Transcript

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Great to be here, thank you for this invitation. Thank you for finding me. It's great to see the great work that is coming out of the CIC and uniting us, trying to understand how these uncertain times are going to affect our world. I'm here to talk to you briefly about our COMBO Initiative, or COVID-19 Mother-Baby Outcomes Initiative that we spearheaded at Columbia University. Lauren [Close] found me because we had one early NIH grant to study brain behavior and functioning. I'll tell you a little bit about this, but broadly speaking, this is a much bigger initiative than that.

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I wear a lot of different hats at Columbia University, but one of them is a neuroscientist. I actually study the neural circuits of resilience. That is all I did pretty much up until the pandemic in my lab.

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Second, I am one of the newborn hospitalists in our Well Baby Nursery. I'm not a neurologist, I don't deal with sick babies, I deal with healthy babies. That accounted for 20% of my time and before the pandemic I used to say that this was my vacation time away from the lab where things are never working out. I get to spend time with new parents and their adorable babies.

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However, on March 13, 2020, all that changed. I'm not sure of the composition of the webinar in terms of whether or not you're from New York or are familiar with the fact that we were the first

epicenter of the pandemic, including for pregnant and laboring women. March 13, 2020 is the date in the U.S. where the first woman in labor was diagnosed with COVID-19. That baby was coming to our nursery and the world was looking towards our nursery to come up with protocols for infection and protection protocols as well. Scientists were learning from our experience in terms of what to expect from these babies and so on.

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As a neuroscientist, and a developmental neuroscientist in particular, one of the things that I immediately thought about is the concept of the developmental origins of health and disease, or DOHAD.

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This is also called prenatal programming, where we have really learned in the last couple of decades that virtually anything that happens to mom while she is pregnant can affect the fetus. Viruses and the consequent maternal immune activation are some of the insights. There are a lot of examples from the literature. Zika, for example, even in children that are not actually infected with the Zika virus, can be associated with language deficits. A variety of viruses have been associated with psychotic disorders all the way into adulthood and there are many other examples. We also know that things like natural exposure to any kind of stressor like famine or natural disasters or war have also been associated with increased risk to offspring, including schizophrenia, language and cognitive deficits, and difficult infant temperament. Of course, the COVID-19 pandemic was this perfect intersection of these really influential impacts during pregnancy.

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As we were entering the summer of 2020, we also began to think about being born into an altered world. So adverse childhood experiences have been shown to be dose-dependently involved and increase a risk of different diseases and disorders. Some things you can think about very easily like depression and anxiety, but they also increase the risk of things like cancer and even broken bones later in life.

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We very rapidly mobilized to start COMBO. The very first dyad was actually enrolled on May 26, 2020. We began with simple phone calls that physicians we were making to the families that had been hospitalized in our Well Baby Nursery. We were just wanting to check up on the baby and then rapidly began to add surveys. We also included a prenatal arm to enroll pregnant individuals. We've been following this cohort ever since then. We just began our four to five year assessment and as funding became available, we began to add things like biospecimens, video visits, brain MRIs of both moms and babies. We've also added cool stuff like smell tests for the mothers. We have entry points between birth and 24 months to capture as big of a population as we can. We've been very fortunate to have early and sustained funding since the spring of 2020 through both federal and non-federal funds.

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Most importantly, this is a big initiative. This is a picture of COMBO from the summer 2020, a group of 77 people. We are now well over that.

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We've had about 200 contributing members to date. We've enrolled 2,000 mother-baby dyads. We were able to expand outside of New York into Utah and Alabama thanks to a CDC contract. We just gather so much data that we don't know what to do with it. If anybody here is interested in collaborating with us, we're completely open source and have open science approach, minus the fact that we don't have the infrastructure to generate data fast enough and set up collaborations fast enough. We are really interested in any kind of collaborative effort. We've generated over 20 publications at this point. We've had many trainees that have used this data for their thesis - for their T32s and KI9s.

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We've generated some of the most foundational data on what is happening to the COVID-19 generation. This is coverage from an early paper that I'll tell you a bit about today.

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What I'm going to do because this is a ten minute talk is cover four papers - just to give you the highlights of some of the biggest findings that we've had. This is our first paper that we put together in exactly 14 days in April 2020. We looked at the rate of vertical transmission - if mom has COVID while she is pregnant and delivering, is an infant at a higher risk of infection? In this study, we looked at the electronic health records of the first 101 infants born to COVID-positive moms at Columbia University. These babies were born in March and April 2020, which was that really acute peak of the first wave of the pandemic. As I mentioned, there were 101 infants born during that time. That was a period of about 6 weeks. And the most important part of this research was that we were one of the only hospitals that did not separate moms and babies. We felt this was a really important thing to do early on - both to protect our own patients, but also to contribute to the research necessary for the rest of the world to follow suit and stop the separation. We know it is very dangerous to separate moms and babies. What we found was that there was a very low risk of vertical transmission. The two babies that did test positive did not have any symptoms. This was work that contributed to changes in policy, including by the CDC and World Health Organization - the ending of the mother-baby separation. I have QR codes for each of the four papers, I forgot to mention, so if you're interested in reading the rest of the manuscript, please feel free to take a snapshot.

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The next paper that I'm going to tell you about came out in January 2022. This was the first paper worldwide to look at the neurodevelopment of these infants. For this paper, we used the ASQ-3, or Ages and Stages Questionnaire, which is widely used in both clinical settings as well as research settings. These are online surveys filled out by mothers. This was specifically

targeting six month-olds born between March 2020 and December 2020. This was restricted to our population around Columbia University. In this paper, we covered 317 infants. We knew that 141 had not been exposed to COVID in utero. I'm not going to review the paper thoroughly, but if anyone has questions, we have some of the world's most characterized maternal infections for the year of 2020 thanks to both hospital policies that were implemented very early, universal testing, as well as research strategies. We had 141 infants that we knew to be exposed either in the first, second, or third trimester to maternal infection. We were very fortunate to be able to include 62 infants that had been born in our hospital system in the preceding 3 years before the pandemic. To summarize the finding of this paper, we found no effects of COVID exposure, but we did see some small decrements in pandemic-born children. This indicated to us that it might be the maternal stress or distress experienced during pregnancy as a result of the pandemic rather than an actual viral infection.

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Of course, that was a maternal report. The gold standard in the field is to actually test infants with objective measures of development with actual neurodevelopmental assessments performed by clinical or research staff. In this second paper, we followed up using an observational tool called a DAYC-2. For those of you who know a bit about childhood development, this is very similar to [inaudible]. We were able to adapt the DAYC-2s easily to Zoom. We are still looking at infants that are six to twelve months old - still very young. We've expanded a bit in this paper on the data on births. We have infants born between March 2020 and November 2021. We also expanded in this paper into Utah and Alabama, so that includes a really nice geographic coverage. We have a larger sample size of 407 infants. Unfortunately, we didn't have any pre-pandemic born infants, but we have a nice division between unexposed and exposed infants. We also have a small group of infants whose exposure status is unknown, so we consider them a separate group. The good news about this paper is that we found absolutely no effects of COVID exposure once again through this expanded assessment. This, unfortunately, made less worldwide news because it was only good news. This was a really phenomenal finding - a very thorough assessment which showed no differences between groups.

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Finally, I'm going to tell you about a paper that came out just a few months ago. This is the world's first paper evaluating the possible increased risk of autism using screening rates among pandemic-born infants, considering their COVID status. Here, we use both electronic health records as well as our COMBO cohort with online surveys. We looked at infants between 16 and 30 months of age. The DOB for all the infants we looked at was between January 2018 to September 2021. These infants were born at Columbia University but also had follow-ups within our clinic system. We had about 2,000 infants total between the electronic health records and our COMBO cohort. The really good news here is that we found absolutely no effects of either COVID or the pandemic environment on infant autism rates. This was really really good news, but unfortunately, it's hard to make a good scientific career out of negative findings. However, this was the best negative finding of my career.

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I will end by showing you this infographic of our collaborations. We are happy and thrilled when people want to join us. We've been adding a variety of components to this cohort based on the investigators that come and are interested in working with us.

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With that, I will thank all of the many contributors and funders. Please follow us at @COMBOstudy on X/Twitter or if you just Google "Columbia and COMBO", we will be the first thing that comes up.