WEBVTT

1 00:06:17.340 --> 00:06:22.400 Alixandra Rachman: It's my great pleasure today to introduce of the colleague, Dr. The home

2 00:06:22.640 --> 00:06:23.949 Alixandra Rachman: broken them.

3~00:06:24.520 --> 00:06:41.730 Alixandra Rachman: I try to. So Tom is a assistant professor here at the department of chronic disease ongoing projects

4 00:06:41.870 --> 00:07:00.169 Alixandra Rachman: during the

 $5\ 00:07:00.170 \longrightarrow 00:07:23.910$ Alixandra Rachman: technology and before. So we have a lot ongoing work. I want to measure that company is also a fit, in fact, in the house. So we're very delighted to have him.

6 00:07:24.370 --> 00:07:25.350 Alixandra Rachman: Thank you.

7 00:07:27.660 --> 00:07:30.230 Alixandra Rachman: But find introduction. I'm just

8 00:07:30.620 --> 00:07:51.430 Alixandra Rachman: okay. Yeah. Thank you for having me. My name is and yeah, I'm trained as a medical doctor and perinatal epidemiologist. So I think that my background, entering the space of climate change and health research is slightly different compared to many. Hopefully, that can

 $9\ 00:07:51.510$ --> 00:07:57.969 Alixandra Rachman: send some some, some new or hopefully, we can send us some new questions without

10 00:07:58.000 --> 00:08:02.120 Alixandra Rachman: but but I do have a very

11 00:08:02.150 --> 00:08:18.980 Alixandra Rachman: I do have a passion for research on how climate change affects pregnancy, and for reasons that we look at a bit. I argue that this is a very under appreciated kind of question whether high ambit temperatures affects the pregnant population.

 $12\,00:08:19.210$ -->00:08:29.809Alixandra Rachman: So we've all seen headlines such as this, and sort of get this impression that we're heading for a dooms do stay in the future. And and the question is, how can we

13 00:08:30.210 \rightarrow 00:08:36.130 Alixandra Rachman: make sure that the pregnant population and the coming generations are as little as effective as possible.

14 00:08:37.770 --> 00:08:48.849 Alixandra Rachman: And the structure for today's agenda is that we're first going to talk about and build current literature on how extreme heat and high ambient temperatures affect pregnancy.

15 00:08:49.090 --> 00:09:15.189 Alixandra Rachman: And then we're going to focus on that final chapter on how exposure to high end temperatures to pregnancy affect offspring outcomes, and, as you will see in a bit, I argue that there is currently very little research on this space, which is why I'm focusing on

our project for this last chapter and focusing on other research groups research in this first chapter.

16 00:09:15.440 \rightarrow 00:09:23.560 Alixandra Rachman: So in the first section, we're first going to have a look at the exposure version to find ambient temperatures in pregnancy.

17 00:09:23.740 --> 00:09:33.350 Alixandra Rachman: And then we're going to look at the hypothetical biological pathways linking heat exposure in pregnancy to adverse pregnancy outcomes.

18 00:09:34.200 --> 00:09:48.719 Alixandra Rachman: And finally, we're going to look at whether the map fits the terrain, and whether, the epidemiological literature actually shows what it shows in terms of the link between high ambulance temperatures and adverse things outcomes

19 $00:09:49.570 \dashrightarrow 00:09:57.249$ Alixandra Rachman: for the final chapter, and I'm going to talk about 2 projects that we have ongoing. And the first one is on

20 $00:09:57.600 \dashrightarrow 00:10:01.830$ Alixandra Rachman: and the second one is on. Boss breaks through

21 00:10:04.430 --> 00:10:08.270 Alixandra Rachman: so extreme heat in pregnancy. And I'm just

22 00:10:08.270 --> 00:10:31.110 Alixandra Rachman: want to flag that. And I am going to focus on extreme heat, and I acknowledge that climate change is much more than just high end temperatures and high under temperatures, of course, doesn't work in a in a silo or isolation. It have this interactive effects with air pollution of ports, and you have these pistol effects or distal consequence. So heat, such as drought

23 00:10:31.110 --> 00:10:41.399 Alixandra Rachman: and displacement, etc. But for this presentation, in order to fit it into 45 min presentation. We're just going to focus on more the direct consequences of

24 00:10:41.400 --> 00:10:42.560 Alixandra Rachman: extreme heaps of

25 00:10:44.330 --> 00:10:46.350 Alixandra Rachman: so, as you know.

26 00:10:46.390 --> 00:11:00.279 Alixandra Rachman: heatwave or increasingly common. So that what mind here is that global average. And if we compare, if you look at the pregnant population today, compared to 2030 years ago. It's estimated that

27 00:11:00.340 \rightarrow 00:11:07.719 Alixandra Rachman: that current pregnant population is exposed to roughly twice as many heatwave days compared to 2030 years ago.

28 00:11:08.270 --> 00:11:15.810 Alixandra Rachman: and not only are the heat waves more common, they also are longer, and they are more intense.

29 00:11:15.920 --> 00:11:25.500 Alixandra Rachman: And it looks like the heatwaves aren't aren't here to stay with us, and are probably going to become increasingly worse for the coming decades.

30 00:11:25.540 --> 00:11:28.930 Alixandra Rachman: So heat rates aren't going away. The question is, how many we deal with them.

31 00:11:30.280 --> 00:11:31.180 Alixandra Rachman: So

32 00:11:31.650 --> 00:11:57.450 Alixandra Rachman: this is really one of the key reasons why I'm so passionate about the topic of heat exposure in privacy, because I feel like this is a very underappreciated topic. So if we look at the official governmental State guidelines in terms of identifying who is at risk at times of heat, stress, or in terms of heat waves. If you look at to Canada, for instance, and we like to look to Canada

33 00:11:57.450 --> 00:12:06.490 Alixandra Rachman: often in admiration, while this time not in admiration because they haven't. They have identified several vulnerable groups at times of extreme heat.

 $34\ 00:12:06.490$ -->00:12:19.290 Alixandra Rachman: All of these groups should be at a cared for in particular, but they have not identified the pregnant population. If you look to the Uk, the same groups have been identified, same thing in Australia.

35 00:12:19.450 --> 00:12:24.649 Alixandra Rachman: in South Africa they have identifying the French population as a risk group

 $36\ 00:12:25.360 \longrightarrow 00:12:35.429$ Alixandra Rachman: in the Us. We actually have identified friend women as a group that is at risk, security, heat waste, and also the who acknowledge this.

37 00:12:36.210 --> 00:12:43.390 Alixandra Rachman: So this is just a quick look at what is sort of the official policies from these different countries.

38 00:12:43.430 --> 00:13:03.699 Alixandra Rachman: So I chose countries where it was easy to find available and guidelines and available to me in English. But the point is, if I didn't find II mean it might have hidden away somewhere deep in a data brief, that the pregnant population is also vulnerable. But if I wasn't able to find it, the general population is also not able to find it.

39 00:13:04.160 --> 00:13:22.689 Alixandra Rachman: and sort of the the official the official attitudes, or the the governmental attitudes of who is at risk during heat waves, of course, also will be reflected in the general population, and what the general population thinks about, who is at risk during

40 00:13:22.750 --> 00:13:24.639 Alixandra Rachman: periods of extreme heat.

41 00:13:24.650 --> 00:13:29.669 Alixandra Rachman: So there have been several surveys, and we're going to look at 2 of them.

42 00:13:29.810 --> 00:13:37.399 Alixandra Rachman: So in this first study they interviewed passersby in Lisbon or Lisbon and Madrid, Portugal, and in Spain.

43 00:13:37.410 --> 00:13:42.860 Alixandra Rachman: where only 6 and 5% of those who are surveyed.

44 00:13:42.940 --> 00:13:48.660 Alixandra Rachman: that I then defined the pregnant population as vulnerable at times of extreme heat.

45 00:13:48.890 --> 00:13:55.610 Alixandra Rachman: A similar survey was conducted in Georgia, Tunisia, and Israel. where again.

46 00:13:55.670 --> 00:14:05.350 Alixandra Rachman: only 12% of those who were surveyed spontaneously identified the pregnant population as a risk group at times of extreme heat.

47 00:14:05.440 --> 00:14:11.350 Alixandra Rachman: So this gets me up in the morning because I think I think this needs to change.

48 00:14:11.760 --> 00:14:14.979 Alixandra Rachman: and hopefully he will agree with me in in half an hour.

49 00:14:15.840 --> 00:14:16.740 Alixandra Rachman: So

50 00:14:16.990 --> 00:14:43.779 Alixandra Rachman: why is it that that we should care in particular for the pregnant population? Well put for those of us who are sort of doing research in the perinatal epidemiological space. Anyways, I mean to us is obvious. Right? Like everyone should care about this. But to state out the obvious. If you have a if you have an an environmental hazard, a heat wave that occurs in pregnancy, of course it can affect or see it might affect.

51 00:14:43.780 --> 00:15:13.500 Alixandra Rachman: and pregnancy outcomes like immediate brain outcomes. It might increase the hypertent or increase the risk of gestational hypertension and pre collapse out, you might increase the incident of early labor and preterm birth, and these will have negative impacts on the mother. Of course, you'll also affect the offspring. So it's 2 generations here that might be affected and adverse outcomes of the offspring, such as preterm birth and birth defects might have

 $52\ 00{:}15{:}13.500$ --> $00{:}15{:}21.699$ Alixandra Rachman: long lasting consequences. So freedom, birth, and birth. Defects, for instance, are the 2 most important causes of infant death

53 00:15:22.490 $\rightarrow 00:15:24.469$ Alixandra Rachman: and preterm birth.

54 00:15:25.060 --> 00:15:35.119 Alixandra Rachman: but at the population level those who are born of return are at greater risk of cardiovascular diseases, infectious diseases. decades into adult life.

55 00:15:35.240 \rightarrow 00:15:37.699 Alixandra Rachman: So we have this full cycle

 $56\ 00:15:37.790 \longrightarrow 00:15:44.629$ Alixandra Rachman: where it can come to a complete cycle at the time that the offspring themselves wants to have children.

57 00:15:44.690 --> 00:15:46.419 Alixandra Rachman: so in theory

58 00:15:46.480 --> 00:15:52.289 Alixandra Rachman: that heat stress at the time of one pregnancy can have

59 00:15:52.970 --> 00:15:56.860 Alixandra Rachman: directly direct effects on generations to come.

 $60\ 00:15:57.870 \longrightarrow 00:15:58.880$ Alixandra Rachman: This is.

61 00:15:59.140 --> 00:16:01.089 Alixandra Rachman: in theory at least.

62 00:16:01.530 --> 00:16:08.500 Alixandra Rachman: so what are the hypothesized pathways from high ambient temperatures to pregnancy complications?

 $63~00:16:08.670 \rightarrow 00:16:17.890$ Alixandra Rachman: And I say hypothesize, because there's very little literature looking at heat, exposure, and biological pathways of the pregnant population.

 $64\ 00{:}16{:}17.900$ --> $00{:}16{:}26.120$ Alixandra Rachman: So we have to sort of steal from other areas. So studies of on animals and on and non pregnant populations, etc.

 $65\ 00{:}16{:}26{.}520$ --> $00{:}16{:}32{.}560$ Alixandra Rachman: But what we do know is that there are several relevant physiological changes that occur during trends.

66 00:16:32.920 --> 00:16:48.270 Alixandra Rachman: The most obvious, of course, is that there's the fetus with its placenta there, and the fetus will have its metabolic processes to generate heat and energy, and needs to get rid of that heat through the medical port. And it needs to get rid of the waste products.

67 00:16:49.160 --> 00:17:07.740 Alixandra Rachman: And the percent, of course, needs a lot of blood as well. So the fetal placental unit demands roughly, 10% of the maternal cardic output. So to accommodate that the maternal cardic output increases by 30 to 50% towards the end of pregnancy.

68 00:17:07.920 --> 00:17:09.690 Alixandra Rachman: which, of course, puts

69 00:17:09.770 --> 00:17:14.509 Alixandra Rachman: additional stress to the maternal cardiovascular system.

 $70\ 00:17:15.250 \longrightarrow 00:17:34.490$ Alixandra Rachman: and there are also changes in the maternal or temperature and maternal thermo regulation. So towards the end of pregnancy, the mother is less heat tolerant compared to earlier in pregnancy, so she gets more uncomfortable at the same temperatures compared with outside.

71 00:17:35.250 --> 00:17:38.860 Alixandra Rachman: And finally, pregnancy is this hyper global state?

 $72\ 00:17:38.950\ -->\ 00:17:54.020$ Alixandra Rachman: Where the risk of from boxes and blood cuts increase in pregnancy in general and heat stress increase

 \mathbf{So}

the risk of blood clots. So you can think that the 2 combined point increase the risk of.

 $73\ 00:17:55.120 \longrightarrow 00:17:59.230$ Alixandra Rachman: and what are the potential biological effects of high ambient temperatures?

 $74~00{:}18{:}00{.}020$ --> $00{:}18{:}10{.}490$ Alixandra Rachman: Well, for one, if the mother isn't able to sufficiently cool down the maternal core, ambient temperatures will increase, which will directly

75 00:18:11.060 --> 00:18:15.710 Alixandra Rachman: be associated with fetal core temperatures. and

76 00:18:16.690 --> 00:18:24.249 Alixandra Rachman: from from animal studies and from other costs of of high fetal core temperatures, such as fever. We know that it

 $77\ 00{:}18{:}24{.}260$ --> $00{:}18{:}27{.}150$ Alixandra Rachman: is associated with an increased risk of birth defects.

78 00:18:27.190 $\rightarrow 00:18:33.949$ Alixandra Rachman: We will have a look at the epistemological literature for ambient temperature in a bit to see whether this is true also for ambient temperature, exposure.

79 00:18:35.850 --> 00:18:49.119 Alixandra Rachman: dehydration might might happen when you're exposed to extreme heat, and when you have dehydration you might have decreased blood volume, and with decreased blood volume there might be decreased uterine blood flow

 $80\ 00{:}18{:}49{.}530$ --> $00{:}18{:}57{.}509$ Alixandra Rachman: which in turn means less nutrients and less oxygen to the fetus which in turn can lead to fecal growth, restriction.

81 00:18:58.370 --> 00:19:16.889 Alixandra Rachman: And there's also this thing where, when the placenta receives too little blood, it will tend to start secreting prostaglandins and Prostaglandins is one of those hormones that can trigger nutrient contractilities. And if this happens too early, it's associated with an increase, risk complete or birth.

82 00:19:18.290 --> 00:19:29.239 Alixandra Rachman: When the mother is warm, or when anyone is warm, we will have a redistribution of our blood flow, so that less is to the internal organs, more to the skin, so that we can release all of that extra heat

83 00:19:29.830 --> 00:19:33.469 Alixandra Rachman: meaning there might be decreased future in blood flow.

84 00:19:34.610 \rightarrow 00:19:57.689 Alixandra Rachman: And then this is a very odd thing where we want to sweat when we warm right? So we want to produce as little urine as possible. We need it to be as concentrated as possible, so that we don't waste fluid to the urine. And in order to do that, we produce

and secrete anti-directic hormone adh, which happens to be secreted from the posterior land, where also

85 00:19:57.690 --> 00:20:11.339 Alixandra Rachman: oxytocin is released from and from non pregnant populations. We've seen that with adh release. There is this. Often there's this code release of oxytocin. We don't know where that's functional, but it it happens so

86 00:20:11.350 --> 00:20:24.730 Alixandra Rachman: when, when during history stress, there, it's a tendency of oxytocin release and oxytocin for those who didn't labor know that this is one thing that we give to pregnant women in order to stimulate labor even further. Right?

87 00:20:27.130 --> 00:20:55.270 Alixandra Rachman: Also, with heat stress, there will be a common release from the adrenal glands. And finally, there's an increase in inflammatory biomarkers, heat proteins and oxidative stress in response to heat stress. So if you found this confusing, you can think that it's intentional in order, like a pedagogical tool and trick for you to think. Well, this sure was complicated, and it is, but there's no reason that we should ignore

 $88\ 00:20:55.270$ -->00:21:11.299 Alixandra Rachman: the pregnant population. There are enough plausible biological pathways there that we should be at least interested in evaluating the epidemiological literature of whether there is a link between key stress and adverse outcomes, because there are many things to tag those effects on.

89 00:21:12.430 --> 00:21:13.350 Alixandra Rachman: So.

90 00:21:15.520 --> 00:21:28.800 Alixandra Rachman: yeah, yeah, this is this is just I wanted to illustrate one very innovative study that look at actually the biological pathways. Because I said that there we are learning learning all of this from the nonpregnant population.

91 00:21:28.830 --> 00:21:29.970 Alixandra Rachman: What they're

92 00:21:30.640 \rightarrow 00:21:34.510 Alixandra Rachman: there are few and far between studies. But one of them actually do look at

93 00:21:34.880 --> 00:21:48.830 Alixandra Rachman: what is the direct biological consequences of heat stress. And this is a study that was conducted in rural parts of the Gambia, between 2,019 and 2,020 of 92 pregnant women prospectively followed.

94 00:21:49.640 --> 00:21:54.770 Alixandra Rachman: Each stress was measured by the hourly wet, cold globe temperature scale.

95 00:21:55.340 --> 00:21:59.750 Alixandra Rachman: and they use doppler ultrasound to ascertain the fetal heart rate.

96 00:21:59.910 \rightarrow 00:22:15.829 Alixandra Rachman: and also the umbilical artery resistance index. So they they measured whether it was fetal strain. If

the female heart rate was too high or too low, or whether there was inadequate fetal blood flow through the placenta ducts.

 $97\ 00:22:16.520 \longrightarrow 00:22:21.960$ Alixandra Rachman: and this was measured at rest, and during working periods. and what they found was that

 $98\ 00:22:22.320$ --> 00:22:35.400 Alixandra Rachman: per degree per one degree, Celsius of ambient temperature. The risk of feeble strain increased by 20%. So with increasing ambient temperature, there was an increase in people, heart rate.

99 00:22:35.440 --> 00:22:40.560 Alixandra Rachman: And also, if you looked at in isolation, at maternal heat stream.

 $100\ 00:22:41.400 \longrightarrow 00:22:48.570$ Alixandra Rachman: and regardless of ambient temperature when the mother experienced heat strain, so did the fetus.

101 00:22:48.900 --> 00:22:50.540 Alixandra Rachman: So this is sort of

102 00:22:50.860 --> 00:22:56.359 Alixandra Rachman: direct study, linking exposure to heat, stress to feeble strain.

103 00:22:58.240 --> 00:23:01.840 Alixandra Rachman: And now let's look at the epidemological literature.

104 00:23:03.080 --> 00:23:15.910 Alixandra Rachman: So the perinatal period is this period. It's even starts before conception. But we're going to focus on from conception to the time of earth. And then you have these outcomes that occur after birth.

105 00:23:16.240 --> 00:23:20.370 Alixandra Rachman: and the vast majority of the literature is

 $106\ 00{:}23{:}20.590$ --> $00{:}23{:}25.430$ Alixandra Rachman: studies that are developing outcomes occurring at the time of birth

107 00:23:25.960 --> 00:23:37.349 Alixandra Rachman: and lengthugestation, or Peter birth is the single most studied outcome when it comes to heat, stress and adverse outcomes. So we're going to look at 3 examples

108 00:23:37.570 --> 00:23:40.920 Alixandra Rachman: of that of such such an association

109 00:23:41.710 --> 00:23:45.529 Alixandra Rachman: and 3 studies that use very different approaches.

110 00:23:45.590 --> 00:23:51.459 Alixandra Rachman: But I think it's illustrative, because it shows sort of the breadth of these studies.

111 00:23:51.900 --> 00:23:53.789 Alixandra Rachman: So in the first example.

112 00:23:54.420 \rightarrow 00:24:09.129 Alixandra Rachman: this was published earlier this year by Wu and colleagues. It's a population based prospective corpo-

rate study in 16 cities, in China, of women who attempted to get into become pregnant, and and they evaluated

113 00:24:09.490 --> 00:24:11.899 Alixandra Rachman: roughly 200,000 births.

114 00:24:12.050 --> 00:24:15.759 Alixandra Rachman: of which 18,000 were free tournaments.

115 00:24:17.500 --> 00:24:28.089 Alixandra Rachman: and they evaluated. What is the association between ambient temperature the week before birth, or in gestation weeks? 36 for those who gave birth at terms and the risk of pre-trum birth.

116 00:24:29.560 --> 00:24:41.539 Alixandra Rachman: they adjusted for some confounding factors, and they did not adjust for seasonality or for a year, and which I think you can confuse these results. But let's look at the results, anyways.

117 00:24:41.760 --> 00:24:50.390 Alixandra Rachman: And this figure doesn't look as good on the windows computer as it does on my Mac. So we're we're missing missing parts here. But

118 00:24:51.190 --> 00:24:54.429 Alixandra Rachman: from 20°C there is

119 $00{:}24{:}54.850 \dashrightarrow 00{:}24{:}58.620$ Alixandra Rachman: an increased risk of preterm birth.

 $120\ 00{:}24{:}59{.}080$ --> $00{:}25{:}05{.}989$ Alixandra Rachman: That's what this nonlinear graph shows. And if we're comparing in the week before birth, the 90 fifth

121 00:25:06.120 --> 00:25:08.460 Alixandra Rachman: and into temperature

122 00:25:08.480 --> 00:25:14.599 Alixandra Rachman: percentile compared with a median, we see that there's a 36% increased risk of prejudone birth.

123 00:25:14.940 --> 00:25:20.990 Alixandra Rachman: Now, I said that this study might be subject to some residual confounding.

 $124\ 00{:}25{:}21{.}480$ --> $00{:}25{:}28{.}600$ Alixandra Rachman: But there was another study published same year, or this year, which also was a prospective cohort study in China.

125 00:25:28.810 --> 00:25:44.570 Alixandra Rachman: And what they did here is very innovative, and I'm almost a bit mad at them because they they did what what we had wanted to do. I think this is the first sibling comparison study of ambient temperature, exposure. So what they did was that they compared

126 00:25:45.260 --> 00:25:58.970 Alixandra Rachman: pregnancies were or or birth, where the pregnant woman had given birth to 2 children and 2 siblings, and one of them was born preterm, and the other was not born preterm. And then they compared what was the ambient temperature of the week before birth.

127 00:25:58.980 --> 00:26:06.369 Alixandra Rachman: and by doing the sibling comparison you account for a lot of those residual, confounding factors that at least are constant within the mother.

128 00:26:06.770 --> 00:26:28.070 Alixandra Rachman: such as maternal and genetic makeup, etc. And they also adjusted for seasonal conception, which was missing from this period of analysis. And what did they find? You find an offs ratio, which was almost spot on the same as the previous one. So if you're compared to the 90 fifth ambient temperature compared with the Median, there was a 39% increase odds of pre-term birth.

129 00:26:28.390 \rightarrow 00:26:33.720 Alixandra Rachman: The conference interval included the null. but that was because it was a much smaller study.

130 00:26:34.910 --> 00:26:39.839 Alixandra Rachman: So that is, that was one line of studies. Let's look at another example.

131 00:26:40.480 --> 00:26:42.650 Alixandra Rachman: This is a case. Crossover study

132 00:26:42.700 --> 00:27:00.529 Alixandra Rachman: look from from Australia. So in a case cross case cross over you only compare cases to themselves. So you're looking at a hazard period. Let's say the day before birth. If that was a Tuesday, you compare that Tuesday to other Tuesdays within the same month

133 00:27:00.840 --> 00:27:05.600 Alixandra Rachman: effectively account for confounding that are constant within this this mother.

134 00:27:05.830 --> 00:27:09.000 Alixandra Rachman: So they looked at 15,000 pre tumorists

135 00:27:11.000 --> 00:27:12.280 Alixandra Rachman: and

136 00:27:13.330 --> 00:27:25.599 Alixandra Rachman: this figure also does not look as kept on the windows. Anyways, they find very much the same pattern of association, so that from 20°C ambient temperature, there is an increased risk of predator birth.

137 00:27:26.000 \rightarrow 00:27:40.250 Alixandra Rachman: and when comparing the Ninety-fifth with a median, they find in all 3. So 1, 3. But it's so. The magnitude of association is not as pronounced as previously, which might be, because this is a case crossover and not the traditional

138 00:27:40.360 --> 00:27:41.430 Alixandra Rachman: and

139 00:27:42.440 --> 00:27:57.040 Alixandra Rachman: prospective cohort study analysis, but the significance in terms of terms of p-value which we, of course, don't care about. I mean, it's the compass it towards very narrow. So it's it's a very significant and statistically significant environment.

140 00:27:57.790 --> 00:27:59.830 Alixandra Rachman: The final example I'm going to show you.

141 00:27:59.870 \rightarrow 00:28:11.360 Alixandra Rachman: Is this demographic study. So yet another completely different study design set in the Us. Between 1,969, and evaluating 56 million births.

142 00:28:11.910 --> 00:28:13.720 Alixandra Rachman: What they did here was that they

143 00:28:14.020 --> 00:28:23.280 Alixandra Rachman: looked at, and it looked at, and the birthrates in a given county, and looked at whether a high ambient temperature shock

144 00:28:23.860 $\rightarrow 00:28:28.989$ Alixandra Rachman: what's associated with a birthrate in that kind of county on that day and the subsequent days.

145 00:28:29.620 --> 00:28:42.260 Alixandra Rachman: So they they adjusted for county level effects day or year, effects, precipitation, and the surrounding surrounding days. The ambient temperature in the surrounding days. So what they effectively did was that they

146 00:28:42.490 --> 00:28:51.970 Alixandra Rachman: in a county they compared. What is the birth rate? If this was a hot day compared with other days in compared with the same

147 00:28:51.990 --> 00:28:53.969 Alixandra Rachman: date in other years.

148 00:28:54.100 --> 00:28:58.270 Alixandra Rachman: while accounting for the the

149 00:28:58.470 --> 00:29:03.050 Alixandra Rachman: trends in in birth, rates in the Us. As a whole.

150 00:29:03.790 --> 00:29:07.040 Alixandra Rachman: And what did they find? They found that

151 00:29:07.340 --> 00:29:11.530 Alixandra Rachman: on a day of high ambulance temperatures, with this heat shock

152 00:29:11.570 --> 00:29:22.140 Alixandra Rachman: there was an increase in the birth rate. This is for all births, not only preterum birth for all birds. and same for the day after. There's also an increase in the birthrate.

153 00:29:22.410 --> 00:29:37.579 Alixandra Rachman: but 2 days after. There are fewer birds. That's because the births have been shifted. So they're occurring earlier. So you have this heat shock that is, triggering labor, just like we saw in the slide of the hypothesized pathways that there might actually be something to it. Right?

154 00:29:39.040 --> 00:29:54.829 Alixandra Rachman: Okay. So I know what you're thinking. You're thinking, I cherry-picked 3 studies that support my argument, that we should pay more attention to the pregnant population. But if we do an even if we cast our net even wider. Let's look at the most recent and robust systematic review on this topic.

155 00:29:54.840 --> 00:29:58.289 Alixandra Rachman: This is a paper that was published in D
mj. In 2020

156 00:29:58.620 --> 00:30:01.350 Alixandra Rachman: where they included 70 studies.

157 00:30:02.400 --> 00:30:13.479 Alixandra Rachman: And this is one of their key findings, which is that when you're experiencing a heat wave, you have a roughly 15 or 16% increase risk of pre-term birth.

158 00:30:14.580 --> 00:30:21.930 Alixandra Rachman: So this is across many, many studies across all studies, really. And one thing to note, however, is that

159 00:30:22.080 --> 00:30:47.100 Alixandra Rachman: it's very difficult to compare these studies head to head, let alone to create one aggregate estimate, because these studies have been conducted in so different ways, like, what is the heat wave? Is it 2 consecutive days? Is it 3 consecutive or 4 consecutive days of high temperatures? Are we looking at the week before birth, or the trying, the full third trimester? Or are we looking at the second gestational week.

160 00:30:47.100 --> 00:30:58.740 Alixandra Rachman: and and also the setting and the underlying susceptibility to pre-term birth in these different populations. It's very difficult to compare head to head, but it's I would say that it's very reassuring that we have all of these

161 00:30:59.370 --> 00:31:05.159 Alixandra Rachman: different study designs that more or less come to the same solution, that there appears to be

162 00:31:05.250 --> 00:31:09.099 Alixandra Rachman: an association between high ambient temperatures and risk of pretern birth.

163 00:31:10.230 --> 00:31:22.509 Alixandra Rachman: They also evaluate low birth weight within. Roughly, 10% increased risk of low birth weight experiencing a heat wave. And roughly, a 50% increased risk of stillbirth. When you're experiencing a heatwave.

164 00:31:22.930 --> 00:31:41.869 Alixandra Rachman: And all of the examples I've given before were from studies published after this systematic review was conducted because this was the search was ended in 2019, and since then many, many, many studies have been published that generally support these findings.

165 00:31:44.020 --> 00:31:57.409 Alixandra Rachman: It should also be noted that, as unfortunately, is the case for almost all exposure outcome associations that we look at in the printing setting. There is racial disparity also here. So

166 00:31:57.610 --> 00:31:58.670 Alixandra Rachman: when

167 00:31:59.250 --> 00:32:04.180 Alixandra Rachman: non-hispanic black and Hispanic pregnant women are exposed to

168 00:32:04.220 --> 00:32:07.150 Alixandra Rachman: high ambient temperatures that 169 00:32:07.540 --> 00:32:17.110 Alixandra Rachman: associated increased risk of these adverse outcomes. Freedom, birth, birth, rate, and silver are stronger compared with non-hispanic white, pregnant women.

170 00:32:20.230 --> 00:32:22.930 Alixandra Rachman: So I would argue that

171 00:32:24.150 --> 00:32:31.900 Alixandra Rachman: for all of these 3 outcomes, so life ifestation or pre-term birth, birth, weight, or low birth, weight and still birth, there is

 $172\;00{:}32{:}31{.}940 \dashrightarrow 00{:}32{:}36{.}070$ Alixandra Rachman: very robust and evidence to suggest that there is

173 00:32:36.340 --> 00:32:39.990 Alixandra Rachman: an association between high ambient temperatures and deep outcomes.

 $174~00{:}32{:}40.030 \dashrightarrow 00{:}32{:}43.539$ Alixandra Rachman: and there are other outcomes that have been evaluated as well.

175 00:32:43.960 --> 00:32:47.350 Alixandra Rachman: one of which is congenital malformations.

176 00:32:47.410 --> 00:32:58.380 Alixandra Rachman: I put this in the italics and the question mark because, I wouldn't say that it's definite, definite at this point. But there are certainly studies that do suggest such an association.

177 00:32:59.060 --> 00:33:02.880 Alixandra Rachman: And for these and outcomes that occurred earlier.

178 00:33:03.200 $\rightarrow 00:33:12.719$ Alixandra Rachman: there are several candidates. So some studies suggest a reduced acuity, meaning a reduced biological ability of conceiving

179 00:33:13.840 --> 00:33:17.600 Alixandra Rachman: several studies indicate an increased risk of miscarriage.

180 00:33:18.340 --> 00:33:24.069 Alixandra Rachman: increased risk of pistachio dietas, or we go hydrant. So, too, little amiotic fluid around the fetus

181 00:33:24.110 --> 00:33:29.399 Alixandra Rachman: option, meaning that that detaches from you. Chris.

182 00:33:29.470 --> 00:33:31.390 Alixandra Rachman: Frequency. So high.

183 00:33:31.710 --> 00:33:38.960 Alixandra Rachman: so gestational hypertension in in pregnancy. This actually, perhaps shouldn't be in italics anymore, because

184 00:33:39.340 --> 00:33:46.270 Alixandra Rachman: there are very, very many studies suggesting that this association is is true

 $185\ 00{:}33{:}46.650$ --> $00{:}33{:}58.870$ Alixandra Rachman: and then severe maternal morbidity. So severe, adverse maternal outcomes. and if we're looking at short or long-term outcomes.

 $186\ 00:33:59.200 \longrightarrow 00:34:11.000$ Alixandra Rachman: there are very few studies that directly evaluate the association between ambient temperature and long-term outcomes of the offspring.

187 00:34:11.540 --> 00:34:19.980 Alixandra Rachman: And I would just like to point out the fact. It's it's also obvious. Everything I'm saying is quite obvious. But but

188 00:34:21.350 --> 00:34:23.460 Alixandra Rachman: hey? Because

189 00:34:23.570 --> 00:34:32.440 Alixandra Rachman: because these 3 outcomes have been robustly associated with ambient temperature exposure, it doesn't mean that these are the ones that are truly

190 00:34:32.469 --> 00:34:34.309 Alixandra Rachman: the most causally

191 00:34:34.449 --> 00:34:38.820 Alixandra Rachman: related to ambient temperature. It means that these are the easiest to study.

192 00:34:39.050 --> 00:34:46.810 Alixandra Rachman: because how are you going to study risk of miscarriage? Miscarriages are very often not even recorded, let alone

193 00:34:47.460 --> 00:34:56.289 Alixandra Rachman: known about by by the by, the woman herself, if they happen very, very brutal. So how do you go about studying that. So?

194
 $00{:}34{:}56{.}550 \dashrightarrow 00{:}34{:}58{.}819$ Alixandra Rachman: So these are very important outcomes.

 $195\ 00:34:59.490$ --> 00:35:03.099 Alixandra Rachman: But it doesn't mean that these are the only ones that are

196 00:35:03.180 --> 00:35:05.970 Alixandra Rachman: causally related. And the same is true, for

197 00:35:06.530 --> 00:35:15.650 Alixandra Rachman: for the long-term outcomes. Because how would you go about studying an outcome that occurs here later? Here you only need birth record data.

198 00:35:16.550 --> 00:35:26.130 Alixandra Rachman: but it gets more complicated when you're looking at things that happen during pregnancy. and especially things that happen late or like years after crazy.

199 00:35:26.380 --> 00:35:29.650 Alixandra Rachman: which is why we find this

20000:35:29.750-->00:35:32.160Alixandra Rachman: particularly intriguing. And so

201 00:35:32.200 \rightarrow 00:35:45.440 Alixandra Rachman: this brings us to the final chapter, which is offering outcomes, which is where my colleagues and I

have have done some studies, and I'm going to talk about 2 of them or some ongoing studies.

202
 00:35:46.820 --> 00:35:51.149 Alixandra Rachman: So
 2 of the projects I'm going to talk about

203 00:35:51.920 --> 00:36:04.930 Alixandra Rachman: are a Charlotte, and the other is through bill policy. I'm going to spend the most time talking about this outcome, because this has come the furthest but I'll also very briefly mentioned this one.

 $204\ 00:36:07.820 \longrightarrow 00:36:12.769$ Alixandra Rachman: So childhood, acute with plastic leukemia, is the most common childhood cancer.

 $205\ 00:36:13.380 \longrightarrow 00:36:25.510$ Alixandra Rachman: Luckily it has a fantastic five-year survival rate, but the incidence rate has increased over the last decades, for reasons that are unknown largely.

206 00:36:25.890 --> 00:36:29.430 Alixandra Rachman: and it it affects

207 00:36:29.660 --> 00:36:33.319 Alixandra Rachman: Hispanic children more than not. Hispanic children.

208 00:36:33.800 --> 00:36:36.029 Alixandra Rachman: Also, for reasons that we don't really know.

209 00:36:36.660 --> 00:36:39.720 Alixandra Rachman: This figure also looks a bit odd

210 00:36:39.780 --> 00:36:45.319 Alixandra Rachman: on this computer. But anyways, this is attempting to show that the

211 00:36:45.500 --> 00:36:49.640 Alixandra Rachman: incidents. the age of of onset

212 00:36:49.960 --> 00:36:53.770 Alixandra Rachman: or the age when the disease is recognized

213 00:36:54.190 --> 00:36:57.719 Alixandra Rachman: is typically. that's 5 years or earlier.

214 00:37:02.190 --> 00:37:18.899 Alixandra Rachman: So this is the the pre print for the the study that I'm going to talk about. So this has been submitted to a journal, and out of respect for the journal and the editors and reviewers. I'm not going to talk about anything related to the review process.

215 00:37:18.970 --> 00:37:23.560 Alixandra Rachman: I'm only going to talk about things that are publicly available in this free prince.

 $216\ 00:37:24.440 \longrightarrow 00:37:51.490$ Alixandra Rachman: and I also want to flag or to to mention that this work was made possible. But the collaboration with this really fantastic team of of researchers and and Philip we? We often do, saying that this has been like a collaborative approach, etc. But this is particularly

true, this project, because we come at this this question from very different backgrounds. So my background is in clinical medicine technology.

217 00:37:51.900 --> 00:38:07.520 Alixandra Rachman: But then on this team, we have climate change, health researchers, environmental epidemiologists, cancer epidemiologists by statisticians. And it's just it's been a. It's really been a huge learning and opportunity for me as well to to work with these researchers.

218 00:38:07.780 --> 00:38:09.489 Alixandra Rachman: many of which are here at Yale.

219 00:38:10.490 --> 00:38:24.119 Alixandra Rachman: So for this project we received funding from the Yale Center on Climate Change and Health, the climate Change and Health research program which really made it possible for us to kick off this project, and I have received funding through the Ycci.

220 00:38:24.260 --> 00:38:27.220 Alixandra Rachman: I've received like a Ycci scholar award.

221 00:38:27.540 \rightarrow 00:38:41.229 Alixandra Rachman: which is this sort of backdoor opportunity to get nih funding for those of us who are immigrants and not eligible for a K. Award, and so shout out through the Yci program. So that's that's a fantastic opportunity.

222 00:38:41.500 --> 00:38:47.979 Alixandra Rachman: And for the background of this project we know that

223 00:38:48.190 --> 00:38:50.860 Alixandra Rachman: Tomokimeta has a prenatal onset.

 $224\ 00:38:50.910$ --> 00:38:56.010 Alixandra Rachman: and we know this, because if we're looking at the blood spots at the time of birth

 $225\ 00:38:56.090$ --> 00:39:00.459 Alixandra Rachman: of children who are later diagnosed with childhood leukemia.

 $226\ 00{:}39{:}00.610$ --> $00{:}39{:}09.280$ Alixandra Rachman: many, if not most have pre-lechemic clones at the time of birth. So this means that the disease onset starts to feed alive.

227 00:39:10.480 --> 00:39:15.249 Alixandra Rachman: We know that oxidative stress may cause prebook chemical pose.

228 00:39:15.510 \rightarrow 00:39:24.610 Alixandra Rachman: It's been suspected, at least, and we also know from the nonpregnant population that high ambient temperatures may increase obsidative stress

229 00:39:25.580 --> 00:39:27.190 Alixandra Rachman: in terms of timing.

230 00:39:27.210 --> 00:39:33.320 Alixandra Rachman: We know that lymphocy starts around the station week 8. So

231 00:39:34.040 --> 00:39:37.630 Alixandra Rachman: acutely for plastic leukemia stems from the lymphocytes.

232 00:39:38.270 --> 00:39:50.299 Alixandra Rachman: And this there's this general rule internally, technology that period when the tissue is the most vulnerable is the period when it's also the most immature.

233 00:39:51.200 --> 00:39:55.780 Alixandra Rachman: So it's reasonable to expect that the tissue

234 00:39:55.800 --> 00:40:00.420 Alixandra Rachman: relevant for toilet. Leukemia is most vulnerable around gestation. Week 8.

235 00:40:00.430 --> 00:40:01.850 Alixandra Rachman: That's our hypothesis

236 00:40:02.990 --> 00:40:04.350 Alixandra Rachman: and

 $237\ 00:40:05.470$ --> 00:40:16.780 Alixandra Rachman: sort of supporting that that hypothesis is epidemiological studies showing that and children which all leukemia are more likely to be born in late winter.

238 00:40:16.800 --> 00:40:25.240 Alixandra Rachman: which can have all sorts of causes. Why there is such an association, but one of those can be that they're exposed to high ambient temperatures in early pranks.

239 00:40:26.740 \rightarrow 00:40:32.719 Alixandra Rachman: and we also know that air pollution in early pregnancy is associated with an increased risk of childhood leukemia.

240 00:40:33.680 --> 00:40:40.570 Alixandra Rachman: And finally, we know that all sorts of other stressors, such as infections, are associated with an increased risk of holiday cancer.

241 00:40:40.850 --> 00:40:42.180 Alixandra Rachman: So this is sort of

242 00:40:42.640 --> 00:40:45.880 Alixandra Rachman: why we wanted to to evaluate this particular association.

243 00:40:47.780 --> 00:40:56.890 Alixandra Rachman: And our research question was, Is there an association between high admin temperature through pregnancy and risk of childhood, acute lymphoblastic leukemia.

244 00:40:57.630 --> 00:41:01.480 Alixandra Rachman: And this is the hypothesis association. So

245 00:41:01.610 --> 00:41:07.360 Alixandra Rachman: we anticipated, or we hypothesized, that the

246 00:41:08.180 --> 00:41:11.510 Alixandra Rachman: per unit increase in ambient temperature.

247 00:41:11.720 --> 00:41:19.519 Alixandra Rachman: the the greatest magnitude of the association would be around the station week 8 to 12, for the reasons that I talked about earlier.

248 00:41:19.560 --> 00:41:33.439 Alixandra Rachman: and we also included this pre-pregnancy period, because we didn't expect there to be any direct effect of heat exposure prior to conception, because the tissue doesn't yet exist.

249 00:41:33.840 --> 00:41:43.390 Alixandra Rachman: We can talk about at length other reasons why there actually might be a pre-pregnacy effect. But but we hypothesize that there there wouldn't be an important pre-pregnancy effect.

 $250\ 00{:}41{:}47{.}740$ --> $00{:}41{:}57{.}700$ Alixandra Rachman: So what did we do. And we used data from the calcic study. So the California linkage study of early onset cancers which.

251 00:41:57.800 --> 00:42:06.709 Alixandra Rachman: has birth records from California between 1,982 and 2,015, linked to the California Cancer Registry from 88 to 2,015.

 $252\ 00{:}42{:}07.770$ --> 00:42:18.109 Alixandra Rachman: And we match cases to controls by a one to 15 ratio matched on last menstrual period, race ethnicity, and sex.

253 00:42:18.190 --> 00:42:28.400 Alixandra Rachman: And the reason why it matched on date of Lnp, so Lnp is sort of what tells us when conception occurs, because it on average occurs 2 weeks later.

254 00:42:28.630 --> 00:42:43.959 Alixandra Rachman: We don't know when the perception occurs, but we do know when Lp hats so by matching on date of lmp, we make sure that the cases and the matched controls are pregnant at the same stage of pregnancy at the same time.

255 00:42:45.610 --> 00:42:54.940 Alixandra Rachman: So this yielded 6,258 leukemia cases and 300,000 controls, making it one of the biggest studies on on leukemia

256 00:42:56.870 --> 00:43:09.110 Alixandra Rachman: and for exposure ascertainment we use ambient temperature estimated as a one kilometer grid. and we adjusted for key confounders. In addition to the matching factors.

 $257\ 00:43:10.300 \longrightarrow 00:43:16.989$ Alixandra Rachman: and we ran the analysis in 2 steps. In the first step we conducted conditional logistic regression.

258 00:43:17.150 --> 00:43:19.799 Alixandra Rachman: evaluating each week individually.

259 00:43:19.860 --> 00:43:27.420 Alixandra Rachman: and then we created these smooth curves between the weeks by using this Bayesian Meta regression method.

 $260\ 00:43:29.340 \longrightarrow 00:43:41.809$ Alixandra Rachman: And because we're only interested in high ambient temperatures, we only considered the warm season. So the station week had to had to occur between May and September.

261 00:43:44.330 --> 00:43:48.839 Alixandra Rachman: So remember, this is the hypothesized association

 $262\ 00{:}43{:}49{.}320$ --> $00{:}44{:}00{.}630$ Alixandra Rachman: before we had any of the temperature data before we had run annual analysis. And these are our results. and which

263 00:44:01.180 --> 00:44:06.309 Alixandra Rachman: I would say, look very much like the Hypoxide Association.

264 00:44:06.470 --> 00:44:07.720 Alixandra Rachman: And so

 $265\ 00{:}44{:}07{.}810$ --> $00{:}44{:}11{.}439$ Alixandra Rachman: we were very happy with this, where

266 00:44:11.470 --> 00:44:12.710 Alixandra Rachman: we found.

267 00:44:12.960 --> 00:44:17.359 Alixandra Rachman: just as hypothesized, that the the peak.

268 00:44:17.690 --> 00:44:22.279 Alixandra Rachman: the greatest magnitude of association, was the invasion week 8. So for

269 00:44:22.320 --> 00:44:33.900 Alixandra Rachman: every 5°C increase in ambient temperature, or every 10 Fahrenheit increases. There was an associated 7% increased risk of childhood leukemia.

270 00:44:35.780 --> 00:44:40.210 Alixandra Rachman: So focusing more on that gestation week 8, which was that the peak of this

271 00:44:40.450 --> 00:44:41.290 Alixandra Rachman: her

272 00:44:43.260 --> 00:44:45.040 Alixandra Rachman: we did subanuses.

273 00:44:46.140 --> 00:44:59.860 Alixandra Rachman: and so, in the stratified analysis by by Latino or non latino white. We did expect there to be a slightly stronger magnitude of association for the Latino pregnancies and offspring, because

274 00:45:00.130 --> 00:45:04.420 Alixandra Rachman: Latino children have the greatest burden of trilochemia

275 00:45:04.500 --> 00:45:15.079 Alixandra Rachman: and other literature has suggested that Latino, pregnant women are more exposed to high ambient temperatures compared with non Latino, white pregnant women.

 $276~00{:}45{:}15{.}200 \dashrightarrow > 00{:}45{:}17{.}909$ Alixandra Rachman: and there was a tendency of a greater effect.

277 00:45:17.970 --> 00:45:20.619 Alixandra Rachman: But it was not that significant. 278 00:45:21.470 --> 00:45:31.140 Alixandra Rachman: When we did sub analysis based on the age of diagnosis, we see that there was no Association for the late Onset Childhood Cancers, which

279 00:45:31.210 --> 00:45:35.439 Alixandra Rachman: sort of makes sense, because those plate onset charged cancers.

280 00:45:35.580 --> 00:45:40.129 Alixandra Rachman: or on average less likely to have this prenatal onset.

281 00:45:42.470 --> 00:45:47.450 Alixandra Rachman: We also did nonlinear analysis. In Music Week 8,

282 00:45:47.750 --> 00:45:48.670 Alixandra Rachman: which

283 00:45:48.800 --> 00:45:55.030 Alixandra Rachman: we had hypothesized, we would have sort of this hockey stick association. But this is

284 00:45:55.050 --> 00:45:58.420 Alixandra Rachman: fairly linear, really, and the contents intervals are very wide.

 $285\ 00{:}46{:}00.710$ --> $00{:}46{:}08.959$ Alixandra Rachman: And then we did a secondary matched analysis or a sensitivity analysis, because when we matched on

286 00:46:09.200 --> 00:46:11.170 Alixandra Rachman: on lmp.

287 00:46:11.740 --> 00:46:20.089 Alixandra Rachman: we sort of made sure that the pregnancy that the case of the controls were pregnant in the same stage at the same time.

288 00:46:20.250 --> 00:46:27.080 Alixandra Rachman: So in order for there to be exposure or contrast between them. They had to live at different locations.

289 00:46:27.670 --> 00:46:29.840 Alixandra Rachman: So here we're

290 00:46:29.870 --> 00:46:40.670 Alixandra Rachman: location A, let's say, Sacramento and Location B. San Diego. So they had to be pregnant, and the same essential stage at the same time as living in different places in California.

291 00:46:41.990 --> 00:46:58.379 Alixandra Rachman: But for our sensitive analysis we wanted to check, because there might be other difference between Sacramento and San Diego than just temperature. And so we wanted to do some steep analysis where we matched on Lnp. Occurring within 365 days, so within a year.

 $292\ 00:46:58.490$ --> 00:47:07.370 Alixandra Rachman: but that they lived within 10 kilometers of one another, so thereby ensuring that they lived at the same place. They were pregnant

293 00:47:07.710 --> 00:47:11.750 Alixandra Rachman: within the same year. But exposure, contrast. So now we're comparing

 $294\ 00:47:11.790 \longrightarrow 00:47:18.290$ Alixandra Rachman: those living in San Diego to one another, but being pregnant at the same cessation stage, but at different times within that same year.

295 00:47:19.390 --> 00:47:26.070 Alixandra Rachman: thus inducing all sorts of bias due to seasonality. So by design. We're doing that.

 $296\ 00:47:26.310 \longrightarrow 00:47:33.119$ Alixandra Rachman: But but this was sensitivity analysis, and what we found was this, where we again see this.

297 00:47:33.380 --> 00:47:37.939 Alixandra Rachman: It's positive association in early pregnancy.

298 00:47:37.970 --> 00:47:46.860 Alixandra Rachman: and risk of child leukemia, and by design. If the case are more likely to be the station of Week 2 in July, they are

299 00:47:47.180 --> 00:47:49.930 Alixandra Rachman: necessarily need need to be

 $300\;00{:}47{:}50{.}240$ --> $00{:}48{:}01{.}179$ Alixandra Rachman: in this ational week, 25 in December, 6 months later, you will have this sort of biased other directional effect.

 $301\ 00{:}48{:}02.390$ --> $00{:}48{:}07.890$ Alixandra Rachman: But these were the findings from this study, and finally, I would like to

 $302\ 00:48:07.920$ --> 00:48:18.560 Alixandra Rachman: mentioned the the other project that we have ongoing on the risk of cerebral palsy. Also. Here we have received funding from the Yield planetary Solutions project.

 $303\ 00:48:18.620 \longrightarrow 00:48:26.419$ Alixandra Rachman: Again. I'm just going to talk about what is already publicly available. But we've put together the epic team of researchers here at Yale.

304 00:48:28.440 --> 00:48:30.510 Alixandra Rachman: and and

 $305\ 00:48:30.750$ --> 00:48:41.109 Alixandra Rachman: what we know is that cerebral palsy is the most common neuro motor condition in childhood. Inflammation in pregnancy and to increase the risk of cerebral palsy

 $306\ 00:48:41.530 \longrightarrow 00:48:46.029$ Alixandra Rachman: and heat stress increases the risk of implementing or increases inflammatory bio markers.

 $307\ 00:48:47.450 \longrightarrow 00:48:57.959$ Alixandra Rachman: We know that high ambient temperature. Pregnancies are associated with impaired fetal head growth and impaired fetal head growth in turn is associated with your cognitive lace.

 $308\ 00{:}48{:}58{.}790$ --> $00{:}49{:}11{.}310$ Alixandra Rachman: and finally, freedom. Birth is the most important risk factor for cerebral palsy, and as we have established high ambient temperatures, is likely associated with an increased risk of freedom birth.

309 00:49:12.310 --> 00:49:15.270 Alixandra Rachman: So what we're doing in this study is that we are

310 00:49:15.550 --> 00:49:34.999 Alixandra Rachman: looking at children with cerebral palsy in California, born between 2,000, 2,015, roughly 10,000, and compare them to a 20% random sample of the birth cohort within those same years. So roughly, 1.6 million. And we're going to do additional observational analysis, and we're also going to do a sibling comparison.

311 00:49:35.000 --> 00:49:47.309 Alixandra Rachman: And at the time that we pitched this project we thought it was the first sibling comparison study, but I've shown you the first, so this will probably be the second or third. I don't know fifth or tenth at the time, and it reaches publication.

312 00:49:47.900 --> 00:49:52.909 Alixandra Rachman: So so we're very excited about this project as well. And hopefully, we'll get

313 00:49:52.970 --> 00:49:55.650 Alixandra Rachman: going with the analysis within much too long.

314 00:49:56.430 --> 00:49:57.310 Alixandra Rachman: So

315 00:49:58.400 --> 00:50:02.330 Alixandra Rachman: some concluding remarks towards the end.

316 00:50:03.500 --> 00:50:07.500 Alixandra Rachman: I argue that the pregnant population is vulnerable.

317 00:50:07.820 --> 00:50:22.989 Alixandra Rachman: and during PE periods of high ambient temperatures, and I think this is under appreciated, and I think that policies and public health recommendations and clinical recommendations need to acknowledge that the pride population is vulnerable during heat phase.

318 00:50:24.250 --> 00:50:27.670 Alixandra Rachman: and I argue that we

319 00:50:27.760 --> 00:50:40.700 Alixandra Rachman: should suspect that there might be an association between exposure to high ambient temperatures in pregnancy and long-term offspring outcomes. This has not yet been robustly established.

 $320\ 00:50:40.830 \longrightarrow 00:50:46.050$ Alixandra Rachman: but I think we should look into it, and I hypothesize that there is such a link.

321 00:50:46.760 --> 00:51:03.789 Alixandra Rachman: So in terms of the research gaps, this is one of the the research gaps. I think that we need to look at the long term outcomes for the offspring, for being exposed to high end temperatures in pregnancy, not only saying that because that this is where we're doing research, and we need funding. But I actually do think so.

322 00:51:04.680 --> 00:51:05.740 Alixandra Rachman: And

 $323\ 00:51:06.250$ --> 00:51:12.799 Alixandra Rachman: and we also need to establish what are the pathways between heat stress in pregnancy and adverse

pregnancy outcomes?

324 00:51:13.870 --> 00:51:20.970 Alixandra Rachman: We need to establish what is the threshold for safe and unsafe individual level exposure to high-ambid temperatures.

 $325\ 00:51:21.100 \longrightarrow 00:51:32.180$ Alixandra Rachman: And finally, because the heat waves aren't going away, we need to know how we can protect the current population for them and for future generations.

 $326\ 00:51:32.480 \longrightarrow 00:51:37.810$ Alixandra Rachman: So with that I thank you for your attention, and I would be happy to for any questions

327 00:51:44.020 --> 00:51:47.610 Alixandra Rachman: so due to the time, limitation, less tapes.

 $328\ 00:51:47.810$ --> 00:51:59.550 Alixandra Rachman: I was wondering you saw any changes, and how like maternal age impacted whether they were successful to extreme heat during pregnancy, or if there are any other factors like

329 00:52:00.180 --> 00:52:02.479 Alixandra Rachman: how he interpreted the

330 00:52:02.680 \rightarrow 00:52:04.659 Alixandra Rachman: that's a really cool

331 00:52:05.210 --> 00:52:24.909 Alixandra Rachman: point. We actually didn't. So we adjusted for maternal light and maternal and paternal light or risk factors for toler leukemia. So that's actually a very good point. But we didn't. But but yeah, that would be interesting to look at.

332 00:52:29.890 --> 00:52:32.730 Alixandra Rachman: sure. Oh, but there's something in the chat.

333 00:52:41.790 --> 00:52:43.689 Alixandra Rachman: Yes, so

334 00:52:44.810 --> 00:52:50.209 Alixandra Rachman: great questions. So we want to stratify by

335 00:52:50.370 --> 00:53:03.920 Alixandra Rachman: by other racial and ethnic groups, but because cholera cancer is fortunately not. It's not super common. And it's most common among Hispanic or Latino.

336 $00{:}53{:}03{.}980 \dashrightarrow 00{:}53{:}09{.}450$ Alixandra Rachman: So we only had power to look at

337 00:53:09.820 --> 00:53:11.709 Alixandra Rachman: Latino and and non

338 00:53:11.750 --> 00:53:21.640 Alixandra Rachman: and latino white. And there were very few black children with with total email. So so we weren't able to to look at that

339 00:53:21.660 --> 00:53:28.360 Alixandra Rachman: And in terms of socioe-conomic factors. That's also a great

340 00:53:28.410 --> 00:53:51.730 Alixandra Rachman: point. We we could in theory strat, do a stratified analysis based on on socioeconomic indicators. We have educational level, and we have sort of neighborhood level as well. So so that is something we definitely could consider. But we we actually didn't do it. We, we felt like we were doing a lot of analysis. So we wanted to restrict ourselves a bit. But but yeah, that's a great suggestion.

341 00:53:53.510 --> 00:53:56.570 Alixandra Rachman: There's Anomala on the first on the first one. Yeah. Yeah.

342 00:53:58.790 --> 00:54:15.559 Alixandra Rachman: yeah, the the mechanisms linking high temperature during pregnancy and high risk each other looking up. That's the 1 million dollar question. So we, of course we don't. Really, we don't really know exactly what those mechanisms would be, which is the case

343 00:54:15.560 --> 00:54:35.290 Alixandra Rachman: for all of these adverse pregnancy outcomes. By the way, we don't know why heat stresses or is associated with increases computer mirth. We do suspect several mechanisms, but we don't know it yet. And the same is true for Toler. We we don't know exactly why, but the reason why we were interested in it

 $344\ 00:54:35.450 \longrightarrow 00:54:54.230$ Alixandra Rachman: to to study. It was for those reasons that I talked about in those previous slides that we know that other environmental hazards in pregnancy are linked to it, and we know that it has this prenatal onset. And we know that, for instance, one potential biological pathway is that

345 00:54:54.250 --> 00:55:16.819 Alixandra Rachman: heat stress in the non pregnant population increases oxidative stress, and some studies have just have suggested that oxidative stress can induce the production of pre-lechamic clones. But we don't know whether this is the mechanism here. But but that would. But I can say as much as this is something that we are interested in looking at further.

346 00:55:17.360 --> 00:55:23.960 Alixandra Rachman: So I say another question, but due to the time intuition, let's make at least the final Q. And a okay. Thank you.

347 00:55:24.400 --> 00:55:26.160 Alixandra Rachman: Mike Bracken, and

348 00:55:29.330 --> 00:55:36.910 Alixandra Rachman: yes. great question. Thank you. bracken, my bracken, and so

349 00:55:37.260 --> 00:55:43.800 Alixandra Rachman: And for for our project we haven't looked at access to air conditioning. I think that's

 $350\ 00:55:43.890 \longrightarrow 00:55:48.410$ Alixandra Rachman: very interesting for for this, for for any pregnancy

351 00:55:48.720 --> 00:55:51.679 Alixandra Rachman: complications. Really, it's it's an interesting and

352 00:55:51.770 --> 00:56:04.559 Alixandra Rachman: question to look at risk mitigation. But I do want to show you, because you asked, and to do have a bonus like I have. So like, this presentation actually lasted one and a half hours. So you're you're lucky to get off

353 00:56:04.950 \rightarrow 00:56:10.850 Alixandra Rachman: early off. But let's see here, I do have a slide on that that I took out this morning

354 00:56:11.990 --> 00:56:12.860 Alixandra Rachman: here.

355 00:56:17.860 --> 00:56:20.699 Alixandra Rachman: so as you can see here.

356 00:56:21.580 \rightarrow 00:56:23.050 Alixandra Rachman: this is looking at.

 $357\ 00{:}56{:}23{.}210$ --> $00{:}56{:}31{.}359$ Alixandra Rachman: the effects of high ambient. This is the the demographic study from the US. Look at those 56 million births.

358 00:56:31.380 --> 00:56:34.410 Alixandra Rachman: the effects of of high

359 00:56:34.650 --> 00:56:36.400 Alixandra Rachman: minimum temperatures

 $360\ 00:56:36.470 --> 00:56:46.740$ Alixandra Rachman: daily, I mean, daily temperature. So that's reflected more than night time temperature. Increases the risk or increases the birth rate on that day and executive days. But

 $361\ 00:56:46.850$ --> 00:57:01.850 Alixandra Rachman: if we model that the current population, or whether the population have full access to air conditioning which they could do in the study because they had. There was a very large increase in the access of air conditioning units. They could actually model that

362 00:57:02.120 --> 00:57:03.869 Alixandra Rachman: there would be a reduction.

 $363\ 00:57:04.180$ --> 00:57:17.190 Alixandra Rachman: and by 3 quarters of the induced birth rate. So so yes, I think that access to air conditioning is one of those those factors that actually can

 $364\ 00{:}57{:}17{.}340$ --> $00{:}57{:}21{.}209$ Alixandra Rachman: modulate the association between high temperatures and adverse outcomes.

365 00:57:23.560 --> 00:57:28.160 Alixandra Rachman: Right? I think we at the end that we'll send that. Thank you so much.

366 00:57:31.720 --> 00:57:36.050 Alixandra Rachman: Thank you.