[MUSIC PLAYING]

MYLYNDA MASSART: We'll talk about the risks and benefits of sharing your DNA. So first, as always with all conferences, I need to disclose that I have no conflicts of interest. However, since it's a genetics talk, I thought I should disclose my genetic risk factors. I do have a less than average Neanderthal DNA. So I won't share what company that result comes from, but may be important to know about me.

What's probably more important to know about me is that I am hypersensitive to warfarin. So if any of you end up treating me in the future and need to put me on warfarin therapy, please know that I'm very sensitive to it. I also have a slightly increased risk for age-related macular degeneration, and I suspect that's probably true, as my father actually did lose his eyesight at 74.

So as you're all probably aware, there's been a massive increase in awareness about genetics over the last 20 years or so since completion of the Human Genome Project. There's been both public awareness, as well as increased utilization in clinical and research studies. Many of you have probably seen these covers of popular magazines.

Most of this started after completion of the Human Genome Project back in 2003, and I remember this project fondly, as part of it was happening at the University of Utah where I went to graduate school. And at the time, if any of you are also aware of any of this research, the size of the DNA sequencing machines were pretty much the size of an entire laboratory room. And if you've seen a DNA sequencing machine lately, you will now know that they're small enough to actually fit on the tables right in front of you where you're having your lunch, so things have really evolved in that time.

But not only that technology has evolved, more importantly, the cost has dropped dramatically. Back in 2003 when we were doing the Human Genome Project, it cost over $100 million to sequence one genome. And now, anyone have a guess on how much it costs if you were to order whole genome sequencing?

Yeah, I heard someone say about $600, and I think that's about for $400 to $600 now per genome, which is pretty amazing. And because of this decrease in cost, the testing technology has really become accessible and viable as an option for really nearly everyone. It's now estimated that by 2024, there will be a $22 billion industry in genetic testing, which is quite amazing and impressive.

So there are several DNA testing technologies out there, many of which you probably heard and are familiar with, and if any of you, like myself did research way back when, you may remember sequencing gel that you see in the bottom corner there. I'm not sure how much radiation exposure I had from all of that sequencing back then, but I'm sure it was not insignificant. And then now what we come to know as more modern day sequencing images at the top of the screen there. And most often, you will also see something called SNP chip arrays.

So SNP chip arrays are looking at single nucleotide polymorphisms or single base pair changes, and they are selected representation of single base pair changes across the genome that are placed on these chips and analyzed. And this is what a lot of the common technology is in the direct to consumer testing that you'll see out there. As well as now whole genome sequencing and whole exome sequencing, and then of course, we still do targeted sequencing for very specific questions around genetic diagnosis.

Technology has advanced so much, we now are very proud that we've launched our own Genome Center here at UPMC. For those of you who don't know about it yet, it's actually in Shady Side next to the Giant Eagle market district in a big, brown nondescript building, and we're quite proud of the Genome Center. It's both CLIA and CAP certified for clinical testing, and at the Genome Center, we can do whole genome sequencing, whole exome sequencing, RNA sequencing, even single cell sequencing, as well as pharmacogenomics, which has been established for one of my research projects that I'm going to talk to you about later.

And you can see, actually, the five sequence stars down below and how much smaller they are in comparison to where they were, historically. So with all this technology and ability to do testing, there's now many different methods that we ourselves and our patients are finding that they can share their DNA, and that's really what we're going to focus on today. What are the risks and benefits of sharing our DNA?

So one of course is clinical testing. We have a lot more advances in clinical testing and indications for clinical testing that we're going to talk about. Direct to consumer testing, which has really grown as a market, and then of course, large genomic research projects like All of Us project. So on the research side, as I mentioned, there are numerous projects now in place collecting and biobanking genomic samples.

There's a lot of research that's happening for disease specific genetic research, which is looking at identifying and characterizing very specific rare genetic disorders, there's a lot of work and interest being done now in polygenic disorders, which is identifying and characterizing those single nucleotide polymorphisms that together, lead to predisposition for specific diseases, and I think this is going to impact us the most in medicine but not quite yet, and then there's precision medicine, which is characterizing the interactions between the genome and the environment. So many of these large projects are actually happening right here in our own state. So as was mentioned in the introduction, I am one of the co-investigators for All of Us Pennsylvania, which is part of the national All of Us biobank project, which is in effect right now, and we are currently recruiting a million people across the country to join that genomic biobank.

There's Geisinger here happening in the state of Pennsylvania and their My Code project, as well as the Million Veterans project being led out of Philadelphia, and our local Pitt Plus Me discovery biobank, which I'll tell you more about later, as well as major, major international projects. Many of you have probably heard about the UK biobank, which is now starting to actually publish quite significant findings, and in other countries such as China. That's a picture of me in the lower right-hand corner at that China National Gene Bank last year, which was extremely impressive.

So what are some of the risks and benefits to sharing our DNA in research studies? So on the benefit side, there's altruism. So I like to always say, I'm not in a place to donate $1 million to the University of Pittsburgh, but I can spit in a test tube for them, and that's really being a DNA benefactor, right? So that donation-- that one time donation-- is something that will really contribute to a lot of research over a long time, so that's the altruistic benefit.

There can be personal gain. In particular, if return of results is happening with a specific research project, and there could be also family gain. If it may help a specific family member with the known or needing to be identified disease. And of course, there's always financial remuneration for research. So what are some of the risks on the other side of participating in research?

In terms of procedural risk, it's fairly minimal, right? We're drawing blood, or collecting saliva, so not a huge amount of risk there. There's always potential for data security and privacy breaches. And then if we are returning results with any of these research studies, there's emotional risks around incidental findings so things we may not have expected to find. Variance of unknown significance, so the stress that may cause if we can't explain what that variant actually means and what it's causing.

Insufficient informed consent. So someone didn't truly understand what they might potentially receive by joining the research study. Inadequate support of return of results, so if research participants are given back genomic results but aren't really supported in how to understand and process that information. Downstream health care costs. So again, if someone receives a genomic result, they may need to go follow up with a provider or have further testing done, which could incur clinical costs that they may not have been anticipating.

And finally, need for disclosure to other family members, to health insurance, to their health providers. On the clinical side, as I said, testing is really advancing. For a long time now, we've been using a lot of genetics and oncology for both prognosis and treatment guidance. We are also doing in primary care. A lot of genetic cancer risk assessment through family health histories.

On the pharmacogenomic side, we are seeing more and more preemptive pharmacogenomics, which is actually having your pharmogenomics tested once and for all so that the data is always available at the time of prescribing in the electronic health record, as well as reactive testing, which is what we're currently deploying at the Presby Cath lab here around CYP2C19 and metabolism of clopidogrel. So reactive testing is a little bit challenging because there is a delay in the time that the test is ordered and the results is received and prescribing can actually be implemented. We're also seeing expanded prenatal carrier testing recommendations come out from the American College of Obstetrics and Gynecology, and additional use of genetics now in pre-implantation genetics and in vitro fertilization.

And again, as I mentioned before, probably the most interesting to us in primary care is genetics of chronic disease and polygenic risk scores, which are all being researched right now and are not currently available for clinical use at this time. And finally, disease-specific testing. Confirming a diagnosis of Huntington's chorea or looking at familial hypercholesterolemia.

On the clinical side, what are the benefits of testing? Well, of course, diagnostic confirmation and care planning is the most useful. Family planning if it's around carrier testing. Risk reduction, especially for genetic cancer risk assessment, and improve outcomes of care, and of course, avoidance of adverse drug reactions and possible increase to time to therapeutic treatment in the case of pharmacogenomics.

So what are some of the risks of clinical genomic testing? Again, there's very minimal procedural risk. There's always, again, the potential for data, security, and privacy violations. Emotional risk with result return, discoverability of that results in the chart, and that gets to the concept of insurance discoverability, which we're going to talk about later. Inadequate results storage in the electronic health records.

So where do we put those genetic results? Can all doctors access them and see them readily? As well as inadequate decision support. We don't yet have decision support integrated into the electronic health record to inform us clinicians how to use that data, and with that inadequate clinical guidelines and downstream health care costs for follow up, again, for the patient.

So what about direct to consumer testing? So right now with direct to consumer testing, you can get ancestry genetics, you can get health genetics, and you can get what I call, you name it, we will sell it to you genetics, and these are just a few of my favorites. The first one Athletigen. You can actually have your children tested to see what kind of athletic prowess they have.

I didn't have to genetically test my children. I can tell you that none of them favor athletics. The next one is you can test your DNA of your dog, so this can actually be used to identify the ancestry of your dog, its purity if you need to know its purity, but it's also been used when that pesky pup keeps pooping on your lawn and you don't know who it is, people have done fecal DNA testing to identify what local neighbor dog has been offending their front lawn.

And of course, my favorite. You can actually test what genetics-- what, by your genetics, wine you prefer. And don't you worry. They'll actually set it up so you can get a delivery every month of the wine that you are genetically prone to prefer.

[LAUGHTER]

That's my favorite. I'll take a subscription anytime. So of course, what are the risks to direct to consumer testing and the benefits? On the benefit side, you can get lineage confirmation, right? So you can find out if you really are related to Marie Antoinette if that's important to you.

You might find a hint about your ancestral origins. They're not fully accurate, because the data set that they're referencing, of course, is modern DNA, so it's really referencing where your representative ancestry is currently, it's not really telling you where your ancestors lived 500 years ago. You can learn fun facts like, can you smell asparagus in your urine? And I hope most of you already know that by now, but you can find out genetically if you're supposed to be able to do that or not.

You also can find family members, and we see a lot of this now published in the popular press, as well as interesting and possibly important health information. So what are the risks? Well, on the flip side, you can find lineage non-confirmation, which may come as quite a shock or a surprise to certain people.

You can have other surprises about your ancestral origins and find something that you weren't expecting. This can be anxiety provoking, as well as anxiety provoking health information that you might find out, and this may be inadequate or unsupported or may even lack evidence yet for intervention. So what do you do when you're at home at night at 10:00 PM and you get a direct to consumer test that comes back and says you're at risk for Parkinson's or Alzheimer's?

There's always data security and privacy issues, again, with direct to consumer testing, as well as the fact that most of the DNA is being sold to companies for research. Law enforcement is now accessing this data. So you, by participating in direct to consumer testing, may be providing access to yourself as well as to your distant relatives.

There is insurance vulnerability, and again, there may be downstream health care costs incurred for follow up. Specifically, if any clinically useful information is returned. So some of the examples of the popular press in the headlines that we've seen. Some of them can seem entertaining, and some of them, if you really think about it, can be quite disturbing.

I actually gave a talk last year in Arizona about ancestry testing, and afterwards, had a physician come up and tell me that her spouse, who is also a physician, was a sperm donor in medical school, and now through 23andMe, they've identified over 23 of his children. And he had not disclosed to his family originally that he had been a sperm donor, and so after he had joined 23andMe, and this started happening, he had to disclose to his biological family, and they together decided to open up their house to all of these children, and they don't know how many that number is actually going to reach, and some of you may have seen that just last week, this happened to another doctor who was a medical student at OHSU.

This happens to be from my hometown in Corvallis, Oregon and my Med school, so it definitely caught my eye, but it's actually very, very concerning, and he's suing primarily because he was given reassurance that this was not going to happen and that the children who were offspring would be-- that these sperm samples would be sent around the country so that they would not grow up adjacent to each other, and it turned out that there's over 17 so far children that have been identified and they are all living in the same region, which means the likelihood of them actually meeting each other and potentially dating or marrying is rather significant.

So because of this, he's actually filing a lawsuit, which I think is great, and might actually change some of the laws around sperm donation and how many parents a single donor can parent, or how many children a single donor can parent. In addition, we've seen some pretty significant data breaches in public media about some of the direct to consumer testing record companies. And then of course, these cases that have shown that they are now sharing the DNA with various different research companies, and there is consent for all of this built into the actual websites when people join the direct to consumer testing, but often, we do not pay much attention to what we're signing to and what we're consenting for, especially if we have a specific interest or goal that we're trying to reach by accomplishing this.

So it's becoming more and more transparent that these direct to consumer companies are selling the data the data and partnering with major research venues. So what are some of the legal implications? Well, what is the standard of care for providers and what is our liability? As these clinical guidelines and research guidelines are changing and evolving very quickly, the FDA is trying to keep up. They are putting out new information and recommendations about what we can use and cannot use for clinical decision making, but I'm not really sure how well that's reaching all of us and that we have a clear set of standard of care.

Also, what are the legal implications of data in the electronic health record for our patients in terms of discoverability? Again, our protection from different insurance discrimination is very minimal, and so if we enter any of this type of data into the health record, it becomes discoverable, and we have to be aware of that in the legal ramifications for our patients. And then is there a legal implication of having genetic data out there? So again, we're seeing these major crime solving cases and access to relatives who may not have consented to participate in the DNA database itself, but because genetics is shared at such a high degree, it's easy then to tract down even third and fourth and fifth cousins.

So these are some of those headlines that we have all seen in the last few years, where genetic genealogy databases have been used to solve some pretty outstanding crimes. And again, these were not the actual perpetrators who had participated in these genetic databases, they were third degree relatives, and that was enough to actually identify the perpetrators. So with all this in mind, we really have to think about the ethical implications of genetic testing, both for ourselves if we decide to engage in genetic testing, as well as for our patients.

And as always, we need to consider the autonomy, the beneficence, the non-maleficence and the justice in terms of what we're going to obtain and what we may potentially risk by having genetic testing done. A specific caveat I wanted to mention today is pediatric testing, and I know that probably the majority of you in the room do not necessarily directly treat pediatric patients, but you are guiding their parents, and that genetic testing in children has new and additional caveats on top of things. We really want there to be a timely medical benefit for clinical testing for pediatric patients, so we try not to do any testing before the age of 18, unless there's going to be a significant impact before age 18 on their health.

And direct to consumer testing is not very well regulated and should also not be done before 18. However, we know of many, many cases, because there's no chain of custody with direct to consumer testing, parents order the kits and have their children spit into the tubes instead, and so then they're really obtaining their children's genetic results prior to the age of 18, probably without consent or assent, and this is a real concern. Now, often this is being done because the parents are frustrated and probably looking to diagnose some undiagnosed health condition, but it's really going through not the proper channels, and so that's where we can provide good advice. Prenatal genetic testing is recommended for a limited number of severe childhood onset diseases. So again, you can imagine, we don't want to open Pandora's box and start testing before conception for every possible genetic condition, but again, it could be very helpful for ones that we know are early lethal or ones where we know there could be an intervention either during pregnancy or after birth that could change potential outcomes.

And then what are the ethical implications on other family members? So as I mentioned earlier, genetic testing results impact family members, right? There's a high degree of shared genetics amongst all of us. In fact, one of my favorite trivia points is that we are all actually 99.9% genetically identical, which is truly amazing, right? If you look to the left and the right of you, and then imagine the conserved DNA between you and your families.

And so when you learn something about yourself, there is a high likelihood that it will impact others in your family as well. And so one concept that has come up over the last few years is the duty of confidentiality versus duty to warn, and these are conflicting concepts in ethics, but when it comes to genetics and family members, we are often finding now that the duty to warn outweighs the duty of confidentiality. This is actually being debated in many legal cases. This is about two cases that are happening currently in Europe.

The first cases about a woman who was actually pregnant, and while she was pregnant her father was diagnosed with Huntington's chorea, and she was not informed of the genetic test result until after she had her child, and about a year or so later, found out that she indeed also tested positive for Huntington's chorea, so she is now suing because she had met she might have made different reproductive choices had she known the test result earlier about her father. The second case is actually the opposite scenario, and so it creates a real challenge of really, where does the ethics lie for this?

The second case is a woman whose ex-husband-- with consent-- was informed that he tested positive for Huntington's chorea, and so she was very angry because her three children were all under the age of 18, and she is actually suing because now she has the burden of this knowledge about her children each having a 50% of having Huntington's chorea, and she did not want to be the bearer of that burden prior to them being 18 years old. So you can see this is really conflicting and people are fighting this out in the courts. So I mentioned earlier many potential insurance ramifications, especially with data being recorded in the electronic health record and discoverability of these results, and that's because of the Genetic Information Nondiscrimination Act, which was put into place just over 10 years ago to protect genetic information.

However, it only protects against employment discrimination and health insurance discrimination, and it does not cover long-term care insurance or life insurance, and this is really important for our patients to know. If they're about to undergo genetic testing, for example, they have a very high family history of breast and ovarian cancer, and you're concerned that they might be a BRCA2 or BRCA1 mutation carrier, if they tell you that they're about to change jobs in one month and apply for new life insurance, then they need to know that if this genetic test result comes back positive they are not protected, and their life insurance may be actually denied. So these are really, really important things that we can empower our patients by making sure they understand these concepts.

This also goes into play with direct to consumer results. So I strongly encourage all of you, if a patient does bring you direct to consumer results, even if there is something clinically useful, to not scan that into the electronic health record and make it discoverable, because they will have to disclose that they've had that testing done if they apply for long-term care or life insurance, and then that can be discovered in your records. So this slide is to discuss what I call the genetic panopticon, and this is a concept that I recently started discussing with some of my colleagues.

Are any of you familiar with the panopticon? Couple heads. So the panopticon on the far left originally was a prison that was designed so that the warden from a center point could actually see into every single cell chamber in the prison at one point in time, and this was actually a concept that was developed like hundreds and hundreds of years ago. Recently, there's been a lot of discussion about Facebook and social media and the panopticon, and how really, by placing so much information on the internet through social media, we are really exposing ourselves to everyone, and now, we are discussing the genetic panopticon, that again, if you share your genetic data, again, that genetic data is highly traceable.

It's your own unique fingerprint, and you are providing insight to the rest of the world who has access to that genomic data. And if you think about combining this the last two, both social media plus genetic data, they're really leaves very, very little that could be private. Informed consent if we are obtaining any genetic testing clinically is very, very important. And I would argue that none of us were really taught about informed consent very well in medical school.

In fact, every time you do a CBC on a patient, how many of you tell them that you might discover they have cancer? It's very quiet in the room. Exactly. Me either. But the truth is, you could, even though that wasn't necessarily why you ordered it.

So informed consent is really important if we're ordering any type of genetic testing. We need to provide education about GINA and its inadequacies to our patients. We need to refer to genetic specialists if we're unable to provide informed consent and pre and post-test counseling around genetic testing results.

We need to be willing to discuss the risks and benefits of research participation, and we need to explain to patients why we cannot use their direct to consumer results, nor scan them in the chart. And just for one major takeaway point today, I just want you to know that the FDA has said that we are not allowed to use any direct to consumer genetic testing results for clinical decision making. So if someone does bring you something and they are releasing more and more clinically interesting information, it has to be clinically validated before it can be utilized for decision making.

And to recognize when direct to consumer results have utility and repeat them again with clinically validating testing. What's our responsibility for those of us who our research investigators in the room? Probably, most of you know what this picture is. Informed consent is meaningful delivery. Consider new methods of engaging and delivering informed consent.

We're currently looking at ways to do informed consent through videos and through multiple languages. We even, on the All of Us, have a short quiz at the end of the informed consent, which is delivered through a video, to capture how well the potential research participants actually understood the consent. Place an emphasis on risks and benefits and don't try to bury them in complicated consents that no one will read.

And just remember, if we break the trust of research participants, we will have to work generations to earn that trust back. I don't know if any of you saw this, there's been a couple articles published of similar research, but this one was called, Will You Give away Your First Born Child, and Deloitte survey of 2000 consumers in the US found that 91% of people consented to legal terms and services, including giving away they're first born child. And in ages 18 to 34, it was even higher with 97% agreeing to conditions before reading them, right?

So research participation and clinical consent shouldn't be just scrolling and hitting the I agree button. It really has to be explicit. So what is true informed consent? It's really not a form, but a process. And I think when you think about it that way, it's very, very helpful. It's a voluntary agreement to participate in research or have clinical testing done and obtaining consent involves informing the subject about their rights, the purpose of the study, the procedures that they'll be undergone, and all the potential risks and benefits of the participation.

In addition, we are now getting into as I mentioned the risk of data privacy and security breaches, and I feel like a very comparable analogy to genetic security and privacy is social security numbers. So do remember all of you 10, 15 years ago when we were panicked if someone had access to our social security number? And now, probably any 12-year-old could Google our social security number in about five seconds flat. So the same is with genetic data, right?

So instead of thinking about how can we protect the genetic data, we need to think about, how can we make it not useful anymore if it gets into the wrong hands? In addition to that, there are many, many big thinkers out there who are trying to drive new methods of how someone who shares genomic data with a research project like these large national biobanks that are now existing would retain authority and consent and same with direct to consumer testing, and this is just one model that was recently published by Dr. Church and his team using blockchain.

And one of the big things is that we can never anonymize genomic data. So basic blockchain itself doesn't actually work, because genomic data, by nature, again, is our most unique fingerprint. But what we can do is go through a series of blockchain, where each time a researcher or investigator or a new lab that someone wants to sell the DNA data to actually has to request permission from the original donor through a series of block chain mechanisms so that no one is actually identified and remains anonymity through that method, but is able to individually provide consent.

I think right now, these concepts are still really convoluted, but I think it's going to be really interesting over the next five years to see how this plays out and what kind of ingenuity is applied to data storage and safety. Next is certificates of confidentiality. So I don't know if many of you have heard about this, but the NIH a few years ago instituted this. So now, all NIH research protocols have a certificate of confidentiality automatically included, but direct to consumer companies and projects that are not funded through the NIH do not automatically have this, and this is very, very important.

This is what actually prevents the government from accessing the genomic biobanks for solving crimes like we're seeing with some of the direct to consumer testing. So this is incredibly important to be able to advise patients to look for this. And ultimately, I think the future of health care really could go two ways, right? So with any new technology, we have a lot of responsibility and genetics certainly at the very top of that list.

I don't know how many of you have been fans of the Black Mirror episodes. Not a lot of nods. That's OK. I actually haven't watched very many of them, because I find them really hard to watch. They're very dark reflections on technology and the impact of technology on our society, and there was a specific episode, where actually the military were fighting and defending the rest of the country from zombies, and it turned out that one of the soldiers somehow injured his head in one of these combat situations with the zombies, and all of a sudden, when he looked at the zombies, they were no longer these horrible, man-eating, screaming, altered looking zombies. They were normal everyday human beings.

And what had happened is that genetic technology had reached a level in this society, where they could tell who was at risk for asthma, who was at risk for cancer, who was at risk for developing under other chronic conditions like diabetes, and they were deemed to be of low value to society. And so the military knew that the army, the military would not go out and fight everyday normal citizens if they looked normal, and so they put these implants in to everyone's brain to see them as these man-eating horrible zombies. So I watched this episode, and then I laid there and reflected that, this is terrifying. This is where our technology could go if we don't have control over it.

So I really always encourage everyone that we need to be very, very responsible about genetics. We have a lot of responsibility as a society to make sure that decisions, both on the research side and the clinical side, always move towards a better utility and a better health future. And my representation of a better health care future, of course, is Star Trek on the right, which I grew up as a Trekkie in my family in my house, and I always loved the pictures of the double helix that would show up on the medical board behind the patients in the sickbay.

And so I really look forward, instead, that we'll be able to apply genetics with my tricorder and scan any patient in the future and have their DNA be projected up and where we'll be instantly able to repair it. So this is our responsibility. So I couldn't get up here and now talk a little bit about all of us, just because it is so important and a big part of what I work on every day.

For those of you who are not familiar yet, All of Us is the national study to create a national biobank of 1 million genomes over the country, and we here at Pennsylvania and at Pittsburgh have one of the grants to enroll 120,000 of that 1 million. We are attempting to enroll the most diverse data set ever possible, so that in order to do precision medicine research, we really have to have representation from everyone and to truly understand environmental influences on genetics and on health. We also have another local study called Pitt Plus Me discovery through CTSI, and this is our local Pitt genomic biobank that we started last year.

We already have over 4,000 local UPMC patients who are enrolled in this biobank, and it will be available for access soon to investigators at Pitt for precision medicine research. But one of the great things about this is in order to engage the patients in participating, we are returning pharmacogenomic results, and we're actually in the final pathway right now of building all the clinical decision support into Epic and Cerner in order to return these first 4,000 preemptive pharmacogenomic testing results. And last but not least, I just want to announce our new primary care precision medicine service. As I talked about a lot of different things today, this is very complicated.

The technology is very new to a lot of us, and we decided that we needed to create a service in the meantime to be able to meet patient needs and providers needs who need consultation on how to interpret results, where to do clinical validation of the testing, and to provide national guidelines for the test results as they come in, as well as the return of results from some of these national biobank and large studies. And with that, I will end.

[APPLAUSE]