WEBVTT

NOTE duration:"00:16:16.2130000"

NOTE language:en-us

NOTE Confidence: 0.81772685

00:00:00.000 --> 00:00:02.968 It's my pleasure to now introduce our

NOTE Confidence: 0.81772685

00:00:02.968 --> 00:00:05.430 next speaker Doctor Chris Christie,

NOTE Confidence: 0.81772685

00:00:05.430 --> 00:00:06.861 office Doctor Kostakis,

NOTE Confidence: 0.81772685

00:00:06.861 --> 00:00:09.246 graduated from the Imperial College

NOTE Confidence: 0.81772685

00:00:09.246 --> 00:00:12.017 London and earned his PhD at the

NOTE Confidence: 0.81772685

00:00:12.017 --> 00:00:14.509 University of New South Wales in Sydney.

NOTE Confidence: 0.81772685

00:00:14.510 --> 00:00:16.162 After postdoctoral training at

NOTE Confidence: 0.81772685

00:00:16.162 --> 00:00:18.227 the Broad Institute and MTH,

NOTE Confidence: 0.81772685

00:00:18.230 --> 00:00:20.516 where he undertook some of the

NOTE Confidence: 0.81772685

00:00:20.516 --> 00:00:22.040 first Genome wide Association

NOTE Confidence: 0.81772685

00:00:22.105 --> 00:00:24.009 studies in autoimmune disease,

NOTE Confidence: 0.81772685

00:00:24.010 --> 00:00:26.080 he joined Yale in 2010.

NOTE Confidence: 0.81772685

00:00:26.080 --> 00:00:27.712 His laboratory uses genetics,

NOTE Confidence: 0.81772685

00:00:27.712 --> 00:00:28.936 genomics and epidemiological

NOTE Confidence: 0.81772685

00:00:28.936 --> 00:00:30.643 approaches to identify the

NOTE Confidence: 0.81772685

00:00:30.643 --> 00:00:31.927 biology underlying autoimmune.

NOTE Confidence: 0.81772685

00:00:31.930 --> 00:00:33.253 And neurological diseases

NOTE Confidence: 0.81772685

00:00:33.253 --> 00:00:35.017 dersum floor is yours,

NOTE Confidence: 0.81772685

00:00:35.020 --> 00:00:35.910 Doctor Kostakis.

NOTE Confidence: 0.8266911

00:00:39.040 --> 00:00:39.898 Thank you Nicole.

NOTE Confidence: 0.8266911

00:00:39.900 --> 00:00:41.755 I'm afraid I can't start my video

NOTE Confidence: 0.8266911

00:00:41.755 --> 00:00:43.864 so it's the tech people would like

NOTE Confidence: 0.8266911

00:00:43.864 --> 00:00:47.500 to start that, but it's fine.

NOTE Confidence: 0.8266911

00:00:47.500 --> 00:00:49.030 There we go. Hello everyone,

NOTE Confidence: 0.8266911

00:00:49.030 --> 00:00:51.018 I also have no disclosures and I

NOTE Confidence: 0.8266911

00:00:51.018 --> 00:00:53.072 would like to take the next few

NOTE Confidence: 0.8266911

00:00:53.072 --> 00:00:55.174 minutes to tell you a little bit

NOTE Confidence: 0.8266911

00:00:55.174 --> 00:00:57.172 about some of the things we've

NOTE Confidence: 0.8266911

00:00:57.172 --> 00:00:59.089 been thinking about in my lab.

NOTE Confidence: 0.8763021

00:01:02.220 --> 00:01:04.430 Specifically, how to use large

NOTE Confidence: 0.8763021

00:01:04.430 --> 00:01:07.167 scale data of both clinical and

NOTE Confidence: 0.8763021

00:01:07.167 --> 00:01:09.861 genetic data to make discoveries in

NOTE Confidence: 0.8763021

00:01:09.861 --> 00:01:12.359 diseases that we're interested in,

NOTE Confidence: 0.8763021

00:01:12.360 --> 00:01:15.620 specifically multiple sclerosis and epilepsy.

NOTE Confidence: 0.8763021

00:01:15.620 --> 00:01:17.780 And I chose these two projects

NOTE Confidence: 0.8763021

00:01:17.780 --> 00:01:20.041 to talk about because they are

NOTE Confidence: 0.8763021

00:01:20.041 --> 00:01:22.273 quite early on in their inception,

NOTE Confidence: 0.8763021

00:01:22.280 --> 00:01:24.500 so we're still not 100% sure

NOTE Confidence: 0.8763021

00:01:24.500 --> 00:01:25.980 what the story is,

NOTE Confidence: 0.8763021

00:01:25.980 --> 00:01:29.340 but I think it is instructive to

NOTE Confidence: 0.8763021

00:01:29.340 --> 00:01:33.029 look at what we can do with data.

NOTE Confidence: 0.8763021

00:01:33.030 --> 00:01:36.117 So the first story is multiple sclerosis.

NOTE Confidence: 0.8763021

00:01:36.120 --> 00:01:38.820 This is a large scale project

NOTE Confidence: 0.8763021

00:01:38.820 --> 00:01:41.429 out of the from the EU,

NOTE Confidence: 0.8763021

00:01:41.430 --> 00:01:43.640 primarily funded by one of

NOTE Confidence: 0.8763021

00:01:43.640 --> 00:01:45.408 the EU horizon programs.

NOTE Confidence: 0.8763021

00:01:45.410 --> 00:01:47.960 It's led by colleagues at the

NOTE Confidence: 0.8763021

00:01:47.960 --> 00:01:50.270 Carolyn Skirt Institute in Sweden,

NOTE Confidence: 0.8763021

00:01:50.270 --> 00:01:52.480 and it covers 10 countries,

NOTE Confidence: 0.8763021

00:01:52.480 --> 00:01:56.458 including site at Yale and a site at UCSF,

NOTE Confidence: 0.8763021

00:01:56.460 --> 00:01:59.748 and all the other partners are

NOTE Confidence: 0.8763021

00:01:59.748 --> 00:02:03.110 in in Europe and our main.

NOTE Confidence: 0.8763021

00:02:03.110 --> 00:02:07.870 Or our main focus is on multiple sclerosis,

NOTE Confidence: 0.8763021

00:02:07.870 --> 00:02:10.365 which is a predominantly autoimmune

NOTE Confidence: 0.8763021

00:02:10.365 --> 00:02:13.868 disease of the brain where the immune

NOTE Confidence: 0.8763021

00:02:13.868 --> 00:02:17.081 system basically decides that it does not

NOTE Confidence: 0.8763021

00:02:17.081 --> 00:02:20.686 like the myelin sheath around white matter.

NOTE Confidence: 0.8763021

00:02:20.690 --> 00:02:22.658 In neurons you get

NOTE Confidence: 0.8763021

00:02:22.658 --> 00:02:24.626 infiltration of immune cells.

NOTE Confidence: 0.8763021

00:02:24.630 --> 00:02:27.394 Stereotypically T cells that

NOTE Confidence: 0.8763021

00:02:27.394 --> 00:02:30.158 cause myelin stripping around.

NOTE Confidence: 0.8763021

00:02:30.160 --> 00:02:32.290 Blood vessels in the brain and

NOTE Confidence: 0.8763021

00:02:32.290 --> 00:02:34.583 you get these large lesions in

NOTE Confidence: 0.8763021

00:02:34.583 --> 00:02:36.573 the brain and progressively get

NOTE Confidence: 0.8763021

00:02:36.573 --> 00:02:39.049 more and more lesions overtime.

NOTE Confidence: 0.8763021

00:02:39.050 --> 00:02:41.878 And that leads to a relapsing remitting,

NOTE Confidence: 0.8763021

00:02:41.880 --> 00:02:43.156 usually mode of disease,

NOTE Confidence: 0.8763021

00:02:43.156 --> 00:02:45.070 where there is both physical and

NOTE Confidence: 0.8763021

00:02:45.129 --> 00:02:46.897 cognitive decline and eventually

NOTE Confidence: 0.8763021

00:02:46.897 --> 00:02:48.665 this becomes permanent and

NOTE Confidence: 0.8763021

00:02:48.665 --> 00:02:50.590 patients experience ongoing and

NOTE Confidence: 0.8763021

00:02:50.590 --> 00:02:51.570 progressive disability.

NOTE Confidence: 0.8763021

00:02:51.570 --> 00:02:53.590 It is a lifelong disease.

NOTE Confidence: 0.8763021

00:02:53.590 --> 00:02:55.610 There are disease modifying therapies,

NOTE Confidence: 0.8763021

00:02:55.610 --> 00:02:57.926 but there exists no cure and

NOTE Confidence: 0.8763021

00:02:57.926 --> 00:03:01.505 it is one of the more common

NOTE Confidence: 0.8763021

00:03:01.505 --> 00:03:04.089 neurological diseases out there.

NOTE Confidence: 0.8763021

00:03:04.090 --> 00:03:06.090 And like most such diseases,

NOTE Confidence: 0.8763021

00:03:06.090 --> 00:03:08.925 you can find some families where the

NOTE Confidence: 0.8763021

00:03:08.925 --> 00:03:11.688 disease appears to run in the families,

NOTE Confidence: 0.8763021

00:03:11.690 --> 00:03:13.690 but most cases are sporadic.

NOTE Confidence: 0.8763021

00:03:13.690 --> 00:03:15.800 It looks like familiar landmass

NOTE Confidence: 0.8763021

00:03:15.800 --> 00:03:18.890 is not a single gene form of Ms.

NOTE Confidence: 0.8763021

00:03:18.890 --> 00:03:21.290 It is exactly like the sporadic

NOTE Confidence: 0.8763021

00:03:21.290 --> 00:03:22.890 form it is polygenic.

NOTE Confidence: 0.8763021

00:03:22.890 --> 00:03:24.358 It is extremely complex.

NOTE Confidence: 0.8763021

00:03:24.358 --> 00:03:28.178 We have at least 200 loci mapped from large

NOTE Confidence: 0.8763021

00:03:28.178 --> 00:03:30.748 scale genome wide Association studies.

NOTE Confidence: 0.8763021

00:03:30.750 --> 00:03:32.830 We estimate there's probably another

NOTE Confidence: 0.8763021

00:03:32.830 --> 00:03:35.990 800 to 1000 out there in the genome,

NOTE Confidence: 0.8763021

00:03:35.990 --> 00:03:38.839 and a large effort now across the

NOTE Confidence: 0.8763021

00:03:38.839 --> 00:03:42.033 world is has been initiated to try

NOTE Confidence: 0.8763021

00:03:42.033 --> 00:03:45.210 and figure out what those genes do.

NOTE Confidence: 0.8763021

00:03:45.210 --> 00:03:47.418 But also to see how we can use

NOTE Confidence: 0.8763021

00:03:47.418 --> 00:03:49.616 some of this information and one

NOTE Confidence: 0.8763021

00:03:49.616 --> 00:03:51.968 of the problems has been that

NOTE Confidence: 0.8763021

00:03:52.050 --> 00:03:54.160 this disease is quite common,

NOTE Confidence: 0.8763021

00:03:54.160 --> 00:03:56.666 but it's not type 2 diabetes comma,

NOTE Confidence: 0.8763021

00:03:56.670 --> 00:03:58.812 so it's about one in 1000

NOTE Confidence: 0.8763021

00:03:58.812 --> 00:03:59.883 in European population,

NOTE Confidence: 0.8763021

00:03:59.890 --> 00:04:01.278 so it's fairly common,

NOTE Confidence: 0.8763021

00:04:01.278 --> 00:04:04.185 but no one really has a cohort of

NOTE Confidence: 0.8763021

00:04:04.185 --> 00:04:06.775 20 or 30,000 patients who have all

NOTE Confidence: 0.8763021

00:04:06.775 --> 00:04:09.946 been seen for a very long time in one

NOTE Confidence: 0.8763021

00:04:09.946 --> 00:04:13.150 clinic where data have been collected.

NOTE Confidence: 0.8763021

00:04:13.150 --> 00:04:14.550 In the same way,

NOTE Confidence: 0.8763021

00:04:14.550 --> 00:04:15.950 by the same people.

NOTE Confidence: 0.8763021

00:04:15.950 --> 00:04:19.496 And So what you have to do is Unite

NOTE Confidence: 0.8763021

00:04:19.496 --> 00:04:21.970 data across many centers.

NOTE Confidence: 0.8763021

00:04:21.970 --> 00:04:23.974 Often with differing practices

NOTE Confidence: 0.8763021

00:04:23.974 --> 00:04:25.477 with differing CHRS,

NOTE Confidence: 0.8763021

00:04:25.480 --> 00:04:28.702 or before that just paper records

NOTE Confidence: 0.8763021

00:04:28.702 --> 00:04:32.310 and try and put these data

NOTE Confidence: 0.8763021

00:04:32.310 --> 00:04:35.675 together in some meaningful way.

NOTE Confidence: 0.8763021

00:04:35.680 --> 00:04:38.270 So you can make large scale inferences

NOTE Confidence: 0.8763021

00:04:38.270 --> 00:04:40.844 and this goes back to what IRA

NOTE Confidence: 0.8763021

00:04:40.844 --> 00:04:42.932 said initially about how even as

NOTE Confidence: 0.8404903

00:04:43.011 --> 00:04:45.395 a biobank we need to be one of

NOTE Confidence: 0.8404903

00:04:45.395 --> 00:04:47.690 the network of biomax and this is

NOTE Confidence: 0.8404903

00:04:47.690 --> 00:04:49.796 very much what we've been trying

NOTE Confidence: 0.8404903

00:04:49.796 --> 00:04:52.183 to do in a disease focused way,

NOTE Confidence: 0.8404903

00:04:52.190 --> 00:04:54.212 and so this project has been

NOTE Confidence: 0.8404903

00:04:54.212 --> 00:04:55.980 aiming to do exactly that,

NOTE Confidence: 0.8404903

00:04:55.980 --> 00:04:58.374 and then from these large scale data,

NOTE Confidence: 0.8404903

00:04:58.380 --> 00:05:00.417 try and see if there are subsets

NOTE Confidence: 0.8404903

00:05:00.417 --> 00:05:02.353 of patients who seem to respond

NOTE Confidence: 0.8404903

00:05:02.353 --> 00:05:04.684 differently to therapy who seem to have

NOTE Confidence: 0.8404903

00:05:04.753 --> 00:05:07.118 different outcomes that is predictable.

NOTE Confidence: 0.8404903

00:05:07.120 --> 00:05:09.610 And that might maybe mechanistic because

NOTE Confidence: 0.8404903

00:05:09.610 --> 00:05:12.870 the problem is like most complex diseases,

NOTE Confidence: 0.8404903

00:05:12.870 --> 00:05:15.516 Ms is extremely heterogeneous at diagnosis.

NOTE Confidence: 0.8404903

00:05:15.520 --> 00:05:18.022 There is effectively no prognosis that

NOTE Confidence: 0.8404903

00:05:18.022 --> 00:05:22.013 one can give to a patient 'cause they may

NOTE Confidence: 0.8404903

00:05:22.013 --> 00:05:24.800 be severely disabled within five years,

NOTE Confidence: 0.8404903

00:05:24.800 --> 00:05:27.775 or they may be just fine 20

NOTE Confidence: 0.8404903

00:05:27.775 --> 00:05:29.660 years down the line,

NOTE Confidence: 0.8404903

00:05:29.660 --> 00:05:32.078 it's very hard to tell anything

NOTE Confidence: 0.8404903

00:05:32.078 --> 00:05:34.520 to tell a patient anything,

NOTE Confidence: 0.8404903

00:05:34.520 --> 00:05:37.856 and that is a major issue.

NOTE Confidence: 0.8404903

00:05:37.860 --> 00:05:40.803 And So what we've been doing is we have

NOTE Confidence: 0.8404903

00:05:40.803 --> 00:05:43.449 been warehousing both clinical and

NOTE Confidence: 0.8404903

00:05:43.449 --> 00:05:46.254 genetic data across these collections.

NOTE Confidence: 0.8404903

00:05:46.260 --> 00:05:49.214 And what I'm showing you so far

NOTE Confidence: 0.8404903

00:05:49.214 --> 00:05:51.560 is the progress we've done.

NOTE Confidence: 0.8404903

00:05:51.560 --> 00:05:54.206 We've made with the genetic data,

NOTE Confidence: 0.8404903

00:05:54.210 --> 00:05:57.563 which is about 45,000 Ms patients across

NOTE Confidence: 0.8404903

00:05:57.563 --> 00:06:01.177 10 centers and 26,000 controls to date.

NOTE Confidence: 0.8404903

00:06:01.180 --> 00:06:03.346 And this by itself has been

NOTE Confidence: 0.8404903

00:06:03.346 --> 00:06:04.790 a fairly major nightmare,

NOTE Confidence: 0.8404903

00:06:04.790 --> 00:06:07.798 not least of which has been the paperwork

NOTE Confidence: 0.8404903

00:06:07.798 --> 00:06:10.291 becauses the GDP are the privacy law

NOTE Confidence: 0.8404903

00:06:10.291 --> 00:06:12.730 that is come into effect in Europe,

NOTE Confidence: 0.8404903

00:06:12.730 --> 00:06:15.834 has really done a number of this on

NOTE Confidence: 0.8404903

00:06:15.834 --> 00:06:18.726 this and we've had like a major.

NOTE Confidence: 0.8404903

00:06:18.730 --> 00:06:22.500 It took us a year and a half to unwind

NOTE Confidence: 0.8404903

00:06:22.602 --> 00:06:25.677 the legal implications of that,

NOTE Confidence: 0.8404903

00:06:25.680 --> 00:06:28.050 but these are real issues that

NOTE Confidence: 0.8404903

00:06:28.050 --> 00:06:31.860 will have to be faced when we think

NOTE Confidence: 0.8404903

00:06:31.860 --> 00:06:34.004 about federations of biobanks,

NOTE Confidence: 0.8404903

00:06:34.010 --> 00:06:37.244 or of case control cohorts across places,

NOTE Confidence: 0.8404903

00:06:37.250 --> 00:06:40.946 and we're also trying to Unite clinical data.

NOTE Confidence: 0.8404903

00:06:40.950 --> 00:06:43.911 We have about 60,000 patients worth of

NOTE Confidence: 0.8404903

00:06:43.911 --> 00:06:46.292 clinical data with different amounts

NOTE Confidence: 0.8404903

00:06:46.292 --> 00:06:48.887 of data for different patients.

NOTE Confidence: 0.8404903

00:06:48.890 --> 00:06:51.426 And we are still trying to resolve those,

NOTE Confidence: 0.8404903

00:06:51.430 --> 00:06:53.509 and ultimately what we want to be

NOTE Confidence: 0.8404903

00:06:53.509 --> 00:06:56.010 able to do is to build predictors

NOTE Confidence: 0.8404903

00:06:56.010 --> 00:06:58.320 of outcomes which we have captured

NOTE Confidence: 0.8404903

00:06:58.388 --> 00:07:00.548 in the clinical data using both.

NOTE Confidence: 0.8404903

00:07:00.550 --> 00:07:03.366 Other data that we have on the data

NOTE Confidence: 0.8404903

00:07:03.366 --> 00:07:06.670 on the patients and the genetic data.

NOTE Confidence: 0.8404903

00:07:06.670 --> 00:07:09.090 Just the genetic data,

NOTE Confidence: 0.8404903

00:07:09.090 --> 00:07:12.720 which is a fairly standard platform.

NOTE Confidence: 0.8404903

00:07:12.720 --> 00:07:13.695 Gina type this.

NOTE Confidence: 0.8404903

00:07:13.695 --> 00:07:15.645 The vast majority of this is

NOTE Confidence: 0.8404903

00:07:15.645 --> 00:07:17.220 genotyping relevant sequencing.

NOTE Confidence: 0.8404903

00:07:17.220 --> 00:07:18.720 There are different platforms

NOTE Confidence: 0.8404903

00:07:18.720 --> 00:07:20.595 on which one can genotype,

NOTE Confidence: 0.8404903

00:07:20.600 --> 00:07:22.100 but they're fairly standard.

NOTE Confidence: 0.8404903

00:07:22.100 --> 00:07:24.350 It's a fairly homogeneous data type.

NOTE Confidence: 0.8404903

00:07:24.350 --> 00:07:26.870 It has taken us about a year to put

NOTE Confidence: 0.8404903

00:07:26.870 --> 00:07:28.889 these data together because there

NOTE Confidence: 0.8404903

00:07:28.889 --> 00:07:31.391 is a pretty significant amount of

NOTE Confidence: 0.8404903

00:07:31.460 --> 00:07:33.962 work involved in actually Q seeing

NOTE Confidence: 0.8404903

00:07:33.962 --> 00:07:35.213 and processing data,

NOTE Confidence: 0.8404903

00:07:35.220 --> 00:07:37.470 and so just that has been

NOTE Confidence: 0.8404903

00:07:37.470 --> 00:07:38.595 a nontrivial challenge.

NOTE Confidence: 0.8404903

00:07:38.600 --> 00:07:40.470 We have now overcome this.

NOTE Confidence: 0.8404903

00:07:40.470 --> 00:07:42.828 We now have this unified collection.

NOTE Confidence: 0.8404903

00:07:42.830 --> 00:07:44.588 Unlike most case control cohorts where

NOTE Confidence: 0.8404903

00:07:44.588 --> 00:07:46.869 we do genome wide Association studies,

NOTE Confidence: 0.8404903

00:07:46.870 --> 00:07:48.865 we actually have deeper information

NOTE Confidence: 0.8404903

00:07:48.865 --> 00:07:50.860 rather than just whether someone

NOTE Confidence: 0.8404903

00:07:50.920 --> 00:07:52.270 is a case or a control,

NOTE Confidence: 0.8404903

00:07:52.270 --> 00:07:54.727 and we're now trying to put these

NOTE Confidence: 0.8404903

00:07:54.727 --> 00:07:57.167 data together so this the next couple

NOTE Confidence: 0.8404903

00:07:57.167 --> 00:07:59.851 of years I think are going to be

NOTE Confidence: 0.8404903

00:07:59.851 --> 00:08:02.056 very exciting here as we try and

NOTE Confidence: 0.8404903

00:08:02.056 --> 00:08:04.445 figure out if there are predictors

NOTE Confidence: 0.8404903

00:08:04.445 --> 00:08:06.510 for both outcomes and treatment

NOTE Confidence: 0.86289924

00:08:06.580 --> 00:08:08.080 outcomes in treatment

NOTE Confidence: 0.86289924

00:08:08.080 --> 00:08:10.080 responses in these patients.

NOTE Confidence: 0.86289924

00:08:10.080 --> 00:08:13.419 What we have so far in the clinical data,

NOTE Confidence: 0.86289924

00:08:13.420 --> 00:08:16.017 I will show you there very briefly.

NOTE Confidence: 0.86289924

00:08:16.020 --> 00:08:18.764 These are all sorts of lifestyle and clinical

NOTE Confidence: 0.86289924

00:08:18.764 --> 00:08:21.210 data that seem to segregate patients.

NOTE Confidence: 0.86289924

00:08:21.210 --> 00:08:23.382 This is a principle components analysis

NOTE Confidence: 0.86289924

00:08:23.382 --> 00:08:25.290 of our entire phenotype matrix,

NOTE Confidence: 0.86289924

00:08:25.290 --> 00:08:27.887 and you can see that there are.

NOTE Confidence: 0.8717199

00:08:30.000 --> 00:08:32.400 Phenotypes seem to correlate with age.

NOTE Confidence: 0.8717199

00:08:32.400 --> 00:08:35.694 In the top left you can see that the

NOTE Confidence: 0.8717199

00:08:35.694 --> 00:08:38.220 dominant trend in our patients is

NOTE Confidence: 0.8717199

00:08:38.220 --> 00:08:41.600 actually age and that kind of makes sense.

NOTE Confidence: 0.8717199

00:08:41.600 --> 00:08:43.200 It's a progressive disease.

NOTE Confidence: 0.8717199

00:08:43.200 --> 00:08:44.800 It's a lifelong disease.

NOTE Confidence: 0.8717199

00:08:44.800 --> 00:08:47.600 Older individuals tend to have more symptoms,

NOTE Confidence: 0.8717199

00:08:47.600 --> 00:08:50.800 and you can definitely see things like that,

NOTE Confidence: 0.8717199

00:08:50.800 --> 00:08:53.600 but that's an important confounder as well.

NOTE Confidence: 0.8717199

00:08:53.600 --> 00:08:57.002 Age is an important aspect of disease

NOTE Confidence: 0.8717199

00:08:57.002 --> 00:09:00.179 that we often don't talk about.

NOTE Confidence: 0.8717199

00:09:00.180 --> 00:09:02.365 We see more interesting things

NOTE Confidence: 0.8717199

00:09:02.365 --> 00:09:05.481 if you look at that second panel

NOTE Confidence: 0.8717199

00:09:05.481 --> 00:09:08.407 from from the left on the top.

NOTE Confidence: 0.8717199

00:09:08.410 --> 00:09:09.706 There's a correlation with

NOTE Confidence: 0.8717199

00:09:09.706 --> 00:09:10.678 natural UV exposure,

NOTE Confidence: 0.8717199

00:09:10.680 --> 00:09:13.146 'cause it turns out the vitamin D is actually

NOTE Confidence: 0.8717199

00:09:13.146 --> 00:09:15.537 an important component of Ms Pathology.

NOTE Confidence: 0.8717199

00:09:15.540 --> 00:09:17.160 It is a risk factor.

NOTE Confidence: 0.8717199

00:09:17.160 --> 00:09:19.421 It appears to be causal in ways

NOTE Confidence: 0.8717199

00:09:19.421 --> 00:09:21.760 that we don't really understand.

NOTE Confidence: 0.8717199

00:09:21.760 --> 00:09:23.410 But there are lifestyle exposures

NOTE Confidence: 0.8717199

00:09:23.410 --> 00:09:25.746 like that as well and they are

NOTE Confidence: 0.8717199

00:09:25.746 --> 00:09:27.937 definitely coming out of the the data.

NOTE Confidence: 0.8717199

00:09:27.940 --> 00:09:29.560 We also see smoking behaviors.

NOTE Confidence: 0.8717199

00:09:29.560 --> 00:09:32.160 Gender is an important component and so on.

NOTE Confidence: 0.8717199

00:09:32.160 --> 00:09:34.239 So as we start pulling all of

NOTE Confidence: 0.8717199

00:09:34.239 --> 00:09:35.740 these clinical data together,

NOTE Confidence: 0.8717199

00:09:35.740 --> 00:09:37.365 we were getting patterns even

NOTE Confidence: 0.8717199

00:09:37.365 --> 00:09:38.340 from very simple.

NOTE Confidence: 0.82994473

00:09:40.490 --> 00:09:43.794 Views of data. This is like a very

NOTE Confidence: 0.82994473

00:09:43.794 --> 00:09:46.298 naive exploratory way to look at data,

NOTE Confidence: 0.82994473

00:09:46.300 --> 00:09:49.388 but we're seeing patterns even in that way,

NOTE Confidence: 0.82994473

00:09:49.390 --> 00:09:52.099 just for the remainder of the time.

NOTE Confidence: 0.82994473

00:09:52.100 --> 00:09:55.106 I'd like to switch for a second and tell

NOTE Confidence: 0.82994473

00:09:55.106 --> 00:09:58.079 you about a different project that is

NOTE Confidence: 0.82994473

00:09:58.079 --> 00:10:00.999 still quite similar in flavor I think,

NOTE Confidence: 0.82994473

00:10:01.000 --> 00:10:02.544 which is about epilepsy.

NOTE Confidence: 0.82994473

00:10:02.544 --> 00:10:03.702 Identifying predictors of

NOTE Confidence: 0.82994473

00:10:03.702 --> 00:10:05.168 psychiatric disease, and epilepsy.

NOTE Confidence: 0.82994473

00:10:05.168 --> 00:10:07.920 This is funded by the NINDS and it

NOTE Confidence: 0.82994473

00:10:07.995 --> 00:10:10.290 is a collaboration between Yale,

NOTE Confidence: 0.82994473

00:10:10.290 --> 00:10:11.092 Arhus University,

NOTE Confidence: 0.82994473

00:10:11.092 --> 00:10:12.696 Helsinki University and the.

NOTE Confidence: 0.82994473

00:10:12.700 --> 00:10:17.930 Rodents chew epilepsy is a.

NOTE Confidence: 0.82994473

00:10:17.930 --> 00:10:19.878 Basically it disease where

NOTE Confidence: 0.82994473

00:10:19.878 --> 00:10:22.313 of seizures in the brain.

NOTE Confidence: 0.82994473

00:10:22.320 --> 00:10:25.600 It is abnormal electrical activity.

NOTE Confidence: 0.82994473

00:10:25.600 --> 00:10:27.324 That is often repeated.

NOTE Confidence: 0.82994473

00:10:27.324 --> 00:10:31.349 You see 2 broad types of seizures on EG.

NOTE Confidence: 0.82994473

00:10:31.350 --> 00:10:34.116 You see either a generalized seizure

NOTE Confidence: 0.82994473

00:10:34.116 --> 00:10:37.291 pattern that takes up a large portion

NOTE Confidence: 0.82994473

00:10:37.291 --> 00:10:40.189 of a hemisphere or the entire brain,

NOTE Confidence: 0.82994473

00:10:40.190 --> 00:10:44.369 or you see very focal abnormal electrical

NOTE Confidence: 0.82994473

00:10:44.369 --> 00:10:48.160 activity in one area of the brain.

NOTE Confidence: 0.82994473

00:10:48.160 --> 00:10:48.658 Again,

NOTE Confidence: 0.82994473

00:10:48.658 --> 00:10:51.646 it is a common neurological disease

NOTE Confidence: 0.82994473

00:10:51.646 --> 00:10:54.980 about one and 26 people in the

NOTE Confidence: 0.82994473

00:10:54.980 --> 00:10:57.596 US have a diagnosis of epilepsy.

NOTE Confidence: 0.82994473

00:10:57.600 --> 00:10:59.960 It is a complex disease.

NOTE Confidence: 0.82994473

00:10:59.960 --> 00:11:02.840 There exist certain single gene forms

NOTE Confidence: 0.82994473

00:11:02.840 --> 00:11:06.566 of it that explain about 14% of cases,

NOTE Confidence: 0.82994473

00:11:06.566 --> 00:11:10.624 but the other 8586% is this more common

NOTE Confidence: 0.82994473

00:11:10.624 --> 00:11:13.870 complex form again polygenic many genes.

NOTE Confidence: 0.82994473

00:11:13.870 --> 00:11:14.292 Heritable,

NOTE Confidence: 0.82994473

00:11:14.292 --> 00:11:15.980 but not simply heritable.

NOTE Confidence: 0.8422435

00:11:18.660 --> 00:11:21.000 And what we've been doing has

NOTE Confidence: 0.8422435

00:11:21.000 --> 00:11:23.169 been working with some colleagues

NOTE Confidence: 0.8422435

00:11:23.169 --> 00:11:25.799 at Arhus University in Denmark.

NOTE Confidence: 0.8422435

00:11:25.800 --> 00:11:28.470 Like many of the Nordic countries,

NOTE Confidence: 0.8422435

00:11:28.470 --> 00:11:31.070 Denmark has an integrated.

NOTE Confidence: 0.8422435

00:11:31.070 --> 00:11:35.053 Our health care system for which records

NOTE Confidence: 0.8422435

00:11:35.053 --> 00:11:37.358 are completely available for research,

NOTE Confidence: 0.8422435

00:11:37.360 --> 00:11:39.665 so the population of Denmark

NOTE Confidence: 0.8422435

00:11:39.665 --> 00:11:41.509 is about 5,000,000 people.

NOTE Confidence: 0.8422435

00:11:41.510 --> 00:11:43.615 There are records roughly for

NOTE Confidence: 0.8422435

00:11:43.615 --> 00:11:45.720 about 2,000,000 people who have

NOTE Confidence: 0.8422435

00:11:45.794 --> 00:11:48.419 interactions with the hospital system.

NOTE Confidence: 0.8422435

00:11:48.420 --> 00:11:51.980 We we tend to limit this to people

NOTE Confidence: 0.8422435

00:11:51.980 --> 00:11:55.149 who've had interactions recently.

NOTE Confidence: 0.8422435

00:11:55.150 --> 00:11:58.828 By which I mean after 1981.

NOTE Confidence: 0.8422435

00:11:58.830 --> 00:12:01.255 Becauses people born after 1981

NOTE Confidence: 0.8422435

00:12:01.255 --> 00:12:03.680 also have blood spots stored

NOTE Confidence: 0.8422435

00:12:03.765 --> 00:12:05.990 in the Staten Serum Institute

NOTE Confidence: 0.8422435

00:12:05.990 --> 00:12:08.620 from which we can extract DNA.

NOTE Confidence: 0.8422435

00:12:08.620 --> 00:12:10.918 So you can do population level

NOTE Confidence: 0.8422435

00:12:10.918 --> 00:12:13.119 genetics based on the hospital

NOTE Confidence: 0.8422435

00:12:13.119 --> 00:12:16.069 registers across the entire population.

NOTE Confidence: 0.8422435

00:12:16.070 --> 00:12:19.150 And so we limited this to this

NOTE Confidence: 0.8422435

00:12:19.150 --> 00:12:22.860 and one of the things that we

NOTE Confidence: 0.8422435

00:12:22.860 --> 00:12:26.274 observed about four years ago now.

NOTE Confidence: 0.8422435

00:12:26.280 --> 00:12:30.382 Is that if you look at individuals

NOTE Confidence: 0.8422435

00:12:30.382 --> 00:12:33.640 with a diagnosis of epilepsy,

NOTE Confidence: 0.8422435

00:12:33.640 --> 00:12:37.570 you find a strong overrepresentation

NOTE Confidence: 0.8422435

00:12:37.570 --> 00:12:40.714 of mental illness diagnosis.

NOTE Confidence: 0.8422435

00:12:40.720 --> 00:12:41.869 In that population.

NOTE Confidence: 0.8422435

00:12:41.869 --> 00:12:44.960 So if you look right at the top,

NOTE Confidence: 0.8422435

00:12:44.960 --> 00:12:47.012 there's about 1.3 million people who

NOTE Confidence: 0.8422435

00:12:47.012 --> 00:12:49.959 do not have a diagnosis of epilepsy,

NOTE Confidence: 0.8422435

00:12:49.960 --> 00:12:51.400 and there are reference.

NOTE Confidence: 0.8422435

00:12:51.400 --> 00:12:54.031 And there's about 10 and a half

NOTE Confidence: 0.8422435

00:12:54.031 --> 00:12:56.401 thousand people who do have a

NOTE Confidence: 0.8422435

00:12:56.401 --> 00:12:58.818 diagnosis of epilepsy and they have

NOTE Confidence: 0.8422435

00:12:58.818 --> 00:13:01.122 somewhere between 1.4 and 1.6 fold.

NOTE Confidence: 0.8422435

00:13:01.130 --> 00:13:02.670 Higher rates of psychiatric

NOTE Confidence: 0.8422435

00:13:02.670 --> 00:13:03.440 illness diagnosis.

NOTE Confidence: 0.8422435

00:13:03.440 --> 00:13:04.976 These are all diagnosis

NOTE Confidence: 0.8422435

00:13:04.976 --> 00:13:06.128 from hospital registers.

NOTE Confidence: 0.8422435

00:13:06.130 --> 00:13:07.670 They're not necessarily strong,

NOTE Confidence: 0.8422435

00:13:07.670 --> 00:13:09.595 strongly followed by individual physician,

NOTE Confidence: 0.8422435

00:13:09.600 --> 00:13:13.100 so this is not a cohort, these are.

NOTE Confidence: 0.8422435

00:13:13.100 --> 00:13:16.075 Medical records and that's worth.

NOTE Confidence: 0.8422435

00:13:16.080 --> 00:13:18.820 Highlighting, however.

NOTE Confidence: 0.8422435

00:13:18.820 --> 00:13:21.040 Psychiatric illness is itself genetic.

NOTE Confidence: 0.8422435

00:13:21.040 --> 00:13:23.160 Again, it is complex.

NOTE Confidence: 0.8422435

00:13:23.160 --> 00:13:25.280 There have been many.

NOTE Confidence: 0.8422435

00:13:25.280 --> 00:13:27.616 Genetic studies of that and so is epilepsy.

NOTE Confidence: 0.8422435

00:13:27.620 --> 00:13:30.175 And So what we are trying to

NOTE Confidence: 0.8422435

00:13:30.175 --> 00:13:32.578 figure out is if we can ask.

NOTE Confidence: 0.8422435

00:13:32.580 --> 00:13:35.748 Does the epilepsy cause psychiatric illness,

NOTE Confidence: 0.8422435

00:13:35.750 --> 00:13:39.272 or are these both either independent

NOTE Confidence: 0.8422435

00:13:39.272 --> 00:13:43.019 effects or both effects of a

NOTE Confidence: 0.8422435

00:13:43.019 --> 00:13:44.957 shared underlying pathology?

NOTE Confidence: 0.8422435

00:13:44.960 --> 00:13:46.524 That's an interesting question,

NOTE Confidence: 0.8422435

00:13:46.524 --> 00:13:49.460 because we think we can then develop.

NOTE Confidence: 0.8422435

00:13:49.460 --> 00:13:53.858 Predictors for given.

NOTE Confidence: 0.8422435

00:13:53.860 --> 00:13:56.289 That you have a diagnosis of epilepsy.

NOTE Confidence: 0.8422435

00:13:56.290 --> 00:13:58.830 What is the probability that

NOTE Confidence: 0.8422435

00:13:58.830 --> 00:14:00.354 you actually develop?

NOTE Confidence: 0.8422435

00:14:00.360 --> 00:14:02.456 Psychiatric illness post epilepsy.

NOTE Confidence: 0.8422435

00:14:02.456 --> 00:14:06.944 It's not even we can see in the data

NOTE Confidence: 0.8422435

00:14:06.944 --> 00:14:09.863 that not everyone is at equal risk,

NOTE Confidence: 0.8422435

00:14:09.870 --> 00:14:12.048 but we do not yet understand

NOTE Confidence: 0.8422435

00:14:12.048 --> 00:14:14.000 who is a higher risk,

NOTE Confidence: 0.8422435

00:14:14.000 --> 00:14:16.045 and so we're taking everything

NOTE Confidence: 0.8422435

00:14:16.045 --> 00:14:18.090 from school records which exist

NOTE Confidence: 0.8422435

00:14:18.163 --> 00:14:20.461 in separate registers which can be

NOTE Confidence: 0.8422435

00:14:20.461 --> 00:14:22.578 cross referenced to the hospital

NOTE Confidence: 0.8422435

00:14:22.578 --> 00:14:24.638 registers to genetic profiles.

NOTE Confidence: 0.8422435

00:14:24.640 --> 00:14:27.725 Two prescription reimbursements to see

NOTE Confidence: 0.8422435

00:14:27.725 --> 00:14:30.810 whether people have refractory disease,

NOTE Confidence: 0.8422435

00:14:30.810 --> 00:14:34.445 or whether they've cycled through

NOTE Confidence: 0.8422435

00:14:34.445 --> 00:14:36.626 many antiepileptic medications.

NOTE Confidence: 0.8422435

00:14:36.630 --> 00:14:39.444 And we're trying to build these predictors,

NOTE Confidence: 0.8422435

00:14:39.450 --> 00:14:41.170 becauses it seems rather important

NOTE Confidence: 0.8422435

00:14:41.170 --> 00:14:43.414 to know who is at substantial

NOTE Confidence: 0.8422435

00:14:43.414 --> 00:14:45.694 additional risk given a diagnosis

NOTE Confidence: 0.8422435

00:14:45.694 --> 00:14:48.320 of epilepsy relative to the others.

NOTE Confidence: 0.8422435

00:14:48.320 --> 00:14:50.770 I will just finish with a small

NOTE Confidence: 0.8422435

00:14:50.770 --> 00:14:52.784 little vignettes of almost accidental

NOTE Confidence: 0.8422435

00:14:52.784 --> 00:14:55.460 findings that we've seen again looking

NOTE Confidence: 0.8422435

00:14:55.460 --> 00:14:58.018 in these registers because we have

NOTE Confidence: 0.8422435

00:14:58.018 --> 00:15:00.406 an entire population to look at.

NOTE Confidence: 0.91636133

00:15:02.470 --> 00:15:07.408 We observe that. People with epilepsy

NOTE Confidence: 0.91636133

00:15:07.408 --> 00:15:10.624 are more likely to have a mother with

NOTE Confidence: 0.91636133

00:15:10.624 --> 00:15:13.246 epilepsy than a father with epilepsy.

NOTE Confidence: 0.8610867

00:15:15.430 --> 00:15:17.628 For reasons that we do not understand,

NOTE Confidence: 0.8610867

00:15:17.630 --> 00:15:19.200 there exists this maternal effect.

NOTE Confidence: 0.8610867

00:15:19.200 --> 00:15:21.078 If you just see in red,

NOTE Confidence: 0.8610867

00:15:21.080 --> 00:15:24.368 there's about a 1 1/2 fold.

NOTE Confidence: 0.8610867

00:15:24.370 --> 00:15:25.550 Enrichment of.

NOTE Confidence: 0.8610867

00:15:25.550 --> 00:15:28.500 Maternal epilepsy than paternal epilepsy.

NOTE Confidence: 0.8610867

00:15:28.500 --> 00:15:31.020 We're not sure if this is genetic

NOTE Confidence: 0.8610867

00:15:31.020 --> 00:15:33.427 or if something else is going on.

NOTE Confidence: 0.8610867

00:15:33.430 --> 00:15:35.536 This is a very unexpected finding.

NOTE Confidence: 0.8610867

00:15:35.540 --> 00:15:39.708 It's been reported at least once before in.

NOTE Confidence: 0.8610867

00:15:39.710 --> 00:15:41.446 In much smaller cohorts,

NOTE Confidence: 0.8610867

00:15:41.446 --> 00:15:44.537 and there's been a long standing dispute

NOTE Confidence: 0.8610867

00:15:44.537 --> 00:15:47.785 in the field about whether this is true,

NOTE Confidence: 0.8610867

00:15:47.790 --> 00:15:50.265 and across about 1.75 million

NOTE Confidence: 0.8610867

00:15:50.265 --> 00:15:52.245 people in Denmark weekend.

NOTE Confidence: 0.8610867

00:15:52.250 --> 00:15:54.686 Unequivocally see there is a sort of

NOTE Confidence: 0.8610867

00:15:54.686 --> 00:15:57.092 fairly meaningful increase in this risk and

NOTE Confidence: 0.8610867

00:15:57.092 --> 00:15:59.048 quite well underlies this maternal effect.

NOTE Confidence: 0.8610867

00:15:59.050 --> 00:16:01.802 We don't know, but it ties into our

NOTE Confidence: 0.8610867

00:16:01.802 --> 00:16:04.104 interest in *** bias in disease,

NOTE Confidence: 0.8610867

00:16:04.104 --> 00:16:05.856 and we're looking forward

NOTE Confidence: 0.8610867

00:16:05.856 --> 00:16:07.470 to following this up.

NOTE Confidence: 0.8610867

00:16:07.470 --> 00:16:09.798 So I want to just leave that there.

NOTE Confidence: 0.8610867

00:16:09.800 --> 00:16:12.285 Ask and I'll hand back to Nicole,

NOTE Confidence: 0.8610867

00:16:12.290 --> 00:16:14.234 who I think will introduce the

NOTE Confidence: 0.8610867

00:16:14.234 --> 00:16:16.213 next speaker or handle questions.