750063
00:06:13.315 --> 00:06:13.815 outcomes.
NOTE Confidence: 0.82905316
00:06:14.770 --> 00:06:15.270 Perfect.
NOTE Confidence: 0.69819957
00:06:15.810 --> 00:06:17.169 So just a nine to
NOTE Confidence: 0.69819957
00:06:17.169 --> 00:06:18.449 twenty graph, did this check
NOTE Confidence: 0.69819957
00:06:18.449 --> 00:06:19.349 this is for,
NOTE Confidence: 0.7747838
00:06:19.889 --> 00:06:21.729 practitioners that are involved with
NOTE Confidence: 0.7747838
00:06:21.969 --> 00:06:23.089 Yeah. Well, I think it's
NOTE Confidence: 0.7747838
00:06:23.089 --> 00:06:24.529 just wash hands. One of
NOTE Confidence: 0.7747838
00:06:24.529 --> 00:06:25.509 the things is,
NOTE Confidence: 0.9337836
00:06:27.185 --> 00:06:29.265 make sure that the mother
NOTE Confidence: 0.9337836
00:06:29.265 --> 00:06:30.245 gets oxytocin
NOTE Confidence: 0.7070716
00:06:30.545 --> 00:06:32.545 during delivery. That's during the
NOTE Confidence: 0.7070716
00:06:32.865 --> 00:06:33.365 Very,
NOTE Confidence: 0.95750666
00:06:34.065 --> 00:06:36.225 very specific things that happened
NOTE Confidence: 0.95750666
00:06:36.225 --> 00:06:36.725 around
NOTE Confidence: 0.85630614

00:06:37.345 --> 00:06:38.785 In and around childhood. There's,
NOTE Confidence: 0.85630614

00:06:38.785 --> 00:06:40.065 like, I think twenty seven
NOTE Confidence: 0.85630614

00:06:40.065 --> 00:06:40.565 different
NOTE Confidence: 0.9973581

00:06:41.029 --> 00:06:42.389 recommended things that should be
NOTE Confidence: 0.9973581

00:06:42.389 --> 00:06:42.889 done
NOTE Confidence: 0.9085847

00:06:44.229 --> 00:06:45.990 before, during, and right after
NOTE Confidence: 0.9085847

00:06:45.990 --> 00:06:47.430 your childbirth, and most of
NOTE Confidence: 0.9085847

00:06:47.430 --> 00:06:49.130 them are very low tech.
NOTE Confidence: 0.7557005

00:06:49.990 --> 00:06:51.210 That works in hand.
NOTE Confidence: 0.9542585

00:06:52.069 --> 00:06:52.810 That's simple.
NOTE Confidence: 0.81733155

00:06:54.104 --> 00:06:54.904 But the third time not
NOTE Confidence: 0.81733155

00:06:54.904 --> 00:06:56.125 everybody does that.
NOTE Confidence: 0.89576936

00:06:58.745 --> 00:07:00.365 We looked at package components
NOTE Confidence: 0.89576936

00:07:00.664 --> 00:07:02.585 intervention, launch units, the number
NOTE Confidence: 0.89576936

00:07:02.585 --> 00:07:04.824 of coaching visits, and a
NOTE Confidence: 0.89576936

00:07:04.824 --> 00:07:06.365 data feedback form

NOTE Confidence: 0.9672163
00:07:06.800 --> 00:07:08.720 And, so what we are
NOTE Confidence: 0.9672163
00:07:08.720 --> 00:07:10.000 going to do is figure
NOTE Confidence: 0.9672163
00:07:10.000 --> 00:07:11.200 out how we could have
NOTE Confidence: 0.9672163
00:07:11.200 --> 00:07:13.120 used Laval in order to
NOTE Confidence: 0.9672163
00:07:13.120 --> 00:07:13.620 improve
NOTE Confidence: 0.92195326
00:07:14.080 --> 00:07:15.520 the outcomes for the better
NOTE Confidence: 0.92195326
00:07:15.520 --> 00:07:16.020 start.
NOTE Confidence: 0.9058167
00:07:19.885 --> 00:07:21.265 Judith, some of the people
NOTE Confidence: 0.9058167
00:07:21.325 --> 00:07:22.925 online said that if you
NOTE Confidence: 0.9058167
00:07:22.925 --> 00:07:24.205 move away from, I guess,
NOTE Confidence: 0.9058167
00:07:24.205 --> 00:07:25.805 the computers where the mic
NOTE Confidence: 0.9058167
00:07:25.805 --> 00:07:27.485 is, they're having trouble hearing
NOTE Confidence: 0.9058167
00:07:27.485 --> 00:07:29.085 you. Oh, okay. So it's
NOTE Confidence: 0.9058167
00:07:29.085 --> 00:07:30.225 a little bit weird.
NOTE Confidence: 0.846899
00:07:31.420 --> 00:07:32.380 And I think the AV
NOTE Confidence: 0.846899

00:07:32.380 --> 00:07:33.820 guys coming back can help
NOTE Confidence: 0.846899

00:07:33.820 --> 00:07:35.100 too. There's also a coating
NOTE Confidence: 0.846899

00:07:35.100 --> 00:07:36.140 that you'd be more comfortable
NOTE Confidence: 0.846899

00:07:36.140 --> 00:07:37.020 with. Would that be easier
NOTE Confidence: 0.846899

00:07:37.020 --> 00:07:38.860 for you? Yes. Let's do
NOTE Confidence: 0.846899

00:07:38.860 --> 00:07:41.040 that. Let me load. Sure.
NOTE Confidence: 0.84943056

00:07:45.475 --> 00:07:46.515 While while you're doing that,
NOTE Confidence: 0.7997924

00:07:47.315 --> 00:07:48.595 before you even talk about
NOTE Confidence: 0.7997924

00:07:48.595 --> 00:07:49.815 including the outcomes,
NOTE Confidence: 0.9813948

00:07:50.275 --> 00:07:51.415 what were the outcomes?
NOTE Confidence: 0.8356944

00:07:52.995 --> 00:07:55.095 So they looked at
NOTE Confidence: 0.9627307

00:07:56.199 --> 00:07:57.639 The primary outcome of the
NOTE Confidence: 0.9627307

00:07:57.639 --> 00:07:59.560 study was a combined outcome
NOTE Confidence: 0.9627307

00:07:59.560 --> 00:08:01.659 of maternal mortality and neonatal
NOTE Confidence: 0.9627307

00:08:01.800 --> 00:08:02.300 mortality.
NOTE Confidence: 0.86953735

00:08:03.560 --> 00:08:05.020 And it's a huge trial,

NOTE Confidence: 0.86953735

00:08:05.159 --> 00:08:06.440 like, you know, something like

NOTE Confidence: 0.86953735

00:08:06.440 --> 00:08:07.560 over a hundred and fifty

NOTE Confidence: 0.86953735

00:08:07.560 --> 00:08:07.875 thousand

NOTE Confidence: 0.89141655

00:08:08.435 --> 00:08:10.215 births or something like that.

NOTE Confidence: 0.89141655

00:08:10.355 --> 00:08:11.955 Yeah. We've heard six hundred.

NOTE Confidence: 0.89141655

00:08:11.955 --> 00:08:12.995 Based on the way they've

NOTE Confidence: 0.89141655

00:08:12.995 --> 00:08:14.295 done it done the trial?

NOTE Confidence: 0.72326934

00:08:14.915 --> 00:08:16.375 Yeah. Yeah. Exactly. Exactly.

NOTE Confidence: 0.81560785

00:08:18.035 --> 00:08:19.475 These colleagues are all evidence

NOTE Confidence: 0.81560785

00:08:19.475 --> 00:08:20.375 based interventions

NOTE Confidence: 0.9240513

00:08:21.070 --> 00:08:22.590 that are routinely all done

NOTE Confidence: 0.9240513

00:08:22.590 --> 00:08:24.110 in high income countries where

NOTE Confidence: 0.9240513

00:08:24.110 --> 00:08:25.810 we have very, very low,

NOTE Confidence: 0.74047136

00:08:26.670 --> 00:08:28.770 maternal mortality rates and neonatal

NOTE Confidence: 0.74047136

00:08:28.910 --> 00:08:30.670 mortality rates. And those are

NOTE Confidence: 0.74047136

00:08:30.670 --> 00:08:32.429 all not in the US.
NOTE Confidence: 0.74047136

00:08:32.429 --> 00:08:33.410 We have high rates.
NOTE Confidence: 0.84307575

00:08:34.725 --> 00:08:35.765 So it couldn't be down
NOTE Confidence: 0.84307575

00:08:35.765 --> 00:08:36.565 the US because we have
NOTE Confidence: 0.84307575

00:08:36.565 --> 00:08:37.845 high rates. We have high
NOTE Confidence: 0.84307575

00:08:37.845 --> 00:08:38.804 rates. Yeah. We have high
NOTE Confidence: 0.84307575

00:08:38.804 --> 00:08:39.765 rates higher than in the
NOTE Confidence: 0.84307575

00:08:39.765 --> 00:08:41.684 Dallas. Very common. Excuse me.
NOTE Confidence: 0.84307575

00:08:41.684 --> 00:08:42.965 That's right. But it is
NOTE Confidence: 0.84307575

00:08:42.965 --> 00:08:44.725 very it's very this this
NOTE Confidence: 0.84307575

00:08:44.725 --> 00:08:46.165 terrible. Somebody like me is
NOTE Confidence: 0.84307575

00:08:46.165 --> 00:08:47.205 not at risk because I
NOTE Confidence: 0.84307575

00:08:47.205 --> 00:08:48.245 go to Brigham and Women's
NOTE Confidence: 0.84307575

00:08:48.245 --> 00:08:48.745 Hospital.
NOTE Confidence: 0.9594045

00:08:49.449 --> 00:08:50.269 Other people,
NOTE Confidence: 0.7799816

00:08:51.050 --> 00:08:52.190 oh, yeah. Other other

NOTE Confidence: 0.7019
00:08:53.370 --> 00:08:53.870 people,
NOTE Confidence: 0.78968924
00:08:54.649 --> 00:08:55.550 are not affected.
NOTE Confidence: 0.8074864
00:08:56.009 --> 00:08:56.970 You can get lucky you
NOTE Confidence: 0.8074864
00:08:56.970 --> 00:08:57.870 can get notified.
NOTE Confidence: 0.9464287
00:09:00.329 --> 00:09:01.149 It's a problem.
NOTE Confidence: 0.841927
00:09:04.214 --> 00:09:06.375 So this randomized leopovirus had
NOTE Confidence: 0.841927
00:09:06.375 --> 00:09:07.654 thirty six or more patients
NOTE Confidence: 0.841927
00:09:07.654 --> 00:09:08.694 and still on the back
NOTE Confidence: 0.841927
00:09:08.694 --> 00:09:10.214 primary outcome, they didn't have
NOTE Confidence: 0.841927
00:09:10.214 --> 00:09:11.514 a significant result.
NOTE Confidence: 0.9955362
00:09:13.415 --> 00:09:13.915 So,
NOTE Confidence: 0.7769335
00:09:14.375 --> 00:09:15.115 the Golub,
NOTE Confidence: 0.847124
00:09:15.495 --> 00:09:17.175 Lago study is now how
NOTE Confidence: 0.847124
00:09:17.175 --> 00:09:18.855 the probability of success. For
NOTE Confidence: 0.847124
00:09:18.855 --> 00:09:19.620 example, the percentage of
NOTE Confidence: 0.85553026

00:09:20.820 --> 00:09:22.600 developed birth checklist is used

NOTE Confidence: 0.9095346

00:09:23.220 --> 00:09:24.920 depends on the intervention package

NOTE Confidence: 0.9095346

00:09:25.220 --> 00:09:27.059 x. Let's say x consists

NOTE Confidence: 0.9095346

00:09:27.059 --> 00:09:28.339 of both the launch duration

NOTE Confidence: 0.9095346

00:09:28.339 --> 00:09:29.720 and the number of coaching

NOTE Confidence: 0.9095346

00:09:29.779 --> 00:09:32.085 visits. This will be, considered

NOTE Confidence: 0.9095346

00:09:32.085 --> 00:09:33.065 in the middle of study

NOTE Confidence: 0.9095346

00:09:33.205 --> 00:09:34.905 because there were more intervention

NOTE Confidence: 0.9095346

00:09:35.045 --> 00:09:35.545 components,

NOTE Confidence: 0.85565513

00:09:36.165 --> 00:09:37.865 but they were highly coordinated.

NOTE Confidence: 0.85565513

00:09:38.005 --> 00:09:38.885 So we looked only at

NOTE Confidence: 0.85565513

00:09:38.885 --> 00:09:39.625 these two.

NOTE Confidence: 0.9340373

00:09:40.645 --> 00:09:42.325 For example, finding the intervention

NOTE Confidence: 0.9340373

00:09:42.325 --> 00:09:43.385 package xopt

NOTE Confidence: 0.98567986

00:09:43.765 --> 00:09:45.684 so that, it solves that

NOTE Confidence: 0.98567986

00:09:45.684 --> 00:09:47.385 the probability of success

NOTE Confidence: 0.9912346
00:09:47.840 --> 00:09:49.280 is at least zero point
NOTE Confidence: 0.9912346
00:09:49.280 --> 00:09:49.780 nine
NOTE Confidence: 0.9842418
00:09:50.160 --> 00:09:52.000 by minimizing the cost of
NOTE Confidence: 0.9842418
00:09:52.000 --> 00:09:52.500 x
NOTE Confidence: 0.9882142
00:09:52.880 --> 00:09:54.900 and subject to natural constraints
NOTE Confidence: 0.9882142
00:09:54.960 --> 00:09:56.080 on x. When you look
NOTE Confidence: 0.9882142
00:09:56.080 --> 00:09:57.840 at launch duration, you can
NOTE Confidence: 0.9882142
00:09:57.840 --> 00:09:59.360 probably imagine that it's probably
NOTE Confidence: 0.9882142
00:09:59.360 --> 00:10:00.320 not a good idea to
NOTE Confidence: 0.9882142
00:10:00.320 --> 00:10:01.600 have a launch duration of
NOTE Confidence: 0.9882142
00:10:01.600 --> 00:10:03.040 more than three or four
NOTE Confidence: 0.9882142
00:10:03.040 --> 00:10:03.540 days.
NOTE Confidence: 0.89088213
00:10:05.654 --> 00:10:07.015 And there's also a minimum
NOTE Confidence: 0.89088213
00:10:07.015 --> 00:10:08.375 because we cannot be we
NOTE Confidence: 0.89088213
00:10:08.375 --> 00:10:09.735 we we're assuming that at
NOTE Confidence: 0.89088213

00:10:09.735 --> 00:10:11.175 least the intervention needs to
NOTE Confidence: 0.89088213

00:10:11.175 --> 00:10:12.214 be rolled out so it
NOTE Confidence: 0.89088213

00:10:12.214 --> 00:10:13.815 would be considered a launch
NOTE Confidence: 0.89088213

00:10:13.815 --> 00:10:15.255 duration also of at least
NOTE Confidence: 0.89088213

00:10:15.255 --> 00:10:16.075 one day.
NOTE Confidence: 0.9535917

00:10:17.770 --> 00:10:19.690 In March, Exoq minimizes the
NOTE Confidence: 0.9535917

00:10:19.690 --> 00:10:21.290 cost of the intervention package
NOTE Confidence: 0.9535917

00:10:21.290 --> 00:10:22.809 while keeping the probability of
NOTE Confidence: 0.9535917

00:10:22.809 --> 00:10:24.090 success to be at least
NOTE Confidence: 0.9535917

00:10:24.090 --> 00:10:24.990 ninety percent.
NOTE Confidence: 0.2105784

00:10:26.370 --> 00:10:26.870 In
NOTE Confidence: 0.8542746

00:10:28.250 --> 00:10:29.850 the present of center effects,
NOTE Confidence: 0.8542746

00:10:29.850 --> 00:10:31.255 one could look at the
NOTE Confidence: 0.8542746

00:10:31.255 --> 00:10:32.695 average log or the centers
NOTE Confidence: 0.8542746

00:10:32.695 --> 00:10:34.295 of this probability of success
NOTE Confidence: 0.8542746

00:10:34.295 --> 00:10:35.255 and that's what we have

NOTE Confidence: 0.8542746
00:10:35.255 --> 00:10:36.714 been doing in the POLISA
NOTE Confidence: 0.8542746
00:10:36.774 --> 00:10:37.274 study.
NOTE Confidence: 0.94692355
00:10:37.815 --> 00:10:39.175 So the POLISA study is
NOTE Confidence: 0.94692355
00:10:39.175 --> 00:10:40.934 currently ongoing. I cannot show
NOTE Confidence: 0.94692355
00:10:40.934 --> 00:10:41.975 you results. That's why I
NOTE Confidence: 0.94692355
00:10:41.975 --> 00:10:42.855 don't have it on the
NOTE Confidence: 0.94692355
00:10:42.855 --> 00:10:44.650 slides. But the POLISA study
NOTE Confidence: 0.94692355
00:10:44.650 --> 00:10:46.090 is one where we are
NOTE Confidence: 0.94692355
00:10:46.090 --> 00:10:47.950 currently doing level optimization.
NOTE Confidence: 0.93579525
00:10:48.410 --> 00:10:49.290 So we are looking at
NOTE Confidence: 0.93579525
00:10:49.290 --> 00:10:51.230 this, at this particular
NOTE Confidence: 0.96262825
00:10:51.690 --> 00:10:53.470 outcome goal, we call it.
NOTE Confidence: 0.9143884
00:10:54.730 --> 00:10:56.590 So in MERGE, actual minimizes
NOTE Confidence: 0.9143884
00:10:56.730 --> 00:10:57.950 the cost of the intervention
NOTE Confidence: 0.9143884
00:10:58.095 --> 00:10:59.694 package while keeping the average
NOTE Confidence: 0.9143884

00:10:59.694 --> 00:11:01.295 probability of success to be
NOTE Confidence: 0.9143884

00:11:01.295 --> 00:11:02.595 at least ninety percent.
NOTE Confidence: 0.9192161

00:11:05.615 --> 00:11:06.975 So the level, the learn
NOTE Confidence: 0.9192161

00:11:06.975 --> 00:11:08.495 as you go aspect, we
NOTE Confidence: 0.9192161

00:11:08.495 --> 00:11:10.274 will start with two stages.
NOTE Confidence: 0.9192161

00:11:10.334 --> 00:11:11.694 Like, the level can also
NOTE Confidence: 0.9192161

00:11:11.694 --> 00:11:12.814 be done for more than
NOTE Confidence: 0.9192161

00:11:12.814 --> 00:11:13.554 two stages,
NOTE Confidence: 0.94910425

00:11:13.880 --> 00:11:15.399 But the basic things of
NOTE Confidence: 0.94910425

00:11:15.399 --> 00:11:17.080 the how we roll it
NOTE Confidence: 0.94910425

00:11:17.080 --> 00:11:18.360 out and what are the
NOTE Confidence: 0.94910425

00:11:18.360 --> 00:11:19.800 things that we do is
NOTE Confidence: 0.94910425

00:11:19.800 --> 00:11:21.080 better explained to the only
NOTE Confidence: 0.94910425

00:11:21.080 --> 00:11:21.740 two stages.
NOTE Confidence: 0.8806725

00:11:22.519 --> 00:11:24.440 And we consider the stage
NOTE Confidence: 0.8806725

00:11:24.600 --> 00:11:26.519 the situation where the stage

NOTE Confidence: 0.8806725
00:11:26.519 --> 00:11:27.339 one attaches
NOTE Confidence: 0.82775915
00:11:27.915 --> 00:11:30.015 determining amount because what capability
NOTE Confidence: 0.82775915
00:11:30.235 --> 00:11:31.274 you have to play your
NOTE Confidence: 0.82775915
00:11:31.274 --> 00:11:32.955 trial. And then what happens
NOTE Confidence: 0.82775915
00:11:32.955 --> 00:11:34.415 in the first stage happens.
NOTE Confidence: 0.87202525
00:11:34.875 --> 00:11:36.475 In the second stage, we
NOTE Confidence: 0.87202525
00:11:36.475 --> 00:11:38.154 will calculate a re a
NOTE Confidence: 0.87202525
00:11:38.154 --> 00:11:39.375 recommended intervention
NOTE Confidence: 0.95858717
00:11:40.075 --> 00:11:41.355 to use in the next
NOTE Confidence: 0.95858717
00:11:41.355 --> 00:11:42.795 stage of the trial. And
NOTE Confidence: 0.95858717
00:11:42.795 --> 00:11:43.455 that recommended
NOTE Confidence: 0.96826404
00:11:43.890 --> 00:11:44.630 intervention typically
NOTE Confidence: 0.9940649
00:11:45.090 --> 00:11:46.770 depends on the stage one
NOTE Confidence: 0.9940649
00:11:46.770 --> 00:11:48.210 data. So what you get
NOTE Confidence: 0.9940649
00:11:48.210 --> 00:11:49.809 is a dependence between the
NOTE Confidence: 0.9940649

00:11:49.809 --> 00:11:51.090 stage one data and the
NOTE Confidence: 0.9940649

00:11:51.090 --> 00:11:52.150 stage two data
NOTE Confidence: 0.98173904

00:11:52.690 --> 00:11:55.010 because the recommended intervention is
NOTE Confidence: 0.98173904

00:11:55.010 --> 00:11:55.510 learned
NOTE Confidence: 0.9964544

00:11:55.970 --> 00:11:57.510 from the stage one data.
NOTE Confidence: 0.9493916

00:11:58.535 --> 00:12:00.055 And the typical reason for
NOTE Confidence: 0.9493916

00:12:00.055 --> 00:12:01.575 wanting to learn as you
NOTE Confidence: 0.9493916

00:12:01.575 --> 00:12:03.335 go is, okay, we are
NOTE Confidence: 0.9493916

00:12:03.335 --> 00:12:05.095 in this trial and if
NOTE Confidence: 0.9493916

00:12:05.095 --> 00:12:06.695 it's broken, let's try to
NOTE Confidence: 0.9493916

00:12:06.695 --> 00:12:08.535 fix it. So Donna found
NOTE Confidence: 0.9493916

00:12:08.535 --> 00:12:09.895 out through her study group
NOTE Confidence: 0.9493916

00:12:09.895 --> 00:12:11.595 that it is also actually
NOTE Confidence: 0.9493916

00:12:11.655 --> 00:12:12.955 happening in the practice
NOTE Confidence: 0.97965634

00:12:13.280 --> 00:12:14.480 that people do want to
NOTE Confidence: 0.97965634

00:12:14.480 --> 00:12:15.760 learn. They see that their

NOTE Confidence: 0.97965634
00:12:15.760 --> 00:12:17.440 trial is not working and
NOTE Confidence: 0.97965634
00:12:17.440 --> 00:12:18.559 they do want to adapt
NOTE Confidence: 0.97965634
00:12:18.559 --> 00:12:20.080 the intervention to keep to
NOTE Confidence: 0.97965634
00:12:20.080 --> 00:12:21.380 be able to keep going,
NOTE Confidence: 0.97965634
00:12:21.600 --> 00:12:23.220 hoping for trial success.
NOTE Confidence: 0.9685849
00:12:26.275 --> 00:12:28.434 So when we learn as
NOTE Confidence: 0.9685849
00:12:28.434 --> 00:12:29.635 we go and we have
NOTE Confidence: 0.9685849
00:12:29.635 --> 00:12:32.035 a stage two intervention that
NOTE Confidence: 0.9685849
00:12:32.035 --> 00:12:33.715 depends on the stage one
NOTE Confidence: 0.9685849
00:12:33.715 --> 00:12:35.715 data, then we lose one
NOTE Confidence: 0.9685849
00:12:35.715 --> 00:12:36.215 important
NOTE Confidence: 0.99867606
00:12:36.915 --> 00:12:38.355 tool that we have in
NOTE Confidence: 0.99867606
00:12:38.355 --> 00:12:38.855 statistics
NOTE Confidence: 0.9933209
00:12:39.410 --> 00:12:40.950 and that is the independence
NOTE Confidence: 0.9933209
00:12:41.090 --> 00:12:43.250 of data across centers, the
NOTE Confidence: 0.9933209

00:12:43.250 --> 00:12:43.750 independence
NOTE Confidence: 0.98173

00:12:44.130 --> 00:12:44.870 of data,
NOTE Confidence: 0.8665596

00:12:46.210 --> 00:12:47.190 between stages.
NOTE Confidence: 0.99799746

00:12:47.809 --> 00:12:48.309 Because
NOTE Confidence: 0.97221947

00:12:48.690 --> 00:12:50.450 the outcomes in the second
NOTE Confidence: 0.97221947

00:12:50.450 --> 00:12:51.970 stage are going to depend
NOTE Confidence: 0.97221947

00:12:51.970 --> 00:12:53.330 on the outcomes in the
NOTE Confidence: 0.97221947

00:12:53.330 --> 00:12:54.230 first stage,
NOTE Confidence: 0.9769731

00:12:54.725 --> 00:12:56.325 especially if the treatment has
NOTE Confidence: 0.9769731

00:12:56.325 --> 00:12:57.145 any effect
NOTE Confidence: 0.9326311

00:12:57.525 --> 00:12:58.665 because the learning
NOTE Confidence: 0.99687153

00:12:59.365 --> 00:13:01.065 of the recommended intervention
NOTE Confidence: 0.9922222

00:13:01.765 --> 00:13:03.625 depends on the first stage.
NOTE Confidence: 0.9314579

00:13:04.085 --> 00:13:06.085 So the usual techniques that
NOTE Confidence: 0.9314579

00:13:06.085 --> 00:13:07.705 you use to prove consistency
NOTE Confidence: 0.9314579

00:13:07.925 --> 00:13:09.840 and asymptotic normality if your

NOTE Confidence: 0.9314579
00:13:09.920 --> 00:13:10.740 estimators feel
NOTE Confidence: 0.96104926
00:13:11.520 --> 00:13:13.520 miserably in this case because
NOTE Confidence: 0.96104926
00:13:13.520 --> 00:13:15.460 there's dependence between the stages.
NOTE Confidence: 0.96104926
00:13:15.680 --> 00:13:17.140 And that means that also
NOTE Confidence: 0.96104926
00:13:17.200 --> 00:13:19.200 between the different centers, even
NOTE Confidence: 0.96104926
00:13:19.200 --> 00:13:19.860 if they
NOTE Confidence: 0.6687572
00:13:20.240 --> 00:13:20.980 if they're
NOTE Confidence: 0.9977941
00:13:21.680 --> 00:13:23.220 having independent patients,
NOTE Confidence: 0.98341614
00:13:23.574 --> 00:13:24.695 their dates are going to
NOTE Confidence: 0.98341614
00:13:24.695 --> 00:13:26.954 be dependent because their interventions
NOTE Confidence: 0.98341614
00:13:27.095 --> 00:13:28.475 are going to be dependent.
NOTE Confidence: 0.8900195
00:13:31.894 --> 00:13:32.714 Here we have
NOTE Confidence: 0.9604692
00:13:33.654 --> 00:13:35.274 a long list of things.
NOTE Confidence: 0.9604692
00:13:35.520 --> 00:13:36.720 So we do two stages
NOTE Confidence: 0.9604692
00:13:36.720 --> 00:13:38.080 for now and no early
NOTE Confidence: 0.9604692

00:13:38.080 --> 00:13:39.440 stopping that we can also
NOTE Confidence: 0.9604692

00:13:39.440 --> 00:13:39.940 relax.
NOTE Confidence: 0.8780324

00:13:40.480 --> 00:13:42.100 Penny will be the notation
NOTE Confidence: 0.8780324

00:13:42.240 --> 00:13:43.059 for stage.
NOTE Confidence: 0.9770285

00:13:43.600 --> 00:13:44.880 We are assuming the same
NOTE Confidence: 0.9770285

00:13:44.880 --> 00:13:46.320 number of patients in both
NOTE Confidence: 0.9770285

00:13:46.320 --> 00:13:47.760 stages for now. This can
NOTE Confidence: 0.9770285

00:13:47.760 --> 00:13:49.040 be relaxed. It's really not
NOTE Confidence: 0.9770285

00:13:49.040 --> 00:13:49.780 big deal.
NOTE Confidence: 0.94323665

00:13:50.475 --> 00:13:51.775 X one is the recommended
NOTE Confidence: 0.94323665

00:13:51.835 --> 00:13:52.335 intervention
NOTE Confidence: 0.9603614

00:13:52.875 --> 00:13:54.875 at stage one. It's free
NOTE Confidence: 0.9603614

00:13:54.875 --> 00:13:56.235 trial, so I denote it
NOTE Confidence: 0.9603614

00:13:56.235 --> 00:13:57.915 with a little x. And
NOTE Confidence: 0.9603614

00:13:57.915 --> 00:13:59.275 x two n is the
NOTE Confidence: 0.9603614

00:13:59.275 --> 00:14:01.915 recommended multivariate intervention at stage

NOTE Confidence: 0.9603614

00:14:01.915 --> 00:14:03.309 two. And we are assuming

NOTE Confidence: 0.9603614

00:14:03.309 --> 00:14:04.589 that it's a bounded random

NOTE Confidence: 0.9603614

00:14:04.589 --> 00:14:05.950 variable that is learned from

NOTE Confidence: 0.9603614

00:14:05.950 --> 00:14:07.630 the stage one data. So

NOTE Confidence: 0.9603614

00:14:07.630 --> 00:14:08.830 that's also the reason that

NOTE Confidence: 0.9603614

00:14:08.830 --> 00:14:10.830 it's x two n. So

NOTE Confidence: 0.9603614

00:14:10.830 --> 00:14:12.110 x one doesn't need an

NOTE Confidence: 0.9603614

00:14:12.110 --> 00:14:13.649 n because it's free trial,

NOTE Confidence: 0.9858438

00:14:13.950 --> 00:14:15.309 but x two n depends

NOTE Confidence: 0.9858438

00:14:15.309 --> 00:14:16.910 on how many patients are

NOTE Confidence: 0.9858438

00:14:16.910 --> 00:14:18.725 there in stage one and

NOTE Confidence: 0.9858438

00:14:18.725 --> 00:14:19.845 who is in stage one

NOTE Confidence: 0.9858438

00:14:19.845 --> 00:14:21.145 and what were their outcomes.

NOTE Confidence: 0.9858438

00:14:21.445 --> 00:14:23.285 So in order to, stress

NOTE Confidence: 0.9858438

00:14:23.285 --> 00:14:24.725 that, we have x two

NOTE Confidence: 0.9858438

00:14:24.725 --> 00:14:25.225 m.
NOTE Confidence: 0.9571665

00:14:26.965 --> 00:14:28.405 Then we are assuming that
NOTE Confidence: 0.9571665

00:14:28.405 --> 00:14:30.725 maybe in these trials, not
NOTE Confidence: 0.9571665

00:14:30.725 --> 00:14:32.670 everybody does ex every center
NOTE Confidence: 0.9571665

00:14:32.670 --> 00:14:34.530 does exactly as the recommended
NOTE Confidence: 0.9571665

00:14:34.670 --> 00:14:36.050 intervention is recommended.
NOTE Confidence: 0.9484451

00:14:36.590 --> 00:14:37.550 So we have a different
NOTE Confidence: 0.9484451

00:14:37.550 --> 00:14:39.410 notation, a j k n,
NOTE Confidence: 0.9484451

00:14:39.710 --> 00:14:41.550 for the actual intervention in
NOTE Confidence: 0.9484451

00:14:41.550 --> 00:14:43.470 center or side j of
NOTE Confidence: 0.9484451

00:14:43.470 --> 00:14:44.610 stage k.
NOTE Confidence: 0.91449666

00:14:45.295 --> 00:14:46.575 And we are assuming that
NOTE Confidence: 0.91449666

00:14:46.575 --> 00:14:47.935 it depends on maybe on
NOTE Confidence: 0.91449666

00:14:47.935 --> 00:14:50.095 the recommended intervention, hopefully on
NOTE Confidence: 0.91449666

00:14:50.095 --> 00:14:51.235 the recommended intervention,
NOTE Confidence: 0.99010617

00:14:51.855 --> 00:14:53.615 but not further on prior

NOTE Confidence: 0.99010617

00:14:53.615 --> 00:14:55.375 data. And that means that

NOTE Confidence: 0.99010617

00:14:55.375 --> 00:14:56.595 learning is done

NOTE Confidence: 0.96135527

00:14:56.970 --> 00:14:59.050 through the recommended intervention and

NOTE Confidence: 0.96135527

00:14:59.050 --> 00:15:01.050 that's it, not also through

NOTE Confidence: 0.96135527

00:15:01.050 --> 00:15:02.649 other means. This is a

NOTE Confidence: 0.96135527

00:15:02.649 --> 00:15:04.329 restriction that we need to

NOTE Confidence: 0.96135527

00:15:04.329 --> 00:15:05.389 ensure the validity

NOTE Confidence: 0.8348031

00:15:06.089 --> 00:15:08.329 of the conference intervals and

NOTE Confidence: 0.8348031

00:15:08.329 --> 00:15:08.990 the estimators.

NOTE Confidence: 0.947898

00:15:11.274 --> 00:15:13.035 Then we have y for

NOTE Confidence: 0.947898

00:15:13.035 --> 00:15:14.954 outcomes. $Y_{k,n}$ is

NOTE Confidence: 0.947898

00:15:14.954 --> 00:15:16.394 the outcomes of the n

NOTE Confidence: 0.947898

00:15:16.394 --> 00:15:16.894 participants

NOTE Confidence: 0.945857

00:15:17.355 --> 00:15:18.574 in stage k .

NOTE Confidence: 0.9302714

00:15:18.875 --> 00:15:20.714 And their binary outcomes in

NOTE Confidence: 0.9302714

00:15:20.714 --> 00:15:22.074 this case, I can do
NOTE Confidence: 0.9302714

00:15:22.074 --> 00:15:23.595 it also for continuous, but
NOTE Confidence: 0.9302714

00:15:23.595 --> 00:15:24.520 let's set the the stage
NOTE Confidence: 0.9302714

00:15:24.520 --> 00:15:25.820 for binary outcomes.
NOTE Confidence: 0.9944757

00:15:26.279 --> 00:15:26.680 And,
NOTE Confidence: 0.90380454

00:15:27.240 --> 00:15:28.360 y I k n is
NOTE Confidence: 0.90380454

00:15:28.360 --> 00:15:30.600 the outcome of participant I
NOTE Confidence: 0.90380454

00:15:30.600 --> 00:15:31.980 in stage k.
NOTE Confidence: 0.97064084

00:15:33.560 --> 00:15:34.839 That means that y I
NOTE Confidence: 0.97064084

00:15:34.839 --> 00:15:36.040 one n and y I
NOTE Confidence: 0.97064084

00:15:36.040 --> 00:15:37.720 two n denote outcomes of
NOTE Confidence: 0.97064084

00:15:37.720 --> 00:15:38.940 two different participants.
NOTE Confidence: 0.9690751

00:15:40.015 --> 00:15:41.774 This comes from stage one,
NOTE Confidence: 0.9690751

00:15:41.774 --> 00:15:42.915 and this is a participant
NOTE Confidence: 0.9690751

00:15:43.214 --> 00:15:44.435 in stage two.
NOTE Confidence: 0.942181

00:15:45.535 --> 00:15:47.135 The n superscript is needed

NOTE Confidence: 0.942181
00:15:47.135 --> 00:15:48.895 in stages after stage one
NOTE Confidence: 0.942181
00:15:48.895 --> 00:15:50.035 because the intervention
NOTE Confidence: 0.9809387
00:15:50.415 --> 00:15:52.175 in those stages depends on
NOTE Confidence: 0.9809387
00:15:52.175 --> 00:15:54.015 the prior outcomes from stage
NOTE Confidence: 0.9809387
00:15:54.015 --> 00:15:54.515 one,
NOTE Confidence: 0.760108
00:15:56.759 --> 00:15:57.800 under the councilman. Luke. Yeah.
NOTE Confidence: 0.760108
00:15:58.040 --> 00:15:58.680 Just wanna,
NOTE Confidence: 0.6772207
00:15:59.160 --> 00:15:59.660 clarification.
NOTE Confidence: 0.9093275
00:16:00.600 --> 00:16:01.560 Stop if this is a
NOTE Confidence: 0.9093275
00:16:01.560 --> 00:16:02.920 silly question. But you said
NOTE Confidence: 0.9093275
00:16:02.920 --> 00:16:03.959 that we're assuming that we're
NOTE Confidence: 0.9093275
00:16:03.959 --> 00:16:05.980 only learning from the intervention,
NOTE Confidence: 0.93184316
00:16:06.735 --> 00:16:07.695 I think you meant, in
NOTE Confidence: 0.93184316
00:16:07.695 --> 00:16:09.295 this study. But I think
NOTE Confidence: 0.93184316
00:16:09.295 --> 00:16:10.894 that, often we might be
NOTE Confidence: 0.93184316

00:16:10.894 --> 00:16:11.394 learning
NOTE Confidence: 0.9925743

00:16:11.855 --> 00:16:12.735 at the same time from
NOTE Confidence: 0.9925743

00:16:12.735 --> 00:16:13.935 other studies that are not
NOTE Confidence: 0.9925743

00:16:13.935 --> 00:16:15.875 involved. Is that, a problem?
NOTE Confidence: 0.99938554

00:16:16.575 --> 00:16:17.454 So this might be a
NOTE Confidence: 0.99938554

00:16:17.454 --> 00:16:18.834 problem for the FDA
NOTE Confidence: 0.9460243

00:16:19.454 --> 00:16:21.075 because they want things preplanned.
NOTE Confidence: 0.95756876

00:16:22.140 --> 00:16:23.260 It might not be as
NOTE Confidence: 0.95756876

00:16:23.260 --> 00:16:24.940 much of a problem in
NOTE Confidence: 0.95756876

00:16:24.940 --> 00:16:27.340 other settings where the the
NOTE Confidence: 0.95756876

00:16:27.340 --> 00:16:29.260 important thing with LAGO is
NOTE Confidence: 0.95756876

00:16:29.260 --> 00:16:30.780 that we can somehow assume
NOTE Confidence: 0.95756876

00:16:30.780 --> 00:16:31.840 that the intervention,
NOTE Confidence: 0.9995435

00:16:33.100 --> 00:16:34.560 in the second stage
NOTE Confidence: 0.9849444

00:16:35.260 --> 00:16:36.480 converges in probability.
NOTE Confidence: 0.9997073

00:16:37.845 --> 00:16:38.345 So

NOTE Confidence: 0.97544473
00:16:40.725 --> 00:16:41.765 if we look at the
NOTE Confidence: 0.97544473
00:16:41.765 --> 00:16:42.665 stage one
NOTE Confidence: 0.9456952
00:16:43.285 --> 00:16:45.365 outcomes, we can learn from
NOTE Confidence: 0.9456952
00:16:45.365 --> 00:16:46.885 an MLE. We can learn
NOTE Confidence: 0.9456952
00:16:46.885 --> 00:16:48.485 from averages. We can learn
NOTE Confidence: 0.9456952
00:16:48.485 --> 00:16:50.165 from average purchase outcomes. Doesn't
NOTE Confidence: 0.9456952
00:16:50.165 --> 00:16:51.045 need to be the bias.
NOTE Confidence: 0.9456952
00:16:51.045 --> 00:16:52.345 It can be something else,
NOTE Confidence: 0.9456952
00:16:52.620 --> 00:16:53.900 but it needs to converge
NOTE Confidence: 0.9456952
00:16:53.900 --> 00:16:54.560 in probability.
NOTE Confidence: 0.99834293
00:16:55.100 --> 00:16:56.140 So if you have these
NOTE Confidence: 0.99834293
00:16:56.140 --> 00:16:57.520 outside things happening,
NOTE Confidence: 0.9130064
00:16:57.980 --> 00:16:58.860 we also have to at
NOTE Confidence: 0.9130064
00:16:58.860 --> 00:16:59.760 least conceptualize
NOTE Confidence: 0.9757204
00:17:00.140 --> 00:17:01.340 that they could converge to
NOTE Confidence: 0.9757204

00:17:01.340 --> 00:17:01.840 something.
NOTE Confidence: 0.9463857

00:17:09.575 --> 00:17:11.255 So the recommended intervention x
NOTE Confidence: 0.9463857

00:17:11.255 --> 00:17:12.775 two n is random determined
NOTE Confidence: 0.9463857

00:17:12.775 --> 00:17:13.895 by some function of the
NOTE Confidence: 0.9463857

00:17:13.895 --> 00:17:15.575 prior data. It depends on
NOTE Confidence: 0.9463857

00:17:15.575 --> 00:17:17.975 what researchers decide upon looking
NOTE Confidence: 0.9463857

00:17:17.975 --> 00:17:19.515 at the stage one results.
NOTE Confidence: 0.93200135

00:17:19.880 --> 00:17:21.240 And if at all possible,
NOTE Confidence: 0.93200135

00:17:21.240 --> 00:17:22.380 it should be preplanned.
NOTE Confidence: 0.9789271

00:17:23.240 --> 00:17:24.360 And that means in terms
NOTE Confidence: 0.9789271

00:17:24.360 --> 00:17:25.500 of random variables,
NOTE Confidence: 0.98784393

00:17:26.040 --> 00:17:27.560 x two n is not
NOTE Confidence: 0.98784393

00:17:27.560 --> 00:17:29.080 independent of the stage one
NOTE Confidence: 0.98784393

00:17:29.080 --> 00:17:30.840 data, and so outcomes in
NOTE Confidence: 0.98784393

00:17:30.840 --> 00:17:32.520 different stages are going to
NOTE Confidence: 0.98784393

00:17:32.520 --> 00:17:33.180 be dependent.

NOTE Confidence: 0.96721256

00:17:36.155 --> 00:17:37.115 We are now going to

NOTE Confidence: 0.96721256

00:17:37.115 --> 00:17:38.315 assume that x two and

NOTE Confidence: 0.96721256

00:17:38.315 --> 00:17:40.494 the recommended intervention depends determin-
istically

NOTE Confidence: 0.9704801

00:17:41.115 --> 00:17:42.315 on the stage one data

NOTE Confidence: 0.9704801

00:17:42.315 --> 00:17:43.135 in a prespecified

NOTE Confidence: 0.96031725

00:17:43.595 --> 00:17:44.095 rule,

NOTE Confidence: 0.9182692

00:17:44.554 --> 00:17:46.015 in order to not jeopardize

NOTE Confidence: 0.9182692

00:17:46.234 --> 00:17:47.820 the validity of the trial.

NOTE Confidence: 0.9182692

00:17:48.139 --> 00:17:49.820 For example, the decision goal

NOTE Confidence: 0.9182692

00:17:49.820 --> 00:17:51.100 could be based based, as

NOTE Confidence: 0.9182692

00:17:51.100 --> 00:17:52.539 I said, about means and

NOTE Confidence: 0.9182692

00:17:52.539 --> 00:17:53.039 averages,

NOTE Confidence: 0.9996498

00:17:54.059 --> 00:17:55.519 in the entire sample

NOTE Confidence: 0.98563606

00:17:55.820 --> 00:17:57.440 in a smooth and differentiable

NOTE Confidence: 0.9667254

00:17:57.740 --> 00:17:59.580 way. The decision rule should

NOTE Confidence: 0.9667254
00:17:59.580 --> 00:18:00.940 be based on an MLE
NOTE Confidence: 0.9667254
00:18:00.940 --> 00:18:02.619 calculated from the stage one
NOTE Confidence: 0.9667254
00:18:02.619 --> 00:18:03.600 data in a smooth
NOTE Confidence: 0.9044804
00:18:03.955 --> 00:18:05.234 differentiable data would be the
NOTE Confidence: 0.9044804
00:18:05.234 --> 00:18:06.055 other option.
NOTE Confidence: 0.9108984
00:18:08.915 --> 00:18:10.295 We are looking at asymptotic
NOTE Confidence: 0.9108984
00:18:10.515 --> 00:18:11.795 inference. In the meta birth
NOTE Confidence: 0.9108984
00:18:11.795 --> 00:18:12.835 study, that is not a
NOTE Confidence: 0.9108984
00:18:12.835 --> 00:18:13.955 big deal. In the POLISA
NOTE Confidence: 0.9108984
00:18:13.955 --> 00:18:15.155 trial, that is also not
NOTE Confidence: 0.9108984
00:18:15.155 --> 00:18:16.435 a big deal because in
NOTE Confidence: 0.9108984
00:18:16.435 --> 00:18:18.115 typically, these are large scale
NOTE Confidence: 0.9108984
00:18:18.115 --> 00:18:19.260 intervention trials,
NOTE Confidence: 0.98290235
00:18:19.820 --> 00:18:21.119 implementation trials.
NOTE Confidence: 0.9834734
00:18:22.060 --> 00:18:23.260 And we assume that the
NOTE Confidence: 0.9834734

00:18:23.260 --> 00:18:24.700 number of observations in each
NOTE Confidence: 0.9834734

00:18:24.700 --> 00:18:26.060 of the stages gets large
NOTE Confidence: 0.9834734

00:18:26.060 --> 00:18:27.119 at the same rate.
NOTE Confidence: 0.9625065

00:18:30.060 --> 00:18:31.119 So the main,
NOTE Confidence: 0.9512632

00:18:31.580 --> 00:18:33.415 the main assumption in LAGO
NOTE Confidence: 0.9512632

00:18:33.415 --> 00:18:34.875 is that given the recommended
NOTE Confidence: 0.9512632

00:18:35.015 --> 00:18:36.615 intervention, the stage two data
NOTE Confidence: 0.9512632

00:18:36.615 --> 00:18:38.055 are independent of the stage
NOTE Confidence: 0.9512632

00:18:38.055 --> 00:18:39.895 one data. So conditional on
NOTE Confidence: 0.9512632

00:18:39.895 --> 00:18:41.975 the recommended state intervention for
NOTE Confidence: 0.9512632

00:18:41.975 --> 00:18:42.875 stage two,
NOTE Confidence: 0.9635803

00:18:43.175 --> 00:18:45.195 the treatment and the outcomes
NOTE Confidence: 0.9635803

00:18:45.335 --> 00:18:46.075 in stage
NOTE Confidence: 0.98716754

00:18:46.960 --> 00:18:48.400 two are independent of the
NOTE Confidence: 0.98716754

00:18:48.400 --> 00:18:49.920 stage one data, both the
NOTE Confidence: 0.98716754

00:18:49.920 --> 00:18:51.540 treatment and the outcomes.

NOTE Confidence: 0.92987525
00:18:52.800 --> 00:18:54.740 So learning is only through
NOTE Confidence: 0.92987525
00:18:54.800 --> 00:18:56.260 the recommended intervention.
NOTE Confidence: 0.97835004
00:18:59.075 --> 00:19:00.515 And then the second assumption
NOTE Confidence: 0.97835004
00:19:00.515 --> 00:19:02.055 is that the recommended intervention
NOTE Confidence: 0.97835004
00:19:02.275 --> 00:19:03.955 converges in probability to a
NOTE Confidence: 0.97835004
00:19:03.955 --> 00:19:05.475 constant as the number of
NOTE Confidence: 0.97835004
00:19:05.475 --> 00:19:05.975 observations
NOTE Confidence: 0.99630135
00:19:06.275 --> 00:19:07.555 in stage one goes to
NOTE Confidence: 0.99630135
00:19:07.555 --> 00:19:08.055 infinity.
NOTE Confidence: 0.99938875
00:19:11.395 --> 00:19:12.695 The actual intervention
NOTE Confidence: 0.9836416
00:19:12.994 --> 00:19:14.615 is assumed to be a
NOTE Confidence: 0.9906246
00:19:15.130 --> 00:19:15.630 fixed
NOTE Confidence: 0.9381921
00:19:16.169 --> 00:19:16.669 function,
NOTE Confidence: 0.9195711
00:19:16.970 --> 00:19:18.350 maybe center specific,
NOTE Confidence: 0.9365344
00:19:18.970 --> 00:19:20.510 of the recommended intervention,
NOTE Confidence: 0.96440446

00:19:20.970 --> 00:19:22.990 and this makes sure that
NOTE Confidence: 0.8568636

00:19:23.690 --> 00:19:25.390 this function is also deterministically
NOTE Confidence: 0.8568636

00:19:25.690 --> 00:19:27.150 continuous and bounded
NOTE Confidence: 0.9515992

00:19:27.565 --> 00:19:29.405 that the actual intervention in
NOTE Confidence: 0.9515992

00:19:29.405 --> 00:19:31.805 the center also converges in
NOTE Confidence: 0.9515992

00:19:31.805 --> 00:19:33.885 probability to something fixed. And
NOTE Confidence: 0.9515992

00:19:33.885 --> 00:19:35.165 that's something that we really
NOTE Confidence: 0.9515992

00:19:35.165 --> 00:19:36.465 use in their proofs.
NOTE Confidence: 0.9958545

00:19:38.685 --> 00:19:39.185 The
NOTE Confidence: 0.97416246

00:19:40.020 --> 00:19:42.660 binary outcome label typically assumes
NOTE Confidence: 0.97416246

00:19:42.660 --> 00:19:44.340 a logistic regression for the
NOTE Confidence: 0.97416246

00:19:44.340 --> 00:19:46.200 outcome given the intervention.
NOTE Confidence: 0.9919796

00:19:46.660 --> 00:19:47.540 So if this is the
NOTE Confidence: 0.9919796

00:19:47.540 --> 00:19:49.480 intervention in center j ,
NOTE Confidence: 0.962619

00:19:50.020 --> 00:19:51.220 then an outcome of a
NOTE Confidence: 0.962619

00:19:51.220 --> 00:19:53.415 patient in center j follows

NOTE Confidence: 0.962619
00:19:53.415 --> 00:19:55.735 a logistic regression model with
NOTE Confidence: 0.962619
00:19:55.735 --> 00:19:58.315 parameters that depend that that
NOTE Confidence: 0.962619
00:19:58.455 --> 00:19:59.515 determine how
NOTE Confidence: 0.99186385
00:19:59.815 --> 00:20:00.315 the
NOTE Confidence: 0.99037886
00:20:00.615 --> 00:20:01.915 probability of success
NOTE Confidence: 0.86623096
00:20:02.295 --> 00:20:03.995 depends on the different intervention
NOTE Confidence: 0.86623096
00:20:04.215 --> 00:20:04.715 components.
NOTE Confidence: 0.93744415
00:20:06.410 --> 00:20:07.690 And then this case, the
NOTE Confidence: 0.93744415
00:20:07.690 --> 00:20:09.929 outcome goal would be that
NOTE Confidence: 0.93744415
00:20:09.929 --> 00:20:10.429 the,
NOTE Confidence: 0.9834511
00:20:11.690 --> 00:20:13.549 average probability of success,
NOTE Confidence: 0.90969056
00:20:15.130 --> 00:20:16.350 that is is,
NOTE Confidence: 0.9995067
00:20:16.730 --> 00:20:17.470 at least
NOTE Confidence: 0.9385719
00:20:18.055 --> 00:20:19.815 point nine where we look
NOTE Confidence: 0.9385719
00:20:19.815 --> 00:20:21.415 at the probability of set
NOTE Confidence: 0.9385719

00:20:21.575 --> 00:20:22.395 of success
NOTE Confidence: 0.96779114

00:20:22.935 --> 00:20:24.935 under the estimated beta, where
NOTE Confidence: 0.96779114

00:20:24.935 --> 00:20:26.615 beta is estimated based on
NOTE Confidence: 0.96779114

00:20:26.615 --> 00:20:27.815 the stage one data that
NOTE Confidence: 0.96779114

00:20:27.815 --> 00:20:28.635 are known
NOTE Confidence: 0.97137344

00:20:28.935 --> 00:20:30.055 at the time that this
NOTE Confidence: 0.97137344

00:20:30.055 --> 00:20:30.875 level optimization
NOTE Confidence: 0.9271369

00:20:31.335 --> 00:20:32.155 takes place.
NOTE Confidence: 0.94407034

00:20:32.970 --> 00:20:34.650 And this while minimizing the
NOTE Confidence: 0.94407034

00:20:34.650 --> 00:20:36.169 cost. If it was not
NOTE Confidence: 0.94407034

00:20:36.169 --> 00:20:37.530 minimizing the cost, we would
NOTE Confidence: 0.94407034

00:20:37.530 --> 00:20:38.990 not find a unique solution.
NOTE Confidence: 0.94407034

00:20:39.130 --> 00:20:40.410 We would just max out
NOTE Confidence: 0.94407034

00:20:40.410 --> 00:20:42.250 all the effective components, and
NOTE Confidence: 0.94407034

00:20:42.250 --> 00:20:43.869 that is not, believable.
NOTE Confidence: 0.9232387

00:20:47.225 --> 00:20:48.265 So stage one, we have

NOTE Confidence: 0.9232387
00:20:48.265 --> 00:20:50.585 a recommending settling intervention, collects
NOTE Confidence: 0.9232387
00:20:50.585 --> 00:20:52.905 outcomes, recommend intervention. We we
NOTE Confidence: 0.9232387
00:20:52.905 --> 00:20:54.505 calculate that. That's what we
NOTE Confidence: 0.9232387
00:20:54.505 --> 00:20:56.205 are currently doing for POLISA
NOTE Confidence: 0.8505998
00:20:56.585 --> 00:20:57.965 and then collects outcomes.
NOTE Confidence: 0.99784833
00:20:58.505 --> 00:21:00.425 And then we are going
NOTE Confidence: 0.99784833
00:21:00.425 --> 00:21:01.325 to estimate
NOTE Confidence: 0.9994243
00:21:01.890 --> 00:21:03.910 the parameters in this logistic
NOTE Confidence: 0.9994243
00:21:04.130 --> 00:21:05.350 regression model
NOTE Confidence: 0.9790599
00:21:05.730 --> 00:21:07.010 in order to figure out
NOTE Confidence: 0.9790599
00:21:07.010 --> 00:21:07.890 at the end of the
NOTE Confidence: 0.9790599
00:21:07.890 --> 00:21:09.910 study what is a good
NOTE Confidence: 0.9462881
00:21:10.530 --> 00:21:12.550 intervention or the optimal intervention,
NOTE Confidence: 0.9462881
00:21:12.609 --> 00:21:14.130 so the one that has
NOTE Confidence: 0.9462881
00:21:14.130 --> 00:21:15.990 success probability of at least
NOTE Confidence: 0.9996351

00:21:16.345 --> 00:21:16.845 ninety
NOTE Confidence: 0.7571535

00:21:17.305 --> 00:21:19.165 percent by minimizing costs.
NOTE Confidence: 0.9841589

00:21:19.705 --> 00:21:21.145 And we would do that
NOTE Confidence: 0.9841589

00:21:21.145 --> 00:21:23.545 final estimate of beta or
NOTE Confidence: 0.9841589

00:21:23.545 --> 00:21:24.905 the and and the final
NOTE Confidence: 0.9841589

00:21:24.905 --> 00:21:25.405 optimization
NOTE Confidence: 0.9964893

00:21:26.105 --> 00:21:27.305 based on the data from
NOTE Confidence: 0.9964893

00:21:27.305 --> 00:21:28.685 all stages combined.
NOTE Confidence: 0.9856759

00:21:29.000 --> 00:21:30.280 And this is different from
NOTE Confidence: 0.9856759

00:21:30.280 --> 00:21:31.640 a design that is called
NOTE Confidence: 0.9856759

00:21:31.640 --> 00:21:32.140 MOST,
NOTE Confidence: 0.92224365

00:21:32.600 --> 00:21:34.220 where they optimize the intervention
NOTE Confidence: 0.92224365

00:21:34.359 --> 00:21:35.580 in the first stage
NOTE Confidence: 0.9097419

00:21:35.960 --> 00:21:36.619 and then
NOTE Confidence: 0.90791047

00:21:36.920 --> 00:21:38.200 implement it in the second
NOTE Confidence: 0.90791047

00:21:38.200 --> 00:21:39.480 stage and then only the

NOTE Confidence: 0.90791047
00:21:39.480 --> 00:21:40.935 estimate use the second
NOTE Confidence: 0.8055728
00:21:42.135 --> 00:21:43.675 stage data to look at
NOTE Confidence: 0.8055728
00:21:43.675 --> 00:21:44.655 the effect of the intervention.
NOTE Confidence: 0.8055728
00:21:44.655 --> 00:21:45.435 In Lago,
NOTE Confidence: 0.8760656
00:21:46.375 --> 00:21:47.255 the idea is to use
NOTE Confidence: 0.8760656
00:21:47.255 --> 00:21:47.915 all data
NOTE Confidence: 0.9513451
00:21:48.215 --> 00:21:48.715 combined
NOTE Confidence: 0.907042
00:21:49.095 --> 00:21:50.615 at the final analysis to
NOTE Confidence: 0.907042
00:21:50.615 --> 00:21:53.495 estimate this logistic regression model
NOTE Confidence: 0.907042
00:21:53.495 --> 00:21:54.935 and also to determine the
NOTE Confidence: 0.907042
00:21:54.935 --> 00:21:55.835 optimal intervention.
NOTE Confidence: 0.9260135
00:21:59.710 --> 00:22:00.670 Here, I'm going to go
NOTE Confidence: 0.9260135
00:22:00.670 --> 00:22:01.170 fast
NOTE Confidence: 0.96803313
00:22:01.550 --> 00:22:02.510 because I think that is
NOTE Confidence: 0.96803313
00:22:02.510 --> 00:22:03.410 more for tomorrow.
NOTE Confidence: 0.9786662

00:22:04.110 --> 00:22:05.390 We have a likelihood here.
NOTE Confidence: 0.9786662

00:22:05.390 --> 00:22:07.090 So we have the probability
NOTE Confidence: 0.9786662

00:22:07.390 --> 00:22:08.369 of the first
NOTE Confidence: 0.96053255

00:22:09.225 --> 00:22:11.405 data by one, second stage,
NOTE Confidence: 0.9826595

00:22:11.865 --> 00:22:13.545 outcomes by two, and then
NOTE Confidence: 0.9826595

00:22:13.545 --> 00:22:15.165 the both interventions.
NOTE Confidence: 0.99453676

00:22:16.105 --> 00:22:17.725 And this is a fixed,
NOTE Confidence: 0.92103624

00:22:18.665 --> 00:22:20.924 intervention because it's pretrial determined.
NOTE Confidence: 0.92471075

00:22:21.225 --> 00:22:22.265 And this is the beta
NOTE Confidence: 0.92471075

00:22:22.265 --> 00:22:23.385 this is the beta that
NOTE Confidence: 0.92471075

00:22:23.385 --> 00:22:24.285 comes from.
NOTE Confidence: 0.6701915

00:22:25.830 --> 00:22:26.490 Where is
NOTE Confidence: 0.8454998

00:22:27.190 --> 00:22:28.869 where is my beta? Here's
NOTE Confidence: 0.8454998

00:22:28.869 --> 00:22:29.530 my beta.
NOTE Confidence: 0.9951918

00:22:29.910 --> 00:22:30.650 That beta.
NOTE Confidence: 0.9671329

00:22:33.670 --> 00:22:35.690 So first, the actual interventions

NOTE Confidence: 0.9671329

00:22:35.910 --> 00:22:37.905 come based on x one,

NOTE Confidence: 0.9671329

00:22:37.984 --> 00:22:39.984 and we're assuming that, it's

NOTE Confidence: 0.9671329

00:22:39.984 --> 00:22:41.425 not depending on beta, so

NOTE Confidence: 0.9671329

00:22:41.425 --> 00:22:43.285 this this this goes out.

NOTE Confidence: 0.9560254

00:22:43.665 --> 00:22:44.865 And then we have the

NOTE Confidence: 0.9560254

00:22:44.865 --> 00:22:47.025 first stage outcomes. They depend

NOTE Confidence: 0.9560254

00:22:47.025 --> 00:22:47.685 on beta.

NOTE Confidence: 0.96502686

00:22:49.345 --> 00:22:50.965 And then we have the

NOTE Confidence: 0.8520513

00:22:52.040 --> 00:22:53.820 the second stage interventions.

NOTE Confidence: 0.92522776

00:22:54.840 --> 00:22:56.280 They depend on the prior

NOTE Confidence: 0.92522776

00:22:56.280 --> 00:22:57.960 outcomes, but they typically don't

NOTE Confidence: 0.92522776

00:22:57.960 --> 00:22:59.560 depend on beta. And then

NOTE Confidence: 0.92522776

00:22:59.560 --> 00:23:01.320 you get the second stage

NOTE Confidence: 0.92522776

00:23:01.320 --> 00:23:03.020 outcomes and those do the.

NOTE Confidence: 0.99375695

00:23:04.035 --> 00:23:04.915 If you look at the

NOTE Confidence: 0.99375695

00:23:04.915 --> 00:23:06.915 MLE or whatever you wanna
NOTE Confidence: 0.99375695

00:23:06.915 --> 00:23:08.435 call this, then it will
NOTE Confidence: 0.99375695

00:23:08.435 --> 00:23:10.455 solve the same score equations
NOTE Confidence: 0.99375695

00:23:10.515 --> 00:23:11.734 that you would solve
NOTE Confidence: 0.9454995

00:23:12.115 --> 00:23:13.795 had the intervention not been
NOTE Confidence: 0.9454995

00:23:13.795 --> 00:23:14.295 learned.
NOTE Confidence: 0.9960931

00:23:14.675 --> 00:23:15.795 So this would be maybe
NOTE Confidence: 0.9960931

00:23:15.795 --> 00:23:16.935 the end of story
NOTE Confidence: 0.90224576

00:23:17.470 --> 00:23:18.670 if it wasn't the case
NOTE Confidence: 0.90224576

00:23:18.670 --> 00:23:20.110 that, okay, this tells the
NOTE Confidence: 0.90224576

00:23:20.110 --> 00:23:22.290 same score equations, that's great.
NOTE Confidence: 0.90224576

00:23:22.510 --> 00:23:23.890 But these score equations
NOTE Confidence: 0.99983716

00:23:24.350 --> 00:23:25.010 are highly
NOTE Confidence: 0.99975044

00:23:25.390 --> 00:23:25.890 unusual
NOTE Confidence: 0.9486666

00:23:26.910 --> 00:23:28.850 because what would usually happen
NOTE Confidence: 0.9486666

00:23:29.070 --> 00:23:30.434 is that these two terms

NOTE Confidence: 0.9486666

00:23:30.434 --> 00:23:32.434 are independent. They involve different

NOTE Confidence: 0.9486666

00:23:32.434 --> 00:23:33.794 patients who are treated in

NOTE Confidence: 0.9486666

00:23:33.794 --> 00:23:36.215 different ways, so why bother?

NOTE Confidence: 0.9486666

00:23:36.434 --> 00:23:37.955 But we bother because these

NOTE Confidence: 0.9486666

00:23:37.955 --> 00:23:39.734 two terms are actually dependent

NOTE Confidence: 0.99244535

00:23:40.195 --> 00:23:41.554 and this term is highly

NOTE Confidence: 0.99244535

00:23:41.554 --> 00:23:43.414 dependent on what happens here

NOTE Confidence: 0.99910593

00:23:43.720 --> 00:23:45.320 through the learning of the

NOTE Confidence: 0.99910593

00:23:45.320 --> 00:23:45.820 intervention.

NOTE Confidence: 0.94284195

00:23:49.800 --> 00:23:51.320 So, we can show that

NOTE Confidence: 0.94284195

00:23:51.320 --> 00:23:53.400 they're unbiased estimating equations. That's

NOTE Confidence: 0.94284195

00:23:53.400 --> 00:23:54.920 not a big deal. But

NOTE Confidence: 0.94284195

00:23:54.920 --> 00:23:55.420 then,

NOTE Confidence: 0.9451843

00:23:56.040 --> 00:23:56.540 consistently

NOTE Confidence: 0.99893445

00:23:57.234 --> 00:23:59.414 consistency doesn't immediately follow

NOTE Confidence: 0.99676055

00:23:59.794 --> 00:24:01.255 from theory about,
NOTE Confidence: 0.9083091

00:24:01.875 --> 00:24:04.115 estimating equations because that's mostly
NOTE Confidence: 0.9083091

00:24:04.115 --> 00:24:05.174 on IID observations.
NOTE Confidence: 0.9928462

00:24:05.875 --> 00:24:06.914 So we had to use
NOTE Confidence: 0.9928462

00:24:06.914 --> 00:24:07.414 tricks.
NOTE Confidence: 0.96071637

00:24:08.434 --> 00:24:09.475 If you wanna know those
NOTE Confidence: 0.96071637

00:24:09.475 --> 00:24:10.514 tricks, you have to come
NOTE Confidence: 0.96071637

00:24:10.514 --> 00:24:11.494 to the talk
NOTE Confidence: 0.9401606

00:24:11.869 --> 00:24:13.710 of the of the of
NOTE Confidence: 0.9401606

00:24:13.710 --> 00:24:15.390 Tuna's course tomorrow because then
NOTE Confidence: 0.9401606

00:24:15.390 --> 00:24:16.430 I will show how that
NOTE Confidence: 0.9401606

00:24:16.430 --> 00:24:16.930 works.
NOTE Confidence: 0.56589925

00:24:19.150 --> 00:24:20.290 As I told you, normality,
NOTE Confidence: 0.9981382

00:24:20.590 --> 00:24:21.090 so
NOTE Confidence: 0.9758423

00:24:21.470 --> 00:24:22.430 I think you have seen
NOTE Confidence: 0.9758423

00:24:22.430 --> 00:24:23.390 things like this if you

NOTE Confidence: 0.9758423
00:24:23.390 --> 00:24:25.090 are a little bit, familiar
NOTE Confidence: 0.9758423
00:24:25.150 --> 00:24:25.575 with
NOTE Confidence: 0.93432975
00:24:26.054 --> 00:24:27.355 the estimating equations.
NOTE Confidence: 0.96349066
00:24:27.734 --> 00:24:29.014 You would solve the score
NOTE Confidence: 0.96349066
00:24:29.014 --> 00:24:30.615 equations. So you set the
NOTE Confidence: 0.96349066
00:24:30.615 --> 00:24:32.054 derivative of the log likelihood
NOTE Confidence: 0.96349066
00:24:32.054 --> 00:24:33.734 to zero. So you solve
NOTE Confidence: 0.96349066
00:24:33.734 --> 00:24:34.934 the score equations, and then
NOTE Confidence: 0.96349066
00:24:34.934 --> 00:24:36.615 you do this standard Taylor
NOTE Confidence: 0.96349066
00:24:36.615 --> 00:24:37.115 expansion
NOTE Confidence: 0.94530416
00:24:37.494 --> 00:24:38.955 around beta star.
NOTE Confidence: 0.968273
00:24:39.575 --> 00:24:41.255 And you'll find that, okay.
NOTE Confidence: 0.968273
00:24:41.255 --> 00:24:42.270 This is great. So I
NOTE Confidence: 0.968273
00:24:42.270 --> 00:24:43.150 can put this to the
NOTE Confidence: 0.968273
00:24:43.150 --> 00:24:44.750 other side, and then I
NOTE Confidence: 0.968273

00:24:44.750 --> 00:24:46.270 divide by the inverse of
NOTE Confidence: 0.968273

00:24:46.270 --> 00:24:47.150 this thing, and it will
NOTE Confidence: 0.968273

00:24:47.150 --> 00:24:48.050 all be fine.
NOTE Confidence: 0.9807557

00:24:48.350 --> 00:24:50.030 The problem is going to
NOTE Confidence: 0.9807557

00:24:50.030 --> 00:24:52.030 be that even though this
NOTE Confidence: 0.9807557

00:24:52.030 --> 00:24:53.170 could be fine,
NOTE Confidence: 0.9618354

00:24:53.630 --> 00:24:54.830 this is not the sum
NOTE Confidence: 0.9618354

00:24:54.830 --> 00:24:56.369 of IID terms.
NOTE Confidence: 0.96335196

00:24:57.405 --> 00:24:58.845 So even here, we are
NOTE Confidence: 0.96335196

00:24:58.845 --> 00:25:00.765 not at home yet because
NOTE Confidence: 0.96335196

00:25:00.765 --> 00:25:01.965 typically you would say this
NOTE Confidence: 0.96335196

00:25:01.965 --> 00:25:03.484 goes nicely to a normal
NOTE Confidence: 0.96335196

00:25:03.484 --> 00:25:05.405 random variable because it's IID
NOTE Confidence: 0.96335196

00:25:05.405 --> 00:25:07.565 terms. No. They're not IID
NOTE Confidence: 0.96335196

00:25:07.565 --> 00:25:09.025 terms. There's the two stages.
NOTE Confidence: 0.9997096

00:25:09.565 --> 00:25:10.785 So what we did

NOTE Confidence: 0.9961396
00:25:11.325 --> 00:25:12.705 was do a trick.
NOTE Confidence: 0.9979562
00:25:13.940 --> 00:25:15.460 We have been doing we
NOTE Confidence: 0.9979562
00:25:15.460 --> 00:25:17.700 have been replacing the outcomes
NOTE Confidence: 0.9979562
00:25:17.700 --> 00:25:19.160 in the second stage
NOTE Confidence: 0.99904174
00:25:19.540 --> 00:25:21.560 by outcomes that are coupled
NOTE Confidence: 0.8983022
00:25:21.940 --> 00:25:23.240 with the fixed design.
NOTE Confidence: 0.9460061
00:25:23.940 --> 00:25:25.540 And the fixed design is
NOTE Confidence: 0.9460061
00:25:25.540 --> 00:25:27.619 where the limiting you have
NOTE Confidence: 0.9460061
00:25:27.619 --> 00:25:28.760 this this this
NOTE Confidence: 0.9766369
00:25:29.095 --> 00:25:29.915 stage two interventions.
NOTE Confidence: 0.97881985
00:25:30.935 --> 00:25:32.695 We have been assuming through
NOTE Confidence: 0.97881985
00:25:32.695 --> 00:25:33.675 different stages
NOTE Confidence: 0.8962782
00:25:34.055 --> 00:25:35.595 that the this this,
NOTE Confidence: 0.9568569
00:25:36.935 --> 00:25:38.535 this intervention in the second
NOTE Confidence: 0.9568569
00:25:38.535 --> 00:25:40.155 stage conversion probability
NOTE Confidence: 0.98887134

00:25:40.775 --> 00:25:42.535 to a constant intervention. Let's
NOTE Confidence: 0.98887134

00:25:42.535 --> 00:25:43.915 call it little a.
NOTE Confidence: 0.9983473

00:25:44.490 --> 00:25:46.350 Under the little a intervention,
NOTE Confidence: 0.9768134

00:25:46.730 --> 00:25:48.490 we have that's a fixed
NOTE Confidence: 0.9768134

00:25:48.490 --> 00:25:50.010 intervention, so we lose all
NOTE Confidence: 0.9768134

00:25:50.010 --> 00:25:50.750 these dependencies.
NOTE Confidence: 0.9374939

00:25:52.250 --> 00:25:53.290 But we don't have data
NOTE Confidence: 0.9374939

00:25:53.290 --> 00:25:54.730 from the limiting intervention. We
NOTE Confidence: 0.9374939

00:25:54.730 --> 00:25:56.190 have from the actual intervention.
NOTE Confidence: 0.9374939

00:25:56.410 --> 00:25:57.690 So what we don't really
NOTE Confidence: 0.9374939

00:25:57.690 --> 00:25:58.910 couple the outcomes.
NOTE Confidence: 0.9981322

00:25:59.465 --> 00:25:59.965 And,
NOTE Confidence: 0.8211753

00:26:00.345 --> 00:26:01.705 you have all probably, if
NOTE Confidence: 0.8211753

00:26:01.705 --> 00:26:03.005 you have that one simulation,
NOTE Confidence: 0.8211753

00:26:03.145 --> 00:26:04.265 you have probably a couple
NOTE Confidence: 0.8211753

00:26:04.265 --> 00:26:04.845 of outcomes.

NOTE Confidence: 0.9808687

00:26:05.465 --> 00:26:06.665 Because what you do is

NOTE Confidence: 0.9808687

00:26:06.665 --> 00:26:08.605 you have these these outcomes

NOTE Confidence: 0.9808687

00:26:08.825 --> 00:26:10.445 that have similar probabilities.

NOTE Confidence: 0.95813143

00:26:10.905 --> 00:26:11.865 You can say, okay. The

NOTE Confidence: 0.95813143

00:26:11.865 --> 00:26:13.225 probability is a little bit

NOTE Confidence: 0.95813143

00:26:13.225 --> 00:26:14.345 higher, a little bit lower,

NOTE Confidence: 0.95813143

00:26:14.345 --> 00:26:15.780 but not too much difference.

NOTE Confidence: 0.99883974

00:26:16.160 --> 00:26:17.700 We can make these variables

NOTE Confidence: 0.99967796

00:26:18.080 --> 00:26:19.220 almost the same

NOTE Confidence: 0.9974133

00:26:19.520 --> 00:26:21.700 by using the same uniform

NOTE Confidence: 0.9970012

00:26:22.559 --> 00:26:24.400 to decide on success versus

NOTE Confidence: 0.9970012

00:26:24.400 --> 00:26:24.900 failure

NOTE Confidence: 0.94404703

00:26:25.280 --> 00:26:26.480 because you can have a

NOTE Confidence: 0.94404703

00:26:26.480 --> 00:26:28.800 success probability that depends on

NOTE Confidence: 0.94404703

00:26:28.800 --> 00:26:30.055 a uniform. If you have

NOTE Confidence: 0.94404703

00:26:30.055 --> 00:26:31.255 p is, p is point
NOTE Confidence: 0.94404703

00:26:31.255 --> 00:26:32.535 six, you draw a uniform,
NOTE Confidence: 0.94404703

00:26:32.535 --> 00:26:33.655 you say, okay, if it's
NOTE Confidence: 0.94404703

00:26:33.655 --> 00:26:34.695 less than point six, it's
NOTE Confidence: 0.94404703

00:26:34.695 --> 00:26:36.375 a success. If it's over
NOTE Confidence: 0.94404703

00:26:36.375 --> 00:26:37.575 point six, it's a it's
NOTE Confidence: 0.94404703

00:26:37.575 --> 00:26:38.795 a failure. Right?
NOTE Confidence: 0.985864

00:26:39.175 --> 00:26:40.375 Now you have a different
NOTE Confidence: 0.985864

00:26:40.375 --> 00:26:40.875 probability,
NOTE Confidence: 0.99826497

00:26:41.590 --> 00:26:42.869 but it's similar. If you
NOTE Confidence: 0.99826497

00:26:42.869 --> 00:26:44.250 use the same uniform,
NOTE Confidence: 0.9432994

00:26:44.630 --> 00:26:45.830 these outcomes are going to
NOTE Confidence: 0.9432994

00:26:45.830 --> 00:26:47.050 be almost the same.
NOTE Confidence: 0.99583495

00:26:47.430 --> 00:26:48.890 And the beauty of asymptotic
NOTE Confidence: 0.99583495

00:26:49.030 --> 00:26:50.630 normality is that you don't
NOTE Confidence: 0.99583495

00:26:50.630 --> 00:26:51.690 need to show

NOTE Confidence: 0.9805622
00:26:52.070 --> 00:26:53.770 that the original converges
NOTE Confidence: 0.55514765
00:26:54.150 --> 00:26:55.290 except because
NOTE Confidence: 0.9745781
00:26:55.705 --> 00:26:57.725 asymptotic normality is a distributional
NOTE Confidence: 0.9745781
00:26:58.025 --> 00:26:58.525 result.
NOTE Confidence: 0.99926984
00:26:59.145 --> 00:27:00.285 So you can replace
NOTE Confidence: 0.9728692
00:27:01.305 --> 00:27:03.385 these outcomes that you have
NOTE Confidence: 0.9728692
00:27:03.385 --> 00:27:05.785 under the actual design by
NOTE Confidence: 0.9728692
00:27:05.785 --> 00:27:07.405 outcomes that are coupled
NOTE Confidence: 0.86252975
00:27:07.990 --> 00:27:08.809 with the limiting
NOTE Confidence: 0.98979104
00:27:09.429 --> 00:27:11.369 design without changing the distribution
NOTE Confidence: 0.98979104
00:27:11.590 --> 00:27:12.649 of what you have.
NOTE Confidence: 0.9677123
00:27:13.830 --> 00:27:15.190 It's a trick, just a
NOTE Confidence: 0.9677123
00:27:15.190 --> 00:27:16.090 dirty trick.
NOTE Confidence: 0.99874073
00:27:17.830 --> 00:27:18.330 So
NOTE Confidence: 0.92406327
00:27:18.630 --> 00:27:20.230 you change them you the
NOTE Confidence: 0.92406327

00:27:20.470 --> 00:27:21.130 you change
NOTE Confidence: 0.9985637

00:27:21.669 --> 00:27:22.169 the
NOTE Confidence: 0.9769429

00:27:22.804 --> 00:27:24.405 things that you have by
NOTE Confidence: 0.9769429

00:27:24.405 --> 00:27:25.605 something that has the same
NOTE Confidence: 0.9769429

00:27:25.605 --> 00:27:27.785 distribution, and that doesn't affect
NOTE Confidence: 0.9769429

00:27:27.924 --> 00:27:29.525 the limiting results. So that's
NOTE Confidence: 0.9769429

00:27:29.525 --> 00:27:30.405 what we did. If you
NOTE Confidence: 0.9769429

00:27:30.405 --> 00:27:31.684 wanna know more about that,
NOTE Confidence: 0.9769429

00:27:31.684 --> 00:27:33.225 again, you can come tomorrow.
NOTE Confidence: 0.74463224

00:27:34.804 --> 00:27:35.304 K.
NOTE Confidence: 0.98204976

00:27:36.420 --> 00:27:37.320 Twenty nine.
NOTE Confidence: 0.9393567

00:27:39.860 --> 00:27:41.640 Because of the asymptotic normality,
NOTE Confidence: 0.9393567

00:27:41.780 --> 00:27:43.619 Michelle, the Volta likelihood ratio
NOTE Confidence: 0.9393567

00:27:43.619 --> 00:27:44.820 test for beta one is
NOTE Confidence: 0.9393567

00:27:44.820 --> 00:27:46.760 beta one star are asymptotically
NOTE Confidence: 0.9930043

00:27:47.220 --> 00:27:49.220 valid for any beta one

NOTE Confidence: 0.9930043
00:27:49.220 --> 00:27:49.720 star.
NOTE Confidence: 0.91202635
00:27:50.065 --> 00:27:51.505 And now typically you are
NOTE Confidence: 0.91202635
00:27:51.505 --> 00:27:52.865 interested not so much in
NOTE Confidence: 0.91202635
00:27:52.865 --> 00:27:54.244 any beta one star,
NOTE Confidence: 0.9091099
00:27:54.945 --> 00:27:56.625 because typically what you want
NOTE Confidence: 0.9091099
00:27:56.625 --> 00:27:57.825 to do is test the
NOTE Confidence: 0.9091099
00:27:57.825 --> 00:27:58.645 null hypothesis,
NOTE Confidence: 0.9945558
00:27:59.265 --> 00:28:00.945 maybe of no effect of
NOTE Confidence: 0.9945558
00:28:00.945 --> 00:28:02.165 any of the intervention
NOTE Confidence: 0.9969476
00:28:02.705 --> 00:28:03.205 components.
NOTE Confidence: 0.98795205
00:28:03.990 --> 00:28:04.790 So if you want to
NOTE Confidence: 0.98795205
00:28:04.790 --> 00:28:06.470 test the null hypothesis of
NOTE Confidence: 0.98795205
00:28:06.470 --> 00:28:08.250 none of the intervention components,
NOTE Confidence: 0.94528866
00:28:09.430 --> 00:28:10.890 there is a trick again.
NOTE Confidence: 0.99843127
00:28:11.270 --> 00:28:12.950 Because if none of the
NOTE Confidence: 0.99843127

00:28:12.950 --> 00:28:13.450 components
NOTE Confidence: 0.9950064

00:28:13.750 --> 00:28:15.190 has any effect on the
NOTE Confidence: 0.9950064

00:28:15.190 --> 00:28:15.690 outcome,
NOTE Confidence: 0.9863598

00:28:16.150 --> 00:28:17.830 all this learning is pretty
NOTE Confidence: 0.9863598

00:28:17.830 --> 00:28:18.330 irrelevant.
NOTE Confidence: 0.9490133

00:28:19.315 --> 00:28:20.355 And so what we did
NOTE Confidence: 0.9490133

00:28:20.355 --> 00:28:21.955 is figuring out, okay, we
NOTE Confidence: 0.9490133

00:28:21.955 --> 00:28:23.335 want to test the null
NOTE Confidence: 0.9738483

00:28:23.715 --> 00:28:25.075 and it has to remain
NOTE Confidence: 0.9738483

00:28:25.075 --> 00:28:26.915 a valid test under the
NOTE Confidence: 0.9738483

00:28:26.915 --> 00:28:27.415 null.
NOTE Confidence: 0.98497105

00:28:27.795 --> 00:28:28.755 What it does on the
NOTE Confidence: 0.98497105

00:28:28.755 --> 00:28:29.255 alternative,
NOTE Confidence: 0.9867487

00:28:29.555 --> 00:28:31.015 we hope it goes well,
NOTE Confidence: 0.99754995

00:28:31.315 --> 00:28:32.195 but we don't need to
NOTE Confidence: 0.99754995

00:28:32.195 --> 00:28:33.095 prove anything.

NOTE Confidence: 0.9550693
00:28:33.830 --> 00:28:34.790 We just have to make
NOTE Confidence: 0.9550693
00:28:34.790 --> 00:28:36.230 sure that under the now,
NOTE Confidence: 0.9550693
00:28:36.230 --> 00:28:37.590 this is a valid test
NOTE Confidence: 0.9550693
00:28:37.590 --> 00:28:39.350 with the right correct type
NOTE Confidence: 0.9550693
00:28:39.350 --> 00:28:40.170 one error.
NOTE Confidence: 0.91622967
00:28:40.550 --> 00:28:41.750 Now if there's none of
NOTE Confidence: 0.91622967
00:28:41.750 --> 00:28:43.830 the intervention components has any
NOTE Confidence: 0.91622967
00:28:43.830 --> 00:28:44.330 effect,
NOTE Confidence: 0.99890894
00:28:44.630 --> 00:28:46.150 it doesn't matter how you
NOTE Confidence: 0.99890894
00:28:46.150 --> 00:28:46.650 learn
NOTE Confidence: 0.9439742
00:28:47.245 --> 00:28:48.284 because you won't have an
NOTE Confidence: 0.9439742
00:28:48.284 --> 00:28:50.205 effect anyway. So you can
NOTE Confidence: 0.9439742
00:28:50.205 --> 00:28:51.885 learn, and you don't even
NOTE Confidence: 0.9439742
00:28:51.885 --> 00:28:53.725 need to necessarily restrict to
NOTE Confidence: 0.9439742
00:28:53.725 --> 00:28:55.485 this learning on averages and
NOTE Confidence: 0.9439742

00:28:55.485 --> 00:28:57.105 MLEs. You could even learn
NOTE Confidence: 0.9439742

00:28:57.164 --> 00:28:58.605 from donors' results in the
NOTE Confidence: 0.9439742

00:28:58.605 --> 00:28:59.105 trial.
NOTE Confidence: 0.9375783

00:29:00.130 --> 00:29:01.090 Yes. This may be a
NOTE Confidence: 0.9375783

00:29:01.090 --> 00:29:02.230 really dumb question.
NOTE Confidence: 0.8480915

00:29:02.530 --> 00:29:03.429 Totally. But
NOTE Confidence: 0.9217891

00:29:04.049 --> 00:29:05.250 but it it it it
NOTE Confidence: 0.9217891

00:29:05.250 --> 00:29:06.370 seems to be the assumption
NOTE Confidence: 0.9217891

00:29:06.370 --> 00:29:07.410 you're making is that each
NOTE Confidence: 0.9217891

00:29:07.410 --> 00:29:09.010 component of the intervention is
NOTE Confidence: 0.9217891

00:29:09.010 --> 00:29:10.390 independent of each other.
NOTE Confidence: 0.9552528

00:29:12.145 --> 00:29:13.265 No. I'm not making that
NOTE Confidence: 0.9552528

00:29:13.265 --> 00:29:15.025 assumption. I just the null
NOTE Confidence: 0.9552528

00:29:15.025 --> 00:29:16.405 hypothesis that I'm considering
NOTE Confidence: 0.980219

00:29:16.785 --> 00:29:17.905 is that none of the
NOTE Confidence: 0.980219

00:29:17.905 --> 00:29:20.165 intervention components has any effect.

NOTE Confidence: 0.980219
00:29:20.385 --> 00:29:21.345 So it is a very
NOTE Confidence: 0.980219
00:29:21.345 --> 00:29:22.245 sharp null.
NOTE Confidence: 0.7816467
00:29:23.425 --> 00:29:24.705 Not sharp, but but it's
NOTE Confidence: 0.7816467
00:29:24.705 --> 00:29:25.985 a very You're doing a
NOTE Confidence: 0.7816467
00:29:25.985 --> 00:29:27.340 trial of all the components
NOTE Confidence: 0.7816467
00:29:27.340 --> 00:29:28.620 together and then knowing each
NOTE Confidence: 0.7816467
00:29:28.620 --> 00:29:29.679 individual component
NOTE Confidence: 0.7780819
00:29:30.539 --> 00:29:32.059 isn't, for instance, one in
NOTE Confidence: 0.7780819
00:29:32.059 --> 00:29:33.179 one positive, one is it
NOTE Confidence: 0.7780819
00:29:33.179 --> 00:29:34.399 canceling out a negative?
NOTE Confidence: 0.922253
00:29:34.700 --> 00:29:36.000 So that could happen,
NOTE Confidence: 0.96648806
00:29:36.620 --> 00:29:38.140 and, that's not our null
NOTE Confidence: 0.96648806
00:29:38.140 --> 00:29:39.659 hypothesis. Our null hypothesis is
NOTE Confidence: 0.96648806
00:29:39.659 --> 00:29:40.620 really that none of the
NOTE Confidence: 0.96648806
00:29:40.620 --> 00:29:42.295 intervention components has an effect
NOTE Confidence: 0.96648806

00:29:42.295 --> 00:29:43.415 and not that they cancel
NOTE Confidence: 0.96648806

00:29:43.415 --> 00:29:45.175 out. The null hypothesis that
NOTE Confidence: 0.96648806

00:29:45.175 --> 00:29:46.215 we're looking at is really
NOTE Confidence: 0.96648806

00:29:46.215 --> 00:29:47.415 none of the components has
NOTE Confidence: 0.96648806

00:29:47.415 --> 00:29:48.155 an effect.
NOTE Confidence: 0.7922948

00:29:48.455 --> 00:29:49.575 But you can't can't learn
NOTE Confidence: 0.7922948

00:29:49.575 --> 00:29:50.635 that from the data.
NOTE Confidence: 0.8872638

00:29:52.215 --> 00:29:53.175 No. But you can test
NOTE Confidence: 0.8872638

00:29:53.175 --> 00:29:53.675 it.
NOTE Confidence: 0.9685388

00:29:54.690 --> 00:29:55.809 You cannot learn it from
NOTE Confidence: 0.9685388

00:29:55.809 --> 00:29:56.929 the data. You can get
NOTE Confidence: 0.9685388

00:29:56.929 --> 00:29:58.289 an idea about whether it
NOTE Confidence: 0.9685388

00:29:58.289 --> 00:29:59.890 happens because not only are
NOTE Confidence: 0.9685388

00:29:59.890 --> 00:30:01.250 we testing, we are also
NOTE Confidence: 0.9685388

00:30:01.250 --> 00:30:02.529 estimating the effect of all
NOTE Confidence: 0.9685388

00:30:02.529 --> 00:30:03.830 the intervention components.

NOTE Confidence: 0.66574425
00:30:06.945 --> 00:30:07.445 But
NOTE Confidence: 0.9204502
00:30:07.825 --> 00:30:09.345 the the it it is
NOTE Confidence: 0.9204502
00:30:09.345 --> 00:30:10.945 a restriction that we are
NOTE Confidence: 0.9204502
00:30:10.945 --> 00:30:12.144 looking at the null of
NOTE Confidence: 0.9204502
00:30:12.144 --> 00:30:13.265 no effect of any of
NOTE Confidence: 0.9204502
00:30:13.265 --> 00:30:15.345 the intervention components because this
NOTE Confidence: 0.9204502
00:30:15.345 --> 00:30:16.784 might not be true or
NOTE Confidence: 0.9204502
00:30:16.784 --> 00:30:17.745 it's maybe they can come
NOTE Confidence: 0.9204502
00:30:17.745 --> 00:30:18.625 out. So it's a limited
NOTE Confidence: 0.9204502
00:30:18.625 --> 00:30:20.325 case. It's a limited case.
NOTE Confidence: 0.9204502
00:30:20.544 --> 00:30:21.044 Yes.
NOTE Confidence: 0.8735615
00:30:24.740 --> 00:30:25.860 But under the law on
NOTE Confidence: 0.8735615
00:30:26.020 --> 00:30:27.300 under this now, you can
NOTE Confidence: 0.8735615
00:30:27.300 --> 00:30:28.660 learn as you want, not
NOTE Confidence: 0.8735615
00:30:28.660 --> 00:30:29.160 learn.
NOTE Confidence: 0.9420724

00:30:29.700 --> 00:30:31.220 Because because none of none
NOTE Confidence: 0.9420724

00:30:31.220 --> 00:30:32.020 of what you're doing is
NOTE Confidence: 0.9420724

00:30:32.100 --> 00:30:32.980 has an effect on the
NOTE Confidence: 0.9420724

00:30:32.980 --> 00:30:34.580 distribution of the outcome. So
NOTE Confidence: 0.9420724

00:30:34.580 --> 00:30:35.700 it may affect the outcome,
NOTE Confidence: 0.9420724

00:30:35.700 --> 00:30:36.900 but not the distribution of
NOTE Confidence: 0.9420724

00:30:36.900 --> 00:30:37.480 the outcome.
NOTE Confidence: 0.94390196

00:30:42.075 --> 00:30:43.755 They have been lately also
NOTE Confidence: 0.94390196

00:30:43.755 --> 00:30:45.675 focusing on not only an
NOTE Confidence: 0.94390196

00:30:45.675 --> 00:30:47.595 outcome goal, but also a
NOTE Confidence: 0.94390196

00:30:47.595 --> 00:30:48.495 power goal.
NOTE Confidence: 0.9585861

00:30:48.875 --> 00:30:50.395 And a power goal is
NOTE Confidence: 0.9585861

00:30:50.395 --> 00:30:52.460 where after stage one, we
NOTE Confidence: 0.9585861

00:30:52.460 --> 00:30:53.660 sit around and we try
NOTE Confidence: 0.9585861

00:30:53.660 --> 00:30:55.100 to figure out, okay, what
NOTE Confidence: 0.9585861

00:30:55.100 --> 00:30:56.140 do we think? How do

NOTE Confidence: 0.9585861
00:30:56.140 --> 00:30:57.260 we think the trial is
NOTE Confidence: 0.9585861
00:30:57.260 --> 00:30:57.760 going?
NOTE Confidence: 0.90974313
00:30:58.300 --> 00:31:00.060 Are we achieve achieving the
NOTE Confidence: 0.90974313
00:31:00.060 --> 00:31:00.560 power
NOTE Confidence: 0.90885675
00:31:01.100 --> 00:31:01.580 that,
NOTE Confidence: 0.98182166
00:31:01.980 --> 00:31:03.360 that we hoped for?
NOTE Confidence: 0.9963678
00:31:03.820 --> 00:31:05.125 So there's two ways to
NOTE Confidence: 0.9963678
00:31:05.125 --> 00:31:06.085 do this. We can look
NOTE Confidence: 0.9963678
00:31:06.085 --> 00:31:07.865 at conditional or unconditional
NOTE Confidence: 0.99950886
00:31:08.404 --> 00:31:08.904 power.
NOTE Confidence: 0.96226513
00:31:09.205 --> 00:31:10.245 At first, I thought we
NOTE Confidence: 0.96226513
00:31:10.245 --> 00:31:11.605 should just be looking at
NOTE Confidence: 0.96226513
00:31:11.605 --> 00:31:13.945 unconditional power. But in conversations
NOTE Confidence: 0.96226513
00:31:14.005 --> 00:31:15.284 with Donna, we decided we
NOTE Confidence: 0.96226513
00:31:15.284 --> 00:31:16.404 also have to look at
NOTE Confidence: 0.96226513

00:31:16.404 --> 00:31:16.904 unconditional
NOTE Confidence: 0.9854712

00:31:17.284 --> 00:31:18.750 power. And this turns out
NOTE Confidence: 0.9854712

00:31:18.750 --> 00:31:20.210 to be important, especially
NOTE Confidence: 0.9978219

00:31:20.590 --> 00:31:21.330 in cases
NOTE Confidence: 0.97716016

00:31:21.710 --> 00:31:23.310 where the where the power
NOTE Confidence: 0.97716016

00:31:23.310 --> 00:31:24.690 is not very high.
NOTE Confidence: 0.9305267

00:31:25.230 --> 00:31:27.030 If the power is is
NOTE Confidence: 0.9305267

00:31:27.030 --> 00:31:28.990 is is pretty high, when
NOTE Confidence: 0.9305267

00:31:28.990 --> 00:31:31.330 the conditional power works full,
NOTE Confidence: 0.98385084

00:31:31.710 --> 00:31:32.370 if the
NOTE Confidence: 0.9970477

00:31:33.115 --> 00:31:34.554 overall power is not very
NOTE Confidence: 0.9970477

00:31:34.554 --> 00:31:35.515 high, it may be better
NOTE Confidence: 0.9970477

00:31:35.515 --> 00:31:37.615 to look at unconditional power.
NOTE Confidence: 0.9970477

00:31:37.835 --> 00:31:39.054 So what is the difference?
NOTE Confidence: 0.9999462

00:31:39.515 --> 00:31:40.015 Unconditional
NOTE Confidence: 0.9988475

00:31:40.475 --> 00:31:40.975 power

NOTE Confidence: 0.995983
00:31:41.434 --> 00:31:43.215 ignores that we have already,
NOTE Confidence: 0.96960443
00:31:44.554 --> 00:31:46.475 collected the stage one data,
NOTE Confidence: 0.96960443
00:31:46.475 --> 00:31:47.595 and those will be the
NOTE Confidence: 0.96960443
00:31:47.595 --> 00:31:48.919 data that they'll be using
NOTE Confidence: 0.92635775
00:31:49.620 --> 00:31:50.440 at the test.
NOTE Confidence: 0.9147977
00:31:50.820 --> 00:31:52.759 So they consider more variation
NOTE Confidence: 0.9147977
00:31:52.980 --> 00:31:54.340 in the numerator of the
NOTE Confidence: 0.9147977
00:31:54.340 --> 00:31:56.259 test statistic. Because think of
NOTE Confidence: 0.9147977
00:31:56.259 --> 00:31:57.379 this, if you look at
NOTE Confidence: 0.9147977
00:31:57.379 --> 00:31:58.679 at at, at
NOTE Confidence: 0.9042726
00:31:59.700 --> 00:32:00.580 the test at the end
NOTE Confidence: 0.9042726
00:32:00.580 --> 00:32:01.700 of the study, they compare
NOTE Confidence: 0.9042726
00:32:01.700 --> 00:32:03.000 the treated and the untreated.
NOTE Confidence: 0.8609637
00:32:03.485 --> 00:32:04.525 And maybe just that the
NOTE Confidence: 0.8609637
00:32:04.525 --> 00:32:06.125 two sample t test with
NOTE Confidence: 0.8609637

00:32:06.125 --> 00:32:07.565 a variant studies like p
NOTE Confidence: 0.8609637

00:32:07.565 --> 00:32:08.845 one one minus p one
NOTE Confidence: 0.8609637

00:32:08.845 --> 00:32:10.045 p zero one minus p
NOTE Confidence: 0.8609637

00:32:10.045 --> 00:32:11.565 dot p zero with some
NOTE Confidence: 0.8609637

00:32:11.565 --> 00:32:12.845 n 's and square roots and
NOTE Confidence: 0.8609637

00:32:12.845 --> 00:32:13.905 stuff on the board.
NOTE Confidence: 0.9513132

00:32:14.365 --> 00:32:15.805 So when you look at
NOTE Confidence: 0.9513132

00:32:15.805 --> 00:32:17.020 this, you have this p
NOTE Confidence: 0.9513132

00:32:17.020 --> 00:32:18.540 one hat minus p zero
NOTE Confidence: 0.9513132

00:32:18.540 --> 00:32:19.680 hats in the numerator.
NOTE Confidence: 0.9067414

00:32:20.220 --> 00:32:21.500 And part of this p
NOTE Confidence: 0.9067414

00:32:21.500 --> 00:32:22.700 one hats and part of
NOTE Confidence: 0.9067414

00:32:22.700 --> 00:32:23.980 this p zero hats at
NOTE Confidence: 0.9067414

00:32:23.980 --> 00:32:24.940 the end of stage two
NOTE Confidence: 0.9067414

00:32:24.940 --> 00:32:25.680 we have,
NOTE Confidence: 0.9817015

00:32:26.380 --> 00:32:27.500 we have the number of

NOTE Confidence: 0.9817015
00:32:27.500 --> 00:32:29.180 successes in the stage one
NOTE Confidence: 0.9817015
00:32:29.180 --> 00:32:31.115 trial in the stage one,
NOTE Confidence: 0.9817015
00:32:31.115 --> 00:32:32.635 both in the intervention and
NOTE Confidence: 0.9817015
00:32:32.635 --> 00:32:33.855 the control group.
NOTE Confidence: 0.9647201
00:32:34.315 --> 00:32:35.695 When we look at unconditional
NOTE Confidence: 0.9966944
00:32:36.154 --> 00:32:38.575 power, we still consider variation
NOTE Confidence: 0.9966944
00:32:38.794 --> 00:32:40.395 in stage one and stage
NOTE Confidence: 0.9966944
00:32:40.395 --> 00:32:41.914 two. When we look at
NOTE Confidence: 0.9966944
00:32:41.914 --> 00:32:43.934 conditional power, we only consider
NOTE Confidence: 0.9966944
00:32:43.995 --> 00:32:45.375 the stage two variation.
NOTE Confidence: 0.9757041
00:32:45.960 --> 00:32:48.200 So this indicates that if
NOTE Confidence: 0.9757041
00:32:48.200 --> 00:32:49.419 we look at unconditional
NOTE Confidence: 0.9961569
00:32:49.720 --> 00:32:51.179 power, we recommend
NOTE Confidence: 0.9996023
00:32:51.799 --> 00:32:53.820 a more effective intervention
NOTE Confidence: 0.9402553
00:32:54.520 --> 00:32:56.200 than if we look at
NOTE Confidence: 0.9402553

00:32:56.200 --> 00:32:58.440 an at conditional power where
NOTE Confidence: 0.9402553

00:32:58.440 --> 00:32:59.320 we can do with a
NOTE Confidence: 0.9402553

00:32:59.320 --> 00:33:00.460 little bit less
NOTE Confidence: 0.9888021

00:33:01.155 --> 00:33:02.295 effective intervention.
NOTE Confidence: 0.97015554

00:33:02.835 --> 00:33:03.875 So you see that if
NOTE Confidence: 0.97015554

00:33:03.875 --> 00:33:05.075 there is cases where we
NOTE Confidence: 0.97015554

00:33:05.075 --> 00:33:06.935 cannot really reach the uncondition
NOTE Confidence: 0.97015554

00:33:07.235 --> 00:33:09.155 reach the conditional power in
NOTE Confidence: 0.97015554

00:33:09.155 --> 00:33:10.355 many of the in many
NOTE Confidence: 0.97015554

00:33:10.355 --> 00:33:11.255 of the trials,
NOTE Confidence: 0.9973769

00:33:11.555 --> 00:33:12.675 then it's good to have
NOTE Confidence: 0.9973769

00:33:12.675 --> 00:33:13.415 the unconditional
NOTE Confidence: 0.8937714

00:33:13.715 --> 00:33:14.215 power.
NOTE Confidence: 0.9835329

00:33:14.610 --> 00:33:16.070 So based on the uncondition
NOTE Confidence: 0.9993202

00:33:16.370 --> 00:33:17.350 based on the
NOTE Confidence: 0.9933137

00:33:17.730 --> 00:33:18.710 power constraints,

NOTE Confidence: 0.99373156

00:33:19.170 --> 00:33:20.530 we can estimate what is

NOTE Confidence: 0.99373156

00:33:20.530 --> 00:33:21.809 the power of the test

NOTE Confidence: 0.99373156

00:33:21.809 --> 00:33:22.690 at the end of the

NOTE Confidence: 0.99373156

00:33:22.690 --> 00:33:23.190 study.

NOTE Confidence: 0.9884901

00:33:23.730 --> 00:33:25.090 So at at stage one,

NOTE Confidence: 0.9884901

00:33:25.090 --> 00:33:26.210 you could do two things.

NOTE Confidence: 0.9884901

00:33:26.210 --> 00:33:27.970 You can estimate you can

NOTE Confidence: 0.9884901

00:33:27.970 --> 00:33:28.870 work with the

NOTE Confidence: 0.9064983

00:33:29.605 --> 00:33:30.585 outcome goal,

NOTE Confidence: 0.9545027

00:33:30.885 --> 00:33:32.005 and you can work with

NOTE Confidence: 0.9545027

00:33:32.005 --> 00:33:33.225 a power goal.

NOTE Confidence: 0.99389255

00:33:33.765 --> 00:33:35.365 So you can try to

NOTE Confidence: 0.99389255

00:33:35.365 --> 00:33:37.044 have them both be okay.

NOTE Confidence: 0.99389255

00:33:37.044 --> 00:33:38.485 So maybe a power of

NOTE Confidence: 0.99389255

00:33:38.485 --> 00:33:39.304 eighty percent

NOTE Confidence: 0.9606207

00:33:39.845 --> 00:33:41.465 and maybe an outcome
NOTE Confidence: 0.8807776

00:33:41.765 --> 00:33:43.410 goal of ninety percent. And
NOTE Confidence: 0.8807776

00:33:43.410 --> 00:33:44.630 these are two constraints,
NOTE Confidence: 0.9853191

00:33:45.330 --> 00:33:46.370 and you can,
NOTE Confidence: 0.3930352

00:33:46.850 --> 00:33:47.350 minimize
NOTE Confidence: 0.9525395

00:33:47.970 --> 00:33:48.710 the cost
NOTE Confidence: 0.7636693

00:33:49.170 --> 00:33:50.070 by the
NOTE Confidence: 0.88556695

00:33:51.170 --> 00:33:52.230 by the recommended
NOTE Confidence: 0.7594261

00:33:52.610 --> 00:33:53.110 intervention.
NOTE Confidence: 0.7278743

00:33:54.690 --> 00:33:54.940 So,
NOTE Confidence: 0.9271012

00:33:55.945 --> 00:33:58.185 adheres to both constraints, so
NOTE Confidence: 0.9271012

00:33:58.185 --> 00:33:59.865 the power goal and the
NOTE Confidence: 0.9271012

00:33:59.865 --> 00:34:00.685 outcome goal.
NOTE Confidence: 0.916642

00:34:01.305 --> 00:34:03.005 And with these two goals,
NOTE Confidence: 0.916642

00:34:03.065 --> 00:34:04.985 you're still adapting only the
NOTE Confidence: 0.916642

00:34:04.985 --> 00:34:06.905 intervention, not the sample size?

NOTE Confidence: 0.916642

00:34:06.905 --> 00:34:08.130 No. Not the sample size.

NOTE Confidence: 0.916642

00:34:08.210 --> 00:34:09.410 We're for now, we're working

NOTE Confidence: 0.916642

00:34:09.410 --> 00:34:10.609 with sample size fix. It's

NOTE Confidence: 0.916642

00:34:10.609 --> 00:34:12.450 actually an interesting idea to

NOTE Confidence: 0.916642

00:34:12.450 --> 00:34:14.130 also work on sample size

NOTE Confidence: 0.916642

00:34:14.130 --> 00:34:16.150 adjustments for for a level.

NOTE Confidence: 0.916642

00:34:16.289 --> 00:34:17.250 But I think they're not

NOTE Confidence: 0.916642

00:34:17.250 --> 00:34:18.869 there yet because we have,

NOTE Confidence: 0.7960093

00:34:19.489 --> 00:34:21.410 repeated outcomes to work on

NOTE Confidence: 0.7960093

00:34:21.410 --> 00:34:23.175 and confounding by indications work.

NOTE Confidence: 0.7960093

00:34:23.335 --> 00:34:25.015 Right. So, essentially, you're just

NOTE Confidence: 0.7960093

00:34:25.015 --> 00:34:25.675 an intervention,

NOTE Confidence: 0.9347715

00:34:26.055 --> 00:34:27.415 not only to reach that

NOTE Confidence: 0.9347715

00:34:27.415 --> 00:34:28.855 outcome goal, but also there'll

NOTE Confidence: 0.9347715

00:34:28.855 --> 00:34:30.614 be different interventions that have

NOTE Confidence: 0.9347715

00:34:30.614 --> 00:34:32.315 more like, you could achieve
NOTE Confidence: 0.9347715

00:34:32.375 --> 00:34:33.655 more or less power, so
NOTE Confidence: 0.9347715

00:34:33.655 --> 00:34:34.795 you're also
NOTE Confidence: 0.6486076

00:34:35.175 --> 00:34:36.695 changing the Too long strange.
NOTE Confidence: 0.6486076

00:34:36.695 --> 00:34:37.815 Okay. We we we want
NOTE Confidence: 0.6486076

00:34:37.815 --> 00:34:39.035 an intervention
NOTE Confidence: 0.9748237

00:34:39.630 --> 00:34:40.289 that hopefully
NOTE Confidence: 0.9578129

00:34:40.589 --> 00:34:42.130 gets us the outcome goal
NOTE Confidence: 0.9210162

00:34:42.510 --> 00:34:43.890 and the power goal.
NOTE Confidence: 0.7269815

00:34:44.670 --> 00:34:46.670 And And all the models.
NOTE Confidence: 0.7269815

00:34:46.750 --> 00:34:48.930 On those among those two
NOTE Confidence: 0.9229765

00:34:49.469 --> 00:34:51.489 goals, the intervention that satisfy
NOTE Confidence: 0.9229765

00:34:51.630 --> 00:34:52.450 both goals
NOTE Confidence: 0.86814886

00:34:53.154 --> 00:34:54.434 estimated based on the stage
NOTE Confidence: 0.86814886

00:34:54.434 --> 00:34:56.114 found data. Among those, we
NOTE Confidence: 0.86814886

00:34:56.114 --> 00:34:56.994 choose the one that is

NOTE Confidence: 0.86814886
00:34:56.994 --> 00:34:57.815 least cost.
NOTE Confidence: 0.94810945
00:34:59.555 --> 00:35:00.934 Yes. Thank you.
NOTE Confidence: 0.64656645
00:35:04.355 --> 00:35:05.875 Simulation study. How about they
NOTE Confidence: 0.64656645
00:35:05.875 --> 00:35:06.855 stick that, Dona?
NOTE Confidence: 0.9140561
00:35:07.370 --> 00:35:08.489 That sounds like a good
NOTE Confidence: 0.9140561
00:35:08.489 --> 00:35:09.370 idea. We can go over
NOTE Confidence: 0.9140561
00:35:09.370 --> 00:35:11.370 tomorrow in class. Yeah. Which
NOTE Confidence: 0.9140561
00:35:11.370 --> 00:35:12.110 by the way,
NOTE Confidence: 0.94352937
00:35:12.489 --> 00:35:13.610 I told people on chat,
NOTE Confidence: 0.94352937
00:35:13.610 --> 00:35:15.210 but Judith will give a
NOTE Confidence: 0.94352937
00:35:15.210 --> 00:35:16.510 more detailed technical
NOTE Confidence: 0.88901186
00:35:16.810 --> 00:35:18.810 lecture tomorrow, two hour lecture
NOTE Confidence: 0.88901186
00:35:18.810 --> 00:35:19.870 in my course
NOTE Confidence: 0.7304407
00:35:20.735 --> 00:35:21.235 in
NOTE Confidence: 0.8112476
00:35:21.775 --> 00:35:23.135 room one zero two at
NOTE Confidence: 0.8112476

00:35:23.135 --> 00:35:24.435 sixty Public Street.
NOTE Confidence: 0.9197591

00:35:24.895 --> 00:35:25.935 And you're all welcome to
NOTE Confidence: 0.9197591

00:35:25.935 --> 00:35:26.895 join that as well if
NOTE Confidence: 0.9197591

00:35:26.895 --> 00:35:28.094 you wanna hear more about
NOTE Confidence: 0.9197591

00:35:28.094 --> 00:35:29.535 Mago and learn a bit
NOTE Confidence: 0.9197591

00:35:29.535 --> 00:35:30.495 more in in fact the
NOTE Confidence: 0.9197591

00:35:30.495 --> 00:35:31.795 mathematical details.
NOTE Confidence: 0.8619856

00:35:32.750 --> 00:35:33.549 And I can get you
NOTE Confidence: 0.8619856

00:35:33.549 --> 00:35:34.910 that information if you email
NOTE Confidence: 0.8619856

00:35:34.910 --> 00:35:35.790 me on me at j
NOTE Confidence: 0.8619856

00:35:35.790 --> 00:35:36.609 j dot com.
NOTE Confidence: 0.6894621

00:35:38.030 --> 00:35:38.910 Or we can and you
NOTE Confidence: 0.6894621

00:35:38.910 --> 00:35:40.109 can ask anyone who also
NOTE Confidence: 0.6894621

00:35:40.109 --> 00:35:41.809 knows. Sally or me.
NOTE Confidence: 0.92426026

00:35:46.655 --> 00:35:47.395 Oh, cool.
NOTE Confidence: 0.9695365

00:35:47.775 --> 00:35:48.655 Yeah. So,

NOTE Confidence: 0.9239066

00:35:50.415 --> 00:35:51.614 what we have we can

NOTE Confidence: 0.9239066

00:35:51.614 --> 00:35:52.655 do, we can use the

NOTE Confidence: 0.9239066

00:35:52.655 --> 00:35:54.734 resulting estimates and confidence intervals

NOTE Confidence: 0.9239066

00:35:54.734 --> 00:35:56.094 for the beta using the

NOTE Confidence: 0.9239066

00:35:56.094 --> 00:35:57.935 coupling argument. We can find

NOTE Confidence: 0.9239066

00:35:57.935 --> 00:35:58.994 asymptotic normality.

NOTE Confidence: 0.99269134

00:35:59.370 --> 00:36:01.230 We can also find formulas

NOTE Confidence: 0.99269134

00:36:01.290 --> 00:36:02.590 for the confidence intervals.

NOTE Confidence: 0.9951194

00:36:02.970 --> 00:36:04.010 We can use that to,

NOTE Confidence: 0.9951194

00:36:04.490 --> 00:36:06.670 create estimates and confidence regions

NOTE Confidence: 0.997651

00:36:06.970 --> 00:36:08.750 for the optimal intervention

NOTE Confidence: 0.6170638

00:36:09.130 --> 00:36:09.950 x opt.

NOTE Confidence: 0.9658552

00:36:10.410 --> 00:36:12.090 And then we could, maybe

NOTE Confidence: 0.9658552

00:36:12.090 --> 00:36:13.870 keep only package configurations

NOTE Confidence: 0.7233148

00:36:14.170 --> 00:36:14.330 for which the confidence interval

NOTE Confidence: 0.7233148

00:36:14.330 --> 00:36:14.910 for the
NOTE Confidence: 0.73091

00:36:16.775 --> 00:36:17.674 success probability
NOTE Confidence: 0.9899138

00:36:18.295 --> 00:36:20.055 contains zero point nine to
NOTE Confidence: 0.9899138

00:36:20.055 --> 00:36:21.835 create a confidence set
NOTE Confidence: 0.7020379

00:36:22.214 --> 00:36:23.194 for x points.
NOTE Confidence: 0.88176656

00:36:25.015 --> 00:36:26.154 They can also,
NOTE Confidence: 0.9419388

00:36:26.454 --> 00:36:28.135 do a confidence band for
NOTE Confidence: 0.9419388

00:36:28.135 --> 00:36:28.714 the probability
NOTE Confidence: 0.9989189

00:36:29.015 --> 00:36:30.739 of success based on β
NOTE Confidence: 0.51581615

00:36:31.600 --> 00:36:32.660 hat, since Jaffe's,
NOTE Confidence: 0.9377496

00:36:33.520 --> 00:36:34.020 theorem.
NOTE Confidence: 0.92800283

00:36:34.560 --> 00:36:36.400 This is something that, Daniel
NOTE Confidence: 0.92800283

00:36:36.400 --> 00:36:37.440 was able to figure out.
NOTE Confidence: 0.92800283

00:36:37.440 --> 00:36:38.719 Once we have a subdotted
NOTE Confidence: 0.92800283

00:36:38.719 --> 00:36:40.320 normality, we can use standard
NOTE Confidence: 0.92800283

00:36:40.320 --> 00:36:40.820 results,

NOTE Confidence: 0.99389404
00:36:41.280 --> 00:36:42.400 and that gives us an
NOTE Confidence: 0.99389404
00:36:42.400 --> 00:36:44.625 option to create confidence bands
NOTE Confidence: 0.99389404
00:36:44.864 --> 00:36:46.725 for the probability of success
NOTE Confidence: 0.99389404
00:36:47.025 --> 00:36:48.485 under any possible
NOTE Confidence: 0.9270148
00:36:48.864 --> 00:36:51.125 configuration of the inter implementation
NOTE Confidence: 0.99403954
00:36:51.505 --> 00:36:52.005 package.
NOTE Confidence: 0.8656688
00:36:52.305 --> 00:36:53.265 And then we can also
NOTE Confidence: 0.8656688
00:36:53.265 --> 00:36:54.864 get a no confidence interval
NOTE Confidence: 0.8656688
00:36:54.864 --> 00:36:56.465 for success probability on the
NOTE Confidence: 0.8656688
00:36:56.545 --> 00:36:57.765 of x opt
NOTE Confidence: 0.95347303
00:36:58.469 --> 00:37:00.070 that we estimated because we
NOTE Confidence: 0.95347303
00:37:00.070 --> 00:37:01.270 can just look at the
NOTE Confidence: 0.95347303
00:37:01.270 --> 00:37:03.369 confidence bands at x opt.
NOTE Confidence: 0.99147093
00:37:03.910 --> 00:37:05.210 It's a little bit conservative,
NOTE Confidence: 0.99147093
00:37:05.350 --> 00:37:06.250 but it works.
NOTE Confidence: 0.7754245

00:37:09.750 --> 00:37:10.250 Okay.
NOTE Confidence: 0.8811079
00:37:11.694 --> 00:37:12.515 Thirty nine.
NOTE Confidence: 0.7969603
00:37:12.815 --> 00:37:14.094 No. Not thirty nine. Ah,
NOTE Confidence: 0.7969603
00:37:14.094 --> 00:37:14.835 here. Yeah.
NOTE Confidence: 0.8480198
00:37:15.855 --> 00:37:17.535 The better birth starts. We
NOTE Confidence: 0.8480198
00:37:17.535 --> 00:37:18.895 looked at one outcome. It
NOTE Confidence: 0.8480198
00:37:18.895 --> 00:37:20.414 is a process outcome. We
NOTE Confidence: 0.8480198
00:37:20.414 --> 00:37:22.114 looked at our satoshian administration
NOTE Confidence: 0.9956245
00:37:22.575 --> 00:37:23.075 immediately
NOTE Confidence: 0.9980366
00:37:23.375 --> 00:37:24.355 after delivery.
NOTE Confidence: 0.9909966
00:37:24.734 --> 00:37:26.414 This is recommended by the
NOTE Confidence: 0.9909966
00:37:26.414 --> 00:37:26.914 WHO.
NOTE Confidence: 0.9100203
00:37:30.630 --> 00:37:32.790 The intervention components we considered
NOTE Confidence: 0.9100203
00:37:32.790 --> 00:37:33.930 were the number of coaching
NOTE Confidence: 0.9100203
00:37:33.989 --> 00:37:35.610 visits and the launch duration,
NOTE Confidence: 0.9100203
00:37:35.830 --> 00:37:37.030 and we used the center

NOTE Confidence: 0.9100203

00:37:37.030 --> 00:37:38.550 characteristics. I didn't this would

NOTE Confidence: 0.9100203

00:37:38.550 --> 00:37:40.330 be one that we also

NOTE Confidence: 0.9875357

00:37:40.815 --> 00:37:42.575 included in the logistic regression

NOTE Confidence: 0.9875357

00:37:42.575 --> 00:37:44.255 model. It was the monthly

NOTE Confidence: 0.9875357

00:37:44.255 --> 00:37:46.015 birth birth volume because it

NOTE Confidence: 0.9875357

00:37:46.015 --> 00:37:46.835 was highly,

NOTE Confidence: 0.89241844

00:37:48.094 --> 00:37:49.855 highly variable among the centers

NOTE Confidence: 0.89241844

00:37:49.855 --> 00:37:50.835 in bed of birth.

NOTE Confidence: 0.9471778

00:37:52.494 --> 00:37:53.695 And then you can get

NOTE Confidence: 0.9471778

00:37:53.695 --> 00:37:56.020 the, confidence intervals and the

NOTE Confidence: 0.9471778

00:37:56.020 --> 00:37:57.720 estimate decides this is the

NOTE Confidence: 0.9471778

00:37:58.020 --> 00:37:59.860 beta zero hat, beta one

NOTE Confidence: 0.9471778

00:37:59.860 --> 00:38:01.320 hat, beta two hat.

NOTE Confidence: 0.986969

00:38:01.700 --> 00:38:03.220 After stage one, you could

NOTE Confidence: 0.986969

00:38:03.220 --> 00:38:04.740 get an estimate of the

NOTE Confidence: 0.986969

00:38:04.740 --> 00:38:05.800 optimal intervention,
NOTE Confidence: 0.9827772

00:38:06.740 --> 00:38:08.520 and and the recommended intervention
NOTE Confidence: 0.9827772

00:38:08.580 --> 00:38:09.460 in this case would have
NOTE Confidence: 0.9827772

00:38:09.460 --> 00:38:09.960 been
NOTE Confidence: 0.98424673

00:38:10.295 --> 00:38:10.695 one,
NOTE Confidence: 0.93796957

00:38:11.095 --> 00:38:12.795 long day of lunch duration
NOTE Confidence: 0.9767895

00:38:13.255 --> 00:38:15.114 and five coaching visits.
NOTE Confidence: 0.9430732

00:38:15.735 --> 00:38:17.495 And then after stage two,
NOTE Confidence: 0.9430732

00:38:17.495 --> 00:38:19.495 the recommended intervention would be
NOTE Confidence: 0.9430732

00:38:19.495 --> 00:38:20.875 three lunch duration
NOTE Confidence: 0.97205675

00:38:21.175 --> 00:38:23.114 and only one coaching visit.
NOTE Confidence: 0.9979484

00:38:23.495 --> 00:38:25.275 And after the study,
NOTE Confidence: 0.908163

00:38:26.100 --> 00:38:27.940 one could estimate all the
NOTE Confidence: 0.908163

00:38:27.940 --> 00:38:29.300 in the effect of all
NOTE Confidence: 0.908163

00:38:29.300 --> 00:38:30.420 the of of the both
NOTE Confidence: 0.908163

00:38:30.420 --> 00:38:31.560 intervention components

NOTE Confidence: 0.97722936
00:38:32.100 --> 00:38:34.120 and also the recommended optimal
NOTE Confidence: 0.97722936
00:38:34.180 --> 00:38:34.680 intervention.
NOTE Confidence: 0.9575262
00:38:40.065 --> 00:38:41.585 The ninety five percent confidence
NOTE Confidence: 0.9575262
00:38:41.585 --> 00:38:43.125 set for the optimal intervention
NOTE Confidence: 0.96700096
00:38:43.425 --> 00:38:44.885 over the grid of x,
NOTE Confidence: 0.96700096
00:38:45.025 --> 00:38:45.905 we looked at,
NOTE Confidence: 0.9106634
00:38:46.305 --> 00:38:48.065 all possible numbers of coaching
NOTE Confidence: 0.9106634
00:38:48.065 --> 00:38:49.025 visits that can only be
NOTE Confidence: 0.9106634
00:38:49.025 --> 00:38:50.065 half because you have a
NOTE Confidence: 0.9106634
00:38:50.065 --> 00:38:51.344 coaching visit or you don't
NOTE Confidence: 0.9106634
00:38:51.344 --> 00:38:53.070 have it. Launchuation, you could
NOTE Confidence: 0.9106634
00:38:53.070 --> 00:38:54.110 think of having it one
NOTE Confidence: 0.9106634
00:38:54.110 --> 00:38:55.650 or one point five days.
NOTE Confidence: 0.97863704
00:38:56.430 --> 00:38:57.470 And of the three hundred
NOTE Confidence: 0.97863704
00:38:57.470 --> 00:38:59.650 and sixty potential intervention package,
NOTE Confidence: 0.95444465

00:38:59.950 --> 00:39:01.710 we included only ten point
NOTE Confidence: 0.95444465

00:39:01.710 --> 00:39:03.330 five percent in the confidence
NOTE Confidence: 0.95444465

00:39:03.550 --> 00:39:04.050 set.
NOTE Confidence: 0.96429855

00:39:05.795 --> 00:39:07.174 And they had different,
NOTE Confidence: 0.9921741

00:39:07.875 --> 00:39:08.775 different costs.
NOTE Confidence: 0.91320777

00:39:12.515 --> 00:39:13.654 We also created,
NOTE Confidence: 0.87535995

00:39:17.234 --> 00:39:18.614 I think it's right here.
NOTE Confidence: 0.87535995

00:39:18.674 --> 00:39:19.174 Sorry.
NOTE Confidence: 0.9571603

00:39:20.160 --> 00:39:21.859 We also created these conference
NOTE Confidence: 0.9571603

00:39:22.000 --> 00:39:23.839 bands for the probability of
NOTE Confidence: 0.9571603

00:39:23.839 --> 00:39:26.079 success under the different intervention
NOTE Confidence: 0.9571603

00:39:26.079 --> 00:39:27.839 component compositions. So you see
NOTE Confidence: 0.9571603

00:39:27.839 --> 00:39:29.599 the first component here and
NOTE Confidence: 0.9571603

00:39:29.599 --> 00:39:31.520 the second component here, and
NOTE Confidence: 0.9571603

00:39:31.520 --> 00:39:33.200 you can visualize this. This
NOTE Confidence: 0.9571603

00:39:33.200 --> 00:39:35.359 is pictures that Daniel never

NOTE Confidence: 0.9571603
00:39:35.359 --> 00:39:36.855 was able to create in
NOTE Confidence: 0.9571603
00:39:36.855 --> 00:39:37.355 art.
NOTE Confidence: 0.9455978
00:39:42.215 --> 00:39:43.675 And now I'm going.
NOTE Confidence: 0.8426422
00:39:44.135 --> 00:39:45.495 So the adaptive learn as
NOTE Confidence: 0.8426422
00:39:45.495 --> 00:39:46.935 you go, Labo design aims
NOTE Confidence: 0.8426422
00:39:46.935 --> 00:39:48.955 to find the optimal intervention
NOTE Confidence: 0.8426422
00:39:49.094 --> 00:39:49.594 composition
NOTE Confidence: 0.9003854
00:39:50.055 --> 00:39:51.195 and its effect.
NOTE Confidence: 0.95998114
00:39:51.730 --> 00:39:53.330 There's a dependence between stage
NOTE Confidence: 0.95998114
00:39:53.330 --> 00:39:54.610 one and stage two data,
NOTE Confidence: 0.95998114
00:39:54.610 --> 00:39:55.969 which makes it really nice
NOTE Confidence: 0.95998114
00:39:55.969 --> 00:39:56.850 for me to work on
NOTE Confidence: 0.95998114
00:39:56.850 --> 00:39:57.969 this because I am also
NOTE Confidence: 0.95998114
00:39:57.969 --> 00:39:59.650 a medical statistic from time
NOTE Confidence: 0.95998114
00:39:59.650 --> 00:40:01.090 to time. I love doing
NOTE Confidence: 0.95998114

00:40:01.090 --> 00:40:02.930 those math things. We use
NOTE Confidence: 0.95998114

00:40:02.930 --> 00:40:04.710 the coupling argument to provide
NOTE Confidence: 0.95998114

00:40:04.770 --> 00:40:05.270 theoretical
NOTE Confidence: 0.94053066

00:40:06.105 --> 00:40:08.425 justification for using existing software
NOTE Confidence: 0.94053066

00:40:08.425 --> 00:40:10.185 for estimation and inference because
NOTE Confidence: 0.94053066

00:40:10.185 --> 00:40:11.864 these estimating equations that I
NOTE Confidence: 0.94053066

00:40:11.864 --> 00:40:13.545 showed you are actually really
NOTE Confidence: 0.94053066

00:40:13.545 --> 00:40:15.945 just the usual estimating equations
NOTE Confidence: 0.94053066

00:40:15.945 --> 00:40:17.864 that logistic regression solves if
NOTE Confidence: 0.94053066

00:40:17.864 --> 00:40:18.925 you run
NOTE Confidence: 0.7137929

00:40:19.385 --> 00:40:21.244 like a PROC LOGISTIC or,
NOTE Confidence: 0.9571427

00:40:21.969 --> 00:40:22.630 or or,
NOTE Confidence: 0.35420787

00:40:22.930 --> 00:40:24.310 geom with a logic.
NOTE Confidence: 0.8877645

00:40:25.330 --> 00:40:27.170 It provided a confidence set
NOTE Confidence: 0.8877645

00:40:27.170 --> 00:40:28.930 for the optimal intervention and
NOTE Confidence: 0.8877645

00:40:28.930 --> 00:40:30.550 confidence band for the probabilities

NOTE Confidence: 0.9938108
00:40:31.250 --> 00:40:32.150 under any,
NOTE Confidence: 0.9966675
00:40:32.850 --> 00:40:33.910 package composition.
NOTE Confidence: 0.9147575
00:40:36.344 --> 00:40:37.945 Extensions, these are things we
NOTE Confidence: 0.9147575
00:40:37.945 --> 00:40:39.225 have done and I haven't
NOTE Confidence: 0.9147575
00:40:39.225 --> 00:40:39.725 shown.
NOTE Confidence: 0.958752
00:40:40.425 --> 00:40:41.945 Replace n is n one
NOTE Confidence: 0.958752
00:40:41.945 --> 00:40:43.545 and n two with n
NOTE Confidence: 0.958752
00:40:43.545 --> 00:40:44.585 one and n two that
NOTE Confidence: 0.958752
00:40:44.585 --> 00:40:46.685 go, at the same rate.
NOTE Confidence: 0.8671332
00:40:47.730 --> 00:40:49.670 Include center specific covariates
NOTE Confidence: 0.9068294
00:40:50.130 --> 00:40:51.330 in the regression in the
NOTE Confidence: 0.9068294
00:40:51.330 --> 00:40:52.790 logistic regression model,
NOTE Confidence: 0.97886866
00:40:53.090 --> 00:40:55.030 including more than two stages.
NOTE Confidence: 0.8960901
00:40:56.210 --> 00:40:57.489 And, also, we worked on
NOTE Confidence: 0.8960901
00:40:57.489 --> 00:40:59.410 LaVu for continuous outcomes. This
NOTE Confidence: 0.8960901

00:40:59.410 --> 00:41:00.870 is work with my PhD
NOTE Confidence: 0.8960901

00:41:00.930 --> 00:41:03.075 student, advisee, Amta Bing. I
NOTE Confidence: 0.8960901

00:41:03.075 --> 00:41:04.195 think he's home live if
NOTE Confidence: 0.8960901

00:41:04.195 --> 00:41:04.994 you want to ask him
NOTE Confidence: 0.8960901

00:41:04.994 --> 00:41:05.815 about details.
NOTE Confidence: 0.97901815

00:41:06.275 --> 00:41:07.734 So we looked at continuous
NOTE Confidence: 0.97901815

00:41:07.795 --> 00:41:08.295 outcomes,
NOTE Confidence: 0.97338694

00:41:08.594 --> 00:41:10.195 and we looked not only
NOTE Confidence: 0.97338694

00:41:10.195 --> 00:41:11.875 at a linear regression. So
NOTE Confidence: 0.97338694

00:41:11.875 --> 00:41:13.474 with a linear link, we
NOTE Confidence: 0.97338694

00:41:13.474 --> 00:41:15.075 also looked at different link
NOTE Confidence: 0.97338694

00:41:15.075 --> 00:41:15.575 functions.
NOTE Confidence: 0.9978627

00:41:15.920 --> 00:41:17.040 What we did assume so
NOTE Confidence: 0.9978627

00:41:17.040 --> 00:41:18.239 far is that all the
NOTE Confidence: 0.9978627

00:41:18.239 --> 00:41:19.380 errors are identically
NOTE Confidence: 0.97566843

00:41:19.680 --> 00:41:20.180 distributed.

NOTE Confidence: 0.9937861
00:41:21.840 --> 00:41:22.880 And the way he did
NOTE Confidence: 0.9937861
00:41:22.880 --> 00:41:24.580 this was to look at
NOTE Confidence: 0.9937861
00:41:24.719 --> 00:41:25.219 replacing
NOTE Confidence: 0.9995179
00:41:25.520 --> 00:41:27.219 the errors under the
NOTE Confidence: 0.99987376
00:41:27.680 --> 00:41:28.739 actual intervention
NOTE Confidence: 0.99862033
00:41:29.614 --> 00:41:31.694 by errors under the under
NOTE Confidence: 0.99862033
00:41:31.694 --> 00:41:32.434 the limiting
NOTE Confidence: 0.99971014
00:41:32.734 --> 00:41:33.234 intervention
NOTE Confidence: 0.9772211
00:41:33.855 --> 00:41:35.535 without changing the distribution. So
NOTE Confidence: 0.9772211
00:41:35.535 --> 00:41:36.494 it's a little bit like
NOTE Confidence: 0.9772211
00:41:36.494 --> 00:41:36.994 coupling,
NOTE Confidence: 0.95980877
00:41:37.295 --> 00:41:38.895 except for coupling, you cannot
NOTE Confidence: 0.95980877
00:41:38.895 --> 00:41:40.415 really copy them over because
NOTE Confidence: 0.95980877
00:41:40.415 --> 00:41:41.234 they have different
NOTE Confidence: 0.9891367
00:41:41.640 --> 00:41:42.859 different success probabilities.
NOTE Confidence: 0.9109193

00:41:43.319 --> 00:41:44.279 But here, we are showing
NOTE Confidence: 0.9109193

00:41:44.279 --> 00:41:45.480 that the errors are iid,
NOTE Confidence: 0.9109193

00:41:45.480 --> 00:41:46.779 so we can re replace
NOTE Confidence: 0.9109193

00:41:46.920 --> 00:41:48.520 one by the other. The
NOTE Confidence: 0.9109193

00:41:48.520 --> 00:41:49.640 other thing that he needed
NOTE Confidence: 0.9109193

00:41:49.640 --> 00:41:51.640 to do was, use, theory
NOTE Confidence: 0.9109193

00:41:51.640 --> 00:41:52.140 from,
NOTE Confidence: 0.9311119

00:41:53.079 --> 00:41:54.460 from empirical purposes.
NOTE Confidence: 0.69314814

00:42:00.425 --> 00:42:01.805 No. But I do.
NOTE Confidence: 0.63549024

00:42:03.625 --> 00:42:05.145 I'm not fully loading this
NOTE Confidence: 0.63549024

00:42:05.145 --> 00:42:05.645 morning.
NOTE Confidence: 0.90718555

00:42:06.265 --> 00:42:07.405 Let me go fast.
NOTE Confidence: 0.72798127

00:42:21.410 --> 00:42:21.910 Okay.
NOTE Confidence: 0.9898321

00:42:22.625 --> 00:42:23.585 Then another thing,
NOTE Confidence: 0.96357185

00:42:25.105 --> 00:42:26.545 the power constraints, this is
NOTE Confidence: 0.96357185

00:42:26.545 --> 00:42:28.325 still really work in progress.

NOTE Confidence: 0.97631514

00:42:30.625 --> 00:42:32.224 We're almost there. I expect

NOTE Confidence: 0.97631514

00:42:32.224 --> 00:42:33.364 that we can

NOTE Confidence: 0.8346737

00:42:34.440 --> 00:42:35.560 we can send the one

NOTE Confidence: 0.8346737

00:42:35.560 --> 00:42:36.780 liter power constraints

NOTE Confidence: 0.960548

00:42:37.560 --> 00:42:38.940 within a month or so.

NOTE Confidence: 0.960548

00:42:39.000 --> 00:42:39.500 Okay?

NOTE Confidence: 0.9079583

00:42:42.280 --> 00:42:43.660 There's future research.

NOTE Confidence: 0.7833552

00:42:44.680 --> 00:42:45.719 Xin Yu here is still

NOTE Confidence: 0.7833552

00:42:45.800 --> 00:42:47.000 is working on,

NOTE Confidence: 0.8308211

00:42:47.585 --> 00:42:49.664 including random center effects. This

NOTE Confidence: 0.8308211

00:42:49.664 --> 00:42:51.424 is joint work, Jun Jin

NOTE Confidence: 0.8308211

00:42:51.424 --> 00:42:53.344 Yu Yu, Donna Spiegelman and

NOTE Confidence: 0.8308211

00:42:53.344 --> 00:42:55.984 Xin Xu Zhou. I'm also

NOTE Confidence: 0.8308211

00:42:55.984 --> 00:42:57.265 involved. I should have put

NOTE Confidence: 0.8308211

00:42:57.265 --> 00:42:58.864 that. Oh, that's your joint

NOTE Confidence: 0.8308211

00:42:58.864 --> 00:43:00.464 work business. Xin Yu is
NOTE Confidence: 0.8308211

00:43:00.464 --> 00:43:01.290 leading this.
NOTE Confidence: 0.9901678

00:43:02.170 --> 00:43:03.850 Allow centers to contribute to
NOTE Confidence: 0.9901678

00:43:03.850 --> 00:43:05.130 more than one stage. I
NOTE Confidence: 0.9901678

00:43:05.130 --> 00:43:06.250 think that we are there
NOTE Confidence: 0.9901678

00:43:06.250 --> 00:43:06.750 now.
NOTE Confidence: 0.8779779

00:43:07.050 --> 00:43:09.390 Study design, consider help additional
NOTE Confidence: 0.8779779

00:43:09.610 --> 00:43:11.310 ways to choose the recommended
NOTE Confidence: 0.8779779

00:43:11.530 --> 00:43:12.030 intervention,
NOTE Confidence: 0.923805

00:43:13.210 --> 00:43:14.350 but he left. So
NOTE Confidence: 0.8028526

00:43:15.305 --> 00:43:16.425 I don't remember his name,
NOTE Confidence: 0.8028526

00:43:16.425 --> 00:43:17.805 but I also would look
NOTE Confidence: 0.8028526

00:43:18.025 --> 00:43:18.685 look at.
NOTE Confidence: 0.3143883

00:43:19.465 --> 00:43:19.965 So
NOTE Confidence: 0.973558

00:43:20.825 --> 00:43:22.185 far, we have done worked
NOTE Confidence: 0.973558

00:43:22.185 --> 00:43:23.945 with a power goal and

NOTE Confidence: 0.973558

00:43:23.945 --> 00:43:25.865 an outcome sorry, power goal

NOTE Confidence: 0.973558

00:43:25.865 --> 00:43:27.549 and outcome goal, but there

NOTE Confidence: 0.973558

00:43:27.549 --> 00:43:28.510 are other ways to do

NOTE Confidence: 0.973558

00:43:28.510 --> 00:43:29.469 it. It could be based

NOTE Confidence: 0.973558

00:43:29.469 --> 00:43:31.469 on process outcomes. I would

NOTE Confidence: 0.973558

00:43:31.469 --> 00:43:32.750 be curious to see that

NOTE Confidence: 0.973558

00:43:32.750 --> 00:43:34.049 implemented in practice.

NOTE Confidence: 0.93417794

00:43:34.910 --> 00:43:36.829 Replace the logistic regression models

NOTE Confidence: 0.93417794

00:43:36.829 --> 00:43:37.789 for the outcome with a

NOTE Confidence: 0.93417794

00:43:37.789 --> 00:43:39.390 more flexible model. One can

NOTE Confidence: 0.93417794

00:43:39.390 --> 00:43:40.589 think of a probate model.

NOTE Confidence: 0.93417794

00:43:40.589 --> 00:43:41.745 We didn't work with that.

NOTE Confidence: 0.93417794

00:43:41.825 --> 00:43:42.785 Probably that's not a big

NOTE Confidence: 0.93417794

00:43:42.785 --> 00:43:43.665 deal, but it would be

NOTE Confidence: 0.93417794

00:43:43.665 --> 00:43:44.165 interesting.

NOTE Confidence: 0.907902

00:43:44.865 --> 00:43:46.385 Create an R package for
NOTE Confidence: 0.907902

00:43:46.385 --> 00:43:47.825 design. This is joint work
NOTE Confidence: 0.907902

00:43:47.825 --> 00:43:49.265 with Hunter Bing. He is
NOTE Confidence: 0.907902

00:43:49.265 --> 00:43:50.705 at Boston University and on
NOTE Confidence: 0.907902

00:43:50.705 --> 00:43:51.925 the Spiegelman here.
NOTE Confidence: 0.9768908

00:43:52.945 --> 00:43:54.945 Hunter has a package working
NOTE Confidence: 0.9768908

00:43:54.945 --> 00:43:56.130 for the better birth, both
NOTE Confidence: 0.9768908

00:43:56.130 --> 00:43:58.609 for continuous outcome and for,
NOTE Confidence: 0.9501246

00:43:59.250 --> 00:44:00.770 for a binary outcome, both
NOTE Confidence: 0.9501246

00:44:00.770 --> 00:44:02.450 with a logic link, but
NOTE Confidence: 0.9501246

00:44:02.450 --> 00:44:04.289 he's, extending it so that
NOTE Confidence: 0.9501246

00:44:04.289 --> 00:44:05.650 hopefully we can also use
NOTE Confidence: 0.9501246

00:44:05.650 --> 00:44:07.329 it for POLISA in the
NOTE Confidence: 0.9501246

00:44:07.329 --> 00:44:09.010 future and then other people
NOTE Confidence: 0.9501246

00:44:09.010 --> 00:44:10.210 can use it for different
NOTE Confidence: 0.9501246

00:44:10.210 --> 00:44:10.710 studies.

NOTE Confidence: 0.9394777

00:44:12.295 --> 00:44:14.455 Consider confounding by indication. This

NOTE Confidence: 0.9394777

00:44:14.455 --> 00:44:15.975 is joint work with Minh

NOTE Confidence: 0.9394777

00:44:15.975 --> 00:44:16.475 Bui,

NOTE Confidence: 0.91702205

00:44:16.775 --> 00:44:19.015 who is currently also online.

NOTE Confidence: 0.91702205

00:44:19.015 --> 00:44:20.455 So she is in, at

NOTE Confidence: 0.91702205

00:44:20.455 --> 00:44:21.435 Boston University.

NOTE Confidence: 0.94346565

00:44:21.975 --> 00:44:23.460 What if a center adopts

NOTE Confidence: 0.94346565

00:44:23.619 --> 00:44:24.440 the intervention?

NOTE Confidence: 0.99667674

00:44:24.820 --> 00:44:26.280 How they do that correlates

NOTE Confidence: 0.9355572

00:44:26.739 --> 00:44:28.660 with their potential outcomes? Maybe

NOTE Confidence: 0.9355572

00:44:28.660 --> 00:44:30.420 a very successful center Yeah.

NOTE Confidence: 0.9355572

00:44:30.580 --> 00:44:32.339 Will have a a higher

NOTE Confidence: 0.9355572

00:44:32.339 --> 00:44:34.119 intervention component on physician

NOTE Confidence: 0.7948748

00:44:34.500 --> 00:44:35.800 than a not as successful

NOTE Confidence: 0.9970251

00:44:36.180 --> 00:44:37.815 center. So we are considering

NOTE Confidence: 0.9970251

00:44:37.955 --> 00:44:38.695 this now.
NOTE Confidence: 0.99615437
00:44:39.315 --> 00:44:40.375 It seems like
NOTE Confidence: 0.88658124
00:44:40.755 --> 00:44:42.435 it's a permitting approach to
NOTE Confidence: 0.88658124
00:44:42.435 --> 00:44:44.375 include fixed center effects
NOTE Confidence: 0.94422716
00:44:44.835 --> 00:44:46.435 because the fixed center effects
NOTE Confidence: 0.94422716
00:44:46.435 --> 00:44:48.515 could pick up the effects
NOTE Confidence: 0.94422716
00:44:48.515 --> 00:44:50.935 of this successful center.
NOTE Confidence: 0.99003816
00:44:54.055 --> 00:44:54.555 And,
NOTE Confidence: 0.9982105
00:44:55.094 --> 00:44:55.835 I will
NOTE Confidence: 0.99598205
00:44:56.135 --> 00:44:56.955 answer questions.