Welcome to today's ELSI Friday Forum. My name is Dr. Esohe Irabor, and I am a Public Health Laboratory Fellow at the New Jersey Department of Health, as well as the CERA coordinator for today's session. ELSI Friday Forum is a monthly webinar organized by the CERA, which also provides resources and other events through the ELSIhub website.

CERA is funded by the National Human Genome Research Institute. Today's session, entitled "The ELSI of Social Epigenetics." It will address how ELSI research of social epigenetics can address these issues and make social epigenetics more impactful. For logistical information about this webinar's closed-captioning, the chat, or the Q&A feature, please see the information dropped in the chat.

Before we get to today's session, I have a few quick announcements. We are excited about the expansion of the CERA partnership with the *American Journal of Bioethics.* The journal now welcomes proposals for target articles related to ELSI Friday Forum topics, including today's topic and those explored by future forums. You can find the link for submission instructions and monthly deadlines in the chat.

A compiled list of resources to today's panel will be published on ELSIhub, and a link to this page will be provided in the chat. We are pleased to share the technologies to operationalize Indigenous Data Sovereignty. And ELSIhub Collection curated by Maui Hudson and Stephanie Carroll was updated this month. Please find a link to that resource in the chat as well.

And finally, I want to encourage each of you to join the ELSI Scholar Directory and sign up for our newsletter and connect with us on LinkedIn and Bluesky. Please note that this session is being held as a Zoom meeting. So unlike previous sessions, we can all see one another and connect in the chat. Please ask your questions using the Q&A feature and keep yourselves muted. And I mean muted for the duration of the event.

When we transition to the meet the speakers after-party, at the top of the hour, we will stop the recording and invite you to turn on your cameras and participate in that informal part of the discussion. Now, it is my distinct pleasure to introduce our moderator for today's session. Full bios for all speakers are in the chat.

So I will just quickly introduce Martine Lappe, PhD. Dr. Lappe is an Associate Professor of Sociology and Science, Technology, and Society in the Department of Social Sciences at the California Polytechnic State University, San Luis Obispo. She is also a fellow in the Center on the Developing Child at Harvard University.

Dr. Lappe is a feminist sociologist of science, health, and medicine and a previous postdoctoral fellow at Columbia's Center for Excellence in ELSI Research. Her research focuses on the social and ethical dimensions of contemporary life sciences and their intersections with lived experiences of pregnancy and parenting in the United States and Canada. She has published widely on the social and ethical dimensions of social epigenetics and will be moderating today's session. Over to you, Dr. Lappe.

Thank you so much for that thoughtful introduction. It is my pleasure to be here today. Really an honor to be moderating this session about the ethical, legal, and social implications of social epigenetics.

As we will hear in more detail during today's panel, at its core, social epigenetics is a broad field of study that considers how experiences and exposures of various sorts get under the skin affect gene expression and potentially impact health, development, and disease. These experiences and exposures can include everything from what we eat to the environments we live in and the experiences we have. So this is an area of science that truly touches all of our lives.

Over the past decade and more, foundational social epigenetic studies in both animal models and human populations have deepened our understanding of health, development, and disease, while also raising important questions about the social, ethical, and legal implications of this growing area of research. For example, findings from epigenetic research have led to the development of direct-to-consumer testing, particularly associated with biological age. This has captured the interest of the public, venture capitalists, and celebrities alike.

Other findings have sparked ongoing and important discussion about topics with far-reaching implications, including intergenerational inheritance, the effects of early life adversity and care, and questions about the potentially lasting impacts of systemic oppression, environmental degradation, and trauma. Perhaps one of the most fascinating and important aspects of social epigenetics is its potential to inform interventions and support policies that can improve health and well-being in meaningful ways.

So it is for these reasons and many more that we consider the ELSI of social epigenetics during today's panel. And we are very fortunate to have two leading researchers in the field to provide an overview of the science, present their research, and answer your questions and mine about the ELSI of social epigenetics. So, without further delay, I'm very pleased to introduce two esteemed panelists.

Dr. Michael Kobor, PhD, is a Professor in the Department of Medical Genetics at the University of British Columbia, UBC, and the Edwin SH Leong UBC Chair in Healthy Aging, a UBC President's Excellence Chair. Dr. Kobor's world-class interdisciplinary research program employs a society to SEL framework to better understand the mechanisms by which environmental exposures and life experiences can get under the skin to affect health and behavior across the life course.

Dr. Erika Waters, PhD, MPH, is a Professor of Surgery in the Division of Public Health Sciences of the School of Medicine at Washington University in St. Louis. Dr. Waters's research program seeks to understand how people think about health issues and how those thoughts influence their health-related decisions and behaviors. Her scholarships in-- or her scholarship, rather, informs health communication and behavioral interventions that aim to improve health and reduce health disparities. Dr. Kobor will present first, followed by Dr. Waters and our discussion. So I'll turn it over to Dr. Kobor.

Well, thank you so much. It's a real privilege to be here. Much appreciate the invitation and the very kind words. What I'd love to do is to give you sort of a personal perspective on social epigenetics. And Dr. Lappe already has highlighted some of the key and exciting areas that this field has evolved in.

And so I don't claim to cover 9 or 10 minutes, everything that the social epigenetics. So it's a vignette of various pieces that I can speak from my own lived experience, if you wish, as an epigenetic practitioner. So our conceptual framework, very similar to what Dr. Lappe shared with us, is really the idea that there are experiences and environments that, especially during sensitive periods, get under the skin to then affect biological pathways and ultimately, in some cases, end up in the nucleus of the cell to affect gene expression and the structure upon which the DNA is wrapped, which is called chromatin.

And in some cases, this can be in a persistent fashion. And so, of course, this can also then be the other way around to affect downstream lifelong processes as well. Today we're really going to stick primarily to the left side of this framework. But needless to say that the secret to understanding epigenetics is really the chromatin structure and the fact that the DNA is not occurring in the cell in the naked form, but is tightly packed. And I'm happy to talk about this more in the discussion.

One particular aspect of epigenetics in chromatin structure that I think in human populations, at least, is capturing 99.5% of all studies is called DNA methylation. It's just a little attachment of a chemical tag to the DNA itself. And this is really what, in many cases, social epigenetics-- in most cases, social epigenetics is all about. But keep in mind that there's much more to this.

Lots of exciting work has really highlighted the fact that experiences get under the skin. including studies of society to cell studies and nutrition and lifestyle of the mother can affect the epigenome of the child, in some cases, lasting for decades, such in the case of the Dutch famine. Further, something that really captured the attention of the public is work pioneered by my Canadian colleague Dr. Michael Meaney, that showed that postnatally, the quality of the maternal care can associate with the epigenome in the child, both in rodent models but also in humans.

You probably heard a lot about twin studies in your research and in your discussions. They are often used for genetics, but they're also a really powerful illustrator of this idea that experiences can get under the skin. And so you see here these two twins, little cutie on the right and this crying one on the left.

Turns out that identical twins acquire discordant epigenomes during the life course, in particular if they have been separated early in life. In turn, this then can be associated with various health and behavioral outcomes, including chronic diseases, mental health, and so forth. So really an exciting field.

In our own research, we focus this epigenetics at the interface of nature, that being the DNA we're given by our parents, and nurture those being the fertile grounds of our families, of our communities, and such. And ultimately, what we try to do is to get the best starts to our children to life, prevent diseases, and doing so with a life course perspective. As I mentioned earlier, we look at the epigenetics at the interface with the environment.

But increasingly, we are also aware that there is a strong component of genetics, and we're exploring this actively. And again, I'm happy to talk about this in the discussion.

We take a very developmental look to this. So, for example, you can see here on the top that the genome is more or less static throughout the life course. But the epigenome can, quote unquote, "listen" to some extent to the environment.

And in particular, if a particular exposure happens during a sensitive period, in this case during pregnancy or early in life, like we saw these earlier examples, if such an exposure, then might alter the trajectory of distinct epigenetic marks or pathways and end up in a higher risk for, say, chronic diseases many, many years, decades later. If the same exposure happens outside of the sensitive periods, perhaps it doesn't have the same detrimental impact.

Now, of course, this could also be good exposures, and you can easily imagine this being very beneficial.

One of the areas that the field and we in particular have been really focused on is the really striking impact that child poverty can have on lifelong health. And we have written a recent review to illustrate how child poverty gets under the skin, to not only influence child development, but also lifelong health. And outlined in that review the various biological, physiological, and health outcomes.

So I encourage you, those of you, to read this. And I'll just show you some vignettes on how we have then tested the idea that, indeed, child poverty and related child adversities do get under the skin by means of epigenetic biology.

And so early on with Greg Miller and Edith Chen who, for example, showed that early-life social class can leave a biological residue that we can measure at this level of epigenetics and similar marks. With Tom McDade and Chris Kuzawa have shown that in the Philippines, social environment, physical environment in development also predict DNA methylation. We have shown that things like growing up in these atrocious places for the children in Eastern Europe leaves a biological imprint and that we can see at the level of the genome.

And without going into too much detail with folks at Harvard, we have actually shown that in the human sperm, we can find a signature of childhood abuse as well. We have also used this to understand neurodevelopmental diversity more and have looked at things like prenatal exposure to alcohol and how the epigenetic biology might be explaining some of the downstream effects. Needless to say, these kind of studies do attract the public, but not always in the right way.

So I take two of-- a contrast here-- two of our studies, the titles with what they end up in the newspapers. And you can easily appreciate, especially on the first one where it's basically associations of epigenetics with parental stress and no causality versus what the newspaper ends up making of it. And I'm sure we're going to talk about this more later on.

Now, all I've shown you so far is really associations of the epigenome with various exposures in environments. The one area that Dr. Lappe pointed out that's also really captured the imagination of the public is the idea that epigenetic age occurs so that there's an epigenetic clock, if you wish. And this is pioneered by my friend Steve Horvath more than a decade ago.

And here, we basically use the same information of these DNA methylation patterns, but we use machine learning and bioinformatic algorithms to derive a epigenetic age. And the epigenetic age is one and perhaps the original of what we call now DNA methylation risk scores, where we basically take a methylation pattern and you can predict things, including epigenetic age, but also whether somebody has smoked, whether somebody has certain diseases potentially, and inflammation and so forth. So a really rapidly evolving field where I think the ELSI perspective is much needed.

Now, we have put this idea into the concept that most of us live in this Yellow Zone, where basically our chronological-- our epigenetic age predicted-- epigenetic age more or less corresponds to our chronological age. But some folks that go to the gym twice a day or live very healthy lifestyles, they might be epigenetically young. So chronologically, they might be 50, but epigenetically, perhaps they're 40.

And, of course, the opposite is also true. Many, many studies have associated deviations in epigenetic age concordant from the chronological age with various health outcomes. And so generally, folks who tend to be epigenetically older tend to be less healthy by and large.

Now there is a vast field of research, very exciting area. And clocks are evolving very rapidly. So the original clocks, we call them first-generational clocks, like the what you call the Horvath's Clock, for example, they were trained in chronological age. More recent clocks were trained on other outcomes. So with these second-generation clocks, including biomarkers of aging.

And in some cases, even time to death. So there's a thing called GrimAge when the Grim Reaper comes that is trained on, in part, on time to death. And then lastly, there are third-generation clocks, like the DunedinPACE of aging, that are trained on longitudinal samples and patterns of methylation changes over time. So keep that in mind when you see epigenetic clocks.

There are many, many different. And it's important to understand which of these generation clocks are being reported on.

We've been involved with many sort of clock studies, including going back to our work on poverty, showing that growing up in early-life low socioeconomic status is associated with accelerated epigenetic aging. We have looked at these so-called high longevity regions, which previously known as Blue Zones, to document epigenetic age differences there between sexes, biological sexes. We have looked at things like frailty and how that might be associated with epigenetic age deviations.

But as Dr. Lappe pointed out, these things are also rapidly taking hold in intervention studies. And so we've been involved in some rather controversial ones, including the idea that the epigenetic age can be reversed by swallowing a bunch of different compounds, but also more recently about how epigenetic clocks might report on caloric restrictions.

Now, again, there's a huge amount of body of work that we're happy to discuss later on, but I think it's a fascinating field. We ourselves have also focused on the childhood aspect of epigenetic aging, which is an entirely new area that I'm happy to talk about in the discussion. But you probably seen that this has been popularized without sort of advertising this. The Kardashians have popularized the epigenetic test.

And on the right, you see this fellow Bryan Johnson with his teenage son who is very infamous. By putting up this DNA longevity test on the bottom here, I'm not endorsing it by any means, just to illustrate as Dr. Lappe pointed out, as this can be now direct-to-consumer tests. You might be also aware that Bryan Johnson, in particular, has a world record list of epigenetic age reversal, but some of his claims have been reasonably refuted in *The New York Times.*

So with that, I just leave with you that there's really a brave new world of epigenetics. You can do epigenetic yoga. If you sweat a little too much, there's now an epigenetic shampoo for greasy hair that you can buy. And just a quick search last night, there is now epigenetic serums for aging, related skin issues and so forth. And I already mentioned the direct-to-consumer test.

So thank you so very much. Really looking forward to this panel discussion afterwards in the questions.

Wonderful. Thank you so much, Dr. Kobor. We will turn it over to Dr. Waters.

Thank you so much, Dr. Kobor. That was a fascinating talk. And I think I will be able to expand a little bit on some of what you had mentioned. Let's see.

So today I am going to use Dr. Kobor's talk as a springboard to talk about public, the public perspective, on epigenetics. And let me-- I lost my timer. OK.

So first, this talk is informed by the broader literature, but much of it is presenting information gleaned from data collected during a study funded by the National Institutes of Health. And here is a list of the team that really helped make the research happen, as we can't do research. Professors can't do research without our teams. And they have been fantastic all around.

This particular line of research-- in this particular line of research, we really sought to answer four key questions. First, how do members of the public come to interpret, understand, and make meaning of epigenetic information? What implications does this understanding have for key concepts related to ethical, legal, and social implications of epigenetics, such as genetic determinism beliefs, but also including some other beliefs, such as stigmatized beliefs?

Are their communication strategies that can foster public understanding of epigenetic concepts while avoiding perpetuating determinism? And finally, how do sociodemographic characteristics shape public responses to epigenetics information? Basically, how generalizable are the findings across different population groups?

And really, what motivated this research was the fact that epigenetics research in the clinical setting is evolving quite rapidly. There are extensive number of therapeutics being tested in clinical trials. And also, as Dr. Kobor pointed out, information about epigenetics is being disseminated in the lay media.

And so we were really motivated by this question of, if people are taking what they're seeing in the lay media and maybe misinterpreting it or drawing conclusions that may not be supported by the data, how might that affect their openness to therapeutics or their beliefs about the effectiveness of different therapeutics and other technologies?

So we approached this through a variety of research methodologies. As you can see here, we have focus groups, national representative surveys, experiments. And really, we wanted to progress through the research continuum, so to speak, or the research project-- process, excuse me.

First, in our first attempt to understand how people are interpreting epigenetic information, we showed them a video about epigenetics and different news headlines. And our national surveys were refining the epigenetics video in an attempt to increase comprehension, make it a little bit clearer, and also doing some more extensive testing of news headlines.

And then finally, in the experiments, we're going to implement some strategic changes to communication strategies for the epigenetics video and news headlines to really see what communication strategies can we use to really increase people's comprehension and how do those strategies-- [COUGHS] excuse me-- affect the acceptability of epigenetics technologies for clinical use.

And you can see we have different recruitment strategies. We have different perspectives. We have community recruitment.

We have recruitment through national panel called Ipsos. You might have heard about them in the news. They do political polls as well.

Other sorts of internet panels-- we're doing exploratory work, confirmatory work, interventional research. And we're doing this work in fairly large samples, again, in an attempt to increase the generalizability and applicability of our findings to different groups. And you can see that we--

I'm not going to read everything in the table. But you can see that we are stratifying our recruitment orthogonally by race, ethnicity, and education based on the literature's suggestion about what demographic factors might influence comprehension.

We found a lot of elements in our research that really bring us hope. And there are indications that the public also has a very hopeful perspective on the future. In the focus group research, the participants really mentioned the possibility to create novel technologies and therapeutics based off epigenetics to prevent and detect and cure disease, either in oneself or in future generations. So very forward-thinking.

They identified strategies or possibilities for using information about epigenetics research broadly to encourage health promotion and disease detection behaviors, again, to improve the health of themselves and possibly future generations.

One of the things that we were concerned about going into this research was inadvertent endorsement of genetic determinism. We know through research on public interpretations of genetics that there's a lot of deterministic inferences among the public. And we wanted to see if that was the case here.

And in this case, the determinism could have gone one of two ways. It could have gone towards epigenetic determinism in terms of once my epigenome has changed, I am permanently harmed in some way.

Another way it could have gone was more of an environmental determinism, where there were concerns about whether inferences about people who grew up in poverty were permanently damaged because the environmental effects are unchangeable. And we didn't see indication. We didn't see many indications of that.

Participants also identified the possibility to really educate physicians about the importance of history taking, a complete history taking, that included factors that might influence epigenetics, such as your typical diet, tobacco use, physical activity. But also, participants mentioned asking about the environment, the physical environment where people were growing up, was there environmental pollution?

And then also the possibility of epigenetics to help physicians understand and other health care providers understand patient experiences and the importance of patient experiences for health.

Some participants were also optimistic because they thought it's possible that maybe learning about epigenetics and how impactful environmental influences could be on a person's health might motivate social change. Participants mentioned things like improving childcare for very young children, the possibility of reducing poverty through policy, or implementing regulations to try to limit environmental pollution. So these are very forward-thinking possibilities that participants mentioned.

These hopeful perspectives did need to be cautioned by some-- did need to be tempered by some caution, however.

Across the board, participants expressed very serious concerns about the implications of epigenetics research and testing for health insurance coverage, cost of care, and implications for exacerbating current and future health disparities. For example, they mentioned things like concerns about either being denied health insurance coverage,

being removed from health insurance rolls, the cost of care being so much-- even with health insurance-- that we're talking about the possibility of deductibles being so high that even the insured wouldn't be able to care for them. And then they also mentioned the possibility that if only very high-income people can afford this, then over generations,

you have a two-tiered society where you have the more wealthy who have access to these technologies and have very good health contrasting with another stratum of society that don't have access to these technologies and have experienced harms to health. They mentioned the potential for increased stigma, social stigma. There was extensive endorsement of the idea that now--

to paraphrase, now we have the knowledge to really take control over our health. And these conversations were really focused on the individual level of behavior change without acknowledging potential external factors that might constrain people's choices, like, for example, the cost of healthy food or the walkability of neighborhoods, things like that.

In my last minute or so, participants mentioned concerns about who would have access to the data if their epigenetic data would be held private. And then what would happen if there were data breaches or data were shared without their knowledge or permission?

There was also-- I'm going to skip genetic determinism. We already talked a little bit about that. There was also expressions of distrust, fear, and anger at media portrayal of epigenetics findings.

These were some of the headlines that we showed to participants. And you can read them here. They really felt that they were, quote, "clickbait" and could cause a lot of fear and anger, fear within populations that were mentioned by these articles, and anger at the potential for these articles to perpetuate stigma. And so we have several recommendations for different communication strategies, which you can see here on the screen.

But overall, I think this research so far shows that the lay public, even folks with limited formal education, can be savvy in their interpretations of information about epigenetics. However, it is absolutely critical that the information be communicated in a way that is supportive of their knowledge and is not sensational. And I will stop there. Thank you.

Thank you so much. So this has been a really enlightening and fascinating set of talks that are raising a lot of questions that I'm sure some of you have been interested in. And that's why you're here today. As the moderator, I want to take the privilege to open up with a couple of questions.

One is, both Dr. Waters and Dr. Kobor have talked about sort of the implications of social epigenetics very widely, both in terms of the biological elements, as well as the social elements, as well as the sort of potential future that it implicates. I want to ask a little bit about how you both decided to study social epigenetics and what you've taken away from your experience working in the field for the time that you have been studying it, because I think we can all learn a lot from both of your experiences. So I'll open it up to both of you.

Erika, you want to go first? Give me more time to think? [CHUCKLES]

Yeah, sure. I can be thrown under the bus. [CHUCKLES] OK. So brief, slightly embarrassing personal story. I did not-- I first learned about epigenetics when I was doing my MPH after my doctoral work.

And I heard the term in a cancer etiology and epidemiology course. And I didn't understand what it was. It wasn't defined. And so when the class ended, I turned to my friend. And I said--

or they had talked about methylation. And I turned to my friend, and I said, what does menthylation have to do with cancer? And she laughed. And so I laughed. We were good friends.

And she said, no, not menthylation, methylation. And so she explained. And as she was explaining this, me with my health communications background just started having all of these ideas about the potential utility for communicating-- for using epigenetics to perhaps promote healthy behavior change.

And also, I had concerns about potential misuse of this information by the news media. And so that was in 2007. And ever since then, I have been nipping away at small projects here and there to get to where you currently see. And I think the overarching conclusion that I have so far today is really that idea of hope tempered by caution.

There are so many potential benefits to epigenetics technologies. And also, those potential benefits exist in a context where people don't always have the money for the therapies. And the way that the research is framed could be used by people with either malintent or who are looking to make a buck. And so that's what really keeps me fascinated is, how do we develop these strategies to really find that balance between the two?

My story is much less exciting. And so I-- as corny as it sounds, since high school, I had been fascinated by how environments can regulate genes, going back to some very basic bacterial paradigms. And that's how I sort of focused my graduate and postgraduate education. Ended up doing a postdoc at University of California, Berkeley with a wonderful mentor called Jasper Rine, who was not only a broad thinker, but [INAUDIBLE] its own PhD had discovered the key aspect of epigenetic biology in yeast.

And so I had been working in yeast and measuring all kinds of epigenetic things, patterns, and how they respond to when you expose a cell to harmful chemicals and all that fun stuff. And then when I started UBC, I by accident, by chance, maybe-- although I always think chance favors the prepared mind-- got involved with-- got invited to join a group called the Child & Brain Development at the Canadian Institute for Advanced Research, which is one of the sort of most wonderful organizations that I would all of you encouraged to check out. And Michael Meaney was part of that group.

And then at the same time, a particular company had developed technology and just launched technology to measure those methylation marks that Dr. Waters mentioned in fairly high throughput. And so I said, oh, I've done this in yeast for the last decade. I can do that in humans. And so that's how I started.

And then I think what really helped us is that-- and I still think that's true even now. We also started in 2007 doing this, almost 20 years later-- that epigenetics, social epigenetics, lends itself so very well to interdisciplinary research approaches and conversations. And that has really kept me going because anytime I talk to somebody from a different field, we find some common ground. And that common ground tends to be that little methyl mark and the various meanings and factors that shape it.

And this goes from-- as you might know. And I think hopefully I mentioned this. We collaborate with people from anthropology, child development, pediatrics. You name it. And so this is really refreshing. And I think the other aspect that I've been really fascinated by is how much it benefits trainees to be early on in their career exposed to that sort of interdisciplinary mindset.

The one thing I've learned is that it's messy, because especially if you do it in human populations, it's not as clean as some rodent experiment. There is a lot of noise. There's a lot of aspects that need to be considered. But we're improving. And I think discussions like the one we have really help put the field in a more broader, in a more nuanced perspective.

Wonderful. Thank you both for fielding that open-ended question and for taking us through what brought you to the field and where it stands right now. We have a number of really wonderful questions in the Q&A, so I'm going to turn to some of those now.

One of them is about sort of the sensitive period that you had discussed, Dr. Kobor, during your presentation. And Mary [INAUDIBLE] asked, what is it about the DNA of a child that makes it more sensitive to the effects of the environment? And I might just patch on sort of, what are some of the social or ethical implications you think are aligned with that sort of sensitive period?

That is a great question. I think that's probably what is it in the DNA, in the cell, in the metabolism of the cell, in the way that these environments get eventually to the cell that in particular makes the early-life period, quote unquote, "more susceptible" or in the prenatal period. And I dare to say we still don't exactly know the answer.

We have a lot of observations. So I can take methylation profiles from one-year-olds and sort of stack them up every five years across the entire lifespan. And it's clear that some of these methylation marks change much quicker in early life, which coincides with these sensitive periods, to some extent. But why that is? I honestly don't know.

It's a great question. I do think that when you take a step back, what it really means is that we need to be very aware of what we as, say, parents, what we as communities, what we as policymakers put in place to ensure the best possible outcome for our children, whether it's going back to the prenatal period or the early life.

I do also say that I think it's a little bit like looking under the light bulb because so much research has been done in the early-life plasticity sensitive period way beyond DNA methylation, obviously. But I think there are probably other sensitive periods in life that we should explore, such as puberty and adolescence and maybe the transition into older age. So lots of work to do and great, great question.

Thank you. And Dr. Waters, I mean, some of what Dr. Kobor brought up in terms of the social environment and the impacts that that early social environment has on both DNA methylation but also child health and development more broadly really speak to some of your findings in terms of those tempered hopes. So I just wondered from your research if you could comment on where the question of early life came into people's responses or concerns or hopes in your research.

The focus groups were peppered with these discussions throughout across multiple different contexts and topics of discussion. And one of the most salient interactions for me at this point is participants wondering, what have I done to my children and grandchildren? Many people are taking responsibility, personal responsibility, for some things that they had no knowledge of beforehand and cannot be changed now.

And they expressed very deep levels of concern and guilt. And so one of the things that we really struggle with is that communication aspect. How do we communicate the fact that early-life experiences have profound impacts without making people take on too much responsibility for things that weren't necessarily entirely in their control?

Talking about stress-- we know scientifically that experiences of stress run a spectrum from daily hassles to severe chronic traumatic stress brought on by abuse and other adverse childhood experiences. And participants really weren't differentiating among those different types of stresses. And so when you layer on--

if I think about par-- I am not a parent. But when I look at parents and discussions of parenthood and motherhood, in particular now, and the lack of childcare, affordable childcare, life is very stressful for parents. And I worry about-- we had some hard conversations in the team about, do we raise these issues at all about early childhood experiences?

And we decided, yes, we should because it's out there in the broader information environment. And so they will find it. So we need to get in there first to hopefully set them on a path that is a little bit less harmful.

Thank you. Martine, do you mind if I just follow up on this real quick?

Please do.

Because I think Dr. Waters raised some excellent points. And we have been struggling with this because at some point, it's very easy to be a messenger of doom and gloom with some of these findings. And I always point out two things, or maybe three.

The first one is on a technical level, these-- if we look at these associations, even of the worst of experiences with DNA methylation or gene expression, they are never black and white. They are not like the epigenetic profile of a normal cell versus a cancer cell. Not even close. We're talking about maybe if you're lucky, 5% changes at particular, a few of those DNA methylation marks--

so we're not talking about wholesale changes. And related to this thing is, if we, for example, compare two groups, yes, there are differences in their mean methylation patterns. But I would [INAUDIBLE]. And we've probably run 150,000 of these assays.

And there's not a single one where I could say, OK, just based on the methylation profile, I could say whether somebody grew up in poverty or was abused as a child compared-- because it's the mean differences that is very-- they're very strong. They're statistically strong, especially if we have larger numbers. But they're not deterministic at an individual level. And I think that's really important.

It's difficult to communicate because that's not what the newspapers want to hear. They want to say, oh, wow. We see these wholesale changes. And it's all bad or good. But it's so important, I feel.

And then lastly, the related point is that epigenetics is one of many different things. You talk to somebody who studies the microbiome, they will tell you the microbiome is much more important than the epigenome. So it's important to communicate this as excited. As we are about our own research, there's more to life than epigenetics.

Thank you for following up with that. I think that it touches on several of the other questions that we have from our participants in today's session. And one of them is actually about sort of how you would advise researchers to mitigate some of the harms. And, Dr. Kobor, you just spoke to that in terms of the difference between sort of individual implications versus population studies, as well as the degree of risk that any kind of epigenetic finding might infer.

Erika, I wondered if you could speak to some of the recommendations you might have for researchers to mitigate some of the potential harms that you saw in your research that people brought up.

So we have taken a few approaches. One is to acknowledge the uncertainty in the data. We state that it is a science that is still learning a lot of things. And we differentiate between research done in animals and research done in humans, and how we don't know if research done in animals will translate to research done in humans.

We also emphasize the potential positive aspects. So in our most recent communication that we're just finishing up a video, we do talk about severe trauma potentially producing harmful epigenetic changes. But we also talk about the potential positive aspects as well and potential positive behaviors and other things that can have positive effects. So nurturing relationships and things like that.

I think those are the two major things. And then we're very, very careful to not overstate to the best of our ability.

And we have-- George [INAUDIBLE] is a-- he does epigenetics lab work in mice. And he has been speaking of interdiscipline area of research. He has been integral in making sure that we are at an appropriate level of technical accuracy and uncertainty.

Thank you. So we have just a few more minutes in the formal session, and then I just want to remind everyone who's questions that we haven't had a chance to get to or won't have a chance to get to that we will have sort of an open discussion at the hour for the half hour following. So you can pop your cameras on at that point. And please feel free to ask your question, or I can ask them for you from the chat.

But we do have a couple of different questions in the Q&A that raise the question around how we can refute some of the types of determinism that might be particularly troublesome in our social world, particularly around sort of this idea of any kind of biological determinism related to race or racism related to poverty, related to some of those environmental determinisms that you mentioned, and what are your recommendations for ways to refute those, which might be much more consistent with some of the messaging that people receive.

So this is challenging. And I want to have a caveat that we have not tested experimentally all of these strategies yet. These are strategies that we hopefully will be able to test.

One of the key aspects of our communications are to really emphasize the multidimensional nature of human health. And so we talk about-- it's just not all one thing or the other. It is an interaction. And things can change over time.

We do mention the possibility that epigenetic changes can be reversed, but we are also very careful to say that most of that research has been done in mice. And so we're not sure how to translate it. We're not certain that it translates completely to human health.

We do also say just because you have a change doesn't mean that you are destined to have a bad outcome. And I think that is a really important part. And that is also something that we use in just garden variety genetic communication as well. Unless we're talking about Huntington's or something like that, it's different.

Yeah. And just to add, I think what Dr. Waters said is extremely insightful. It is challenging. It's really difficult to sometimes communicate in a nuanced way that avoids stereotypes.

So if you-- probably the worst experience, if I may be open here in my career, has been-- we have been doing a lot of work, as I pointed out very briefly, on fetal alcohol spectrum disorder. And I did a lot of media training on how to communicate this in a respectful way and what it could mean that it is really about helping the children to potentially understand the biology that enables them to further earlier detection so that therapies and things could go on earlier. The reality of it is that at least in Canada, it is very, very biased towards our Indigenous populations. And so I was very careful to communicate this.

And even in the papers, we were very careful. The problem is that then you get the newspapers and the news who try to sensationalize it. And then the worst thing I ever did was looking at the comments of-- and this is in the sort of-- not on a sort of tabloid paper in a very respected-- the comments of the readers. And it was just--

I realized that I had gotten nowhere with what I said because it was all about stigmatizing and using this to stereotype these poor models even further. And so it was a sobering experience, really, and just taught me to be even more careful. And we're starting to see-- because, of course, just like in most other fields, a lot of the studies are done in real populations. And we need to use this also to sort of think much more carefully about race, gender, ethnicity, and so forth in the epigenetic space, which is often--

I think I might have posted. I might have shared with you a recent piece that my wonderful postdoc, Michael [INAUDIBLE], put together about how we can, from an epigenetic lens, perhaps be more careful in looking at these aspects.

Thank you. Oh, yes. Go ahead. Last comment.

Can I add to that real quick? So the postdoc on the epigenetics project on [INAUDIBLE] has a subproject looking at YouTube videos describing epigenetics. And that could be a whole talk on its own. But she is finding things that are very similar to what Dr. Kobor has been talking about these.

Many of the videos include very stigmatizing language. A lot of it centered around this notion of taking control over your own health and really not recognizing these external drivers. They are also very much peppered with advertisements for products that claim to change your epigenome or measure your epigenetic clock or something like that. So social media is a whole other beast that's also going on in the information environment at this time.

Thank you so much, Martine, Mike, and Erika, for today's rich discussion and to our audience for your informed and productive questions. If you can stick around for a bit, you can meet the speakers as we transition to the more informal after-party catch-up. Our next ELSI Journal Club will be on May 30th at 12:00 noon, where we discuss the paper "Parents' perceptions of the utility of genetic testing in the NICU," with author Katharine Press Callahan and discussant Jessica Hunter The registration link is in the chat.

On June 13, we'll have our next ELSI Friday Forum entitled "Rigor, Reproducibility and Responsibility, ELSI Questions in Population Data Practices." The link to register for that session is also in the chat.

Finally, a post-event survey will pop up once this webinar ends. I encourage all of you to complete this as our organizing committee takes your comments and suggestions seriously. It has informed us on how to improve this forum and to bring new topics and speakers to you, so please do fill that out. We will continue the discussion presently.

At this time, we invite you to turn on your cameras and raise your hands to ask questions and join the conversation. We look forward to seeing many of you. I wish you all a wonderful weekend.