00:00:00.000 --> 00:00:05.364 Here and and then Karen take it from there.

00:00:05.370 --> 00:00:09.434 So may I call Doctor Tara Thompson Felix.

00:00:09.440 --> 00:00:10.484 Take it away.

00:00:10.484 --> 00:00:11.878 Doctor Thompson feelings, yeah,

00:00:11.878 --> 00:00:13.270 so good afternoon everyone.

00:00:13.270 --> 00:00:15.010 My name is Tara Thompson.

00:00:15.010 --> 00:00:17.954 Felix I'm one of the first year child

00:00:17.954 --> 00:00:20.104 Psychiatry Fellows so I actually met

00:00:20.104 --> 00:00:22.114 Doctor O'Donnell a few months ago

00:00:22.188 --> 00:00:24.467 on virtually in one of our breakout

00:00:24.467 --> 00:00:26.681 sessions and grand rounds and just

00:00:26.681 --> 00:00:28.924 heard a lot about his research who

00:00:28.924 --> 00:00:31.006 really got me excited because I've

00:00:31.006 --> 00:00:33.097 done some research and in utero,

1

NOTE Confidence: 0.8208883

00:00:33.100 --> 00:00:35.236 and epigenetics and I really wanted

NOTE Confidence: 0.8208883

00:00:35.236 --> 00:00:37.328 the opportunity to kind of explore

NOTE Confidence: 0.8208883

00:00:37.328 --> 00:00:39.018 that more so Doctor O'Donnell

NOTE Confidence: 0.8208883

00:00:39.020 --> 00:00:40.830 has been awesome and discussing.

NOTE Confidence: 0.8208883

00:00:40.830 --> 00:00:42.514 Potential projects with me.

NOTE Confidence: 0.8208883

00:00:42.514 --> 00:00:45.521 Since then an I am very excited

NOTE Confidence: 0.8208883

00:00:45.521 --> 00:00:48.293 to announce that I will be a

NOTE Confidence: 0.8208883

00:00:48.293 --> 00:00:50.078 PhD student in his lab.

NOTE Confidence: 0.8208883

00:00:50.080 --> 00:00:51.538 Starting in July,

NOTE Confidence: 0.8208883

00:00:51.538 --> 00:00:54.940 so I'm very excited to pass it

NOTE Confidence: 0.8208883

00:00:55.047 --> 00:00:58.287 along to Doctor Karen O'Donnell.

NOTE Confidence: 0.8208883

00:00:58.290 --> 00:00:59.756 Thank you.

NOTE Confidence: 0.8208883

00:00:59.756 --> 00:01:00.489 But

NOTE Confidence: 0.8083789

00:01:00.490 --> 00:01:01.978 congratulations again, Tara Anne.

NOTE Confidence: 0.8083789

00:01:01.978 --> 00:01:04.614 I'm very happy that you got into

NOTE Confidence: 0.8083789

00:01:04.614 --> 00:01:06.319 the program and delighted that

NOTE Confidence: 0.8083789

00:01:06.319 --> 00:01:08.240 you'll be working in the lab,

NOTE Confidence: 0.8083789

00:01:08.240 --> 00:01:10.824 and I'll be looking forward to when you

NOTE Confidence: 0.8083789

00:01:10.824 --> 00:01:13.158 were doing Grand Ryans showing some.

NOTE Confidence: 0.8083789

00:01:13.160 --> 00:01:14.920 Hopefully you're very interesting data,

NOTE Confidence: 0.8083789

00:01:14.920 --> 00:01:17.181 fetal exosomes and how they are shaped

NOTE Confidence: 0.8083789

00:01:17.181 --> 00:01:18.880 by exposure to prenatal adversity

NOTE Confidence: 0.8083789

00:01:18.880 --> 00:01:21.520 and how they can inform on child in

NOTE Confidence: 0.8083789

00:01:21.581 --> 00:01:23.716 your development and Doctor Martin.

NOTE Confidence: 0.8083789

00:01:23.720 --> 00:01:25.946 Thank you very much for that

NOTE Confidence: 0.8083789

00:01:25.946 --> 00:01:27.825 kind introduction for not giving

NOTE Confidence: 0.8083789

00:01:27.825 --> 00:01:30.107 the game away about where I am.

NOTE Confidence: 0.8083789

00:01:30.110 --> 00:01:32.726 Chrome I thought I would start by giving

NOTE Confidence: 0.8083789

00:01:32.726 --> 00:01:35.502 you a little bit of a background on

NOTE Confidence: 0.8083789

00:01:35.502 --> 00:01:38.295 how and where I've come from an end to

NOTE Confidence: 0.8083789

00:01:38.295 --> 00:01:40.601 end up here at the Child study Center

NOTE Confidence: 0.8083789

00:01:40.601 --> 00:01:42.498 and as Doctor Martin mentioned, an.

NOTE Confidence: 0.8083789

00:01:42.498 --> 00:01:44.346 If this is an experiment between

NOTE Confidence: 0.8083789

00:01:44.346 --> 00:01:45.984 the Department of Citrix and

NOTE Confidence: 0.8083789

00:01:45.984 --> 00:01:47.280 the Child Study Center,

NOTE Confidence: 0.8083789

00:01:47.280 --> 00:01:49.692 I'm more than happy to be a subject in

NOTE Confidence: 0.8083789

00:01:49.692 --> 00:01:51.890 this study because it's such a pleasure

NOTE Confidence: 0.8083789

00:01:51.890 --> 00:01:54.648 to be acting as a bridge between these

NOTE Confidence: 0.8083789

00:01:54.648 --> 00:01:56.814 two Fantastic Department's an so as

NOTE Confidence: 0.8083789

00:01:56.820 --> 00:01:58.728 Doctor Martin at knows I actually,

NOTE Confidence: 0.8083789

00:01:58.730 --> 00:02:01.138 I'm from the West coast of Ireland.

NOTE Confidence: 0.8083789

00:02:01.140 --> 00:02:02.480 A very small village,

NOTE Confidence: 0.8083789

00:02:02.480 --> 00:02:04.490 around 200 people an on the

NOTE Confidence: 0.8083789

00:02:04.567 --> 00:02:06.279 western coast of Ireland,

NOTE Confidence: 0.8083789

00:02:06.280 --> 00:02:09.208 very close to a small town called Belona.

NOTE Confidence: 0.8083789

00:02:09.210 --> 00:02:11.418 It's right on the Atlantic coast.

NOTE Confidence: 0.8083789

00:02:11.420 --> 00:02:13.667 The red line that you're seeing on

NOTE Confidence: 0.8083789

00:02:13.667 --> 00:02:16.204 this map is what's called the Wild

NOTE Confidence: 0.8083789

00:02:16.204 --> 00:02:18.936 Atlantic way that has a roadway that

NOTE Confidence: 0.8083789

00:02:18.936 --> 00:02:21.324 hugs the Atlantic coast of Ireland.

NOTE Confidence: 0.8083789

00:02:21.330 --> 00:02:23.661 And for those of you who are

NOTE Confidence: 0.8083789

00:02:23.661 --> 00:02:25.730 avid cyclists like Doctor Martin,

NOTE Confidence: 0.8083789

00:02:25.730 --> 00:02:27.812 it's 1500 miles and that you

NOTE Confidence: 0.8083789

00:02:27.812 --> 00:02:29.770 can cycle around our lender,

NOTE Confidence: 0.8083789

00:02:29.770 --> 00:02:32.086 driver and arnensee some fantastic sites.

NOTE Confidence: 0.8083789

00:02:32.090 --> 00:02:34.250 Such as the Stone Age settlement

NOTE Confidence: 0.8083789

00:02:34.250 --> 00:02:36.580 that's around 20 minutes from my home,

NOTE Confidence: 0.8083789

00:02:36.580 --> 00:02:37.876 Amore Dan Patrick head.

NOTE Confidence: 0.8083789

00:02:37.876 --> 00:02:40.624 I can tell you it took a long

NOTE Confidence: 0.8083789

00:02:40.624 --> 00:02:42.439 time to take this photograph.

NOTE Confidence: 0.8083789

00:02:42.440 --> 00:02:44.075 This isn't representative of the

NOTE Confidence: 0.8083789

00:02:44.075 --> 00:02:46.240 weather that we have in Ireland,

NOTE Confidence: 0.8083789

00:02:46.240 --> 00:02:46.573 Ann,

NOTE Confidence: 0.8083789

00:02:46.573 --> 00:02:48.571 but there are some beautiful scenes

NOTE Confidence: 0.8083789

00:02:48.571 --> 00:02:51.180 to be had in the West Coast of

NOTE Confidence: 0.8083789

00:02:51.180 --> 00:02:53.164 Ireland and up until very recently

NOTE Confidence: 0.8083789

00:02:53.164 --> 00:02:55.444 that would have been the most

NOTE Confidence: 0.8083789

00:02:55.444 --> 00:02:57.532 famous thing about where I'm from.

NOTE Confidence: 0.8083789

00:02:57.532 --> 00:02:58.788 This wonderful coastline and

NOTE Confidence: 0.8083789

00:02:58.788 --> 00:03:00.380 this Stone Age settlement.

NOTE Confidence: 0.8083789

00:03:00.380 --> 00:03:02.900 And but then Joe Biden got elected.

NOTE Confidence: 0.8083789

00:03:02.900 --> 00:03:06.156 And his ancestral home is around 20 minutes

NOTE Confidence: 0.8083789

00:03:06.156 --> 00:03:09.770 from my home in a small town called Belle.

NOTE Confidence: 0.8083789

00:03:09.770 --> 00:03:12.794 And all you can see is distant relatives

NOTE Confidence: 0.8083789

00:03:12.794 --> 00:03:15.417 celebrating when the election was announced,

NOTE Confidence: 0.8083789

00:03:15.420 --> 00:03:17.440 and mural that remains in

NOTE Confidence: 0.8083789

00:03:17.440 --> 00:03:19.460 our small town and were,

NOTE Confidence: 0.8083789

00:03:19.460 --> 00:03:20.663 among other works.

NOTE Confidence: 0.8083789

00:03:20.663 --> 00:03:23.910 So where everyone was very excited by this,

NOTE Confidence: 0.8083789

00:03:23.910 --> 00:03:26.190 this is actually the 2nd president

NOTE Confidence: 0.8083789

00:03:26.190 --> 00:03:28.222 that belona can lay claim

NOTE Confidence: 0.8083789

00:03:28.222 --> 00:03:29.966 to because Mary Robinson,

NOTE Confidence: 0.8083789

00:03:29.970 --> 00:03:32.388 the first woman President of Ireland,

NOTE Confidence: 0.8083789

00:03:32.390 --> 00:03:33.136 also hails.

NOTE Confidence: 0.8083789

00:03:33.136 --> 00:03:33.882 From Belona,

NOTE Confidence: 0.8083789

00:03:33.882 --> 00:03:35.747 so a little fun fact,

NOTE Confidence: 0.8083789

00:03:35.750 --> 00:03:37.510 but as Doctor Martin mentioned,

NOTE Confidence: 0.8083789

00:03:37.510 --> 00:03:39.514 I my trading didn't occur in

NOTE Confidence: 0.8083789

00:03:39.514 --> 00:03:42.017 Ireland and I had to travel a

NOTE Confidence: 0.8083789

00:03:42.017 --> 00:03:44.195 little bit further East for that,

NOTE Confidence: 0.8083789

00:03:44.200 --> 00:03:46.531 and that was to London where I

NOTE Confidence: 0.8083789

00:03:46.531 --> 00:03:48.284 completed my undergrad Masters and

NOTE Confidence: 0.8083789

00:03:48.284 --> 00:03:50.354 eventually my PhD where I worked

NOTE Confidence: 0.8083789

00:03:50.354 --> 00:03:52.570 with Vivek Glover and who's an

NOTE Confidence: 0.8083789

00:03:52.570 --> 00:03:54.390 expert and perinatal cycle biology

NOTE Confidence: 0.8083789

00:03:54.390 --> 00:03:56.300 and also with Tom O'Connor.

NOTE Confidence: 0.8083789

00:03:56.300 --> 00:03:58.610 Andthat PhD was actually a little

NOTE Confidence: 0.80372703

00:03:58.679 --> 00:04:01.442 bit of an experiment at the time as well.

NOTE Confidence: 0.80372703

00:04:01.450 --> 00:04:03.700 It was in an NIH funded.

NOTE Confidence: 0.80372703

00:04:03.700 --> 00:04:06.262 PhD occurring in London using the Avon

NOTE Confidence: 0.80372703

00:04:06.262 --> 00:04:08.708 Longitudinal Study of Parents and Children,

NOTE Confidence: 0.80372703

00:04:08.710 --> 00:04:10.762 which is along the Tunal perspective

NOTE Confidence: 0.80372703

00:04:10.762 --> 00:04:12.611 cohort of around 15,000 pregnancies

NOTE Confidence: 0.80372703

00:04:12.611 --> 00:04:14.721 where these children have been

NOTE Confidence: 0.80372703

00:04:14.721 --> 00:04:16.409 followed up continuously there,

NOTE Confidence: 0.80372703

00:04:16.410 --> 00:04:18.330 now approaching their 30s themselves,

NOTE Confidence: 0.80372703

00:04:18.330 --> 00:04:20.260 having children of their own,

NOTE Confidence: 0.80372703

00:04:20.260 --> 00:04:22.710 and I'll talk to you a little

NOTE Confidence: 0.80372703

00:04:22.710 --> 00:04:24.880 bit about that cohort today.

NOTE Confidence: 0.80372703

00:04:24.880 --> 00:04:26.308 Now following my PhD,

NOTE Confidence: 0.80372703

00:04:26.308 --> 00:04:28.942 I moved back out West but much

NOTE Confidence: 0.80372703

00:04:28.942 --> 00:04:31.414 further West than where I'm from.

NOTE Confidence: 0.80372703

00:04:31.420 --> 00:04:33.405 An ended up at McGill

NOTE Confidence: 0.80372703

00:04:33.405 --> 00:04:35.390 University where I completed it.

NOTE Confidence: 0.80372703

00:04:35.390 --> 00:04:37.760 Post doctoral fellowship with Michael Meaney,

NOTE Confidence: 0.80372703

00:04:37.760 --> 00:04:40.245 who many of you will know and

NOTE Confidence: 0.80372703

00:04:40.245 --> 00:04:42.694 it's really been a pioneer in

NOTE Confidence: 0.80372703

00:04:42.694 --> 00:04:44.864 the field of social epigenetics.

NOTE Confidence: 0.80372703

00:04:44.870 --> 00:04:47.240 So how the environment can shape

NOTE Confidence: 0.80372703

00:04:47.240 --> 00:04:48.820 variation in the epigenome?

NOTE Confidence: 0.80372703

00:04:48.820 --> 00:04:51.190 When I talk about the epigenome,

NOTE Confidence: 0.80372703

00:04:51.190 --> 00:04:53.320 I'm talking about chemical marks

NOTE Confidence: 0.80372703

00:04:53.320 --> 00:04:55.843 or modifications that sit on or

NOTE Confidence: 0.80372703

00:04:55.843 --> 00:04:58.090 close to the genome that can change

9

NOTE Confidence: 0.80372703

00:04:58.090 --> 00:05:00.515 the way the genome functions and

NOTE Confidence: 0.80372703

00:05:00.515 --> 00:05:02.650 throughout all of my training.

NOTE Confidence: 0.80372703

00:05:02.650 --> 00:05:06.098 Really, what's been at the heart of my.

NOTE Confidence: 0.80372703

00:05:06.100 --> 00:05:06.465 Fascination,

NOTE Confidence: 0.80372703

00:05:06.465 --> 00:05:09.020 really with science is the idea that

NOTE Confidence: 0.80372703

00:05:09.020 --> 00:05:11.490 the early environment can shape health

NOTE Confidence: 0.80372703

00:05:11.490 --> 00:05:13.585 and disease across the lifespan.

NOTE Confidence: 0.80372703

00:05:13.590 --> 00:05:16.590 Ann and this notion or this idea has

NOTE Confidence: 0.80372703

00:05:16.590 --> 00:05:18.737 been described as the developmental

NOTE Confidence: 0.80372703

00:05:18.737 --> 00:05:21.824 origins of health and disease and which

NOTE Confidence: 0.80372703

00:05:21.899 --> 00:05:24.619 has led to a whole field of research.

NOTE Confidence: 0.80372703

00:05:24.620 --> 00:05:27.259 A SoC adore had society that was

NOTE Confidence: 0.80372703

00:05:27.259 --> 00:05:29.682 really an largely based on findings

NOTE Confidence: 0.80372703

00:05:29.682 --> 00:05:32.100 from the work of David Barker.

NOTE Confidence: 0.80372703

00:05:32.100 --> 00:05:32.844 In fact,

NOTE Confidence: 0.80372703

00:05:32.844 --> 00:05:36.550 it used to be referred to as the Barker.

NOTE Confidence: 0.80372703

00:05:36.550 --> 00:05:38.900 Hypothesis that and the fetal

NOTE Confidence: 0.80372703

00:05:38.900 --> 00:05:40.310 origins of disease,

NOTE Confidence: 0.80372703

00:05:40.310 --> 00:05:42.656 that the the origins of many

NOTE Confidence: 0.80372703

00:05:42.656 --> 00:05:45.285 types of disease could be traced

NOTE Confidence: 0.80372703

00:05:45.285 --> 00:05:47.740 back to the neutral environment

NOTE Confidence: 0.80372703

00:05:47.740 --> 00:05:49.848 and these observations initially

NOTE Confidence: 0.80372703

00:05:49.848 --> 00:05:52.060 stemmed from David's work,

NOTE Confidence: 0.80372703

00:05:52.060 --> 00:05:54.586 where he notice to parallel between

NOTE Confidence: 0.80372703

00:05:54.586 --> 00:05:56.857 high rates of infant mortality

NOTE Confidence: 0.80372703

00:05:56.857 --> 00:05:59.412 and subsequent rates of death

NOTE Confidence: 0.80372703

00:05:59.412 --> 00:06:01.456 from coronary heart disease,

NOTE Confidence: 0.80372703

00:06:01.460 --> 00:06:04.154 and these were largely in deprived

NOTE Confidence: 0.80372703

00:06:04.154 --> 00:06:06.700 areas in the United Kingdom.

NOTE Confidence: 0.80372703

00:06:06.700 --> 00:06:09.031 And what you're looking at here is

NOTE Confidence: 0.80372703

00:06:09.031 --> 00:06:11.130 the relationship of risk from death

NOTE Confidence: 0.80372703

00:06:11.130 --> 00:06:13.200 for death from coronary heart disease

NOTE Confidence: 0.80372703

00:06:13.200 --> 00:06:15.278 as a function of birth weight.

NOTE Confidence: 0.80372703

00:06:15.280 --> 00:06:16.990 I want David Barker noticed,

NOTE Confidence: 0.80372703

00:06:16.990 --> 00:06:19.144 was that lower birth weight was

NOTE Confidence: 0.80372703

00:06:19.144 --> 00:06:21.359 associated with an elevated or an

NOTE Confidence: 0.80372703

00:06:21.359 --> 00:06:23.513 increased risk from death from coronary

NOTE Confidence: 0.80372703

00:06:23.513 --> 00:06:25.567 heart disease before the age of 65,

NOTE Confidence: 0.80372703

00:06:25.570 --> 00:06:28.074 and you can see a greater decline in

NOTE Confidence: 0.80372703

00:06:28.074 --> 00:06:31.047 risk as we move to larger birth weights.

NOTE Confidence: 0.80372703

00:06:31.050 --> 00:06:32.422 These are birth weights

NOTE Confidence: 0.80372703

00:06:32.422 --> 00:06:34.137 expressed in pounds and answers,

NOTE Confidence: 0.80372703

00:06:34.140 --> 00:06:37.026 and then maybe a slight uptick.

NOTE Confidence: 0.80372703

00:06:37.030 --> 00:06:38.902 In at disease risk,

NOTE Confidence: 0.80372703

00:06:38.902 --> 00:06:40.774 and as I mentioned,

NOTE Confidence: 0.80372703

00:06:40.780 --> 00:06:43.454 this is really led to really an

NOTE Confidence: 0.80372703

00:06:43.454 --> 00:06:46.315 expansive literature on how the neutral

NOTE Confidence: 0.80372703

00:06:46.315 --> 00:06:48.507 environment can shape vulnerability

NOTE Confidence: 0.80372703

00:06:48.507 --> 00:06:50.151 for cardiovascular disease,

NOTE Confidence: 0.80372703

00:06:50.160 --> 00:06:53.526 and really a whole host of

NOTE Confidence: 0.80372703

00:06:53.526 --> 00:06:54.648 metabolic phenotypes.

NOTE Confidence: 0.80372703

00:06:54.650 --> 00:06:55.874 But of course,

NOTE Confidence: 0.80372703

00:06:55.874 --> 00:06:58.322 the question is if the cardiovascular

NOTE Confidence: 0.80372703

00:06:58.322 --> 00:07:01.297 system is so sensitive to the unusual

NOTE Confidence: 0.80372703

00:07:01.297 --> 00:07:03.450 environment into adversity in usual,

NOTE Confidence: 0.80372703

00:07:03.450 --> 00:07:05.090 what about the brain?

NOTE Confidence: 0.80372703

00:07:05.090 --> 00:07:08.057 And as we heard from Kartek last

NOTE Confidence: 0.80372703

00:07:08.057 --> 00:07:10.983 week and from Amanda study as well,

NOTE Confidence: 0.80372703

00:07:10.990 --> 00:07:12.985 we know that the prenatal

NOTE Confidence: 0.80372703

00:07:12.985 --> 00:07:14.980 environment can also shape variation

NOTE Confidence: 0.80372703

00:07:15.054 --> 00:07:16.858 in brain related phenotypes.

NOTE Confidence: 0.80372703

00:07:16.860 --> 00:07:18.114 So, for example,

NOTE Confidence: 0.80372703

00:07:18.114 --> 00:07:19.786 at the Dutch hunger,

NOTE Confidence: 0.80372703

00:07:19.790 --> 00:07:22.400 winter and the Holocaust have all

NOTE Confidence: 0.80372703

00:07:22.400 --> 00:07:24.140 been associated with increased

NOTE Confidence: 0.8285338

00:07:24.213 --> 00:07:25.368 risk for adverse.

NOTE Confidence: 0.8285338

00:07:25.370 --> 00:07:27.135 Mental health outcomes in the

NOTE Confidence: 0.8285338

00:07:27.135 --> 00:07:29.680 offspring and in the next generation,

NOTE Confidence: 0.8285338

00:07:29.680 --> 00:07:31.540 and these have largely been

NOTE Confidence: 0.8285338

00:07:31.540 --> 00:07:33.028 from retrospective studies where

NOTE Confidence: 0.8285338

00:07:33.028 --> 00:07:34.779 this evidence first emerged.

NOTE Confidence: 0.8285338

00:07:34.780 --> 00:07:36.999 And of course from our own work

NOTE Confidence: 0.8285338

00:07:36.999 --> 00:07:38.525 with the Avon Longitudinal

NOTE Confidence: 0.8285338

00:07:38.525 --> 00:07:41.045 Study of Parents and Children.

NOTE Confidence: 0.8285338

00:07:41.050 --> 00:07:43.042 What we found is that maternal

NOTE Confidence: 0.8285338

00:07:43.042 --> 00:07:44.370 prenatal anxiety and also

NOTE Confidence: 0.8285338

00:07:44.430 --> 00:07:46.149 maternal prenatal depression,

NOTE Confidence: 0.8285338

14

00:07:46.150 --> 00:07:47.894 associate's with an increased

NOTE Confidence: 0.8285338

00:07:47.894 --> 00:07:50.074 risk for adverse mental health

NOTE Confidence: 0.8285338

00:07:50.074 --> 00:07:52.067 outcomes in the child and what

NOTE Confidence: 0.8285338

00:07:52.067 --> 00:07:54.190 you're looking at here is the

NOTE Confidence: 0.8285338

00:07:54.190 --> 00:07:55.897 predicted population prevalence.

NOTE Confidence: 0.8285338

00:07:55.900 --> 00:07:58.618 Of a probable mental disorder at

NOTE Confidence: 0.8285338

00:07:58.618 --> 00:08:01.458 children from age 4 all the way

NOTE Confidence: 0.8285338

00:08:01.458 --> 00:08:04.562 up to age 13 an and what we can

NOTE Confidence: 0.8285338

00:08:04.562 --> 00:08:07.016 see is that those children born

NOTE Confidence: 0.8285338

00:08:07.016 --> 00:08:09.124 to women that experience high

NOTE Confidence: 0.8285338

00:08:09.124 --> 00:08:11.692 levels of anxiety in the prenatal

NOTE Confidence: 0.8285338

00:08:11.692 --> 00:08:13.332 period have approximately double

NOTE Confidence: 0.8285338

00:08:13.332 --> 00:08:16.430 the risk of ending up in the group

NOTE Confidence: 0.8285338

00:08:16.430 --> 00:08:18.662 that is likely to suffer from

NOTE Confidence: 0.8285338

00:08:18.662 --> 00:08:20.149 a probable mental disorder,

NOTE Confidence: 0.8285338

00:08:20.149 --> 00:08:22.732 and we see this elevated risk across

NOTE Confidence: 0.8285338

00:08:22.732 --> 00:08:24.950 childhood and into early adolescence,

NOTE Confidence: 0.8285338

00:08:24.950 --> 00:08:25.882 and indeed.

NOTE Confidence: 0.8285338

00:08:25.882 --> 00:08:27.746 As studies follow up,

NOTE Confidence: 0.8285338

00:08:27.750 --> 00:08:29.362 studies have been completed

NOTE Confidence: 0.8285338

00:08:29.362 --> 00:08:31.377 now into the early 20s,

NOTE Confidence: 0.8285338

00:08:31.380 --> 00:08:33.624 and Sean a similar pattern of

NOTE Confidence: 0.8285338

00:08:33.624 --> 00:08:35.582 Association between high rates of

NOTE Confidence: 0.8285338

00:08:35.582 --> 00:08:37.178 prenatal anxiety and depression

NOTE Confidence: 0.8285338

00:08:37.178 --> 00:08:39.173 and increase risk for adverse

NOTE Confidence: 0.8285338

00:08:39.236 --> 00:08:40.670 mental health outcomes.

NOTE Confidence: 0.8285338

00:08:40.670 --> 00:08:43.254 And I just want to point out that

NOTE Confidence: 0.8285338

00:08:43.254 --> 00:08:45.077 these effects are independent

NOTE Confidence: 0.8285338

00:08:45.077 --> 00:08:46.730 of socioeconomic status.

NOTE Confidence: 0.8285338

00:08:46.730 --> 00:08:49.474 So you may think that this may be

NOTE Confidence: 0.8285338

00:08:49.474 --> 00:08:51.257 confounded by maternal education

NOTE Confidence: 0.8285338

00:08:51.257 --> 00:08:52.790 or maternal age,

NOTE Confidence: 0.8285338

00:08:52.790 --> 00:08:54.810 or indeed taxol crowding or

NOTE Confidence: 0.8285338

00:08:54.810 --> 00:08:55.618 obstetric outcomes.

NOTE Confidence: 0.8285338

00:08:55.620 --> 00:08:56.532 Birth weight,

NOTE Confidence: 0.8285338

00:08:56.532 --> 00:08:57.444 gestational age.

NOTE Confidence: 0.8285338

00:08:57.444 --> 00:08:59.724 Because of the large sample

NOTE Confidence: 0.8285338

00:08:59.724 --> 00:09:01.270 size of this court,

NOTE Confidence: 0.8285338

00:09:01.270 --> 00:09:03.465 we can statistically control for

NOTE Confidence: 0.8285338

00:09:03.465 --> 00:09:05.660 the effects of those exposures,

NOTE Confidence: 0.8285338

00:09:05.660 --> 00:09:08.564 and we still see this independent

NOTE Confidence: 0.8285338

00:09:08.564 --> 00:09:11.150 Association with maternal prenatal anxiety.

NOTE Confidence: 0.8285338

00:09:11.150 --> 00:09:13.831 So for any of you that have

NOTE Confidence: 0.8285338

00:09:13.831 --> 00:09:15.720 heard me speak before,

NOTE Confidence: 0.8285338

00:09:15.720 --> 00:09:18.352 I always talk about 414 and 44 being

NOTE Confidence: 0.8285338

00:09:18.352 --> 00:09:21.717 one in four women that are likely to

NOTE Confidence: 0.8285338

00:09:21.717 --> 00:09:24.027 experience or struggle with their

NOTE Confidence: 0.8285338

00:09:24.027 --> 00:09:26.919 mental health in and around pregnancy.

NOTE Confidence: 0.8285338

00:09:26.920 --> 00:09:30.248 So I say one in four other estimates

NOTE Confidence: 0.8285338

00:09:30.248 --> 00:09:32.884 they went in five, one in six,

NOTE Confidence: 0.8285338

00:09:32.884 --> 00:09:35.180 and really what I think we're seeing

NOTE Confidence: 0.8285338

00:09:35.249 --> 00:09:37.709 from these epidemiological analysis,

NOTE Confidence: 0.8285338

00:09:37.710 --> 00:09:39.370 particularly the more recent

NOTE Confidence: 0.8285338

00:09:39.370 --> 00:09:40.200 epidemiological analysis,

NOTE Confidence: 0.8285338

00:09:40.200 --> 00:09:41.469 is increased rates.

NOTE Confidence: 0.8285338

00:09:41.469 --> 00:09:43.584 Of perinatal mental health problems.

NOTE Confidence: 0.8285338

00:09:43.590 --> 00:09:43.980 So,

NOTE Confidence: 0.8285338

00:09:43.980 --> 00:09:44.760 for example,

NOTE Confidence: 0.8285338

00:09:44.760 --> 00:09:47.100 Louise Howard Publishing in 2018 and

NOTE Confidence: 0.8285338

00:09:47.100 --> 00:09:49.860 one in four women struggling with their

NOTE Confidence: 0.8285338

00:09:49.860 --> 00:09:52.630 mental health in and around pregnancy.

NOTE Confidence: 0.8285338

00:09:52.630 --> 00:09:53.474 Rebecca Pearson,

NOTE Confidence: 0.8285338

00:09:53.474 --> 00:09:55.584 using the Avon Longitudinal Study

NOTE Confidence: 0.8285338

00:09:55.584 --> 00:09:58.234 of Parents and children using the

NOTE Confidence: 0.8285338

00:09:58.234 --> 00:10:00.424 second generation from that cohort.

NOTE Confidence: 0.8285338

00:10:00.430 --> 00:10:03.210 Showed a generational increase in

NOTE Confidence: 0.8285338

00:10:03.210 --> 00:10:05.990 rates of perinatal mental health

NOTE Confidence: 0.8285338

00:10:06.083 --> 00:10:09.473 problems with again one in four

NOTE Confidence: 0.8285338

00:10:09.473 --> 00:10:11.168 women experiencing perinatal

NOTE Confidence: 0.8285338

00:10:11.168 --> 00:10:13.170 mental health problems.

NOTE Confidence: 0.8285338

00:10:13.170 --> 00:10:15.683 So this is a common problem and

NOTE Confidence: 0.8285338

00:10:15.683 --> 00:10:17.644 what is challenging with this

NOTE Confidence: 0.8285338

00:10:17.644 --> 00:10:20.056 problem is that we're still not

NOTE Confidence: 0.8285338

00:10:20.056 --> 00:10:21.780 screening women effectively,

NOTE Confidence: 0.8285338

00:10:21.780 --> 00:10:24.090 and when we do screen women and

NOTE Confidence: 0.8285338

00:10:24.090 --> 00:10:25.805 they're still not receiving

NOTE Confidence: 0.8285338

00:10:25.805 --> 00:10:27.109 adequate treatment,

NOTE Confidence: 0.8285338

00:10:27.110 --> 00:10:30.008 so we know that around 25% of

NOTE Confidence: 0.8285338

00:10:30.008 --> 00:10:32.198 women who do experience perinatal

NOTE Confidence: 0.8285338

00:10:32.198 --> 00:10:33.950 mental health problems receive

NOTE Confidence: 0.8285338

00:10:34.019 --> 00:10:36.165 treatment and less than 5% of

NOTE Confidence: 0.8285338

00:10:36.165 --> 00:10:37.945 those women achieve remission

NOTE Confidence: 0.8285338

00:10:37.945 --> 00:10:39.725 or experience receive adequate

NOTE Confidence: 0.8285338

00:10:39.725 --> 00:10:41.814 treatment to reduce their symptoms

NOTE Confidence: 0.8285338

00:10:41.814 --> 00:10:43.398 down below clinical levels.

NOTE Confidence: 0.8285338

00:10:43.400 --> 00:10:46.100 So this is a common problem that we are

NOTE Confidence: 0.8285338

00:10:46.100 --> 00:10:49.130 not addressing sufficiently at the moment.

NOTE Confidence: 0.8285338

00:10:49.130 --> 00:10:51.416 It is also a costly problem,

NOTE Confidence: 0.8285338

00:10:51.420 --> 00:10:53.364 so we know that the per

NOTE Confidence: 0.8285338

00:10:53.364 --> 00:10:54.660 year costs of untreated

NOTE Confidence: 0.87315464

00:10:54.729 --> 00:10:56.934 perinatal mental health problems is

NOTE Confidence: 0.87315464

00:10:56.934 --> 00:10:59.830 around 14 billion US dollars per year,

NOTE Confidence: 0.87315464

00:10:59.830 --> 00:11:02.511 with around 40% of those costs attributed

NOTE Confidence: 0.87315464

00:11:02.511 --> 00:11:05.168 to the adverse effects on the child.

NOTE Confidence: 0.87315464

00:11:05.170 --> 00:11:07.468 So that's in the United States.

NOTE Confidence: 0.87315464

00:11:07.470 --> 00:11:10.094 What about the in the UK where the

NOTE Confidence: 0.87315464

00:11:10.094 --> 00:11:12.430 first cost estimate was produced?

NOTE Confidence: 0.87315464

00:11:12.430 --> 00:11:14.440 Well, we see that around.

NOTE Confidence: 0.87315464

00:11:14.440 --> 00:11:17.072 An 8 billion pounds is the cost

NOTE Confidence: 0.87315464

00:11:17.072 --> 00:11:19.164 associated with untreated paradata mental

NOTE Confidence: 0.87315464

00:11:19.164 --> 00:11:21.840 health problems in the United Kingdom,

NOTE Confidence: 0.87315464

00:11:21.840 --> 00:11:24.717 but in contrast to the United States,

NOTE Confidence: 0.87315464

00:11:24.720 --> 00:11:27.184 we see that 72% almost 3/4 of those

NOTE Confidence: 0.87315464

00:11:27.184 --> 00:11:29.786 costs are attributed to the adverse

NOTE Confidence: 0.87315464

00:11:29.786 --> 00:11:32.181 effects of untreated perinatal mental

NOTE Confidence: 0.87315464

00:11:32.181 --> 00:11:34.579 health problems on child outcomes,

NOTE Confidence: 0.87315464

00:11:34.580 --> 00:11:36.080 and you may ask,

NOTE Confidence: 0.87315464

00:11:36.080 --> 00:11:38.330 rightfully So what is the difference

NOTE Confidence: 0.87315464

00:11:38.403 --> 00:11:40.738 between these two cost estimates?

00:11:40.740 --> 00:11:44.970 Why is it 40% in the United States and 72%?

00:11:44.970 --> 00:11:47.184 In the United Kingdom or one

00:11:47.184 --> 00:11:49.483 of the explanations for that is

00:11:49.483 --> 00:11:51.358 because in the United States,

00:11:51.360 --> 00:11:53.230 costs were only calculated on

00:11:53.230 --> 00:11:55.500 child outcomes from zero to five,

00:11:55.500 --> 00:11:57.924 whereas in the United Kingdom costs

00:11:57.924 --> 00:12:00.010 were calculated from zero to 18.

00:12:00.010 --> 00:12:02.890 So I think you can appreciate that if

00:12:02.890 --> 00:12:05.991 we extend the follow up period in the

00:12:05.991 --> 00:12:08.288 United States that 40% an proportion

00:12:08.288 --> 00:12:10.941 of costs is likely to increase in

00:12:10.941 --> 00:12:13.508 addition to the total costs that have

00:12:13.508 --> 00:12:15.940 been reported from that cost analysis.

00:12:15.940 --> 00:12:18.640 In the United States.

00:12:18.640 --> 00:12:19.532 And of course,

NOTE Confidence: 0.87315464

00:12:19.532 --> 00:12:21.708 you may ask about what is the impact

NOTE Confidence: 0.87315464

00:12:21.708 --> 00:12:23.598 of the post Natal environment.

NOTE Confidence: 0.87315464

00:12:23.600 --> 00:12:24.431 And of course,

NOTE Confidence: 0.87315464

00:12:24.431 --> 00:12:26.370 we know that there is an effect

NOTE Confidence: 0.87315464

00:12:26.438 --> 00:12:28.248 of the post Natal environment,

NOTE Confidence: 0.87315464

00:12:28.250 --> 00:12:30.252 and in our studies from the Avon

NOTE Confidence: 0.87315464

00:12:30.252 --> 00:12:32.279 Longitudinal Study of Parents and Children,

NOTE Confidence: 0.87315464

00:12:32.280 --> 00:12:33.520 we see that perhaps,

NOTE Confidence: 0.87315464

00:12:33.520 --> 00:12:34.760 as you would expect,

NOTE Confidence: 0.87315464

00:12:34.760 --> 00:12:36.662 children that are exposed to high

NOTE Confidence: 0.87315464

00:12:36.662 --> 00:12:39.173 levels of anxiety in the pre and post

NOTE Confidence: 0.87315464

00:12:39.173 --> 00:12:41.305 Natal period are the children who do

NOTE Confidence: 0.87315464

00:12:41.305 --> 00:12:43.141 worse than children who are exposed

NOTE Confidence: 0.87315464

00:12:43.141 --> 00:12:45.252 to anxiety at one but not both.

NOTE Confidence: 0.87315464

00:12:45.252 --> 00:12:47.779 Time points end up somewhere in the middle.

NOTE Confidence: 0.87315464

00:12:47.780 --> 00:12:50.705 Now hasten to add, this is not a treatment.

NOTE Confidence: 0.87315464

00:12:50.710 --> 00:12:53.538 And study this is not an intervention.

NOTE Confidence: 0.87315464

00:12:53.540 --> 00:12:55.958 This is simply an epidemiological analysis,

NOTE Confidence: 0.87315464

00:12:55.960 --> 00:12:58.550 but I think it provides proof of

NOTE Confidence: 0.87315464

00:12:58.550 --> 00:13:01.457 principle that if we could pull down

NOTE Confidence: 0.87315464

00:13:01.457 --> 00:13:04.031 or reduce maternal symptoms of anxiety,

NOTE Confidence: 0.87315464

00:13:04.040 --> 00:13:06.060 ideally at both time points,

NOTE Confidence: 0.87315464

00:13:06.060 --> 00:13:08.080 we could improve child outcome.

NOTE Confidence: 0.8589383

00:13:10.380 --> 00:13:13.188 So again, just thinking about what are the

NOTE Confidence: 0.8589383

00:13:13.188 --> 00:13:15.267 consequences for untreated perinatal mental

NOTE Confidence: 0.8589383

00:13:15.267 --> 00:13:17.889 health problems on the next generation?

NOTE Confidence: 0.8589383

00:13:17.890 --> 00:13:21.458 Well, I showed you the effects on child

NOTE Confidence: 0.8589383

00:13:21.458 --> 00:13:24.210 outcomes from 4 to 13 years of age,

NOTE Confidence: 0.8589383

00:13:24.210 --> 00:13:26.180 but this is another study

NOTE Confidence: 0.8589383

00:13:26.180 --> 00:13:27.756 from the same cohort.

NOTE Confidence: 0.8589383

00:13:27.760 --> 00:13:30.394 the Avon Longitudinal Study of Parents

NOTE Confidence: 0.8589383

00:13:30.394 --> 00:13:33.421 and Children where they looked at the

NOTE Confidence: 0.8589383

00:13:33.421 --> 00:13:35.803 rates of prenatal depression in women

NOTE Confidence: 0.8589383

00:13:35.803 --> 00:13:38.606 that were born to ALS back moms who

NOTE Confidence: 0.8589383

00:13:38.606 --> 00:13:40.392 either didn't or did experience.

NOTE Confidence: 0.8589383

00:13:40.392 --> 00:13:41.174 Prenatal depression,

NOTE Confidence: 0.8589383

00:13:41.174 --> 00:13:45.510 and so when we look at the daughters of women

NOTE Confidence: 0.8589383

00:13:45.510 --> 00:13:47.905 who didn't experience prenatal depression,

NOTE Confidence: 0.8589383

00:13:47.910 --> 00:13:50.908 we see that around 16% of those

NOTE Confidence: 0.8589383

00:13:50.908 --> 00:13:53.362 women who want to experience prenatal

NOTE Confidence: 0.8589383

00:13:53.362 --> 00:13:55.760 depression in their own pregnancies.

NOTE Confidence: 0.8589383

00:13:55.760 --> 00:13:58.434 So what about the daughters from women

NOTE Confidence: 0.8589383

00:13:58.434 --> 00:14:00.989 who did experience prenatal depression?

NOTE Confidence: 0.8589383

00:14:00.990 --> 00:14:04.428 Or 54% of those women went on to experience

NOTE Confidence: 0.8589383

00:14:04.428 --> 00:14:07.530 prenatal depression in their own pregnancies.

NOTE Confidence: 0.8589383

00:14:07.530 --> 00:14:11.290 So I think you can begin to appreciate.

NOTE Confidence: 0.8589383

00:14:11.290 --> 00:14:13.732 Add there can be marked intergenerational

NOTE Confidence: 0.8589383

00:14:13.732 --> 00:14:15.846 effects of exposure to prenatal

NOTE Confidence: 0.8589383

00:14:15.846 --> 00:14:18.366 depression and this makes it critically

NOTE Confidence: 0.8589383

00:14:18.366 --> 00:14:20.796 important that we try to support

NOTE Confidence: 0.8589383

00:14:20.796 --> 00:14:22.641 pregnant women and their mental

NOTE Confidence: 0.8589383

00:14:22.641 --> 00:14:24.992 health both for the pregnant woman's,

NOTE Confidence: 0.8589383

00:14:24.992 --> 00:14:27.007 all mental and physical health,

NOTE Confidence: 0.8589383

00:14:27.010 --> 00:14:30.292 but also to potentially mitigate the

NOTE Confidence: 0.8589383

00:14:30.292 --> 00:14:32.480 effects of this intergenerational

NOTE Confidence: 0.8589383

00:14:32.559 --> 00:14:34.200 transmission of risk.

NOTE Confidence: 0.8589383

00:14:34.200 --> 00:14:36.540 But there are some unanswered questions

NOTE Confidence: 0.8589383

00:14:36.540 --> 00:14:39.802 and many of you will be looking at and

NOTE Confidence: 0.8589383

00:14:39.802 --> 00:14:42.185 some of the slides that I presented

NOTE Confidence: 0.8589383

00:14:42.185 --> 00:14:44.905 in some of the data that I presented

NOTE Confidence: 0.8589383

00:14:44.910 --> 00:14:46.585 and thinking about the advances

NOTE Confidence: 0.8589383

00:14:46.585 --> 00:14:48.260 that we've made in characterizing

NOTE Confidence: 0.8589383

00:14:48.312 --> 00:14:49.908 genetic variation and thinking,

NOTE Confidence: 0.8589383

00:14:49.910 --> 00:14:50.288 well,

NOTE Confidence: 0.8589383

00:14:50.288 --> 00:14:52.178 isn't this just all confounded

NOTE Confidence: 0.8589383

00:14:52.178 --> 00:14:53.690 by underlying genetic propensity

NOTE Confidence: 0.8589383

00:14:53.754 --> 00:14:55.454 for psychiatric disorders and and

NOTE Confidence: 0.8589383

00:14:55.454 --> 00:14:57.542 there have been many studies that

NOTE Confidence: 0.8589383

00:14:57.542 --> 00:14:59.187 have attempted to address this,

NOTE Confidence: 0.8589383

00:14:59.190 --> 00:14:59.918 perhaps indirectly,

NOTE Confidence: 0.8589383

00:14:59.918 --> 00:15:02.466 and perhaps the most well established or

NOTE Confidence: 0.8589383

00:15:02.466 --> 00:15:04.970 well known paper to address this question.

NOTE Confidence: 0.8589383

00:15:04.970 --> 00:15:07.994 Was at this study by Hanigan and

NOTE Confidence: 0.8589383

00:15:07.994 --> 00:15:10.476 colleagues based in the mobile

NOTE Confidence: 0.8589383

00:15:10.476 --> 00:15:13.221 quarter large Norwegian study of

NOTE Confidence: 0.8589383

00:15:13.221 --> 00:15:15.450 around 30,000 pregnant women,

NOTE Confidence: 0.8589383

00:15:15.450 --> 00:15:19.178 Ann and they used a children of children

NOTE Confidence: 0.8589383

00:15:19.178 --> 00:15:22.440 and sibling children of Twins design.

NOTE Confidence: 0.8589383

00:15:22.440 --> 00:15:25.116 Basically it's a twin study that

NOTE Confidence: 0.8589383

00:15:25.116 --> 00:15:27.976 looks at the offspring and their

NOTE Confidence: 0.8589383

00:15:27.976 --> 00:15:30.451 conclusion was that a genetic

NOTE Confidence: 0.8589383

00:15:30.451 --> 00:15:32.600 factor that explained relatedness

NOTE Confidence: 0.8589383

00:15:32.600 --> 00:15:35.505 between Twins and siblings was.

NOTE Confidence: 0.8589383

00:15:35.510 --> 00:15:38.108 The explanation for the effects of

NOTE Confidence: 0.8589383

00:15:38.108 --> 00:15:40.460 prenatal depression on child outcome.

NOTE Confidence: 0.8589383

00:15:40.460 --> 00:15:42.992 So they concluded that the entire

NOTE Confidence: 0.8589383

00:15:42.992 --> 00:15:44.680 fetal origins hypothesis was

NOTE Confidence: 0.8589383

00:15:44.755 --> 00:15:47.175 confounded by genetic variation using

NOTE Confidence: 0.8589383

00:15:47.175 --> 00:15:49.595 an indirect assessment of genetic

NOTE Confidence: 0.8589383

00:15:49.665 --> 00:15:51.710 variation using a twin design.

NOTE Confidence: 0.8589383

00:15:51.710 --> 00:15:54.608 So we wanted to revisit this question

NOTE Confidence: 0.8589383

00:15:54.608 --> 00:15:57.627 to really ask and provide a more

NOTE Confidence: 0.8589383

00:15:57.627 --> 00:15:59.737 direct test of this hypothesis

NOTE Confidence: 0.8589383

00:15:59.737 --> 00:16:03.225 as to whether or not there was

NOTE Confidence: 0.8589383

00:16:03.225 --> 00:16:05.209 confounding by underlying genetic

NOTE Confidence: 0.8589383

00:16:05.210 --> 00:16:07.430 propensity or genetic vulnerability.

NOTE Confidence: 0.8589383

00:16:07.430 --> 00:16:10.205 For adverse mental health outcomes

NOTE Confidence: 0.8589383

00:16:10.205 --> 00:16:13.425 now many of you will have heard from

NOTE Confidence: 0.8589383

00:16:13.425 --> 00:16:15.720 our recent ground round sessions.

NOTE Confidence: 0.8589383

00:16:15.720 --> 00:16:18.396 The use of polygenic risk scores

NOTE Confidence: 0.8589383

00:16:18.396 --> 00:16:21.152 to capture common variation that is

NOTE Confidence: 0.8589383

00:16:21.152 --> 00:16:22.936 associated with psychiatric disorders

NOTE Confidence: 0.8589383

00:16:22.936 --> 00:16:26.162 and the use of these genetic tools

NOTE Confidence: 0.8589383

00:16:26.162 --> 00:16:28.886 has really an been greatly facilitated

NOTE Confidence: 0.8589383

00:16:28.886 --> 00:16:31.216 by these incredibly large genome

NOTE Confidence: 0.8589383

00:16:31.216 --> 00:16:33.092 wide Association studies largely

NOTE Confidence: 0.8589383

00:16:33.092 --> 00:16:35.431 conducted by the Psychiatric Genomics

NOTE Confidence: 0.8589383

00:16:35.431 --> 00:16:37.215 Consortium where we have.

NOTE Confidence: 0.8589383

00:16:37.220 --> 00:16:39.788 10s or hundreds of thousands of

NOTE Confidence: 0.8589383

00:16:39.788 --> 00:16:41.914 individuals with a psychiatric disorder

NOTE Confidence: 0.8589383

00:16:41.914 --> 00:16:44.329 and where we look at the snips,

NOTE Confidence: 0.8589383

00:16:44.330 --> 00:16:47.042 the genetic variants that are associated

NOTE Confidence: 0.8589383

00:16:47.042 --> 00:16:48.850 with the psychiatric disorder

NOTE Confidence: 0.8720987

00:16:48.916 --> 00:16:50.812 and that provides us with an

NOTE Confidence: 0.8720987

00:16:50.812 --> 00:16:52.964 effect size for that snip and

NOTE Confidence: 0.8720987

00:16:52.964 --> 00:16:54.600 risk of psychiatric disorder.

NOTE Confidence: 0.8720987

00:16:54.600 --> 00:16:57.624 Now what we can do is take those

NOTE Confidence: 0.8720987

00:16:57.624 --> 00:16:59.873 effect sizes and we can count

NOTE Confidence: 0.8720987

00:16:59.873 --> 00:17:02.533 up and using our own data using

NOTE Confidence: 0.8720987

00:17:02.533 --> 00:17:05.269 genetic data from our own court,

NOTE Confidence: 0.8720987

00:17:05.270 --> 00:17:08.119 we can count up the number of.

NOTE Confidence: 0.8720987

00:17:08.120 --> 00:17:10.766 Risk snips that an individual carries,

NOTE Confidence: 0.8720987

00:17:10.770 --> 00:17:12.210 and we can wait.

NOTE Confidence: 0.8720987

00:17:12.210 --> 00:17:14.907 Each one of those snips by the

NOTE Confidence: 0.8720987

00:17:14.907 --> 00:17:17.571 effect size that has been derived

NOTE Confidence: 0.8720987

00:17:17.571 --> 00:17:20.504 from these very large scale genome

NOTE Confidence: 0.8720987

00:17:20.504 --> 00:17:23.019 wide Association studies and what

NOTE Confidence: 0.8720987

00:17:23.019 --> 00:17:26.000 you get is a simple summary score

NOTE Confidence: 0.8720987

00:17:26.000 --> 00:17:27.576 that reflects an individual's

NOTE Confidence: 0.8720987

00:17:27.576 --> 00:17:29.567 genetic vulnerability for adverse

NOTE Confidence: 0.8720987

00:17:29.567 --> 00:17:31.100 mental health outcomes,

NOTE Confidence: 0.8720987

00:17:31.100 --> 00:17:33.310 whether it be ADHD, schizophrenia,

NOTE Confidence: 0.8720987

00:17:33.310 --> 00:17:34.134 or depression.

NOTE Confidence: 0.8720987

00:17:34.134 --> 00:17:37.018 So the general principle is that once

NOTE Confidence: 0.8720987

00:17:37.018 --> 00:17:39.689 we calculate this summary score.

NOTE Confidence: 0.8720987

00:17:39.690 --> 00:17:41.262 And this polygenic risk,

NOTE Confidence: 0.8720987

00:17:41.262 --> 00:17:43.620 or you will generally see that

NOTE Confidence: 0.8720987

00:17:43.693 --> 00:17:46.048 cases or individuals that have

NOTE Confidence: 0.8720987

00:17:46.048 --> 00:17:48.403 high risk for psychiatric disorder,

NOTE Confidence: 0.8720987

00:17:48.410 --> 00:17:51.105 generally have a higher score

NOTE Confidence: 0.8720987

00:17:51.105 --> 00:17:53.800 than non cases or controls.

NOTE Confidence: 0.8720987

00:17:53.800 --> 00:17:55.888 So we use this methodology and

NOTE Confidence: 0.8720987

00:17:55.888 --> 00:17:58.254 we can talk about the limitations

NOTE Confidence: 0.8720987

00:17:58.254 --> 00:18:00.948 of this methodology and in the

NOTE Confidence: 0.8720987

00:18:00.948 --> 00:18:03.319 question period and but we use

NOTE Confidence: 0.8720987

00:18:03.319 --> 00:18:05.407 this methodology as what we think

NOTE Confidence: 0.8720987

00:18:05.410 --> 00:18:07.622 of as the best approach at the

NOTE Confidence: 0.8720987

00:18:07.622 --> 00:18:09.675 moment to capture genetic risk

NOTE Confidence: 0.8720987

00:18:09.675 --> 00:18:11.220 for psychiatric disorders.

NOTE Confidence: 0.8720987

00:18:11.220 --> 00:18:13.160 We calculated these polygenic risk

NOTE Confidence: 0.8720987

00:18:13.160 --> 00:18:15.100 scores in the Outback children

NOTE Confidence: 0.8720987

00:18:15.166 --> 00:18:17.016 around just over 5000 children.

NOTE Confidence: 0.8720987

00:18:17.020 --> 00:18:18.960 We calculated them for ADHD,

NOTE Confidence: 0.8720987

00:18:18.960 --> 00:18:20.800 schizophrenia and depression and then

NOTE Confidence: 0.8720987

00:18:20.800 --> 00:18:23.210 we used child mental health symptoms,

NOTE Confidence: 0.8720987

00:18:23.210 --> 00:18:25.470 derives from the strength.

NOTE Confidence: 0.8720987

00:18:25.470 --> 00:18:27.730 Difficulties questionnaire from age

NOTE Confidence: 0.8720987

00:18:27.730 --> 00:18:31.568 4 to 16 years of age and then we use

NOTE Confidence: 0.8720987

00:18:31.568 --> 00:18:34.509 long to tude ainle model modeling.

NOTE Confidence: 0.8720987

00:18:34.510 --> 00:18:36.434 Generalized estimating equations to

NOTE Confidence: 0.8720987

00:18:36.434 --> 00:18:39.320 ask whether or not the prediction

NOTE Confidence: 0.8720987

00:18:39.390 --> 00:18:41.534 from maternal prenatal depression

NOTE Confidence: 0.8720987

00:18:41.534 --> 00:18:44.214 or maternal prenatal anxiety was

NOTE Confidence: 0.8720987

00:18:44.214 --> 00:18:46.989 confounded by child genetic risk for ADHD,

NOTE Confidence: 0.8720987

00:18:46.990 --> 00:18:48.520 schizophrenia, or depression.

NOTE Confidence: 0.8720987

00:18:48.520 --> 00:18:49.030 And.

NOTE Confidence: 0.8720987

00:18:49.030 --> 00:18:52.600 And the take home message from these

NOTE Confidence: 0.8720987

00:18:52.600 --> 00:18:55.186 analysis was that even when we

NOTE Confidence: 0.8720987

00:18:55.186 --> 00:18:58.288 adjusted for child genetic risk for ADHD,

NOTE Confidence: 0.8720987

00:18:58.290 --> 00:18:58.701 schizophrenia,

33

NOTE Confidence: 0.8720987

00:18:58.701 --> 00:18:59.523 or depression,

NOTE Confidence: 0.8720987

00:18:59.523 --> 00:19:01.578 we still saw a significant

NOTE Confidence: 0.8720987

00:19:01.578 --> 00:19:03.221 independent effect of maternal

NOTE Confidence: 0.8720987

00:19:03.221 --> 00:19:05.136 prenatal depression on child outcome.

NOTE Confidence: 0.8720987

00:19:05.140 --> 00:19:07.660 And this is just a representative

NOTE Confidence: 0.8720987

00:19:07.660 --> 00:19:09.799 figure using the ADHD polygenic

NOTE Confidence: 0.8720987

00:19:09.799 --> 00:19:12.791 risk score and what you can see is

NOTE Confidence: 0.8720987

00:19:12.791 --> 00:19:15.633 that children with a high burden of

NOTE Confidence: 0.8720987

00:19:15.633 --> 00:19:18.469 genetic risk for ADHD and exposed to

NOTE Confidence: 0.8720987

00:19:18.469 --> 00:19:20.947 high levels of maternal prenatal depression.

NOTE Confidence: 0.8720987

00:19:20.950 --> 00:19:23.080 Show increased symptoms relative to

NOTE Confidence: 0.8720987

00:19:23.080 --> 00:19:25.581 children with low genetic risk for

NOTE Confidence: 0.8720987

00:19:25.581 --> 00:19:27.660 ADHD and low and exposure to low

NOTE Confidence: 0.8720987

00:19:27.660 --> 00:19:30.199 levels of maternal prenatal depression,

NOTE Confidence: 0.8720987

00:19:30.200 --> 00:19:32.612 depression and we see this for

NOTE Confidence: 0.8720987

00:19:32.612 --> 00:19:34.220 the external Ising subscale.

NOTE Confidence: 0.8720987

00:19:34.220 --> 00:19:37.489 We see this for the total symptom

NOTE Confidence: 0.8720987

00:19:37.489 --> 00:19:41.029 scores and we see this at four years

NOTE Confidence: 0.8720987

00:19:41.029 --> 00:19:45.156 of age but also at 16 1/2 years of age.

NOTE Confidence: 0.8720987

00:19:45.160 --> 00:19:45.612 Now,

NOTE Confidence: 0.8720987

00:19:45.612 --> 00:19:47.872 one of the interesting observations

NOTE Confidence: 0.8720987

00:19:47.872 --> 00:19:50.624 from this study was that there

NOTE Confidence: 0.8720987

00:19:50.624 --> 00:19:52.779 was no interaction with time.

NOTE Confidence: 0.8720987

00:19:52.780 --> 00:19:55.810 We found a stable prediction from

NOTE Confidence: 0.8720987

00:19:55.810 --> 00:19:57.830 maternal prenatal depression overtime.

NOTE Confidence: 0.8720987

00:19:57.830 --> 00:20:00.180 Conversely, for both the schizophr.

NOTE Confidence: 0.8720987

00:20:00.180 --> 00:20:02.350 Any other polygenic risk score

NOTE Confidence: 0.8720987

00:20:02.350 --> 00:20:04.520 and for the depression polygenic

NOTE Confidence: 0.8720987

00:20:04.591 --> 00:20:06.985 risk or we found a significant

NOTE Confidence: 0.8720987

00:20:06.985 --> 00:20:09.154 interaction with time where the

NOTE Confidence: 0.8720987

00:20:09.154 --> 00:20:11.634 polygenic risk score for schizophrenia

NOTE Confidence: 0.8720987

00:20:11.634 --> 00:20:14.038 or depression strengthened as these

NOTE Confidence: 0.8720987

00:20:14.038 --> 00:20:15.292 children approached adolescence,

NOTE Confidence: 0.8720987

00:20:15.292 --> 00:20:17.800 so perhaps in the question period

NOTE Confidence: 0.8720987

00:20:17.867 --> 00:20:19.872 we can discuss how developmentally

NOTE Confidence: 0.8720987

00:20:19.872 --> 00:20:21.877 dynamic symptoms or phenotypes may

NOTE Confidence: 0.8720987

00:20:21.939 --> 00:20:23.559 require developmentally informed

NOTE Confidence: 0.8720987

00:20:23.559 --> 00:20:25.719 genome wide Association studies,

NOTE Confidence: 0.831203

00:20:25.720 --> 00:20:28.342 but going back to the question

NOTE Confidence: 0.831203

00:20:28.342 --> 00:20:31.678 at hand as to whether or not.

NOTE Confidence: 0.831203

00:20:31.680 --> 00:20:34.116 Effects of the prenatal environment are

NOTE Confidence: 0.831203

00:20:34.116 --> 00:20:36.410 confounded by child genetic variation.

NOTE Confidence: 0.831203

00:20:36.410 --> 00:20:38.560 At least from this study,

NOTE Confidence: 0.831203

00:20:38.560 --> 00:20:41.256 we can see that our best efforts to

NOTE Confidence: 0.831203

00:20:41.256 --> 00:20:43.443 assess genetic risk for psychiatric

NOTE Confidence: 0.831203

00:20:43.443 --> 00:20:45.838 disorders doesn't seem to confound

NOTE Confidence: 0.831203

00:20:45.838 --> 00:20:48.019 the Association between maternal,

NOTE Confidence: 0.831203

00:20:48.020 --> 00:20:49.740 prenatal depression or maternal

NOTE Confidence: 0.831203

00:20:49.740 --> 00:20:51.890 prenatal anxiety and child outcome,

NOTE Confidence: 0.831203

00:20:51.890 --> 00:20:55.285 and we do see an independent significant

NOTE Confidence: 0.831203

00:20:55.285 --> 00:20:57.664 prediction from child genetic risk

NOTE Confidence: 0.831203

00:20:57.664 --> 00:21:00.196 factors with the child ADHD PRS

NOTE Confidence: 0.831203

00:21:00.196 --> 00:21:02.689 being the strongest predictor.

NOTE Confidence: 0.831203

00:21:02.690 --> 00:21:05.066 Now for many years we spend a lot of

NOTE Confidence: 0.831203

00:21:05.066 --> 00:21:07.173 time talking about the importance

NOTE Confidence: 0.831203

00:21:07.173 --> 00:21:08.945 of maternal mental health,

NOTE Confidence: 0.831203

00:21:08.950 --> 00:21:11.038 but of course maternal mental health

NOTE Confidence: 0.831203

00:21:11.038 --> 00:21:13.137 can be associated with many other

NOTE Confidence: 0.831203

00:21:13.137 --> 00:21:15.081 phenotypes that are also at risk

NOTE Confidence: 0.831203

00:21:15.081 --> 00:21:16.869 factors for adverse mental health

NOTE Confidence: 0.831203

00:21:16.869 --> 00:21:19.023 outcomes and one of the other

NOTE Confidence: 0.831203

00:21:19.023 --> 00:21:20.890 exposures that we were particularly

NOTE Confidence: 0.831203

00:21:20.890 --> 00:21:22.765 interested in assessing and perhaps

NOTE Confidence: 0.831203

00:21:22.765 --> 00:21:24.443 especially relevant in the context

NOTE Confidence: 0.831203

00:21:24.443 --> 00:21:26.003 of an ongoing global pandemic,

NOTE Confidence: 0.831203

00:21:26.010 --> 00:21:28.086 was the role of maternal infection,

NOTE Confidence: 0.831203

00:21:28.090 --> 00:21:30.603 and again with the idea of trying

NOTE Confidence: 0.831203

00:21:30.603 --> 00:21:32.819 to understand whether or not there

NOTE Confidence: 0.831203

00:21:32.819 --> 00:21:34.239 could be synergy between.

NOTE Confidence: 0.831203

00:21:34.240 --> 00:21:37.305 Maternal prenatal anxiety or depression

NOTE Confidence: 0.831203

00:21:37.305 --> 00:21:40.370 and maternal infection to produce

NOTE Confidence: 0.831203

00:21:40.454 --> 00:21:43.681 an works outcomes for the child and

NOTE Confidence: 0.831203

00:21:43.681 --> 00:21:46.800 what you're looking at here in this

NOTE Confidence: 0.831203

00:21:46.800 --> 00:21:49.266 slide is symptoms from the social

NOTE Confidence: 0.831203

00:21:49.270 --> 00:21:50.788 communication disorder checklist,

NOTE Confidence: 0.831203

00:21:50.788 --> 00:21:54.330 which can be thought of as essentially

NOTE Confidence: 0.831203

00:21:54.406 --> 00:21:57.286 symptoms related to autism like features,

NOTE Confidence: 0.831203

00:21:57.290 --> 00:21:58.793 and we cut,

NOTE Confidence: 0.831203

00:21:58.793 --> 00:22:00.797 characterized or assessed maternal

NOTE Confidence: 0.831203

00:22:00.797 --> 00:22:02.300 infection in pregnancy,

NOTE Confidence: 0.831203

00:22:02.300 --> 00:22:04.910 and we particularly focused on.

NOTE Confidence: 0.831203

00:22:04.910 --> 00:22:07.794 Infections that may give rise to systemic,

NOTE Confidence: 0.831203

00:22:07.800 --> 00:22:09.560 an inflammation and infection an

NOTE Confidence: 0.831203

00:22:09.560 --> 00:22:12.271 and what we found was that the

NOTE Confidence: 0.831203

00:22:12.271 --> 00:22:14.486 number of maternal infections was

NOTE Confidence: 0.831203

00:22:14.486 --> 00:22:16.470 associated with increased symptoms.

NOTE Confidence: 0.831203

00:22:16.470 --> 00:22:18.575 Scores for the social communication

NOTE Confidence: 0.831203

00:22:18.575 --> 00:22:20.680 disorder checklist and the question

NOTE Confidence: 0.831203

00:22:20.747 --> 00:22:22.557 was whether or not maternal

NOTE Confidence: 0.831203

00:22:22.557 --> 00:22:24.367 anxiety would have an independent

NOTE Confidence: 0.831203

00:22:24.430 --> 00:22:26.390 effect and multiplicative effect,

NOTE Confidence: 0.831203

00:22:26.390 --> 00:22:28.862 and what we found was indeed

NOTE Confidence: 0.831203

00:22:28.862 --> 00:22:30.098 an additive effect.

NOTE Confidence: 0.831203

00:22:30.100 --> 00:22:31.752 An independent additive effect

NOTE Confidence: 0.831203

00:22:31.752 --> 00:22:33.404 of maternal prenatal anxiety,

NOTE Confidence: 0.831203

00:22:33.410 --> 00:22:35.580 and infection on child symptoms.

NOTE Confidence: 0.831203

00:22:35.580 --> 00:22:37.455 We saw this first social

NOTE Confidence: 0.831203

00:22:37.455 --> 00:22:38.580 communication disorder checklist,

NOTE Confidence: 0.831203

00:22:38.580 --> 00:22:41.898 but also for symptoms of 80 HD.

NOTE Confidence: 0.831203

00:22:41.900 --> 00:22:42.225 So,

NOTE Confidence: 0.831203

00:22:42.225 --> 00:22:45.150 just to summarize this first part of my talk.

NOTE Confidence: 0.831203

00:22:45.150 --> 00:22:47.016 I think that what we've documented

NOTE Confidence: 0.831203

00:22:47.016 --> 00:22:49.158 using the OS backward is that there

NOTE Confidence: 0.831203

00:22:49.158 --> 00:22:51.104 can be a persisting influence of the

NOTE Confidence: 0.831203

00:22:51.164 --> 00:22:53.279 prenatal environment on child outcome,

NOTE Confidence: 0.831203

00:22:53.280 --> 00:22:56.040 and we don't think that this is completely

NOTE Confidence: 0.831203

00:22:56.040 --> 00:22:58.459 confounded by child genetic risk factors.

NOTE Confidence: 0.831203

00:22:58.460 --> 00:23:00.645 Could it be amplified by

NOTE Confidence: 0.831203

00:23:00.645 --> 00:23:02.830 genetic variation in the child?

NOTE Confidence: 0.831203

00:23:02.830 --> 00:23:06.113 That's an open question and we have

NOTE Confidence: 0.831203

00:23:06.113 --> 00:23:08.129 published papers previously showing

NOTE Confidence: 0.831203

00:23:08.129 --> 00:23:10.774 evidence of gene environment interactions

NOTE Confidence: 0.831203

00:23:10.774 --> 00:23:14.009 and the prediction of child outcome.

NOTE Confidence: 0.831203

00:23:14.010 --> 00:23:16.584 Really highlights is that there are

NOTE Confidence: 0.831203

00:23:16.584 --> 00:23:18.731 multiple opportunities to intervene to

NOTE Confidence: 0.831203

00:23:18.731 --> 00:23:20.909 try and improve maternal mental health,

NOTE Confidence: 0.831203

00:23:20.910 --> 00:23:23.472 ideally as early as possible in

NOTE Confidence: 0.831203

00:23:23.472 --> 00:23:25.180 pregnancy and certainly early

NOTE Confidence: 0.831203

00:23:25.250 --> 00:23:27.000 in the post Natal period.

NOTE Confidence: 0.831203

00:23:27.000 --> 00:23:27.614 Of course,

NOTE Confidence: 0.831203

00:23:27.614 --> 00:23:30.070 I think our data also speak to the

NOTE Confidence: 0.831203

00:23:30.148 --> 00:23:32.064 importance of considering maternal

NOTE Confidence: 0.831203

00:23:32.064 --> 00:23:34.938 physical health as another point of

NOTE Confidence: 0.831203

00:23:35.006 --> 00:23:37.508 intervention to ensure that we can

NOTE Confidence: 0.831203

00:23:37.508 --> 00:23:40.408 bolster both maternal well being but

NOTE Confidence: 0.831203

00:23:40.408 --> 00:23:43.478 also potentially improve child outcome.

NOTE Confidence: 0.831203

00:23:43.480 --> 00:23:45.315 Now one of the characteristics

NOTE Confidence: 0.831203

00:23:45.315 --> 00:23:46.783 of this research area,

NOTE Confidence: 0.831203

00:23:46.790 --> 00:23:47.894 the developmental origins

NOTE Confidence: 0.831203

00:23:47.894 --> 00:23:49.366 of health and disease,

NOTE Confidence: 0.831203

00:23:49.370 --> 00:23:51.422 is that there can be marked

NOTE Confidence: 0.831203

00:23:51.422 --> 00:23:52.790 variation or marked individual

NOTE Confidence: 0.831203

00:23:52.851 --> 00:23:55.077 differences in the effects of the

NOTE Confidence: 0.831203

00:23:55.077 --> 00:23:56.561 prenatal environment on child

NOTE Confidence: 0.8619012

00:23:56.628 --> 00:23:58.684 outcome, and the question is,

NOTE Confidence: 0.8619012

00:23:58.684 --> 00:24:01.060 how can we better identify children

NOTE Confidence: 0.8619012

00:24:01.136 --> 00:24:03.826 that are at risk and to try and get at

NOTE Confidence: 0.8619012

00:24:03.898 --> 00:24:06.658 this question or address this question?

NOTE Confidence: 0.8619012

00:24:06.660 --> 00:24:09.000 And I moved to Montreal to

NOTE Confidence: 0.8619012

00:24:09.000 --> 00:24:10.560 study social epigenetics with

00:24:10.631 --> 00:24:12.926 Michael Meaney and that's really.

00:24:12.930 --> 00:24:14.995 Features heavily in my current

00:24:14.995 --> 00:24:16.647 research program because epigenetics,

00:24:16.650 --> 00:24:18.710 really, while it's heavily involved

00:24:18.710 --> 00:24:19.946 in cellular differentiation,

00:24:19.950 --> 00:24:21.960 there was a paradigm shift in

00:24:21.960 --> 00:24:24.560 the early 2000s where we began to

00:24:24.560 --> 00:24:26.535 appreciate that the environment could

00:24:26.535 --> 00:24:29.039 also shape epigenetic modifications.

00:24:29.040 --> 00:24:31.518 But before we get into that,

00:24:31.520 --> 00:24:34.680 I think it's helpful to start with a

00:24:34.680 --> 00:24:37.381 definition of epigenetics and I like

00:24:37.381 --> 00:24:40.129 add this definition that comes from

00:24:40.211 --> 00:24:43.443 the road map project and which is really.

00:24:43.450 --> 00:24:45.315 Markable initiative that sought to

NOTE Confidence: 0.8619012

00:24:45.315 --> 00:24:48.864 act as a parallel to the Human Genome

NOTE Confidence: 0.8619012

00:24:48.864 --> 00:24:51.544 Project and to characterize different

NOTE Confidence: 0.8619012

00:24:51.544 --> 00:24:53.506 epigenetic modifications across the

NOTE Confidence: 0.8619012

00:24:53.506 --> 00:24:55.541 genome and across different cells

NOTE Confidence: 0.8619012

00:24:55.541 --> 00:24:57.572 and tissues and integrate those

NOTE Confidence: 0.8619012

00:24:57.572 --> 00:24:59.978 data to provide a richer perspective

NOTE Confidence: 0.8619012

00:24:59.978 --> 00:25:02.788 and a deeper understanding of the

NOTE Confidence: 0.8619012

00:25:02.788 --> 00:25:05.208 epigenome across cells and tissues.

NOTE Confidence: 0.8619012

00:25:05.210 --> 00:25:05.635 Now,

NOTE Confidence: 0.8619012

00:25:05.635 --> 00:25:08.610 what many of you on the call

NOTE Confidence: 0.8619012

00:25:08.610 --> 00:25:11.860 will probably be aware of is the

NOTE Confidence: 0.8619012

00:25:11.860 --> 00:25:13.708 very controversial area of.

NOTE Confidence: 0.8619012

00:25:13.710 --> 00:25:14.994 Transgenerational epigenetic inheritance,

NOTE Confidence: 0.8619012

00:25:14.994 --> 00:25:16.706 which posits that epigenetics

NOTE Confidence: 0.8619012

00:25:16.706 --> 00:25:18.953 states can be transmitted across

NOTE Confidence: 0.8619012

00:25:18.953 --> 00:25:20.765 multiple generations with Fidelity,

NOTE Confidence: 0.8619012

00:25:20.770 --> 00:25:23.416 and the evidence for that in

NOTE Confidence: 0.8619012

00:25:23.416 --> 00:25:25.180 humans is lacking an.

NOTE Confidence: 0.8619012

00:25:25.180 --> 00:25:26.503 As I mentioned,

NOTE Confidence: 0.8619012

00:25:26.503 --> 00:25:29.149 it is a very controversial subject,

NOTE Confidence: 0.8619012

00:25:29.150 --> 00:25:32.090 and there is an excellent review by

NOTE Confidence: 0.8619012

00:25:32.090 --> 00:25:35.497 Edith Heard for any of you that are

NOTE Confidence: 0.8619012

00:25:35.497 --> 00:25:38.136 interested in getting a having a

NOTE Confidence: 0.8619012

00:25:38.136 --> 00:25:40.606 deeper dive into this controversy,

NOTE Confidence: 0.8619012

00:25:40.610 --> 00:25:43.795 but also the evidence we can see.

NOTE Confidence: 0.8619012

00:25:43.800 --> 00:25:45.120 Evidence for transgenerational

NOTE Confidence: 0.8619012

00:25:45.120 --> 00:25:46.880 epigenetic inheritance in C.

NOTE Confidence: 0.8619012

00:25:46.880 --> 00:25:47.282 Elegans.

NOTE Confidence: 0.8619012

00:25:47.282 --> 00:25:48.488 In certain plants,

NOTE Confidence: 0.8619012

00:25:48.488 --> 00:25:51.351 an Indra Sofala fruit flies and but

NOTE Confidence: 0.8619012

00:25:51.351 --> 00:25:53.637 again trying to establish that evidence

NOTE Confidence: 0.8619012

00:25:53.637 --> 00:25:56.560 in humans is particularly challenging.

NOTE Confidence: 0.8619012

00:25:56.560 --> 00:25:59.640 It doesn't rule out the possibility an,

NOTE Confidence: 0.8619012

00:25:59.640 --> 00:26:02.657 but there is no clear evidence for

NOTE Confidence: 0.8619012

00:26:02.657 --> 00:26:05.800 that in humans at the current time.

NOTE Confidence: 0.8619012

00:26:05.800 --> 00:26:08.836 But when I think about epigenetics

NOTE Confidence: 0.8619012

00:26:08.836 --> 00:26:11.322 and really the definition that

NOTE Confidence: 0.8619012

00:26:11.322 --> 00:26:13.905 I use in my work is different.

NOTE Confidence: 0.8619012

00:26:13.910 --> 00:26:15.935 The genetic states or epigenetic

NOTE Confidence: 0.8619012

00:26:15.935 --> 00:26:17.960 modifications that can alter the

NOTE Confidence: 0.8619012

00:26:18.025 --> 00:26:20.270 transcriptional potential of a cell,

NOTE Confidence: 0.8619012

00:26:20.270 --> 00:26:23.393 or indeed a system and what I mean by

NOTE Confidence: 0.8619012

00:26:23.393 --> 00:26:27.047 that is directly related to gene expression,

NOTE Confidence: 0.8619012

00:26:27.050 --> 00:26:29.170 so epigenetic modifications have the

NOTE Confidence: 0.8619012

00:26:29.170 --> 00:26:31.290 potential to alter gene expression,

NOTE Confidence: 0.8619012

00:26:31.290 --> 00:26:33.635 and that's one of the reasons that

NOTE Confidence: 0.8619012

00:26:33.635 --> 00:26:36.160 people are so interested in the

NOTE Confidence: 0.8619012

00:26:36.160 --> 00:26:38.570 epigenome trying to understand how

NOTE Confidence: 0.8619012

00:26:38.570 --> 00:26:40.496 these epigenetic modifications can

NOTE Confidence: 0.8619012

00:26:40.496 --> 00:26:43.166 alter the function of the genome.

NOTE Confidence: 0.8619012

00:26:43.170 --> 00:26:44.080 And as.

NOTE Confidence: 0.8619012

00:26:44.080 --> 00:26:46.355 Doctor Martin very kindly pointed

NOTE Confidence: 0.8619012

00:26:46.355 --> 00:26:49.046 out we've written a review on

NOTE Confidence: 0.8619012

00:26:49.046 --> 00:26:51.542 the evidence for and against the

NOTE Confidence: 0.8619012

00:26:51.542 --> 00:26:53.658 epigenome underlying the biological

NOTE Confidence: 0.8619012

00:26:53.658 --> 00:26:56.353 embedding of experience and what

NOTE Confidence: 0.8619012

00:26:56.353 --> 00:26:58.820 we conclude from this review is

NOTE Confidence: 0.8619012

00:26:58.820 --> 00:27:02.495 that there is quite a lot of a good

NOTE Confidence: 0.8619012

00:27:02.495 --> 00:27:04.016 correlational evidence suggesting

NOTE Confidence: 0.8619012

00:27:04.016 --> 00:27:07.350 that the epigenome may underlie the

NOTE Confidence: 0.8619012

00:27:07.350 --> 00:27:09.806 biological embedding of experience,

NOTE Confidence: 0.8619012

00:27:09.810 --> 00:27:12.225 but trying to establish causality

NOTE Confidence: 0.8619012

00:27:12.225 --> 00:27:14.157 does require model or.

NOTE Confidence: 0.8619012

00:27:14.160 --> 00:27:15.720 Organisms and I think,

NOTE Confidence: 0.8619012

00:27:15.720 --> 00:27:18.060 will be greatly facilitated by the

NOTE Confidence: 0.8619012

00:27:18.137 --> 00:27:20.879 advent of EPI genome editing technology,

NOTE Confidence: 0.8619012

00:27:20.880 --> 00:27:22.615 where we can actually directly

NOTE Confidence: 0.8619012

00:27:22.615 --> 00:27:24.350 manipulate in a site specific

NOTE Confidence: 0.8619012

00:27:24.409 --> 00:27:26.281 manner and different epigenetic

NOTE Confidence: 0.8619012

00:27:26.281 --> 00:27:28.153 States and establish functional

NOTE Confidence: 0.8619012

00:27:28.153 --> 00:27:30.030 associations with gene expression

NOTE Confidence: 0.8619012

00:27:30.030 --> 00:27:32.220 and different brain based phenotypes.

NOTE Confidence: 0.8619012

00:27:32.220 --> 00:27:33.836 Now the modification that

NOTE Confidence: 0.8619012

00:27:33.836 --> 00:27:36.260 I'm going to spend most of

NOTE Confidence: 0.8554767

00:27:36.342 --> 00:27:38.477 my time talking about today

NOTE Confidence: 0.8554767

00:27:38.477 --> 00:27:40.612 is that of DNA methylation,

NOTE Confidence: 0.8554767

00:27:40.620 --> 00:27:43.206 which is the addition of a

NOTE Confidence: 0.8554767

00:27:43.206 --> 00:27:44.930 methyl group are represented.

NOTE Confidence: 0.8554767

00:27:44.930 --> 00:27:47.240 Here in red to a cytisine,

NOTE Confidence: 0.8554767

00:27:47.240 --> 00:27:49.935 that's a C in the genetic code,

NOTE Confidence: 0.8554767

00:27:49.940 --> 00:27:52.364 Anne Anne, but I also want to point

NOTE Confidence: 0.8554767

00:27:52.364 --> 00:27:54.367 out from this figure from this

NOTE Confidence: 0.8554767

00:27:54.367 --> 00:27:57.111 review that this is one of many

NOTE Confidence: 0.8554767

00:27:57.111 --> 00:27:59.178 different epigenetic modifications.

NOTE Confidence: 0.8554767

00:27:59.180 --> 00:28:01.400 In fact, some people call them

NOTE Confidence: 0.8554767

00:28:01.400 --> 00:28:03.344 epigenetic systems that work in

NOTE Confidence: 0.8554767

00:28:03.344 --> 00:28:04.948 conjunction with one another,

NOTE Confidence: 0.8554767

00:28:04.950 --> 00:28:07.386 and as we make progress in our

NOTE Confidence: 0.8554767

00:28:07.386 --> 00:28:09.190 understanding of the epigenome,

NOTE Confidence: 0.8554767

00:28:09.190 --> 00:28:10.734 and indeed, social epigenomics,

NOTE Confidence: 0.8554767

00:28:10.734 --> 00:28:12.664 we're beginning to realize the

NOTE Confidence: 0.8554767

00:28:12.664 --> 00:28:14.258 importance of integrating different

NOTE Confidence: 0.8554767

00:28:14.258 --> 00:28:16.173 layers and levels of information.

NOTE Confidence: 0.8554767

00:28:16.180 --> 00:28:17.800 About the epigynum.

NOTE Confidence: 0.8554767

00:28:17.800 --> 00:28:20.500 To fully understand its impact

NOTE Confidence: 0.8554767

00:28:20.500 --> 00:28:22.480 on genome function.

NOTE Confidence: 0.8554767

00:28:22.480 --> 00:28:24.355 So let's think about this

NOTE Confidence: 0.8554767

00:28:24.355 --> 00:28:25.855 in more simple terms.

NOTE Confidence: 0.8554767

00:28:25.860 --> 00:28:28.866 I think it can be very helpful to think

NOTE Confidence: 0.8554767

00:28:28.866 --> 00:28:31.877 about the epigenome in terms of metaphor.

NOTE Confidence: 0.8554767

00:28:31.880 --> 00:28:34.162 And so some great metaphors exist to

NOTE Confidence: 0.8554767

00:28:34.162 --> 00:28:36.768 try and add describe the epigenome.

NOTE Confidence: 0.8554767

00:28:36.770 --> 00:28:38.798 I particularly like the idea of

NOTE Confidence: 0.8554767

00:28:38.798 --> 00:28:40.900 the epigenome as a conductor,

NOTE Confidence: 0.8554767

00:28:40.900 --> 00:28:43.908 so as sheet music and as a conductor.

NOTE Confidence: 0.8554767

00:28:43.910 --> 00:28:46.465 So we think about genes being the

NOTE Confidence: 0.8554767

00:28:46.465 --> 00:28:48.420 individual and instruments or musicians.

NOTE Confidence: 0.8554767

00:28:48.420 --> 00:28:49.138 And really,

NOTE Confidence: 0.8554767

00:28:49.138 --> 00:28:52.640 if we want to create a Symphony to create.

NOTE Confidence: 0.8554767

00:28:52.640 --> 00:28:54.600 A phenotype that makes sense.

NOTE Confidence: 0.8554767

00:28:54.600 --> 00:28:56.808 It's important that all of these

NOTE Confidence: 0.8554767

00:28:56.808 --> 00:28:58.774 different units and work together

NOTE Confidence: 0.8554767

00:28:58.774 --> 00:29:00.478 in a coordinated manner,

NOTE Confidence: 0.8554767

00:29:00.480 --> 00:29:02.692 and one of the ways that they

NOTE Confidence: 0.8554767

00:29:02.692 --> 00:29:05.565 do so is by following the signs

NOTE Confidence: 0.8554767

00:29:05.565 --> 00:29:08.313 of the signals of the conductor.

NOTE Confidence: 0.8554767

00:29:08.320 --> 00:29:10.637 One of the other metaphors that I

NOTE Confidence: 0.8554767

00:29:10.637 --> 00:29:13.477 love to use to describe how the

NOTE Confidence: 0.8554767

00:29:13.477 --> 00:29:15.245 epigenome influences the function

NOTE Confidence: 0.8554767

00:29:15.245 --> 00:29:18.119 of the genome is that of grammar,

NOTE Confidence: 0.8554767

00:29:18.120 --> 00:29:21.288 and so you can have all of the

NOTE Confidence: 0.8554767

00:29:21.288 --> 00:29:22.950 correct letters and text.

NOTE Confidence: 0.8554767

00:29:22.950 --> 00:29:26.874 In a book, but if you don't have punctuation,

NOTE Confidence: 0.8554767

00:29:26.880 --> 00:29:29.070 if you don't have grammar,

NOTE Confidence: 0.8554767

00:29:29.070 --> 00:29:31.910 then you lose all meaning and we all

NOTE Confidence: 0.8554767

00:29:31.910 --> 00:29:34.745 know that grammar can be critically

NOTE Confidence: 0.8554767

00:29:34.745 --> 00:29:37.805 important for our understanding of text,

NOTE Confidence: 0.8554767

00:29:37.810 --> 00:29:39.990 and similarly with the epigenome.

NOTE Confidence: 0.8554767

00:29:39.990 --> 00:29:41.870 Epigenetic modifications are critically

NOTE Confidence: 0.8554767

00:29:41.870 --> 00:29:44.220 important for placing emphasis on

NOTE Confidence: 0.8554767

00:29:44.220 --> 00:29:46.550 certain genes or silencing other genes,

NOTE Confidence: 0.8554767

00:29:46.550 --> 00:29:50.108 so really playing a functional role.

NOTE Confidence: 0.8554767

00:29:50.110 --> 00:29:50.443 Now,

NOTE Confidence: 0.8554767

00:29:50.443 --> 00:29:51.442 historically we've thought

NOTE Confidence: 0.8554767

00:29:51.442 --> 00:29:53.107 about DNA methylation as being

NOTE Confidence: 0.8554767

00:29:53.107 --> 00:29:54.749 a repressive modification.

NOTE Confidence: 0.8554767

00:29:54.750 --> 00:29:57.846 People have likened it to a light switch,

NOTE Confidence: 0.8554767

00:29:57.850 --> 00:30:00.250 so turning a gene on turning.

NOTE Confidence: 0.8554767

00:30:00.250 --> 00:30:02.614 Aging off and the evidence really

NOTE Confidence: 0.8554767

00:30:02.614 --> 00:30:04.190 to support DNA methylation

NOTE Confidence: 0.8554767

00:30:04.256 --> 00:30:06.160 as a repressive modification.

NOTE Confidence: 0.8554767

00:30:06.160 --> 00:30:08.848 Cones from X inactivation where DNA

NOTE Confidence: 0.8554767

00:30:08.848 --> 00:30:11.492 methylation plays a role in silencing

NOTE Confidence: 0.8554767

00:30:11.492 --> 00:30:14.596 one of the X chromosomes an in females,

NOTE Confidence: 0.8554767

00:30:14.600 --> 00:30:17.522 but also from an imprinting where

NOTE Confidence: 0.8554767

00:30:17.522 --> 00:30:20.553 there can be silencing of 1 copy

NOTE Confidence: 0.8554767

00:30:20.553 --> 00:30:22.863 of a gene for ad that occurs

NOTE Confidence: 0.8554767

00:30:22.958 --> 00:30:25.568 in a parent of origin fashion.

NOTE Confidence: 0.8554767

00:30:25.570 --> 00:30:27.859 But we've begun to realize that we

NOTE Confidence: 0.8554767

00:30:27.859 --> 00:30:30.789 as we add more deeply characterized

NOTE Confidence: 0.8554767

00:30:30.789 --> 00:30:32.037 DNA methylation.

NOTE Confidence: 0.8554767

00:30:32.040 --> 00:30:34.170 Is that it's Association with gene

NOTE Confidence: 0.8554767

00:30:34.170 --> 00:30:36.150 expression can be more nuanced.

NOTE Confidence: 0.8554767

00:30:36.150 --> 00:30:39.516 In some cases it can act like a dimmer

NOTE Confidence: 0.8554767

00:30:39.516 --> 00:30:41.390 switch, turning gene expression up,

NOTE Confidence: 0.8554767

00:30:41.390 --> 00:30:42.140 or Dan.

NOTE Confidence: 0.8554767

00:30:42.140 --> 00:30:43.540 Indeed in other situations,

NOTE Confidence: 0.8554767

00:30:43.540 --> 00:30:44.940 demethylation is not associated

NOTE Confidence: 0.8554767

00:30:44.940 --> 00:30:46.250 with gene expression,

NOTE Confidence: 0.8554767

00:30:46.250 --> 00:30:48.666 and in other cases still we can find

NOTE Confidence: 0.8554767

00:30:48.666 --> 00:30:51.024 the DNA methylation at certain sites

NOTE Confidence: 0.8554767

00:30:51.024 --> 00:30:53.538 within a gene can actually alter

NOTE Confidence: 0.8554767

00:30:53.615 --> 00:30:55.925 the product or the splice variant

NOTE Confidence: 0.8554767

00:30:55.925 --> 00:30:58.118 that's produced from a given gene.

NOTE Confidence: 0.8554767

00:30:58.118 --> 00:31:00.710 I think the take home message is that

NOTE Confidence: 0.84403723

00:31:00.784 --> 00:31:03.169 the context is critically important.

NOTE Confidence: 0.84403723

00:31:03.170 --> 00:31:05.215 Another cool curring epigenetic modifications

NOTE Confidence: 0.84403723

00:31:05.215 --> 00:31:08.066 can also have an impact on whether

NOTE Confidence: 0.84403723

00:31:08.066 --> 00:31:10.304 or not DNA methylation is negatively

NOTE Confidence: 0.84403723

00:31:10.304 --> 00:31:12.491 associated with gene expression or

NOTE Confidence: 0.84403723

00:31:12.491 --> 00:31:14.786 positively associated with gene expression,

NOTE Confidence: 0.84403723

00:31:14.790 --> 00:31:17.054 or indeed not associated

NOTE Confidence: 0.84403723

00:31:17.054 --> 00:31:19.884 with gene expression at all.

NOTE Confidence: 0.84403723

00:31:19.890 --> 00:31:22.458 Now, one thing to consider when we look

NOTE Confidence: 0.84403723

00:31:22.458 --> 00:31:25.201 at DNA methylation across the genome is

NOTE Confidence: 0.84403723

00:31:25.201 --> 00:31:28.209 that DNA methylation is a binary event,

NOTE Confidence: 0.84403723

00:31:28.210 --> 00:31:30.466 it's either on or it's off.

NOTE Confidence: 0.84403723

00:31:30.470 --> 00:31:33.134 But throughout my talk you'll hear me talking

NOTE Confidence: 0.84403723

00:31:33.134 --> 00:31:35.390 perhaps about percentage DNA methylation,

NOTE Confidence: 0.84403723

00:31:35.390 --> 00:31:37.658 90% DNA methylation, 60% DNA methylation,

NOTE Confidence: 0.84403723

00:31:37.660 --> 00:31:40.145 or 10% DNA methylation, and that is

NOTE Confidence: 0.84403723

00:31:40.145 --> 00:31:42.947 because when we look at DNA methylation,

NOTE Confidence: 0.84403723

00:31:42.950 --> 00:31:44.414 particularly in clinical studies,

NOTE Confidence: 0.84403723

00:31:44.414 --> 00:31:46.610 we're looking at an average across

NOTE Confidence: 0.84403723

00:31:46.671 --> 00:31:49.850 multiple cells, and so when we look within.

NOTE Confidence: 0.84403723

00:31:49.850 --> 00:31:53.306 Multiple cells we can see that there may

NOTE Confidence: 0.84403723

00:31:53.306 --> 00:31:56.455 be methylation at a given site in one cell,

NOTE Confidence: 0.84403723

00:31:56.460 --> 00:31:57.824 but not in another,

NOTE Confidence: 0.84403723

00:31:57.824 --> 00:32:01.130 and so when we report back DNA methylation,

NOTE Confidence: 0.84403723

00:32:01.130 --> 00:32:03.070 an results were talking about

NOTE Confidence: 0.84403723

00:32:03.070 --> 00:32:04.622 it as percentage metalation.

NOTE Confidence: 0.84403723

00:32:04.630 --> 00:32:05.020 Essentially,

NOTE Confidence: 0.84403723

00:32:05.020 --> 00:32:07.360 the number of metalation marks within

NOTE Confidence: 0.84403723

00:32:07.360 --> 00:32:10.078 the cells of your tissue of interest.

NOTE Confidence: 0.84403723

00:32:10.080 --> 00:32:12.870 And that brings me to one of the issues

NOTE Confidence: 0.84403723

00:32:12.870 --> 00:32:15.519 with epigenetics in clinical studies,

NOTE Confidence: 0.84403723

00:32:15.520 --> 00:32:17.860 and that is the rule of

NOTE Confidence: 0.84403723

00:32:17.860 --> 00:32:18.640 cellular heterogeneity.

NOTE Confidence: 0.84403723

00:32:18.640 --> 00:32:20.625 So one of the principle

NOTE Confidence: 0.84403723

00:32:20.625 --> 00:32:22.213 rules of the epigenome.

NOTE Confidence: 0.84403723

00:32:22.220 --> 00:32:25.041 Is to ensure that there is cellular

NOTE Confidence: 0.84403723

00:32:25.041 --> 00:32:26.879 differentiation and the maintenance

NOTE Confidence: 0.84403723

00:32:26.879 --> 00:32:29.119 of those cellular phenotypes,

NOTE Confidence: 0.84403723

00:32:29.120 --> 00:32:31.941 and in fact where you have disorders

NOTE Confidence: 0.84403723

00:32:31.941 --> 00:32:34.180 related to DNA methylation.

NOTE Confidence: 0.84403723

00:32:34.180 --> 00:32:35.686 Another epigenetic modifications.

NOTE Confidence: 0.84403723

00:32:35.686 --> 00:32:38.196 You can require pluripotency increase

NOTE Confidence: 0.84403723

00:32:38.196 --> 00:32:40.160 the stemness of these cells,

NOTE Confidence: 0.84403723

00:32:40.160 --> 00:32:42.830 giving rise to disorders and

NOTE Confidence: 0.84403723

00:32:42.830 --> 00:32:44.966 diseases such as cancer.

NOTE Confidence: 0.84403723

00:32:44.970 --> 00:32:47.580 But one of the other interesting

NOTE Confidence: 0.84403723

00:32:47.580 --> 00:32:50.500 features of the epigenome and one of

NOTE Confidence: 0.84403723

00:32:50.500 --> 00:32:53.069 the functions that is emerging for the

NOTE Confidence: 0.84403723

00:32:53.152 --> 00:32:56.225 epigenome is the idea of genomic priming.

NOTE Confidence: 0.84403723

00:32:56.230 --> 00:32:58.894 So this is the idea that there can

NOTE Confidence: 0.84403723

00:32:58.894 --> 00:33:02.294 be an exposure that gives rise to a

NOTE Confidence: 0.84403723

00:33:02.294 --> 00:33:05.149 change in an epigenetic state such

NOTE Confidence: 0.84403723

00:33:05.149 --> 00:33:07.847 as DNA methylation, and that am,

NOTE Confidence: 0.84403723

00:33:07.847 --> 00:33:08.246 instills,

NOTE Confidence: 0.84403723

00:33:08.246 --> 00:33:10.640 or instantiates the capacity to then

NOTE Confidence: 0.84403723

00:33:10.710 --> 00:33:13.314 have an even greater response to an

NOTE Confidence: 0.84403723

00:33:13.314 --> 00:33:15.919 exposure subject to subsequent exposures.

NOTE Confidence: 0.84403723

00:33:15.920 --> 00:33:18.398 That an individual or sell may

NOTE Confidence: 0.84403723

00:33:18.398 --> 00:33:19.637 experience as subsequently,

NOTE Confidence: 0.84403723

00:33:19.640 --> 00:33:21.872 and this is really nicely articulated

NOTE Confidence: 0.84403723

00:33:21.872 --> 00:33:24.423 in this paper from my colleague

NOTE Confidence: 0.84403723

00:33:24.423 --> 00:33:25.419 Nadine Provincal,

NOTE Confidence: 0.84403723

00:33:25.420 --> 00:33:27.355 working with Elizabeth ****** where

NOTE Confidence: 0.84403723

00:33:27.355 --> 00:33:28.903 they treated hippocampal stem

NOTE Confidence: 0.84403723

00:33:28.903 --> 00:33:30.380 cells with dexamethasone,

NOTE Confidence: 0.84403723

00:33:30.380 --> 00:33:32.440 which is a synthetic glucocorticoid.

NOTE Confidence: 0.84403723

00:33:32.440 --> 00:33:35.331 And you can think of it like

NOTE Confidence: 0.84403723

00:33:35.331 --> 00:33:36.570 a synthetic cortisol,

NOTE Confidence: 0.84403723

00:33:36.570 --> 00:33:38.615 an that produced widespread changes

NOTE Confidence: 0.84403723

00:33:38.615 --> 00:33:41.146 in DNA methylation and what was

NOTE Confidence: 0.84403723

00:33:41.146 --> 00:33:43.226 interesting about this particular study

NOTE Confidence: 0.84403723

00:33:43.226 --> 00:33:46.188 was that the changes in DNA methylation.

NOTE Confidence: 0.84403723

00:33:46.190 --> 00:33:48.908 Didn't always correlate with the gene

NOTE Confidence: 0.84403723

00:33:48.908 --> 00:33:50.720 expression response to dexamethasone,

NOTE Confidence: 0.84403723

00:33:50.720 --> 00:33:53.096 but the DNA methylation changes that

NOTE Confidence: 0.84403723

00:33:53.096 --> 00:33:55.768 did occur did predict the magnitude

NOTE Confidence: 0.84403723

00:33:55.768 --> 00:33:58.308 of response to subsequent exposures

NOTE Confidence: 0.84403723

00:33:58.308 --> 00:33:59.324 to dexamethasone,

NOTE Confidence: 0.84403723

00:33:59.330 --> 00:34:02.048 supporting this notion of genomic priming,

NOTE Confidence: 0.84403723

00:34:02.050 --> 00:34:04.310 and you may be asking,

NOTE Confidence: 0.84403723

00:34:04.310 --> 00:34:06.580 well, how could that occur?

NOTE Confidence: 0.84403723

00:34:06.580 --> 00:34:09.286 What would be the molecular mechanism?

NOTE Confidence: 0.84403723

00:34:09.290 --> 00:34:09.720 Well,

NOTE Confidence: 0.84403723

00:34:09.720 --> 00:34:12.730 one of the reasons that we're interested

NOTE Confidence: 0.84403723

00:34:12.730 --> 00:34:15.639 in steroid hormones such as cortisol,

NOTE Confidence: 0.84403723

00:34:15.640 --> 00:34:16.554 progesterone, estradiol,

NOTE Confidence: 0.84403723

00:34:16.554 --> 00:34:17.011 testosterone.

NOTE Confidence: 0.84403723

00:34:17.011 --> 00:34:19.296 Is because they are there.

NOTE Confidence: 0.84403723

00:34:19.300 --> 00:34:21.510 Their receptors are nuclear receptors.

NOTE Confidence: 0.84403723

00:34:21.510 --> 00:34:24.394 So when you have high levels of

NOTE Confidence: 0.84403723

00:34:24.394 --> 00:34:26.380 glucocorticoids such as cortisol,

NOTE Confidence: 0.84403723

00:34:26.380 --> 00:34:29.056 they can bind to the glucocorticoid

NOTE Confidence: 0.84403723

00:34:29.056 --> 00:34:31.260 receptor highlighted here in Gray,

NOTE Confidence: 0.84403723

00:34:31.260 --> 00:34:33.450 and the binding of that receptor

NOTE Confidence: 0.84403723

00:34:33.450 --> 00:34:34.910 to the DNA can

NOTE Confidence: 0.8489138

00:34:34.988 --> 00:34:37.784 result in DNA demethylation or changes

NOTE Confidence: 0.8489138

00:34:37.784 --> 00:34:41.222 in DNA methylation at the site that

NOTE Confidence: 0.8489138

00:34:41.222 --> 00:34:43.218 the transcription factor binds.

NOTE Confidence: 0.8489138

00:34:43.220 --> 00:34:45.932 So here you can see before

NOTE Confidence: 0.8489138

00:34:45.932 --> 00:34:47.288 exposure to glucocorticoids.

NOTE Confidence: 0.8489138

00:34:47.290 --> 00:34:49.922 You have higher levels of DNA methylation

NOTE Confidence: 0.8489138

00:34:49.922 --> 00:34:52.568 at this particular site or glucocorticoid

NOTE Confidence: 0.8489138

00:34:52.568 --> 00:34:54.983 response element then you have

NOTE Confidence: 0.8489138

00:34:54.983 --> 00:34:57.018 glucocorticoids binding to its receptor,

NOTE Confidence: 0.8489138

00:34:57.020 --> 00:34:59.120 resulting in changes in DNA methylation

NOTE Confidence: 0.8489138

00:34:59.120 --> 00:35:01.698 and then when you have subsequent

NOTE Confidence: 0.8489138

00:35:01.698 --> 00:35:03.360 exposures to glucocorticoids,

NOTE Confidence: 0.8489138

00:35:03.360 --> 00:35:05.475 you then have enhanced response

NOTE Confidence: 0.8489138

00:35:05.475 --> 00:35:06.744 to that exposure.

NOTE Confidence: 0.8489138

00:35:06.750 --> 00:35:09.865 And I think this is a particularly

NOTE Confidence: 0.8489138

00:35:09.865 --> 00:35:11.704 interesting hypothesis and model

NOTE Confidence: 0.8489138

00:35:11.704 --> 00:35:14.284 when we think about the effects

NOTE Confidence: 0.8489138

00:35:14.284 --> 00:35:16.403 of prenatal adversity or early

NOTE Confidence: 0.8489138

00:35:16.403 --> 00:35:18.278 adversity and how that may.

NOTE Confidence: 0.8489138

00:35:18.280 --> 00:35:22.788 Confer or prime the genome for subsequent

NOTE Confidence: 0.8489138

00:35:22.788 --> 00:35:26.740 exposures or responses to those exposures.

NOTE Confidence: 0.8489138

00:35:26.740 --> 00:35:29.547 So how do we analyze DNA methylation?

NOTE Confidence: 0.8489138

00:35:29.550 --> 00:35:29.952 Well,

NOTE Confidence: 0.8489138

00:35:29.952 --> 00:35:33.168 there are many approaches that we can use.

NOTE Confidence: 0.8489138

00:35:33.170 --> 00:35:35.486 We can use an epigenome wide

NOTE Confidence: 0.8489138

00:35:35.486 --> 00:35:37.030 Association study or metalation

NOTE Confidence: 0.8489138

00:35:37.100 --> 00:35:39.711 wide Association study an if we use

NOTE Confidence: 0.8489138

00:35:39.711 --> 00:35:41.610 whole genome bisulfite sequencing,

NOTE Confidence: 0.8489138

00:35:41.610 --> 00:35:44.452 we can assess roughly around 24 million

NOTE Confidence: 0.8489138

00:35:44.452 --> 00:35:46.840 CPG's more commonly because of cost.

NOTE Confidence: 0.8489138

00:35:46.840 --> 00:35:49.186 We're using an microarray based technology

NOTE Confidence: 0.8489138

00:35:49.186 --> 00:35:51.660 where we assess around 850,000 sites.

NOTE Confidence: 0.8489138

00:35:51.660 --> 00:35:54.228 Now, what you can quickly appreciate

NOTE Confidence: 0.8489138

00:35:54.228 --> 00:35:57.000 is that you're going to need very.

NOTE Confidence: 0.8489138

00:35:57.000 --> 00:35:59.682 Large courts to to adjust for

NOTE Confidence: 0.8489138

00:35:59.682 --> 00:36:01.956 multiple comparisons with so many

NOTE Confidence: 0.8489138

00:36:01.956 --> 00:36:04.362 sites and so what's promising in

NOTE Confidence: 0.8489138

00:36:04.362 --> 00:36:07.188 this regard is the PACE consortium,

NOTE Confidence: 0.8489138

00:36:07.190 --> 00:36:09.788 which is a consortium that's combining

NOTE Confidence: 0.8489138

00:36:09.788 --> 00:36:11.520 multiple different studies to

NOTE Confidence: 0.8489138

00:36:11.591 --> 00:36:13.821 perform meta analysis of prenatal

NOTE Confidence: 0.8489138

00:36:13.821 --> 00:36:15.605 exposures on DNA methylation.

NOTE Confidence: 0.8489138

00:36:15.610 --> 00:36:18.627 So they have performed a meta analysis

NOTE Confidence: 0.8489138

00:36:18.627 --> 00:36:20.894 of maternal prenatal smoking and

NOTE Confidence: 0.8489138

00:36:20.894 --> 00:36:23.139 DNA methylation and cord blood,

NOTE Confidence: 0.8489138

00:36:23.140 --> 00:36:26.008 and found over 2000 sites that

NOTE Confidence: 0.8489138

00:36:26.008 --> 00:36:27.442 survived genome wide.

NOTE Confidence: 0.8489138

00:36:27.450 --> 00:36:29.886 Adjustment and then the figure that

NOTE Confidence: 0.8489138

00:36:29.886 --> 00:36:32.487 you're looking at here on the right

NOTE Confidence: 0.8489138

00:36:32.487 --> 00:36:34.594 is showing all of the sites in

NOTE Confidence: 0.8489138

00:36:34.666 --> 00:36:37.102 blue and red across the different

NOTE Confidence: 0.8489138

00:36:37.102 --> 00:36:39.146 chromosomes in the human genome

NOTE Confidence: 0.8489138

00:36:39.146 --> 00:36:41.226 that were associated with infant

NOTE Confidence: 0.8489138

00:36:41.226 --> 00:36:43.888 birth weight in cord blood and

NOTE Confidence: 0.8489138

00:36:43.888 --> 00:36:45.736 from around 9000 participants.

NOTE Confidence: 0.8489138

00:36:45.740 --> 00:36:46.136 Now,

NOTE Confidence: 0.8489138

00:36:46.136 --> 00:36:49.304 one of the challenges with this approach is,

NOTE Confidence: 0.8489138

00:36:49.310 --> 00:36:52.883 as I said, you need very large sample sizes,

NOTE Confidence: 0.8489138

00:36:52.890 --> 00:36:54.875 but you also ideally would

NOTE Confidence: 0.8489138

00:36:54.875 --> 00:36:56.860 need to have longitudinal data.

NOTE Confidence: 0.8489138

00:36:56.860 --> 00:36:59.422 So for example in the birth weight

NOTE Confidence: 0.8489138

00:36:59.422 --> 00:37:02.018 study that I'm talking about here,

NOTE Confidence: 0.8489138

00:37:02.020 --> 00:37:04.438 they identified around 900 CPG's that

NOTE Confidence: 0.8489138

00:37:04.438 --> 00:37:06.498 were associated with birth weight

NOTE Confidence: 0.8489138

00:37:06.498 --> 00:37:08.766 for a subset of those participants.

NOTE Confidence: 0.8489138

00:37:08.770 --> 00:37:11.248 They then had longitudinal data and

NOTE Confidence: 0.8489138

00:37:11.248 --> 00:37:14.077 what they found was that of those

NOTE Confidence: 0.8489138

00:37:14.077 --> 00:37:16.856 900 sites only around 10% of them.

NOTE Confidence: 0.8489138

00:37:16.856 --> 00:37:18.748 We're still associated with

NOTE Confidence: 0.8489138

00:37:18.748 --> 00:37:21.868 birth weight at 7 years of age,

NOTE Confidence: 0.8489138

00:37:21.870 --> 00:37:24.810 and this highlights a complexity with

NOTE Confidence: 0.8489138

00:37:24.810 --> 00:37:27.588 epigenetic analysis that you don't have

NOTE Confidence: 0.8489138

00:37:27.588 --> 00:37:30.185 as it's not as strong a confounder

NOTE Confidence: 0.8489138

00:37:30.185 --> 00:37:33.009 with genome wide Association studies.

NOTE Confidence: 0.8489138

00:37:33.010 --> 00:37:35.038 This idea that there can be

NOTE Confidence: 0.8489138

00:37:35.038 --> 00:37:37.227 dynamic change in DNA methylation

NOTE Confidence: 0.8489138

00:37:37.227 --> 00:37:39.507 requiring longitudinal sampling.

NOTE Confidence: 0.8489138

00:37:39.510 --> 00:37:41.830 So what approaches can we

NOTE Confidence: 0.8489138

00:37:41.830 --> 00:37:44.150 take to overcome these issues?

NOTE Confidence: 0.8489138

00:37:44.150 --> 00:37:44.626 Well,

NOTE Confidence: 0.8489138

00:37:44.626 --> 00:37:47.958 one approach that has I've used extensively.

NOTE Confidence: 0.8489138

00:37:47.960 --> 00:37:50.280 Is that of an biomarkers?

NOTE Confidence: 0.8489138

00:37:50.280 --> 00:37:52.164 Epigenetic biomarkers that distill

NOTE Confidence: 0.8489138

00:37:52.164 --> 00:37:54.990 down and genome wide data into

NOTE Confidence: 0.8489138

00:37:55.065 --> 00:37:57.240 a single unit of measurements,

NOTE Confidence: 0.8489138

00:37:57.240 --> 00:37:59.560 and perhaps the most well

NOTE Confidence: 0.8489138

00:37:59.560 --> 00:38:01.416 established of these biomarkers,

NOTE Confidence: 0.8489138

00:38:01.420 --> 00:38:03.740 is that of epigenetic age,

NOTE Confidence: 0.8489138

00:38:03.740 --> 00:38:06.060 initially developed by Steve Horvath,

NOTE Confidence: 0.8489138

00:38:06.060 --> 00:38:07.664 an at UCLA Ann,

NOTE Confidence: 0.8489138

00:38:07.664 --> 00:38:10.070 and the idea with these epigenetic

NOTE Confidence: 0.8489138

00:38:10.152 --> 00:38:13.038 biomarkers is that we can identify

NOTE Confidence: 0.8489138

00:38:13.038 --> 00:38:14.962 sites that are predictive

NOTE Confidence: 0.79934704

00:38:15.045 --> 00:38:16.728 of chronological age,

NOTE Confidence: 0.79934704

00:38:16.730 --> 00:38:18.302 and we can create.

NOTE Confidence: 0.79934704

00:38:18.302 --> 00:38:19.874 A measure of epigenetic

NOTE Confidence: 0.79934704

00:38:19.874 --> 00:38:21.849 age for an individual.

NOTE Confidence: 0.79934704

00:38:21.850 --> 00:38:23.830 These clocks now exist with

NOTE Confidence: 0.79934704

00:38:23.830 --> 00:38:25.018 multi tissue predictors,

NOTE Confidence: 0.79934704

00:38:25.020 --> 00:38:27.246 so you can take any biological

NOTE Confidence: 0.79934704

00:38:27.246 --> 00:38:29.916 sample from anyone and you can then

NOTE Confidence: 0.79934704

00:38:29.916 --> 00:38:31.771 measure their epigenetic age and

NOTE Confidence: 0.79934704

00:38:31.771 --> 00:38:34.322 what we notice in population levels

NOTE Confidence: 0.79934704

00:38:34.322 --> 00:38:36.926 is that there are some individuals

NOTE Confidence: 0.79934704

00:38:36.930 --> 00:38:38.920 that you'll hire epigenetic age,

NOTE Confidence: 0.79934704

00:38:38.920 --> 00:38:40.428 relative chronological age and

NOTE Confidence: 0.79934704

00:38:40.428 --> 00:38:42.313 others that show lower epigenetic

NOTE Confidence: 0.79934704

00:38:42.313 --> 00:38:44.218 age relative to their chronological

NOTE Confidence: 0.79934704

00:38:44.218 --> 00:38:46.048 age and what's interesting is

NOTE Confidence: 0.79934704

00:38:46.048 --> 00:38:48.317 that those individuals with higher

NOTE Confidence: 0.79934704

00:38:48.317 --> 00:38:49.697 epigenetic age acceleration.

NOTE Confidence: 0.79934704

00:38:49.700 --> 00:38:55.130 Show increase risk for age related?

NOTE Confidence: 0.79934704

00:38:55.130 --> 00:38:57.682 Disorders including cardiovascular disease,

NOTE Confidence: 0.79934704

00:38:57.682 --> 00:39:00.872 but also all cause mortality.

NOTE Confidence: 0.79934704

00:39:00.880 --> 00:39:03.124 Now, one of the challenges with

NOTE Confidence: 0.79934704

00:39:03.124 --> 00:39:05.066 this epigenetic Clock from the

NOTE Confidence: 0.79934704

00:39:05.066 --> 00:39:06.562 multi tissue epigenetic Clock

NOTE Confidence: 0.79934704

00:39:06.562 --> 00:39:08.877 is that it was developed using

NOTE Confidence: 0.79934704

00:39:08.877 --> 00:39:10.747 primarily samples from adults and

NOTE Confidence: 0.79934704

00:39:10.747 --> 00:39:13.622 they ranged in age from zero to 100,

NOTE Confidence: 0.79934704

00:39:13.622 --> 00:39:15.680 but it was primarily samples from

NOTE Confidence: 0.79934704

00:39:15.748 --> 00:39:18.046 adult participants and the error in

NOTE Confidence: 0.79934704

00:39:18.046 --> 00:39:20.047 the prediction of the epigenetic

NOTE Confidence: 0.79934704

00:39:20.047 --> 00:39:22.423 Clock is around 3.6 years and

NOTE Confidence: 0.79934704

00:39:22.423 --> 00:39:24.757 which obviously is a very long

NOTE Confidence: 0.79934704

00:39:24.757 --> 00:39:27.410 time in the life of a child.

NOTE Confidence: 0.79934704

00:39:27.410 --> 00:39:29.726 So we set about creating a

NOTE Confidence: 0.79934704

00:39:29.726 --> 00:39:30.884 novel pediatric specific.

NOTE Confidence: 0.79934704

00:39:30.890 --> 00:39:31.680 Epigenetic Clock,

NOTE Confidence: 0.79934704

00:39:31.680 --> 00:39:33.655 which was published last year.

NOTE Confidence: 0.79934704

00:39:33.660 --> 00:39:35.645 We used approximately 2000 DNA

NOTE Confidence: 0.79934704

00:39:35.645 --> 00:39:38.106 methylome's and we simply asked what

NOTE Confidence: 0.79934704

00:39:38.106 --> 00:39:40.530 were the sites that were associated

NOTE Confidence: 0.79934704

00:39:40.530 --> 00:39:42.768 with chronological age in this cohort.

NOTE Confidence: 0.79934704

00:39:42.770 --> 00:39:44.690 This is data from longitudinal cohort

NOTE Confidence: 0.79934704

00:39:44.690 --> 00:39:47.055 where we use the original epigenetic

NOTE Confidence: 0.79934704

00:39:47.055 --> 00:39:49.107 Clock with longitudinal samples,

NOTE Confidence: 0.79934704

00:39:49.110 --> 00:39:52.206 and what you can appreciate from this is

NOTE Confidence: 0.79934704

00:39:52.206 --> 00:39:55.436 that the slopes are all over the place.

NOTE Confidence: 0.79934704

00:39:55.440 --> 00:39:57.330 An long digital samples that

NOTE Confidence: 0.79934704

00:39:57.330 --> 00:39:58.842 should be epigenetically older

NOTE Confidence: 0.79934704

00:39:58.842 --> 00:40:00.550 are appearing epigenetic.

NOTE Confidence: 0.79934704

00:40:00.550 --> 00:40:03.310 Younger and you can see this again here,

NOTE Confidence: 0.79934704

00:40:03.310 --> 00:40:05.368 and this simply reflects the error

NOTE Confidence: 0.79934704

00:40:05.368 --> 00:40:07.110 in the conventional epigenetic Clock.

NOTE Confidence: 0.79934704

00:40:07.110 --> 00:40:09.476 When we plot these data using the

NOTE Confidence: 0.79934704

00:40:09.476 --> 00:40:10.900 new pediatric epigenetic Clock,

NOTE Confidence: 0.79934704

00:40:10.900 --> 00:40:13.189 I think you can appreciate that the

NOTE Confidence: 0.79934704

00:40:13.189 --> 00:40:15.390 slopes become a lot more positive,

NOTE Confidence: 0.79934704

00:40:15.390 --> 00:40:18.158 so we brought the error in prediction of

NOTE Confidence: 0.79934704

00:40:18.158 --> 00:40:20.556 epigenetic age down to around six months,

NOTE Confidence: 0.79934704

00:40:20.560 --> 00:40:22.975 and many of you may be thinking,

NOTE Confidence: 0.79934704

00:40:22.980 --> 00:40:24.700 well, you know, that's great.

NOTE Confidence: 0.79934704

00:40:24.700 --> 00:40:26.450 You can just calculate someones

NOTE Confidence: 0.79934704

00:40:26.450 --> 00:40:28.839 age based on their date of birth.

NOTE Confidence: 0.79934704

00:40:28.840 --> 00:40:31.156 What is what value is this?

NOTE Confidence: 0.79934704

00:40:31.160 --> 00:40:33.806 An and so in this particular study,

NOTE Confidence: 0.79934704

00:40:33.810 --> 00:40:35.748 what we found was that children

NOTE Confidence: 0.79934704

00:40:35.748 --> 00:40:37.583 of the autism spectrum disorder

NOTE Confidence: 0.79934704

00:40:37.583 --> 00:40:39.499 had accelerated epigenetic age,

NOTE Confidence: 0.79934704

00:40:39.500 --> 00:40:42.132 an Association that we saw with the

NOTE Confidence: 0.79934704

00:40:42.132 --> 00:40:43.670 pediatric specific epigenetic Clock,

NOTE Confidence: 0.79934704

00:40:43.670 --> 00:40:46.960 but not with the conventional Horvath Clock.

NOTE Confidence: 0.79934704

00:40:46.960 --> 00:40:47.992 But of course,

NOTE Confidence: 0.79934704

00:40:47.992 --> 00:40:51.140 bringing us back to the topic of interest,

NOTE Confidence: 0.79934704

00:40:51.140 --> 00:40:53.800 the fetal origins of health and disease,

NOTE Confidence: 0.79934704

00:40:53.800 --> 00:40:56.271 we wanted to ask whether or not

NOTE Confidence: 0.79934704

00:40:56.271 --> 00:40:57.811 maternal prenatal anxiety would

NOTE Confidence: 0.79934704

00:40:57.811 --> 00:40:59.876 be associated with epigenetic age,

NOTE Confidence: 0.79934704

00:40:59.880 --> 00:41:00.207 acceleration,

NOTE Confidence: 0.79934704

00:41:00.207 --> 00:41:02.823 and to do that we made use of

NOTE Confidence: 0.79934704

00:41:02.823 --> 00:41:04.819 two longitudinal at courts,

NOTE Confidence: 0.79934704

00:41:04.820 --> 00:41:06.340 one from the Netherlands.

NOTE Confidence: 0.79934704

00:41:06.340 --> 00:41:07.860 That's primarily Caucasian one

NOTE Confidence: 0.79934704

00:41:07.860 --> 00:41:08.620 from Singapore,

NOTE Confidence: 0.79934704

00:41:08.620 --> 00:41:11.042 that's multi ethnic and what we found

NOTE Confidence: 0.79934704

00:41:11.042 --> 00:41:13.034 was that maternal prenatal anxiety

NOTE Confidence: 0.79934704

00:41:13.034 --> 00:41:14.798 was associated with accelerated

NOTE Confidence: 0.79934704

00:41:14.798 --> 00:41:17.449 epigenetic age at six years of age.

NOTE Confidence: 0.79934704

00:41:17.450 --> 00:41:20.447 In the 10 years of age in the Bible

NOTE Confidence: 0.79934704

00:41:20.447 --> 00:41:22.631 course and again we replicated

NOTE Confidence: 0.79934704

00:41:22.631 --> 00:41:24.836 this in the coastal court,

NOTE Confidence: 0.79934704

00:41:24.840 --> 00:41:26.452 finding that maternal prenatal

NOTE Confidence: 0.79934704

00:41:26.452 --> 00:41:28.064 anxiety was associated with

NOTE Confidence: 0.79934704

00:41:28.064 --> 00:41:29.120 accelerated epigenetic age,

NOTE Confidence: 0.79934704

00:41:29.120 --> 00:41:31.850 an effect that strengthens overtime

NOTE Confidence: 0.79934704

00:41:31.850 --> 00:41:34.580 is particularly pronounced at 48

NOTE Confidence: 0.8114952

00:41:34.665 --> 00:41:37.345 months of age. Now, one of the questions

NOTE Confidence: 0.8114952

00:41:37.345 --> 00:41:39.513 that again I'm very interested in is

NOTE Confidence: 0.8114952

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00:41:39.513 --> 00:41:41.452 is trying to understand whether or not

NOTE Confidence: 0.8114952

00:41:41.452 --> 00:41:43.858 there are features or aspects of the

NOTE Confidence: 0.8114952

00:41:43.858 --> 00:41:45.738 Pulcinella environment that may be able

NOTE Confidence: 0.8114952

00:41:45.738 --> 00:41:47.730 to buffer or moderate the effects of the

NOTE Confidence: 0.8114952

00:41:47.787 --> 00:41:49.967 prenatal environment on epigenetic states.

NOTE Confidence: 0.8114952

00:41:49.970 --> 00:41:51.570 Because of course it's very

NOTE Confidence: 0.8114952

00:41:51.570 --> 00:41:54.058 depressing to to give a talk and say,

NOTE Confidence: 0.8114952

00:41:54.060 --> 00:41:55.950 well, it's all over at birth,

NOTE Confidence: 0.8114952

00:41:55.950 --> 00:41:57.959 and of course it's much more optimistic

NOTE Confidence: 0.8114952

00:41:57.959 --> 00:42:00.208 and positive to say that there are

NOTE Confidence: 0.8114952

00:42:00.208 --> 00:42:01.878 potential interventions that we can

NOTE Confidence: 0.8114952

00:42:01.878 --> 00:42:03.879 implement that may buffer or mitigate

NOTE Confidence: 0.8114952

00:42:03.879 --> 00:42:05.494 the effects of prenatal adversity.

NOTE Confidence: 0.8114952

00:42:05.500 --> 00:42:08.340 This is a paper from my PhD mentors

NOTE Confidence: 0.8114952

00:42:08.340 --> 00:42:11.130 showing that an infant attachment style,

NOTE Confidence: 0.8114952

00:42:11.130 --> 00:42:13.310 so each child's perception of

00:42:13.310 --> 00:42:15.490 the predictability an index of

00:42:15.562 --> 00:42:17.956 the quality of care in the pools.

00:42:17.960 --> 00:42:19.504 Naval environment moderates the

00:42:19.504 --> 00:42:21.048 Association between prenatal cortisol

00:42:21.048 --> 00:42:23.188 exposure and child cognitive development.

00:42:23.190 --> 00:42:25.200 Of course, other examples exist.

00:42:25.200 --> 00:42:27.606 This is from the Boukris Early

00:42:27.606 --> 00:42:28.408 Intervention Project,

00:42:28.410 --> 00:42:30.780 showing that secure an infant attachment

00:42:30.780 --> 00:42:33.748 can buffer or moderate the effects of

00:42:33.748 --> 00:42:35.943 early adversity on child psychopathology.

00:42:35.950 --> 00:42:36.844 So of course,

00:42:36.844 --> 00:42:38.930 the question we wanted to ask with

00:42:38.993 --> 00:42:41.597 this study was whether or not infant

00:42:41.597 --> 00:42:43.916 attachment would buffer or moderate the

00:42:43.916 --> 00:42:45.806 effects of maternal prenatal anxiety

NOTE Confidence: 0.8114952

00:42:45.806 --> 00:42:47.629 on child epigenetic age acceleration.

NOTE Confidence: 0.8114952

00:42:47.629 --> 00:42:49.394 And this is unpublished data.

NOTE Confidence: 0.8114952

00:42:49.400 --> 00:42:51.677 But what we find is that yes indeed in

NOTE Confidence: 0.8114952

00:42:51.677 --> 00:42:53.368 children that have secure attachment

NOTE Confidence: 0.8114952

00:42:53.368 --> 00:42:55.438 we see a positive but nonsignificant

NOTE Confidence: 0.8114952

00:42:55.492 --> 00:42:57.300 Association between maternal prenatal

NOTE Confidence: 0.8114952

00:42:57.300 --> 00:42:59.560 anxiety and child epigenetic age

NOTE Confidence: 0.8114952

00:42:59.560 --> 00:43:00.012 acceleration,

NOTE Confidence: 0.8114952

00:43:00.020 --> 00:43:01.946 but the effects of maternal prenatal

NOTE Confidence: 0.8114952

00:43:01.946 --> 00:43:03.695 anxiety on child epigenetic age

NOTE Confidence: 0.8114952

00:43:03.695 --> 00:43:04.922 acceleration are particularly

NOTE Confidence: 0.8114952

00:43:04.922 --> 00:43:06.149 pronounced in children.

NOTE Confidence: 0.8114952

00:43:06.150 --> 00:43:08.590 With an insecure attachment style.

NOTE Confidence: 0.8114952

00:43:08.590 --> 00:43:11.985 Again supporting this idea of a potential,

NOTE Confidence: 0.8114952

00:43:11.990 --> 00:43:15.770 pools Natal moderation of infant attachment.

NOTE Confidence: 0.8114952

00:43:15.770 --> 00:43:18.598 Now of course there are other M

NOTE Confidence: 0.8114952

00:43:18.598 --> 00:43:20.503 epigenetic biomarkers that we can

NOTE Confidence: 0.8114952

00:43:20.503 --> 00:43:22.652 use to try and probe our describe

NOTE Confidence: 0.8114952

00:43:22.652 --> 00:43:24.914 the effects of the environment

NOTE Confidence: 0.8114952

00:43:24.914 --> 00:43:26.798 on health related outcomes.

NOTE Confidence: 0.8114952

00:43:26.800 --> 00:43:29.164 This is one that we're starting

NOTE Confidence: 0.8114952

00:43:29.164 --> 00:43:30.740 to make use of.

NOTE Confidence: 0.8114952

00:43:30.740 --> 00:43:32.636 It's a second generation after genetic

NOTE Confidence: 0.8114952

00:43:32.636 --> 00:43:34.834 Clock and what is different about

NOTE Confidence: 0.8114952

00:43:34.834 --> 00:43:37.444 this epigenetic biomarker is that it

NOTE Confidence: 0.8114952

00:43:37.444 --> 00:43:39.211 incorporates information about plasma

NOTE Confidence: 0.8114952

00:43:39.211 --> 00:43:41.301 proteins that are associated with

NOTE Confidence: 0.8114952

00:43:41.301 --> 00:43:43.396 cardiovascular disease risk as well

NOTE Confidence: 0.8114952

00:43:43.396 --> 00:43:45.904 as sites that are associated with.

NOTE Confidence: 0.8114952

00:43:45.910 --> 00:43:47.854 Aging and we wanted to determine

NOTE Confidence: 0.8114952

00:43:47.854 --> 00:43:50.421 whether or not there was any Association

NOTE Confidence: 0.8114952

00:43:50.421 --> 00:43:52.839 between an early adversity and this

NOTE Confidence: 0.8114952

00:43:52.839 --> 00:43:54.524 epigenetic biomarker making use

NOTE Confidence: 0.8114952

00:43:54.524 --> 00:43:56.549 of the Nurse Family Partnership,

NOTE Confidence: 0.8114952

00:43:56.550 --> 00:43:58.755 which many of you will know is

NOTE Confidence: 0.8114952

00:43:58.755 --> 00:44:00.639 a randomized control trial of

NOTE Confidence: 0.8114952

00:44:00.639 --> 00:44:02.391 the perinatal intervention that

NOTE Confidence: 0.8114952

00:44:02.391 --> 00:44:04.143 targets vulnerable low income.

NOTE Confidence: 0.8114952

00:44:04.150 --> 00:44:06.280 First time moms and it provides

NOTE Confidence: 0.8114952

00:44:06.280 --> 00:44:08.525 nurse visitations have been shown to

NOTE Confidence: 0.8114952

00:44:08.525 --> 00:44:10.420 reduce child maltreatment an improve

NOTE Confidence: 0.8114952

00:44:10.420 --> 00:44:12.890 outcomes for both mothers and children.

NOTE Confidence: 0.8114952

00:44:12.890 --> 00:44:14.850 We published the first epigenetic

NOTE Confidence: 0.8114952

00:44:14.850 --> 00:44:16.418 analysis in this cohort.

NOTE Confidence: 0.8114952

00:44:16.420 --> 00:44:18.874 A collaboration with Jim Lechman and

NOTE Confidence: 0.8114952

00:44:18.874 --> 00:44:21.202 Elena Grigorenko when she was based

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NOTE Confidence: 0.8114952

00:44:21.202 --> 00:44:23.682 here and we found that there was some

NOTE Confidence: 0.8114952

00:44:23.753 --> 00:44:25.917 preliminary Association between nurse

NOTE Confidence: 0.8114952

00:44:25.917 --> 00:44:29.163 Visitation and variation in DNA methylation.

NOTE Confidence: 0.8114952

00:44:29.170 --> 00:44:31.676 But really the take home message was

NOTE Confidence: 0.8114952

00:44:31.676 --> 00:44:34.788 that there was a profound effect of

NOTE Confidence: 0.8114952

00:44:34.788 --> 00:44:37.243 childhood maltreatment on DNA methylation,

NOTE Confidence: 0.8114952

00:44:37.250 --> 00:44:39.370 but we couldn't distinguish the

NOTE Confidence: 0.8114952

00:44:39.370 --> 00:44:41.066 effects of maltreatment from,

NOTE Confidence: 0.8114952

00:44:41.070 --> 00:44:42.345 say, for example,

NOTE Confidence: 0.8114952

00:44:42.345 --> 00:44:44.045 the effects of associated

NOTE Confidence: 0.8114952

00:44:44.045 --> 00:44:45.320 confounders like smoking.

NOTE Confidence: 0.8114952

00:44:45.320 --> 00:44:46.685 So what about?

NOTE Confidence: 0.8114952

00:44:46.685 --> 00:44:48.960 This measure of epigenetic age,

NOTE Confidence: 0.8456794

00:44:48.960 --> 00:44:51.704 acceleration in the context of the Nurse,

NOTE Confidence: 0.8456794

00:44:51.710 --> 00:44:52.376 Family, Partnership,

NOTE Confidence: 0.8456794

00:44:52.376 --> 00:44:55.040 or what we see is that children with

NOTE Confidence: 0.8456794

00:44:55.100 --> 00:44:57.656 a documented or substantiated case of

NOTE Confidence: 0.8456794

00:44:57.656 --> 00:44:59.360 child maltreatment show accelerated

NOTE Confidence: 0.8456794

00:44:59.426 --> 00:45:01.526 epigenetic aging using this disease.

NOTE Confidence: 0.8456794

00:45:01.530 --> 00:45:02.943 Relevant epigenetic biomarker.

NOTE Confidence: 0.8456794

00:45:02.943 --> 00:45:06.240 But what about when we break this

NOTE Confidence: 0.8456794

00:45:06.320 --> 00:45:08.438 down by an intervention group or

NOTE Confidence: 0.8456794

00:45:08.438 --> 00:45:11.286 what we find is that in the nurse

NOTE Confidence: 0.8456794

00:45:11.286 --> 00:45:13.712 visit a group in purple here and

NOTE Confidence: 0.8456794

00:45:13.712 --> 00:45:16.064 the yellow is the control group.

NOTE Confidence: 0.8456794

00:45:16.070 --> 00:45:18.150 We find no difference in

NOTE Confidence: 0.8456794

00:45:18.150 --> 00:45:19.398 epigenetic age acceleration.

NOTE Confidence: 0.8456794

00:45:19.400 --> 00:45:21.640 As a function in those individuals that

NOTE Confidence: 0.8456794

00:45:21.640 --> 00:45:24.517 don't have a history of child maltreatment.

NOTE Confidence: 0.8456794

00:45:24.520 --> 00:45:27.337 But when we look in the group that does

NOTE Confidence: 0.8456794

00:45:27.337 --> 00:45:30.008 have a history of child maltreatment,

NOTE Confidence: 0.8456794

00:45:30.010 --> 00:45:31.478 we see significantly increased

NOTE Confidence: 0.8456794

00:45:31.478 --> 00:45:32.579 an epigenetic age,

NOTE Confidence: 0.8456794

00:45:32.580 --> 00:45:34.410 acceleration and those individuals that

NOTE Confidence: 0.8456794

00:45:34.410 --> 00:45:36.657 have a history of child maltreatment

NOTE Confidence: 0.8456794

00:45:36.657 --> 00:45:38.799 that are in the control group.

NOTE Confidence: 0.8456794

00:45:38.800 --> 00:45:40.714 But it seems that exposure to

NOTE Confidence: 0.8456794

00:45:40.714 --> 00:45:42.409 nurse Visitation to that early

NOTE Confidence: 0.8456794

00:45:42.409 --> 00:45:44.209 intervention seems to be buffering

NOTE Confidence: 0.8456794

00:45:44.209 --> 00:45:46.480 the effects of child maltreatment.

NOTE Confidence: 0.8456794

00:45:46.480 --> 00:45:48.044 An epigenetic age acceleration.

NOTE Confidence: 0.8456794

00:45:48.044 --> 00:45:49.608 Now we can discuss.

NOTE Confidence: 0.8456794

00:45:49.610 --> 00:45:51.234 Potential explanations for this

NOTE Confidence: 0.8456794

00:45:51.234 --> 00:45:53.264 one possibility is that perhaps

NOTE Confidence: 0.8456794

00:45:53.264 --> 00:45:55.661 the severity of abuse was less in

NOTE Confidence: 0.8456794

00:45:55.661 --> 00:45:57.790 the nurse visited group that there

NOTE Confidence: 0.8456794

00:45:57.790 --> 00:45:59.740 was greater surveillance of abuse,

NOTE Confidence: 0.8456794

00:45:59.740 --> 00:46:01.990 and the nurse visited group an.

NOTE Confidence: 0.8456794

00:46:01.990 --> 00:46:03.775 An alternative hypothesis is that

NOTE Confidence: 0.8456794

00:46:03.775 --> 00:46:05.560 the early intervention is providing

NOTE Confidence: 0.8456794

00:46:05.617 --> 00:46:06.859 some buffering capacity,

NOTE Confidence: 0.8456794

00:46:06.860 --> 00:46:09.860 so even in the face of child maltreatment,

NOTE Confidence: 0.8456794

00:46:09.860 --> 00:46:12.242 there's less of an impact on

NOTE Confidence: 0.8456794

00:46:12.242 --> 00:46:13.830 epigenetic age acceleration just

NOTE Confidence: 0.8456794

00:46:13.903 --> 00:46:15.859 in the last couple of minutes.

NOTE Confidence: 0.8456794

00:46:15.860 --> 00:46:18.758 I just like to tell you about one of

NOTE Confidence: 0.8456794

00:46:18.758 --> 00:46:21.987 the biomarker that we're making use of.

NOTE Confidence: 0.8456794

00:46:21.990 --> 00:46:24.180 Which is a measure that relates

NOTE Confidence: 0.8456794

00:46:24.180 --> 00:46:26.650 to this paper I highlighted,

NOTE Confidence: 0.8456794

00:46:26.650 --> 00:46:28.350 previously speaking to this

NOTE Confidence: 0.8456794

00:46:28.350 --> 00:46:30.050 idea of genomic priming,

NOTE Confidence: 0.8456794

00:46:30.050 --> 00:46:32.874 and in this paper they created an epigenetic

NOTE Confidence: 0.8456794

00:46:32.874 --> 00:46:35.129 biomarker of glucocorticoid exposure,

NOTE Confidence: 0.8456794

00:46:35.130 --> 00:46:37.601 and so this essentially we can create

NOTE Confidence: 0.8456794

00:46:37.601 --> 00:46:40.908 a an index or a proxy measure for

NOTE Confidence: 0.8456794

00:46:40.908 --> 00:46:42.644 glucocorticoid exposure based on

NOTE Confidence: 0.8456794

00:46:42.644 --> 00:46:45.732 DNA methylation, and so we created.

NOTE Confidence: 0.8456794

00:46:45.732 --> 00:46:47.424 We use this array.

NOTE Confidence: 0.8456794

00:46:47.430 --> 00:46:49.614 Tested this out in a court

NOTE Confidence: 0.8456794

00:46:49.614 --> 00:46:52.170 where we had DNA methylation.

NOTE Confidence: 0.8456794

00:46:52.170 --> 00:46:54.860 Data upper than at one year of age in a

NOTE Confidence: 0.8456794

00:46:54.935 --> 00:46:57.767 cohort from the University of California,

NOTE Confidence: 0.8456794

00:46:57.770 --> 00:46:58.112 Irvine,

NOTE Confidence: 0.8456794

00:46:58.112 --> 00:47:00.506 and we also had structural imaging in

NOTE Confidence: 0.8456794

00:47:00.506 --> 00:47:02.660 this cohort and what we simply asked

NOTE Confidence: 0.8456794

00:47:02.660 --> 00:47:04.958 was whether or not the sites that

NOTE Confidence: 0.8456794

00:47:04.958 --> 00:47:07.028 were associated DNA methylation sites

NOTE Confidence: 0.8456794

00:47:07.028 --> 00:47:08.998 that were associated with maternal

NOTE Confidence: 0.8456794

00:47:08.998 --> 00:47:10.818 prenatal depression did they overlap

NOTE Confidence: 0.8456794

00:47:10.818 --> 00:47:13.064 with the sites that were identified

NOTE Confidence: 0.8456794

00:47:13.064 --> 00:47:14.884 to be glucocorticoid sensitive sites

NOTE Confidence: 0.8456794

00:47:14.884 --> 00:47:17.019 in that paper that I showed you.

NOTE Confidence: 0.8456794

00:47:17.020 --> 00:47:17.790 And indeed,

NOTE Confidence: 0.8456794

00:47:17.790 --> 00:47:19.330 we found significant enrichment

NOTE Confidence: 0.8456794

00:47:19.330 --> 00:47:20.870 of glucocorticoid sensitive sites

NOTE Confidence: 0.8456794

00:47:20.926 --> 00:47:23.026 in the sites that were associated

NOTE Confidence: 0.8456794

00:47:23.026 --> 00:47:24.076 maternal prenatal depression.

NOTE Confidence: 0.8456794

00:47:24.080 --> 00:47:26.504 And when we created this Google

NOTE Confidence: 0.8456794

00:47:26.504 --> 00:47:27.716 Corticoid exposure score,

NOTE Confidence: 0.8456794

00:47:27.720 --> 00:47:30.120 we saw a significant negative Association

NOTE Confidence: 0.8456794

00:47:30.120 --> 00:47:31.720 between maternal prenatal depression

NOTE Confidence: 0.8456794

00:47:31.777 --> 00:47:33.777 and this glucocorticoid exposure score.

NOTE Confidence: 0.8456794

00:47:33.780 --> 00:47:34.902 And interesting Lee,

NOTE Confidence: 0.8456794

00:47:34.902 --> 00:47:37.520 what we found was that this glucocorticoid

NOTE Confidence: 0.8456794

00:47:37.585 --> 00:47:39.730 exposure score at birth predicted

NOTE Confidence: 0.8456794

00:47:39.730 --> 00:47:41.446 lower hippocampal volume birth,

NOTE Confidence: 0.8456794

00:47:41.450 --> 00:47:42.994 and as you'll appreciate,

NOTE Confidence: 0.8456794

00:47:42.994 --> 00:47:44.538 the hippocampus is enriched

NOTE Confidence: 0.8456794

00:47:44.538 --> 00:47:45.900 for glucocorticoid receptors.

NOTE Confidence: 0.8456794

00:47:45.900 --> 00:47:48.280 So we find that the direction of

NOTE Confidence: 0.8456794

00:47:48.280 --> 00:47:49.844 this Association is consistent

NOTE Confidence: 0.8456794

00:47:49.844 --> 00:47:52.199 with a higher maternal prenatal

NOTE Confidence: 0.8456794

00:47:52.199 --> 00:47:54.550 liberation predicting a lower score.

NOTE Confidence: 0.8456794

00:47:54.550 --> 00:47:57.550 And a lower score predicting

NOTE Confidence: 0.8456794

00:47:57.550 --> 00:47:59.350 lower hippocampal volume.

NOTE Confidence: 0.8456794

00:47:59.350 --> 00:48:00.558 So, just to summarize,

NOTE Confidence: 0.8456794

00:48:00.558 --> 00:48:02.821 I think that with some of the

NOTE Confidence: 0.8456794

00:48:02.821 --> 00:48:04.741 studies that I've tried to

NOTE Confidence: 0.8456794

00:48:04.741 --> 00:48:06.277 highlight perhaps very quickly

NOTE Confidence: 0.84173185

00:48:06.342 --> 00:48:08.694 today, we can see that variation in

NOTE Confidence: 0.84173185

00:48:08.694 --> 00:48:10.447 DNA methylation is associated with

NOTE Confidence: 0.84173185

00:48:10.447 --> 00:48:12.337 variation in the early environment.

NOTE Confidence: 0.84173185

00:48:12.340 --> 00:48:14.564 I think as we move towards trying to

NOTE Confidence: 0.84173185

00:48:14.564 --> 00:48:16.899 make these findings clinically relevant,

NOTE Confidence: 0.84173185

00:48:16.900 --> 00:48:18.993 we need to move towards more integrative

NOTE Confidence: 0.84173185

00:48:18.993 --> 00:48:20.386 models where we're incorporating

NOTE Confidence: 0.84173185

00:48:20.386 --> 00:48:22.170 measures of genetic variation,

NOTE Confidence: 0.84173185

00:48:22.170 --> 00:48:23.925 and we're incorporating an greater

NOTE Confidence: 0.84173185

00:48:23.925 --> 00:48:25.680 measures of the social environment,

NOTE Confidence: 0.84173185

00:48:25.680 --> 00:48:28.144 and I think one way that we

NOTE Confidence: 0.84173185

00:48:28.144 --> 00:48:30.000 can really begin to probe.

NOTE Confidence: 0.84173185

00:48:30.000 --> 00:48:32.105 Causal associations between the social

NOTE Confidence: 0.84173185

00:48:32.105 --> 00:48:33.789 environment and epigenetic states

NOTE Confidence: 0.84173185

00:48:33.789 --> 00:48:36.117 is through the use of interventions,

NOTE Confidence: 0.84173185

00:48:36.120 --> 00:48:39.081 and this is an area that I'm

NOTE Confidence: 0.84173185

00:48:39.081 --> 00:48:41.830 particularly keen to do more work in,

NOTE Confidence: 0.84173185

00:48:41.830 --> 00:48:43.852 and one collaboration that I'm very

NOTE Confidence: 0.84173185

00:48:43.852 --> 00:48:46.163 excited about is a cluster randomized

NOTE Confidence: 0.84173185

00:48:46.163 --> 00:48:48.408 control trial of parental intervention

NOTE Confidence: 0.84173185

00:48:48.408 --> 00:48:51.095 that begins in early pregnancy that

NOTE Confidence: 0.84173185

00:48:51.095 --> 00:48:53.215 seeks to reduce prenatal anxiety

NOTE Confidence: 0.84173185

00:48:53.215 --> 00:48:55.698 and depression but also provide an

NOTE Confidence: 0.84173185

00:48:55.698 --> 00:48:57.733 information about nutrition and sleep,

NOTE Confidence: 0.84173185

00:48:57.740 --> 00:49:00.143 trying to reduce domestic violence, an.

NOTE Confidence: 0.84173185

00:49:00.143 --> 00:49:01.958 An increase female empowerment and

NOTE Confidence: 0.84173185

00:49:01.958 --> 00:49:04.285 we're doing this in rural Vietnam

NOTE Confidence: 0.84173185

00:49:04.285 --> 00:49:06.300 with my colleague James Fisher,

NOTE Confidence: 0.84173185

00:49:06.300 --> 00:49:08.382 where one in three women can

NOTE Confidence: 0.84173185

00:49:08.382 --> 00:49:10.254 experience or struggle with their

NOTE Confidence: 0.84173185

00:49:10.254 --> 00:49:11.938 mental health and pregnancy.

NOTE Confidence: 0.84173185

00:49:11.940 --> 00:49:14.220 We're just coordinating to receive

NOTE Confidence: 0.84173185

00:49:14.220 --> 00:49:16.500 samples from approximately 1200 mothers

NOTE Confidence: 0.84173185

00:49:16.563 --> 00:49:18.288 and their infants with biological

NOTE Confidence: 0.84173185

00:49:18.288 --> 00:49:21.332 samples at birth at 12 months and a 24

NOTE Confidence: 0.84173185

00:49:21.332 --> 00:49:23.216 months MA which have been collected

NOTE Confidence: 0.84173185

00:49:23.220 --> 00:49:24.720 in parallel with standardized

NOTE Confidence: 0.84173185

00:49:24.720 --> 00:49:26.595 measures of child newer development.

NOTE Confidence: 0.84173185

00:49:26.600 --> 00:49:29.240 And really the goal with these

NOTE Confidence: 0.84173185

00:49:29.240 --> 00:49:32.149 kind of studies and the goal of.

NOTE Confidence: 0.84173185

00:49:32.150 --> 00:49:33.946 Understanding epigenetic States and

NOTE Confidence: 0.84173185

00:49:33.946 --> 00:49:35.742 modifications and implementing them

NOTE Confidence: 0.84173185

00:49:35.742 --> 00:49:37.780 in clinical studies is really to

NOTE Confidence: 0.84173185

00:49:37.780 --> 00:49:39.869 try and understand how we can make

NOTE Confidence: 0.84173185

00:49:39.869 --> 00:49:41.899 interventions work from war individuals,

NOTE Confidence: 0.84173185

00:49:41.900 --> 00:49:44.511 so I'll leave it there with maybe

NOTE Confidence: 0.84173185

00:49:44.511 --> 00:49:47.150 just one kind of call to action.

NOTE Confidence: 0.84173185

00:49:47.150 --> 00:49:49.398 I was very pleased to be invited to

NOTE Confidence: 0.84173185

00:49:49.398 --> 00:49:51.961 take part in the Scientific Council

NOTE Confidence: 0.84173185

00:49:51.961 --> 00:49:53.897 of Postpartum Support International,

NOTE Confidence: 0.84173185

00:49:53.900 --> 00:49:56.301 and this is a plug for their

NOTE Confidence: 0.84173185

00:49:56.301 --> 00:49:58.695 national strategy on how we can

NOTE Confidence: 0.84173185

00:49:58.695 --> 00:50:00.415 improve perinatal mental health.

NOTE Confidence: 0.84173185

00:50:00.420 --> 00:50:03.201 And so I think this is a societal problem

NOTE Confidence: 0.84173185

00:50:03.201 --> 00:50:05.538 that requires a societal response,

NOTE Confidence: 0.84173185

00:50:05.540 --> 00:50:07.490 and I think we're all responsible

NOTE Confidence: 0.84173185

00:50:07.490 --> 00:50:09.654 for playing our part and trying

NOTE Confidence: 0.84173185

00:50:09.654 --> 00:50:11.644 to support perinatal mental health

NOTE Confidence: 0.84173185

00:50:11.644 --> 00:50:13.624 and recognizing that there are

NOTE Confidence: 0.84173185

00:50:13.624 --> 00:50:15.072 structural and societal factors

NOTE Confidence: 0.84173185

00:50:15.072 --> 00:50:17.984 that we can target and to try and

NOTE Confidence: 0.84173185

00:50:17.984 --> 00:50:19.448 improve perinatal mental health.

NOTE Confidence: 0.84173185

00:50:19.450 --> 00:50:22.117 And this isn't just all pregnant mothers

NOTE Confidence: 0.84173185

00:50:22.117 --> 00:50:24.938 and have another thing to worry about an,

NOTE Confidence: 0.84173185

00:50:24.940 --> 00:50:27.828 so I'll leave it with that and just

NOTE Confidence: 0.84173185

00:50:27.828 --> 00:50:31.206 thank you all for your attention and take.

NOTE Confidence: 0.84173185

00:50:31.210 --> 00:50:31.930 Any questions?

NOTE Confidence: 0.899965584615385

00:50:41.340 --> 00:50:43.026 Fantastic. Questions please.

NOTE Confidence: 0.899965584615385

00:50:43.026 --> 00:50:48.339 Just go for it or put it in the text.

NOTE Confidence: 0.79708225

00:50:50.790 --> 00:50:54.137 Hi, this is Flora. Do you hear me?

NOTE Confidence: 0.79708225

00:50:54.137 --> 00:50:56.641 Yes yes Laura hi sorry hi,

NOTE Confidence: 0.79708225

00:50:56.641 --> 00:50:58.976 how are you really? Nice talk.

NOTE Confidence: 0.79708225

00:50:58.976 --> 00:51:02.182 I had a question um so so as you

NOTE Confidence: 0.79708225

00:51:02.182 --> 00:51:04.447 know epigenetics are very much

NOTE Confidence: 0.79708225

00:51:04.447 --> 00:51:07.263 self type an organ specific so

NOTE Confidence: 0.79708225

00:51:07.263 --> 00:51:10.017 perhaps you can clarify for us.

NOTE Confidence: 0.79708225

00:51:10.020 --> 00:51:12.904 I mean of course studies in humans

NOTE Confidence: 0.79708225

00:51:12.904 --> 00:51:15.634 cannot be done in brain whereas

NOTE Confidence: 0.79708225

00:51:15.634 --> 00:51:18.454 studies in animals can and I'm

NOTE Confidence: 0.79708225

00:51:18.454 --> 00:51:20.946 assuming some of those that you.

NOTE Confidence: 0.79708225

00:51:20.950 --> 00:51:23.355 Elucidated or talked about where

NOTE Confidence: 0.79708225

00:51:23.355 --> 00:51:26.995 done in mouse or rat brains, right?

NOTE Confidence: 0.79708225

00:51:26.995 --> 00:51:28.005 So perhaps,

NOTE Confidence: 0.79708225

00:51:28.005 --> 00:51:30.530 given the course profound difficulties,

NOTE Confidence: 0.79708225

00:51:30.530 --> 00:51:31.914 you know?

NOTE Confidence: 0.79708225

00:51:31.914 --> 00:51:35.374 Same brain samples from humans

NOTE Confidence: 0.79708225

00:51:35.374 --> 00:51:36.758 living individuals.

NOTE Confidence: 0.79708225

00:51:36.760 --> 00:51:41.224 Is it been any study in animals that has?

NOTE Confidence: 0.79708225

00:51:41.230 --> 00:51:43.480 Um illuminated this concept to

NOTE Confidence: 0.79708225

00:51:43.480 --> 00:51:45.280 what extent peripheral samples

NOTE Confidence: 0.79708225

00:51:45.280 --> 00:51:48.056 like blood can inform us on what's

NOTE Confidence: 0.79708225

00:51:48.056 --> 00:51:50.330 actually happening in the brain or

NOTE Confidence: 0.79708225

00:51:50.330 --> 00:51:52.430 the individuals as they grow up,

NOTE Confidence: 0.79708225

00:51:52.430 --> 00:51:54.030 and an and develop.

NOTE Confidence: 0.8073601

00:51:55.020 --> 00:51:56.925 Yeah floor this is such

NOTE Confidence: 0.8073601

00:51:56.925 --> 00:51:58.449 a great great question.

NOTE Confidence: 0.8073601

00:51:58.450 --> 00:52:01.879 And as as you've shown with your own work,

NOTE Confidence: 0.8073601

00:52:01.880 --> 00:52:03.424 talking about somatic mutations,

NOTE Confidence: 0.8073601

00:52:03.424 --> 00:52:06.172 and we know that even genetic variants

NOTE Confidence: 0.8073601

00:52:06.172 --> 00:52:08.338 may not be shared across different

NOTE Confidence: 0.8073601

00:52:08.338 --> 00:52:10.639 tissues and so there have been

NOTE Confidence: 0.8073601

00:52:10.639 --> 00:52:12.549 attempts to address this problem.

NOTE Confidence: 0.8073601

00:52:12.550 --> 00:52:14.034 And so for example,

NOTE Confidence: 0.8073601

00:52:14.034 --> 00:52:15.889 there's a tool called Pecan

NOTE Confidence: 0.8073601

00:52:15.889 --> 00:52:17.498 developed by Michael Horror,

NOTE Confidence: 0.8073601

00:52:17.500 --> 00:52:19.080 Gustavo Tracking Michael Meaney,

NOTE Confidence: 0.8073601

00:52:19.080 --> 00:52:21.862 which actually does a paired comparison of

NOTE Confidence: 0.8073601

00:52:21.862 --> 00:52:23.980 DNA methylation in multiple brain regions,

91

NOTE Confidence: 0.8073601

00:52:23.980 --> 00:52:25.640 and unfortunately is just

NOTE Confidence: 0.8073601

00:52:25.640 --> 00:52:26.885 in peripheral blood.

NOTE Confidence: 0.8073601

00:52:26.890 --> 00:52:29.235 At the moment and looks at the

NOTE Confidence: 0.8073601

00:52:29.235 --> 00:52:31.097 correspondence between DNA methylation and

NOTE Confidence: 0.8073601

00:52:31.097 --> 00:52:33.479 in blood with different brain regions,

NOTE Confidence: 0.8073601

00:52:33.480 --> 00:52:35.727 and they identify CPG's that show a

NOTE Confidence: 0.8073601

00:52:35.727 --> 00:52:38.238 higher degree of concordance than others.

NOTE Confidence: 0.8073601

00:52:38.240 --> 00:52:40.795 I think your point is well taken,

NOTE Confidence: 0.8073601

00:52:40.800 --> 00:52:43.472 this is the idea that we can take

NOTE Confidence: 0.8073601

00:52:43.472 --> 00:52:45.582 a peripheral sample like blood and

NOTE Confidence: 0.8073601

00:52:45.582 --> 00:52:48.115 say that this is going to predict

NOTE Confidence: 0.8073601

00:52:48.115 --> 00:52:50.964 DNA methylation state in a neuron in

NOTE Confidence: 0.8073601

00:52:50.964 --> 00:52:53.244 the dentate gyrus of the hippocampus

NOTE Confidence: 0.8073601

00:52:53.244 --> 00:52:55.440 I think would is a stretch.

NOTE Confidence: 0.8073601

00:52:55.440 --> 00:52:57.708 I think that it's going to.

NOTE Confidence: 0.8073601

00:52:57.710 --> 00:52:59.918 Be very challenging to identify and
NOTE Confidence: 0.8073601

00:52:59.918 --> 00:53:02.728 sites where there is a high degree
NOTE Confidence: 0.8073601

00:53:02.728 --> 00:53:04.833 of correspondence in specific brain
NOTE Confidence: 0.8073601

00:53:04.833 --> 00:53:06.799 nuclei between brain and blood.
NOTE Confidence: 0.8073601

00:53:06.800 --> 00:53:09.304 Where I think we can begin to get
NOTE Confidence: 0.8073601

00:53:09.304 --> 00:53:11.367 a better understanding of pathways
NOTE Confidence: 0.8073601

00:53:11.367 --> 00:53:14.545 that are likely to be shared across
NOTE Confidence: 0.8073601

00:53:14.625 --> 00:53:17.841 brain and periphery is if we focus on
NOTE Confidence: 0.8073601

00:53:17.841 --> 00:53:20.110 specific regions in the genome where
NOTE Confidence: 0.8073601

00:53:20.110 --> 00:53:22.300 there may be snips that influence
NOTE Confidence: 0.8073601

00:53:22.373 --> 00:53:24.809 DNA methylation in the periphery that
NOTE Confidence: 0.8073601

00:53:24.809 --> 00:53:27.818 also are shared snips that influence DNS.
NOTE Confidence: 0.8073601

00:53:27.820 --> 00:53:30.088 Relation in central and we can use
NOTE Confidence: 0.8073601

00:53:30.088 --> 00:53:31.743 the peripheral tissue essentially as
NOTE Confidence: 0.8073601

00:53:31.743 --> 00:53:33.927 a model Organism to say look this
NOTE Confidence: 0.8073601

00:53:33.927 --> 00:53:36.383 proof of principle that this exposure

NOTE Confidence: 0.8073601

00:53:36.383 --> 00:53:38.463 influences DNA methylation or inclusion.

NOTE Confidence: 0.8073601

00:53:38.470 --> 00:53:40.210 Influences the relationship between the

NOTE Confidence: 0.8073601

00:53:40.210 --> 00:53:42.729 snip and DNA methylation in the periphery.

NOTE Confidence: 0.8073601

00:53:42.730 --> 00:53:44.505 And perhaps this could be

NOTE Confidence: 0.8073601

00:53:44.505 --> 00:53:45.925 occurring in the brain.

NOTE Confidence: 0.8073601

00:53:45.930 --> 00:53:48.054 But then we would need to

NOTE Confidence: 0.8073601

00:53:48.054 --> 00:53:49.116 document that experimentally,

NOTE Confidence: 0.8073601

00:53:49.120 --> 00:53:51.250 either in cell culture in ipsc's.

NOTE Confidence: 0.82129586

00:54:03.860 --> 00:54:06.808 Any other questions anyone?

NOTE Confidence: 0.848256866666667

00:54:11.510 --> 00:54:14.066 Well, it's. It is 2:00 o'clock,

NOTE Confidence: 0.848256866666667

00:54:14.070 --> 00:54:15.580 Kieran saved by the Bell.

NOTE Confidence: 0.848256866666667

00:54:15.580 --> 00:54:17.892 But thank you so much that was really

NOTE Confidence: 0.848256866666667

00:54:17.892 --> 00:54:19.827 a marvelous presentation and we learn

NOTE Confidence: 0.848256866666667

00:54:19.827 --> 00:54:22.113 so much and wonderful to have you

NOTE Confidence: 0.848256866666667

00:54:22.113 --> 00:54:24.329 here and we look forward to all that

NOTE Confidence: 0.848256866666667

00:54:24.329 --> 00:54:26.110 you'll teach us another ideal do.

NOTE Confidence: 0.848256866666667

00:54:26.110 --> 00:54:28.217 So thank you here and thank you

NOTE Confidence: 0.817174

00:54:28.220 --> 00:54:29.730 very much. Thank you everyone.