Like. Well, good afternoon everyone, and thank you for joining us at a Cancer Center grand rounds. This is the annual Kingsbury Lecture ship. In honor of breast cancer, I have the profound privilege today to introduce Doctor Lisa Newman. She is a surgical oncologist and someone that I have been in for much of my career. She has a clinical and research practice dedicated to breast cancer management. Her formal title is chief of the section of Breast Surgery at New York.
Presbyterian Weill Cornell Medical Center,
and she leads a multidisciplinary breast program at the David H Koch Center,
also at New York Presbyterian.
Doctor Newman is the new and founding medical director for the International Center for the Study of Breast Cancer Subtypes.
And this was recently headquartered at Wild Cornell as part of Doctor Newman’s recruitment,
she obtained her undergraduate education at Harvard University and attended medical school completing and general surgery residency at the State University of New York.
Downtown Medical Center in Brooklyn.
She went on to pursue fellowship training and surgical oncology at the MD Anderson Cancer Center and joined the faculty there as an assistant professor before going back to Michigan. Doctor Newman has really been a trailblazer in both her research and clinical care. This is focused on ethnicity related variation of breast cancer risk and outcome and the evaluation and management of high risk patients including applications for neoadjuvant chemotherapy. She has a very robust research program and disparities in breast cancer risk and outcomes and has really
been lifted up as a national leader.

In this space, I think on a personal note, she is known as a generous and kind mentor and clinician. And she shared a story with me earlier today about her willingness to give time in the ICU during COVID to call families to update them about their loved ones. And I think this anecdote is a testament to her character. So we are very excited to hear from Doctor Newman today about oncologic, anthropology, breast cancer disparities, and triple negative breast cancer.
and African ancestry welcome.

So it’s a huge, huge honor to be talking to all of you at such an incredible esteemed academic powerhouses, the Yale Cancer Center.

And I first have to express my very deep appreciation to Eric, who, because you have such an incredible leader of your Cancer Center, somebody who is a force of nature in and of himself and has been a leader in the breast oncology world for so many reasons and across so many different types of research. But because of his deep dedication
to HealthEquity and disparity, simply because of who he is and his nature, it’s been a large part to accredit to him that. Disparities research is a field of study in and of itself. And so young minds like Rachel and Elios have been able to do wonderful, because it was made possible by Eric. I really appreciate how you’ve stood by all of us overtime and made this, this field of research possible. So I am over the next few minutes going to talk to you about my work and what my team calls oncologic anthropology.
Which is basically the intersection of research trying to understand how African ancestry in and of itself predisposes individuals to some of the high risk, biologically more aggressive cancers such as triple negative breast cancer. Now, the World Health Organization defines social determinants of health as the conditions in which people are born, grow, live, work, age, and a broader set of forces that shape daily life conditions. And nobody would dispute the fact that poverty is clearly going to be
a determinant of a poorer health,

since the unequal dispute distribution

of wealth in this country leaves

communities of color,

such as African Americans and

the Hispanic Latinx community with the higher rates of poverty,

it’s not surprising that these

issues will go hand in hand with other

metrics of socioeconomic disadvantage,

such as being uninsured and being unemployed.

And then these socioeconomic disadvantages

have a downstream effect on health.

And so communities of color,

such as African Americans and the

Latinx community also have higher
prevalence of metrics of poorer health, including being obese and poorly controlled hypertension.

And then most recently we saw how this played out in terms of the consequences of COVID severity.

However, the very unique history of individuals with African ancestry in this country has led to a very stark and quite large magnitude disparity in health outcomes for African Americans compared to white Americans. And of course, this dates back to the era of slavery,
no autonomy over their own healthcare

00:05:45.082 --> 00:05:47.739 or their healthcare of their families.

But even though slavery was abolished more than 150 years ago,

the consequence is the legacy of it stays with us.

Over several decades that followed the abolition of slavery,

discriminatory banking practices such as redlining,

permitted the banking industry.

To essentially leave many generations of African American families trapped in neighborhoods where they could not own their own businesses or their own homes.

And this led to them living over many
generations and communities featuring more impoverished school systems, which ends up leaving them with fewer professional and educational prospects. And today we see these communities. Continuing to be characterized by other features that affect health, such as food deserts. Less available healthcare resources. And the mere accumulative experiences over a lifetime of discrimination and racism is now being studied in the field of research called Allostatic Rd. where we are learning that these types of experiences not only
have an adverse impact on health, but they also seem to impact on inherent cancer burden. When you look at the specific problem of breast cancer, it’s not surprising that these socioeconomic disadvantages that are so highly prevalent in the African American community is going to have an impact on the higher breast cancer mortality rates that we see in African Americans played out because of the advanced stage distribution that we see for breast cancer related to impaired access to a breast cancer diagnosis and proper treatment.
So this very close correlation between socioeconomic disadvantage and African American identity leads many people to question whether racial ethnic identity has any biologic relevance at all, or is it purely and simply a sociopolitical construct? Well, the answer of course is that both defining components of racial identity are present and they are not mutually exclusive. How we self identify as well as how society labels us will very definitely impact on how we live.
and on how we access healthcare.

However, there are also features of racial identity that are very closely linked to our ancestral heritage and these ancestral genetic factors will also have an impact on health metrics and on cancer burden.

And we’ve actually known for many decades now that when it comes to a diagnosis of breast cancer, there are indeed other factors aside from socioeconomics that are impacting on the outcome disparities that we see.

This slide is now nearly 20 years old and comes from a study that I and some
colleagues from the Harvard School of Public Health it conducted where we simply pulled together all of the data in the published literature looking at breast cancer survival rates for black women compared to white women. After accounting for some measure of socioeconomics, and as you see here from the forest plot, the African American breast cancer patients have a statistically significant nearly 30% higher mortality hazard. And again, this is after accounting for socioeconomic status. Furthermore,
there are several features of the breast cancer burden in the African American community that can’t easily be ascribed to socioeconomics. For example, depending on which study you read, up to 40% of African American breast cancer patients are diagnosed younger than the age of 50, compared to only about 1/5 of white American breast cancer patients being diagnosed in this premenopausal age range. As we will be discussing in this presentation.
We also have a higher risk of the biologically aggressive patterns of breast tumors, the high grade tumors, the hormone receptor negative and the triple negative tumors. We have a higher population based incidence of a primary inflammatory breast cancer and there’s also the very poorly understood higher population based incidence of male breast cancer in the African Community. And so we definitely, definitely need to be exploring tumor biology and genetics.
If we're going to try to comprehensively understand disparities and breast cancer outcome. Now, you might assume that looking at clinical trials data would be the near perfect way of disentangling racial, ethnic, identity and socioeconomics from cancer outcomes. And this was the background, the motivation for a really important study that was conducted several years ago by Kathy Albain and colleagues looking at data and from the Southwest Oncology group.
And in this study, they pulled together the outcomes for a whole variety of adjuvant therapy trials. For different types of cancers and they wanted to see if equal outcomes were achieved in the context of delivering equal care through participation in a clinical trial. Now happily, they did show that for the cancers they looked at, outcomes did equalize given equal treatments regardless of racial, ethnic identity, except when it came to specific cancers.
And for the hormonally driven cancers such as breast cancer and prostate cancer, the African-American clinical trial. Participants continue to have statistically significant worse outcomes. So many of us that have dedicated our careers to disparities research, we’re really excited about Kathy study because we felt that it was going to usher in a whole new generation of young people interested in studying tumor biology and genetics and looking at cancer outcomes. We were there for a little dismayed at thefactthattime.com reviewed her study and called it an example of
NOTE Confidence: 0.86922849375
00:11:56.880 --> 00:11:58.830 racial profiling in medical research.
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00:11:58.830 --> 00:12:01.179 So this we were happy that her study was
NOTE Confidence: 0.86922849375
00:12:01.179 --> 00:12:03.202 getting a lot of publicity, of course.
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00:12:03.202 --> 00:12:05.554 But this title was a little dismaying,
NOTE Confidence: 0.86922849375
00:12:05.560 --> 00:12:07.468 because of course, racial profiling has
NOTE Confidence: 0.86922849375
00:12:07.468 --> 00:12:10.129 a lot of very negative connotations,
NOTE Confidence: 0.86922849375
00:12:10.130 --> 00:12:11.246 and appropriately so.
NOTE Confidence: 0.86922849375
00:12:11.246 --> 00:12:13.850 When it comes to racial profiling and,
NOTE Confidence: 0.86922849375
00:12:13.850 --> 00:12:16.250 for example, the criminal justice system,
NOTE Confidence: 0.86922849375
00:12:16.250 --> 00:12:19.547 but when it comes to cancer biology
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00:12:19.547 --> 00:12:21.820 and studying cancer outcomes,
NOTE Confidence: 0.86922849375
00:12:21.820 --> 00:12:23.330 racial profiling, if you will,
NOTE Confidence: 0.86922849375
00:12:23.330 --> 00:12:25.850 is really just an example of epidemiology.
NOTE Confidence: 0.86922849375
00:12:25.850 --> 00:12:27.734 And we absolutely have an obligation
NOTE Confidence: 0.86922849375
00:12:27.734 --> 00:12:29.864 to study all of the characteristics
NOTE Confidence: 0.86922849375
00:12:29.864 --> 00:12:32.699 of our patients when we’re trying to
understand why some cancer patients have
a better or worse outcome than others.
And this does include characterizing the
racial ethnic identity of our patients.
An example of how important this
racial characterization of our
cancer patients is is shown on the
graphic to the left on this slide,
where we’re looking at the most
basic of epidemiologic statistics,
population based incidence rates of
breast cancer and population based
mortality rates from breast cancer
over the last several decades.
As documented by the surveillance,
epidemiology and end results program.
And what we see here is that over time, incidence rates of breast cancer historically have been lower for black women compared to white women. But the rates typically changed in parallel, indicating comparable effects of different environmental factors. But for mortality rates, shown by the two curves at the bottom of this slide, the mortality rates from breast cancer were equal for black women and white women until we reach the early nine, eight, 1980s and at that point.
Mortality curves separate predominantly because of declining death rates and white women, but largely unchanging rates in black women, and this is probably because the advent of tamoxifen as our first endocrine targeted therapy for breast cancer. The effects of tamoxifen become apparent by the early 1980s, but as shown by the bar graph to the right of this slide, since African American women have significantly lower frequencies. Of the estrogen receptor positive cancers and higher rates of estrogen receptor negative tumors.
We are just not benefiting from the advantages of terrific systemic therapies such as tamoxifen to the same degree as our sisters from other racial ethnic backgrounds. So basically by the early 1980s are seeing the unmasking of differences in tumor biology between African American and white American breast cancer patients. So now of course we’ve gone far beyond simply characterizing breast cancer as the dichotomous hormone receptor positive versus hormone receptor negative tumors. And we know that breast cancer isn’t
comprised of an entire spectrum of intrinsic tumor subtypes with the basal subtype being one of the more virulent subtypes. The patients that we see everyday in clinic are not necessarily going to get complete genomic profiling done on their tumors. So we use immunohistochemistry to look at estrogen receptor, progesterone receptor and hormone and her two new expression as a convenient way to have a surrogate for identifying. The most aggressive of these tumors? And the triple negative breast cancers do tend to correlate with
identifying a patient that has an intrinsic basal type tumor. It’s not a perfect correlation, but it is pretty close. And as shown by the curves on the top right of this slide, women that have the triple negative breast cancers at every stage of breast cancer diagnosis have worse outcomes compared to the women who have the non triple negative breast cancers. And we now know from many studies that African American women have higher frequencies of triple negative breast cancers regardless of
the age at which they’re diagnosed.

And we have higher frequencies of triple negative breast cancer regardless of the stage that the breast cancer is diagnosed.

Now there’s been an interesting phenomenon over the past couple of decades where the population based incidence rates of breast cancer have been rising disproportionately in African American women.

And now over the last ten years or so, breast cancer incidence rates are pretty much equal for black women and white women.

But those rising incidence rates of breast cancer in black women,

coupled with our higher incidence of
the triple negative breast cancer has resulted in a widening of the mortality gap. And today we see about 40% higher breast cancer mortality rates in the African American community compared to the White American community. And it’s impossible to have a discussion about triple negative breast cancer and disparities without making some comment regarding mammography screening recommendations. And as I’m sure all of you are aware, the United States Preventive Services Task Force has been advocating pretty aggressively for average risk American
women to delay initiation of screening mammography until they reach age 50. Many of us that are dedicating our careers to studying breast cancer disparities are really concerned about this. Broad recommendation, because waiting until age 50 for mammography screening can result in an even worsening of the delays in diagnosing biologically aggressive tumors, such as triple negative breast cancers, in African American women, who are already at higher risk for getting these aggressive tumors at younger ages. And so this screening recommendation will likely worsen the
disparities that already exist.

Now, the critics of screening mammography are always quick to point out that mammography is not going to be the be all, end all answer to addressing disparities because it is true that triple negative breast cancers are more challenging to detect on screening mammography and they're more likely to present it as the palpable interval cancers and women that are getting their screening mammograms every year. However,
we do have very strong data showing that early detection of triple negative breast cancer does still make a difference. And an example of those data are shown in the two tables on this slide where investigators from Memorial Sloan Kettering and from the National Comprehensive Cancer Network have both demonstrated that triple negative breast cancers detected at a small size no larger than one centimeter in size, and with nodes negative are by and large going to be screen detected triple negative breast cancers. These tumors have very good outcomes.
regardless of whether the patients receive adjuvant chemotherapy or not. Now those two studies that I showed on the previous slide, we’re looking at early detection of triple negative breast cancer, but they weren’t necessarily looking at mammography, screen detected triple negative breast cancer. And so to address the question of how effective screening mammography is and outcomes in improving outcomes from triple negative breast cancer. Our group pulled together the data.
on triple negative breast cancer

patients from the Metropolitan Detroit area and the Henry Ford Healthcare system and the while Cornell New York Presbyterian Hospital network triple negative breast cancer patients.

And we looked specifically at outcomes from for these patients if with triple negative tumors based upon whether it was screened detected disease or not. And we looked at a whole bunch of different factors that might also impact on outcomes from triple negative breast cancer. For both the white and the African American triple negative breast cancer,
having a mammography screen detected tumor was the strongest predictor of a patient that was going to have a good outcome. So we do indeed have data that mammography screening is effective at early detection of triple negative breast cancer and it does yield some benefits in terms of improving outcomes and that benefit was actually strongest for the African American women. We’ve also been looking at whether or not there might be some precursor lesions in benign breast tissue, identifying women that are at higher.
risk for getting a triple negative breast cancer and whether or not the benign breast patients who require biopsies will still have a higher rate of triple negative breast cancer. Correlating with racial ethnic identity. As all of you are aware, the number of benign breast biopsies that a patient has does correlate with a higher risk of a future breast cancer. Probably because it’s identifying hyperproliferative changes in the breast and This is why number of biopsies and so integrated into many of our risk prediction tools such as the Gale model.
But by and large, multiple biopsies is a predictor of having an estrogen receptor positive breast cancer.

So we utilize the Henry Ford Health system benign breast disease cohort to look at whether fibrocystic breast biopsies predicted for higher rates of triple negative versus hormone receptor positive.

Disease in our black compared to white patients and we had a very large cohort of more than 6000 women who had had benign breast biopsies with robust follow-up of more than 10 years and in evidence that...
these women were receiving equitable treatment over the years.

We actually saw comparable rates of subsequent breast cancers in these women with fibrocystic changes regardless of whether they were black or white. And we saw comparable stage distribution for the cancers that did develop in these patients. However, as shown by this curve, the African American women with benign breast biopsies had about a four-fold higher risk of getting a triple negative breast cancer.
00:21:46.394 --> 00:21:48.626 compared to the white American breast

00:21:48.626 --> 00:21:50.052 fibrocystic change at patients.

00:21:50.052 --> 00:21:51.416 And so there does,

00:21:51.420 --> 00:21:54.236 at least from our experience seem to be

00:21:54.236 --> 00:21:55.841 something inherently different about

00:21:55.841 --> 00:21:58.343 the mammary tissue of African American

00:21:58.343 --> 00:22:00.754 women increasing the susceptibility for

00:22:00.754 --> 00:22:02.770 these biologically aggressive tumors.

00:22:04.554 --> 00:22:07.230 ask is whether or not outcome

00:22:07.307 --> 00:22:09.907 disparities will persist after you

00:22:09.907 --> 00:22:11.987 stratify for tumor phenotype.

00:22:11.990 --> 00:22:13.579 And I’m not going to belabor the

00:22:13.579 --> 00:22:15.130 data on this very busy slide,

00:22:15.130 --> 00:22:17.230 but suffice it to say there are

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actually a number of studies suggesting that when you adjust for stage and treatment that the outcomes from triple negative breast cancer patients might actually be fairly comparable for black women and white women. However, there are numerous studies showing that for hormone receptor positive breast cancer, the disparities persist. Now, whether or not these disparities and outcome in hormone receptor positive disease are related to differences in tumor biology or difference in
response to endocrine treatment or just variation in compliance with the several years that we recommend for endocrine therapies, these are all questions that are continue to be under study. But now we are starting to generate some answers to those questions because a brilliant researchers who’ve been conducting terrific studies about gene expression profiling in women with hormone receptor positive, her two negative breast cancers are now starting to look at their data based upon stratification for race ethnicity.
The TELERX investigators have recently shown that for women undergoing Oncotype 21 gene recurrence score testing for hormone receptor positive, her two negative and no negative breast cancers that in women with the intermediate scores, the African American women have notably higher rates of recurrence and mortality even after adjusting for these intermediate range scores.

And then very recently the investigators for the responder trial reported and the San Antonio Breast Cancer Symposium that among women looking at these 21 gene recurrence scores.
and whether or not they predict for benefit from chemotherapy in the setting of women with no positive disease. They similarly showed that the outcomes for the African American patients were significantly worse compared to the outcomes for the White American patients. And again this is after stratifying. Many investigators have been looking at data from the Cancer Genome Atlas to try to get a deeper dive, basically into looking at tumor biology between black women and
white women with breast cancer.

And I'm summarizing just a few of the studies that have been published utilizing TCG a data on this table. But all of these studies are basically looking at the same group of, more than 700 white American breast cancer patients. And about 170 African American patients that have contributed tumor tissue and clinical information. So it's not surprising that all of these investigators have identified similar patterns. Pam 50 subtyping definitively showing that the African American women
not only have higher frequencies of the triple negative immunohistochemically defined phenotype, but we also have higher rates of the intrinsic basal subtype. The African American patients are more likely to have TP 53 mutations and fewer Pi K3CA mutations, which goes along with the higher frequency of triple negative and lower frequency of hormone receptor positive tumors in these patients. And the phenomenon of seeing higher rates of these biologically aggressive estrogen receptor negative and triple
negative breast cancers in women with African ancestry is actually not something that’s unique to the United States and other countries. The UK, Switzerland, Brazil investigators from these countries have also published data showing that their African ancestry breast cancer patients are more likely to have estrogen receptor negative and triple negative breast cancers compared to their non African ancestry breast cancer patients. So this is why our group has been very excited about looking at international data and in particular
looking at the breast cancer burden on the continent of Africa, to try to tease out the answer to the question of whether or not African ancestry in and of itself is associated with some heritable marker predisposing to risk for triple negative breast cancers. And this I think opens the door not only to exciting ways to understand disparities, but also a very novel ways of trying to understand the Pathogenesis for triple negative breast tumors. So this is just a snapshot of some of our most basic findings.
Looking at the frequency of triple negative breast cancer in women from Ghana representing Western sub-Saharan Africa compared to the triple net, the frequency of triple negative breast cancers in women from Addis Ababa, Ethiopia, representing East Africa. And we see quite high frequencies of triple negative breast cancers in the economy and women, about half of them are triple negative, but the frequency of triple negative breast cancers. And the Ethiopian women is very low at about 15%, similar to what we see in White American.
and European patients with breast cancer.

The frequency of triple negative breast tumors is intermediate for African American women between the rates that we see in Guinea and women and what we see in white American women. Now the American Cancer Society brilliant investigator, Ahmedin Jamal has published data looking at the frequency of ER negative breast tumors, which of course are a subset of the

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triple negative breast tumors in white American breast cancer patients, African American breast cancer patients and women born in West Africa but whose cancers were diagnosed in the United States, and women born in East Africa but whose breast cancers were diagnosed in the United States. And similar to our international data, Amadeen found that we see the highest frequencies of the ER negative tumors in the African American and West African born patients and the lowest frequencies of ER negative tumors in the White American and
East African born patients.

So this is where we’ve coined the nomenclature of oncologic anthropology to try to explain these patterns. And of course, as we all recall from grade school social studies, the transatlantic slave trade brought the ancestors of contemporary western sub-saharan Africans across the ocean to serve as slaves in the colonies. And so today, we have quite a bit of shared genetic ancestry with the contemporary Guineans.
Representing Western sub-Saharan Africans.

But the slave trade from East Africa largely brought the ancestors of contemporary East Africans and Ethiopians further eastward to the Middle East and to Asia.

And so as African Americans, we don’t have quite so much shared ancestry with Ethiopia.

Related to Western sub-Saharan African genetic ancestry.
So one of our terrific and brilliant research partners for my research team, the International Center for the Study of Breast Cancer Subtypes is Doctor John Carton, who runs the Translational Cancer Research program out at USC. And we’ve been really trying to work quite hard to get more of our colleagues in the oncology research world to look at the genetics of race and ethnicity and to quantify germline ancestral genetics with the cancer outcomes. As a way of trying to understand disparities better.
I was absolutely thrilled to be able to recruit one of John’s mentees, Melissa Davis, who is a card carrying PhD geneticist to serve as the scientific director for our International Center for the Study of Breast Cancer subtypes. And our international team for the last nearly 20 years now has been building up this biobank biorepository of tumor specimens for somatic tumor tissue studies. And saliva specimens as well as blood specimens suitable for germline genetic studies from different parts of Africa. And so it was really exciting to get Melissa to serve as our basic science research leader.
So that she could use her tools to tease out some of these differences and understanding the genetics of African ancestry. And for most of Melissa’s career, she’s been a world leading expert in studying a particular gene called the Duffy gene or the Duffy antigen receptor for chemokines. And there’s a particular variant of the Duffy gene that is seen almost exclusively in individuals that have Western sub-saharan African ancestry. It’s widely called the Duffy Gene variant.
And therefore this Duffy null variant is an ancestry informative marker informative of African ancestry. Now, Melissa’s been studying Duffy null for most of her career. Other investigators have kind of happened a Long Duffy Knoll in the context of other studies looking at disparities. And this slide is summarizing the data from a study that came out of the Amber Consortium, a collaborative group of investigators looking at breast cancer disparities related to race. And in this particular publication,
the Amber Consortium investigators were looking at levels of different circulating chemokines that might be associated with cancer and in particular breast cancer risk. They wanted to see if the levels of these different keeps US cytokines were different between black women and white women who had not yet been diagnosed with breast cancer. And then when they did genetic analysis, they found that these differences were explained by the presence...
of the Duffy null genotype.

We’ve also learned overtime that the Duffy Null variant is the variant that’s responsible for a phenomenon called benign ethnic neutropenia, which is the fact that African Americans tend to have a lower circulating white blood cell count. Which doesn’t have any biologic significance, but it is a numeric pattern that seemed pretty consistently. And some investigators are now looking at whether or not Duffy null may be implicated in transplant rejection disparities.
at it in breast cancer, others are looking at it in prostate cancer disparities. Unfortunately, however, when you look at the literature globally, there is a huge gap in terms of what we know about how African ancestral genetics impact on cancer risk because so few of the genomic studies have included significant numbers of individuals with African ancestry. And as shown by this study from cell, only about 2% of individuals contributing to genome wide association.
studies have had African ancestry.

So we were really excited to have Melissa work her magic with her genetics skills to apply them to our international biorepository, which again has been amassing specimens for nearly 20 years.

So I'm Melissa did a really cool study where she looked at Duffy Null compared to a series of other genetic variants that have been potentially linked to risk of breast cancer and hormone receptor negative, triple negative breast cancer.

And in working with this other brilliant researcher,
NOTE Confidence: 0.912492391333333
00:34:16.970 --> 00:34:18.194 our geneticist,
NOTE Confidence: 0.912492391333333
00:34:18.194 --> 00:34:20.642 biostatistician yallah chin from
NOTE Confidence: 0.912492391333333
00:34:20.642 --> 00:34:23.790 the Henry Ford Health system,
NOTE Confidence: 0.912492391333333
00:34:23.790 --> 00:34:26.142 Yalley was able to show that the
NOTE Confidence: 0.912492391333333
00:34:26.142 --> 00:34:28.287 presence of this Duffy Null variant
NOTE Confidence: 0.912492391333333
00:34:28.287 --> 00:34:30.779 was by far and away the strongest
NOTE Confidence: 0.912492391333333
00:34:30.855 --> 00:34:33.150 determinant of having a triple
NOTE Confidence: 0.912492391333333
00:34:33.150 --> 00:34:35.445 negative breast cancer versus having
NOTE Confidence: 0.912492391333333
00:34:35.450 --> 00:34:39.290 a non triple negative breast cancer.
NOTE Confidence: 0.912492391333333
00:34:39.290 --> 00:34:41.814 The phenomenal anthropologist Dr.
NOTE Confidence: 0.912492391333333
00:34:41.814 --> 00:34:46.370 Sarah Tishkoff has shown us very nicely,
NOTE Confidence: 0.912492391333333
00:34:46.370 --> 00:34:48.810 as demonstrated by this graphic,
NOTE Confidence: 0.912492391333333
00:34:48.810 --> 00:34:51.594 that many of the ancestry informative
NOTE Confidence: 0.912492391333333
00:34:51.594 --> 00:34:55.156 markers that we look at aren’t markers
NOTE Confidence: 0.912492391333333
00:34:55.156 --> 00:34:58.408 variants that developed randomly over time.
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Many of them actually represent evolutionary selection pressure over our ancestors to allow our ancestors to survive.

Different threats to longevity, related to infectious diseases, related to climate, related to food sources.

And then today, when we look at the descendants of those populations, you can continue to see many of these ancestry informative markers, regardless of where the descendants reside over the globe.

The Duffy Null variant is just one more
example of such a variant that was acquired over the millennia as a consequence of evolutionary selection pressure. The Duffy Variant is something that became apparent that was adopted in Western sub-Saharan Africa many thousands of years ago, linked to the need to have some resistance to malaria, and malaria became endemic in Western sub-Saharan Africa because of the tropical nature of that. With the geography there with the many watery areas and low altitude areas supporting the lifecycle of the mosquito,
which of course is the host for the malaria parasites. And there are other examples of variants that were acquired to confer some resistance to malaria that thalassemia is seen in European Mediterranean populations. Sickle cell, the Duffy Null variant, doesn’t have quite as many of the adults health consequences as those variants do, and therefore the Duffy null variant is seen in nearly 100% of the descendants of Western sub-saharan Africans. Something occurred about 5-6 thousand years ago called the Band 2 expansion, years ago called the Band 2 expansion, of Western sub-saharan Africans.
migrated across the continent
to populate the various areas of East Africa and South Africa.
And while many of those areas have more mountainous areas that do not support the mosquito life cycle, so they have a different history of endemic malaria in those parts of the continent but with the Bantu expansion. The Duffy Null variant did track across the continent of Africa and you see varying degrees of admixture and the presence of this stuffy null variant in those reasons of Africa. Just as with the transatlantic slave trade,
the Duffy Null variant came across to the Americas and with the genetic admixture that we see in African Americans, this results in about 2/3 to 3/4 of African Americans expressing that Duffy variant and if you overlay a map of the frequency of triple negative. Breast cancer in different parts of the world with a map of the Duffy Null variant, there’s actually a pretty close correlation, so we’ve been exploring. Ways to understand how to connect the dots between the stuff we know variant and the risk of having a triple negative breast cancer.
The reason why that Duffy Null variant confers some resistance to malaria is because if you possess the Duffy null variant, you do not express the Duffy protein on your red blood cell. And the Duffy protein on the red blood cell is kind of the entry portal for the malaria parasites to get into the red blood cell and cause the disease. So now what we are learning and the work that’s ongoing and Melissa let slip is seeking to better understand how this Duffy protein and lack of the Duffy protein on the red
blood cell impacts on circulating chemokines, which would explain the findings of the Amber Consortium that I showed you previously. And how this may have a downstream in fact when the mammary tissue microenvironment and the inflammatory the immune landscape of the Mary mammary tissue. Which can then have an impact on the types of breast tumors that develop.

Melissa has also been doing work with the Cancer Genome Atlas looking at tumor tissue expression presence of the Duffy protein and you see as you would predict lower levels of.
Duffy protein in the breast tumors of African American compared to white women contributing specimens to TCG A. And the lower presence of a Duffy tends to correlate with worse prognosis across the different phenotypes. So this phenotype agnostic. If you will affect on tumor tissue tumor outcome may be what’s explaining what we see in looking at the the impact of race ethnicity on outcomes in women with that have ER positive disease as we saw from the tailor X and the responder trial. Many people are doing very,
very exciting work seeking to subtype
the triple negative breast cancers,
and a lot of this work was pioneered by the Vanderbilt Group identifying about 6 different intrinsic triple negative subtypes initially. However, the publicly available datasets that contribute to the definition of those different triple negative subtypes largely came from communities that had very few, if any. African ancestry individuals. So we really don’t know if those triple negative breast tumor subtypes are applicable to the African ancestry populations that have a
higher inherent risk of developing these triple negative subtypes. In working with Clayton Yates, who used to be at Tuskegee and now he’s recently relocated to Johns Hopkins, Clayton has also been utilizing data from our international buyer repository and has identified the fact that the triple negative breast tumors of African American women does seem to have different signatures compared to what we see in white American women. We’re also utilizing data from TCG a Melissa’s been looking at the impact of tumor infiltrating tumor associated
lymphocytes on breast cancer outcomes. And we typically think of these tumor infiltrating lymphocytes as a favorable prognostic feature. But in this is these are unpublished data and these preliminary data from TCG a, the relationship seems to be flipped for African American women with the higher frequency. Of tumor associated lymphocytes seems to be an adverse prognostic feature. Data correlating with these findings from TCG A have been published, again by members of the Amber Consortium. This comes from a study published by Christine Andersoni and her group where
they looked at the tumor microenvironment signature of breast cancers from African American and white American women. And while they did show that African American women tended to have a more robust tumor infiltrating lymphocyte. Content to their tumors, the lymphocytes of the African American women were more likely to have this T cell exhaustion signature, as they called it. And so their function was different compared to what we see in the white American women with breast cancer.
And this was an intriguing study that was published in Cell just a few years ago where some investigators were looking at immune cells that were basically primed with specific pathogens, looking at the immune activity of these immune cells from patients that were African American compared to white American. And they saw very distinct and different responses in terms of the immune activity of these immune cells. When they're linked to different pathogens. So you can only imagine that if the individuals are responding differently.
to infectious diseases compared to the immune cells of white individuals, there could easily be differences in the way these immune cells function in terms of cancer biology.

So Melissa has been continuing to utilize our international data set in conducting other studies looking at the triple negative breast cancer risk alleles and I’m going to go through these next few slides quickly.

In the interest of time, we’ve also been working with investigators from the University of Michigan been creating PDX models.
based upon our International Studies.

And then very recently a couple of months ago,

we were really excited about our work with triple negative breast cancer subtyping.

Which was the cover article for cancer discovery a couple of months ago.

So to us that was like being on the cover of our vogue magazines.

We were very, very thrilled about this and we were able to show that looking at genetic ancestry does have independent meaning compared to self reported ancestry.

And there were several 100 genes linked to genetic African ancestry.
00:44:13.679 --> 00:44:16.487 that you don’t see if you look only at
self reported racial ethnic identity.

00:44:26.090 --> 00:44:28.386 And this is another slide that came
from that particular publication

00:44:28.386 --> 00:44:29.899 where we’re just demonstrating the
genetic admixture of populations

00:44:29.899 --> 00:44:32.214 specifically looking at Ghanian patients,
African American patients,
Ethiopian patients and European ancestry white American patients.

00:44:34.132 --> 00:44:36.010 in different parts of the world,

00:44:36.010 --> 00:44:38.350 And it’s an example of how much more
you can learn about genetics of
disease by drilling down into the.

00:44:38.350 --> 00:44:39.973 Genetic ancestry.
And African Americans have tremendous, tremendous genetic admixture compared to either Africans or European ancestry people. Individuals and you can’t rely upon self reported ancestry. There are three individuals in the European ancestry group. These are individuals who self reported as being white, but they have between 30 and 80% African genetic ancestry. So you definitely misinformation if you rely. Exclusively upon self reported racial ethnic identity and there are other examples of how genetic ancestry
00:45:31.492 --> 00:45:33.970 might be correlated with health.
00:45:33.970 --> 00:45:36.328 April lipoprotein One is an African ancestry variant that has been linked to severity of kidney disease and we all know that end stage renal disease is more prevalent in the African American community.
00:45:36.328 --> 00:45:38.300 This particular variant is actually a variant that was acquired to develop resistance to the African sleeping sickness disease.
00:45:38.300 --> 00:45:40.310 and we all know that end stage renal disease is more prevalent.
00:45:40.310 --> 00:45:42.772 Also, our wonderful colleague out in California, Lauder Fairman has been doing similar work looking at.
00:45:42.772 --> 00:45:44.512 renal disease is more prevalent in the African American community.
00:45:44.512 --> 00:45:46.920 in the African American community.
00:45:46.920 --> 00:45:49.495 This particular variant is actually a variant that was acquired to develop resistance to the African sleeping sickness disease.
00:45:49.495 --> 00:45:52.396 Also, our wonderful colleague out in California, Lauder Fairman has been doing similar work looking at.
Latin X individuals and Lauda has demonstrated that extent of genetic Native American ancestry reduces the risk of getting breast cancer. On the other hand, higher extent of European ancestry is associated with a higher risk of getting breast cancer. Other investigators have been trying to figure out the germline genetic ancestral causes of the BRC a founder mutations and have been potentially linking some of those founding mutations to fertility over the millennia. So we’ve of course been very,
very excited about our international group with respect to these different research avenues. But it’s also been an incredibly rewarding experience from the perspective of being able to invest in the cancer care resources of the facilities for our partners work. And our mission statement is to reduce the global breast cancer burden through advances in research and delivery of care to diverse populations worldwide. A few examples of how we’ve been making those investments are shown here.
We’ve been able to establish immunohistochemistry training programs so that our colleagues can perform their own immunohistochemistry on site and actually characterize the cancers of the patients that they’re treating. We’ve established core needle biopsy training program so that they can make their diagnosis more efficiently and accelerated through the COVID experience is that we’ve been able to stay in very close contact utilizing zoom meetings and telemedicine tumor board discussions. And now that our program is headquartered at Wild Cornell in New York,
we are able to align our International Studies with the robustly diverse population of New York and we have our New York based breast cancer campuses in Manhattan, Brooklyn and Queens, which has tremendous diversity in those communities. And a lot of our work today is being done in conjunction with the Englander Institute of Precision Medicine. Whenever I talk about breast cancer disparities, I always include these survival rates of 60%, 40% and 20%, which have absolutely
nothing to do with cancer outcomes.

But these are the survival rates for the first class, second class and 3rd class cabin passengers of the Titanic.

And even though my own career in breast Cancer Research and studying disparities has been heavily rooted in trying to understand.

Human biology linked to African ancestry.

We always have to end just the way we began this discussion with an expression of the fact that outcome and the ability to survive any threat is going to be related to access to care.

And just as the third place cabin
passengers of the Titanic did not have equitable access to the lifeboats.

it unfortunately and tragically remains true that communities of color, including African Americans, do not have. Equal access to cancer care, screening, research opportunities.

And as stated by Doctor Martin Luther King Junior, of all the forms of inequality, injustice and health is the most shocking and inhumane. We saw this injustice in the COVID experience.

And as you guys know, it’s been projected that as a
00:49:21.570 --> 00:49:23.903 consequence of the COVID shutdown and
NOTE Confidence: 0.888823984736842
00:49:23.903 --> 00:49:26.429 its downstream impact on Cancer Research
NOTE Confidence: 0.888823984736842
00:49:26.429 --> 00:49:28.918 and cancer screening and treatment,
NOTE Confidence: 0.888823984736842
00:49:28.920 --> 00:49:30.990 we’re probably going to see an
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00:49:30.990 --> 00:49:33.158 excess of about 10,000 deaths from
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00:49:33.158 --> 00:49:35.306 colorectal and breast cancer in the
NOTE Confidence: 0.888823984736842
00:49:35.306 --> 00:49:38.500 next 10 years because of the COVID
NOTE Confidence: 0.888823984736842
00:49:38.500 --> 00:49:40.060 recession was disproportionately
NOTE Confidence: 0.888823984736842
00:49:40.060 --> 00:49:42.319 severe in communities of color.
NOTE Confidence: 0.888823984736842
00:49:42.320 --> 00:49:45.218 We really do have to be proactive.
NOTE Confidence: 0.888823984736842
00:49:45.220 --> 00:49:48.034 In making sure that we protect
NOTE Confidence: 0.888823984736842
00:49:48.034 --> 00:49:49.441 our disadvantaged communities
NOTE Confidence: 0.888823984736842
00:49:49.441 --> 00:49:52.238 from experiencing these excess
NOTE Confidence: 0.888823984736842
00:49:52.238 --> 00:49:53.740 deaths disproportionately,
NOTE Confidence: 0.888823984736842
00:49:53.740 --> 00:49:55.116 we want to get rid of all of
NOTE Confidence: 0.888823984736842
00:49:55.116 --> 00:49:56.694 these excess deaths, of course.
But unless we support our safety net hospitals, which were disproportionately financially devastated by the costs of COVID care, unless we protect our advocacy and philanthropy groups that provide a lot of our free screening programs, and unless we really work with our hospital leadership. To make sure that they don’t cut navigation programs, outreach programs, when they’re trying to balance their budgets in the wake of the COVID experience,
we’re going to have an exacerbation of these types of mortality gaps. But I am an optimist and I do know that by working together we are going to be able to eliminate these disparities. And I look forward to strengthening all of the other partnerships that are already ongoing and bringing researchers from different areas together to try to conquer these problems from all different angles. And in closing, I just want to thank all of the wonderful teams that have supported our research over the years.
And in closing, I do also want to acknowledge this phenomenal woman, my sister Deborah Newman, who passed away almost a year ago today from an incredibly aggressive and virulent inflammatory form of triple negative breast cancer, a Princeton graduate, former US prosecutor. She’s a perfect example of how socioeconomics are not the exclusive explanation for breast cancer disparities. And so it’s an in her memory that I
and my research team continue the work that we’ve been doing so.

I do thank all of you for your time and attention and for inviting me to deliver this presentation.

Thank you so much Doctor Newman for sharing your extraordinary research with our group.

I’d be happy to start with any questions from the audience before we turn to the zoom chat.

One point. Really.

Was how the self reporting of race definitely does not usually capture release what the person is and
that really has me thinking about populations might be able to look at these sort of studies that we are segregating typically but people said decreased sequencing cost and ease of access to that sort of data. Do you and your group’s plan on looking at those populations and identifying specific genetic factors. And if you’re not ready, you seen whether a specific rates have dominance.

Thanks so much for the kind comment and I totally agree with your points that we definitely have an obligation to
look more closely at genetic admixture.

And you're right, self reported race. I mean it’s really primitive.

And as cancer researchers we’ve been so late to bring the technology of quantification of ancestry into our work, but the general population has been doing this for years.

I mean millions of people are purchasing these products or they’ve spent in a cup. And get back their pie diagram of where their ancestors are come from. So I mean I think that this type of work should be routine in our studies because we do have the technology and it’s so much more precise and meaningful.
I agree with you in trying to understand cancer outcomes. Now we do need to look at self-reported race as well because a self-reported identity does have very important relationships to HealthEquity and services that are available to some communities and not available to other communities, but we can’t overlook the genetics components. So that.

Doctor Weiner.
00:54:23.090 --> 00:54:25.859 talk and sorry about your sister
NOTE Confidence: 0.94081753
00:54:25.859 --> 00:54:28.359 and thanks for sharing that.
NOTE Confidence: 0.94081753
00:54:28.360 --> 00:54:30.950 I want to go down a little
NOTE Confidence: 0.94081753
00:54:30.950 --> 00:54:32.970 bit on ERP project.
NOTE Confidence: 0.94081753
00:54:32.970 --> 00:54:36.879 And of course adherence to therapy,
NOTE Confidence: 0.94081753
00:54:36.879 --> 00:54:40.274 Fabian issue, not only adherence
NOTE Confidence: 0.94081753
00:54:40.274 --> 00:54:42.990 but doctors prescribing entering
NOTE Confidence: 0.94081753
00:54:43.086 --> 00:54:45.522 therapy which isn’t really adherence
NOTE Confidence: 0.94081753
00:54:45.522 --> 00:54:47.944 which you think of as a patient
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00:54:47.944 --> 00:55:00.385 issue but maybe a doctor issue.
NOTE Confidence: 0.94081753
00:54:50.990 --> 00:54:54.457 But the the other question with the
NOTE Confidence: 0.94081753
00:54:54.457 --> 00:54:57.460 question I have is to what extent
NOTE Confidence: 0.94081753
00:54:57.553 --> 00:55:00.385 do we know whether simple things
NOTE Confidence: 0.94081753
00:55:00.385 --> 00:55:03.370 like ER expression vary across race?
NOTE Confidence: 0.94081753
00:55:03.370 --> 00:55:05.798 Or whether monumental air
NOTE Confidence: 0.94081753
00:55:05.798 --> 00:55:08.226 versus B percentages bearing.
Yeah, it’s well terrific questions. Now from our biorepository, we definitely see higher frequencies of those weekly positive ER tumors 1 to 9% in the African ancestry patients compared to the white patients. I can’t say that I’ve seen that broadly in publications however, because we usually just talk about your positive or negative using the ASCO CAP guidelines, but in our Database, we do see that. So I do think that it’s a spectrum that’s present. I think you’re probably right that
there are variations in how endocrine therapies are prescribed and how much attention we pay as healthcare providers to adherence to treatment based upon what our patients look like. I think those are very real issues. I am so excited that people like you, the leaders in the clinical trials are paying attention to this. In looking at these, these gene expression profiles, they’re going to be incredibly powerful in studies to come. Presentation of the body of work that features beautifully. Molecular epidemiology,
clinical functions and what you've highlighted cultural. I think you have devoted a lot of time. If I take the same discussion interest cancer in TCG, I'll tell you there are five patients of African argument. And and that’s the disconnect that I’m always struck with, that I’m always struck with, you know so much that threat that biologic androgenicity matters and clinicians have always been able to people like we’ve been able to answer fundamental questions. Yet my worry is in our passion to and
00:57:03.662 --> 00:57:05.976 you track the time article right?
NOTE Confidence: 0.67296178
00:57:05.980 --> 00:57:07.738 And I’ve seen the same thing,
NOTE Confidence: 0.67296178
00:57:07.740 --> 00:57:10.498 that in our desire to be equal,
NOTE Confidence: 0.67296178
00:57:10.500 --> 00:57:14.370 we’re perhaps missing on those.
NOTE Confidence: 0.67296178
00:57:14.370 --> 00:57:16.370 Essential things you pointed out,
NOTE Confidence: 0.67296178
00:57:16.370 --> 00:57:19.082 how do we teach that Vern
NOTE Confidence: 0.67296178
00:57:19.082 --> 00:57:19.986 academic organization?
NOTE Confidence: 0.67296178
00:57:19.990 --> 00:57:22.600 And you have highlighted how clinicians
NOTE Confidence: 0.67296178
00:57:22.600 --> 00:57:25.170 can interact with basic scientists.
NOTE Confidence: 0.67296178
00:57:25.170 --> 00:57:28.210 How do we as leaders make sure we’re
NOTE Confidence: 0.67296178
00:57:28.210 --> 00:57:31.097 pointing that out to the next generation?
NOTE Confidence: 0.67296178
00:57:31.100 --> 00:57:31.930 I
NOTE Confidence: 0.78965661
00:57:32.240 --> 00:57:35.186 would question and it’s something that
NOTE Confidence: 0.78965661
00:57:35.186 --> 00:57:39.560 we all have to keep working on overtime.
NOTE Confidence: 0.78965661
00:57:39.560 --> 00:57:45.790 I again I am very optimistic the fact that.
NOTE Confidence: 0.78965661
00:57:45.790 --> 00:57:51.050 People are documenting cancer outcomes.
Stratified by racial ethnic identity, where it wasn’t necessarily documented in the past, the fact that there’s a very, there’s a lot of momentum to look at the diversity of our workforce and to develop pipeline programs when very little attention was paid for the to little attention was paid for the to this in the past people would remark upon the lack of a workforce diversity, but everybody said well, this is a problem that no group can address overnight and so nobody tried to do anything. To address it, but I think that’s the the COVID experience,
horrific as it was,

the COVID experience with disparities

and COVID outcome hitting us

literally in the face,

coupled with witnessing the

horrific murders of George Floyd,

Brianna Taylor, so many others

in the hands of law enforcement,

all of those events happening.

Together made this an extremely

unique moment in time.

And so I think that the efforts

that we’re seeing now in achieving

HealthEquity are real and I

think that it’s going to make a

difference and accelerate the
00:58:56.970 --> 00:59:00.720 pace of disparities research and.
00:59:00.720 --> 00:59:03.200 Accelerate the pace of trying
00:59:03.200 --> 00:59:04.688 to achieve HealthEquity.
00:59:05.990 --> 00:59:07.445 Breast cancer sort of luminaries
00:59:07.445 --> 00:59:10.055 in the room right now in the
00:59:10.055 --> 00:59:11.438 breast, their breast goes other.
00:59:14.070 --> 00:59:17.094 Problems giving
00:59:17.094 --> 00:59:18.754 their splits the life opportunity.
00:59:21.600 --> 00:59:25.560 Ravens. Give patients the audience.
00:59:26.601 --> 00:59:30.121 And Antonio Wolf and a bunch of us wrote an
00:59:30.121 --> 00:59:32.508 editorial saying that was a horrible idea.
00:59:32.510 --> 00:59:33.834 That about any guide?
00:59:33.834 --> 00:59:36.419 So people are willing to give their data
00:59:36.419 --> 00:59:38.940 yet if they come in for an IRB file,
they’re going to make them really hard and so accurately that makes it very hard for people to happen. And we put so many barriers into look at clinical trials, it’s really hard for people to limited means to come to Cornell or to come to New Haven. So how do we change that because who has the best interest in understanding that patients and yet we make it so complicated. Urge all of us to sort of think about how do we break those barriers to make this, because it’s fundamental. As you said, this was an evolutionary mechanism to survive in Africa, right? Malaria is endemic.
And now we're seeing it makes your hemocyanin your inflammatory. You have this response, but you know, it's the flip side and. So I think that there's a peace for us as leaders of the field to say what are we making researches too complex and simple things like my background. Probably affects how I respond to the world was evolutionary and written into our DNA work thousands of years, right? And we're trying to fix that. You are so right. Yeah. And you hit the nail on the head, I think, in talking about how we've
inadvertently created barriers to diverse populations contributing to research. You know, many studies show that African American cancer patients are at least if not more likely to participate in clinical trials if they’re offered the opportunity to do so. And we’ve created all these barriers where clinicians are less likely to offer them for a whole host of different reasons, implicit biases. Sometimes it’s just. Incidental Mel with well meaning physicians who are worried that they’re going to alienate their patients if they offer an African American cancer
01:01:30.466 --> 01:01:32.755 patient to clinical trial for fear that
NOTE Confidence: 0.71263777
01:01:32.760 --> 01:01:33.966 the patient might think that they’re
NOTE Confidence: 0.71263777
01:01:33.966 --> 01:01:35.532 being treated like * **** Guinea pig.
NOTE Confidence: 0.71263777
01:01:35.532 --> 01:01:37.649 But we have to get over those types
NOTE Confidence: 0.71263777
01:01:37.649 --> 01:01:39.857 of things and we have to offer all
NOTE Confidence: 0.71263777
01:01:39.857 --> 01:01:41.857 treatment opportunities to all of our
NOTE Confidence: 0.71263777
01:01:41.857 --> 01:01:44.456 patients even when it comes to our IRB’s.
NOTE Confidence: 0.71263777
01:01:44.456 --> 01:01:46.878 You know we have all these regulations
NOTE Confidence: 0.71263777
01:01:46.878 --> 01:01:49.053 that try to protect people against
NOTE Confidence: 0.71263777
01:01:49.053 --> 01:01:51.646 coercion and so we don’t want to
NOTE Confidence: 0.71263777
01:01:51.646 --> 01:01:53.286 offer a financial incentives.
NOTE Confidence: 0.71263777
01:01:53.290 --> 01:01:55.700 Patients for fear of more
NOTE Confidence: 0.71263777
01:01:55.700 --> 01:01:57.628 vulnerable patients being coerced.
NOTE Confidence: 0.71263777
01:01:57.630 --> 01:02:00.022 But our socioeconomically disadvantaged
NOTE Confidence: 0.71263777
01:02:00.022 --> 01:02:03.012 patients need that financial support
NOTE Confidence: 0.71263777
in order to take the time off work so that they can come in for the visits. So. Such a broad, sweeping problem to try to meaningfully and thoughtfully get rid of some of these barriers that we've inadvertently created and trying to protect our patients against research and justice. The research abuse is, you know, we can’t let those come back, but we do also have to be thoughtful and make research easier for our patients. Thank.