DAVID WARNER: I'd like welcome everyone to our [INAUDIBLE] Grand Rounds presentation this morning. It's my pleasure to introduce our speaker, Doctor Richard Sharp. Dr. Sharp was educated in Michigan, first at Western Michigan University and then at Michigan State University for his MA and PhD in philosophy. He's gone on to have a quite distinguished career in the field of biomedical ethics. He is the director of the biomedical ethics program here at Mayo.

Prior to joining us in July of 2013 he directed bioethics research at Cleveland Clinic and was the co-director for the Center of Genetic Research Ethics and Law at Case Western Reserve University, one of six NIH centers of excellence in ethics research.

He has published widely in a variety of topics in biomedical ethics, including clinical ethics, consultations, informed consent, financial conflicts of interest, and ethical tensions, and patient advocacy. He has a variety of different research projects going on at the moment, including a variety of topics examining how patients and health care providers view new forms of personalized medicine and clinical interventions enabled by molecular diagnoses.

He's quite in demand as a consultant for health care organizations on ethical issues and has served on advisory committees for the National Institutes of Health, Institute of Medicine, American College of Medical Genetics, and US Environmental Protection Agency. And I might say, unlike most of my philosophy professors in college, he is not only A, a nice guy, but B, an excellent communicator. And I know that you're going to enjoy his topic today. Richard.

RICHARD SHARP: Thanks David. I appreciate it. Thank you, Dr. Warner, for that kind invitation. And it's so nice to see so many familiar faces here.

My journey to Mayo actually began right here at this podium. Like many folks, when I was initially approached to consider a position at Mayo I didn't know much about Rochester and was a little bit apprehensive about the idea of moving out to a small town in the middle of Central Minnesota. In fact, as I recall it, it was a very cold afternoon when that phone call took place initially. And I remember thinking, I don't know about this. But the next step in that conversation began with an invitation to just come out, give a talk. We'll talk after more. We'll see how you like it. And like so many of you, I suspect, once I did get here I immediately knew that this was the right place for me. And I'm very happy that that conversation began, in essence, with a Grand Rounds talk very much like the one that we're doing this afternoon.

It's also nice to be able to say more publicly a thank you for all the support of many of you who are here in the room, including doctors Warner, Khosla, Noseworthy, Farrugia, and a number of others that are here. To be able to say that in a public venue like this is really very satisfying to me. So again, thank you very much for your support.

So I'm going to talk a little bit today-- well, before I disclose, I have no disclosures. I'm going to talk a little bit today about some changes taking place in the delivery of individualized medicine services. I want to talk a little bit about why this movement toward individualized medicine has generated so much interest and excitement. I'm going to say a little bit about how patients are engaging some of these changes, and highlight some of the ethical challenges that we should anticipate along the road to personalized medicine, and suggest some ways in which we might actually address those challenges.

So let me begin by saying several things that I think many of you in this room will be familiar with, but should give us some background assumptions for the remainder of our comments. The first is that over the last 10 to 15 years there have been tremendous advances in what are known as Next-Generation Sequencing technologies. And over the last six to seven years in particular advances in these technologies have greatly reduced the cost of performing high throughput genetic testing.

Those costs have become so low that in many cases the cost of doing an analysis of the entire whole exome of an individual is less than performing a detailed genetic analysis of a single gene. That's a remarkable progression in terms of the technologies, and it's really changing the landscape with regard to the utilization of these technologies. And again, I think another well-understood thing for this group is that, as those costs continue to fall, what we're going to see are greater numbers of institutions beginning to experiment with using those technologies in their practices for a variety of different purposes.

So I wanted to start with those background assumptions and with a quotation. And since we are celebrating our sesquicentennial, I thought it would be nice to look back to a historical figure and share this quote. This is a quote that says, "the doctor of the future will give no medicine but will interest his patients in the care of the human frame, in diet and in the cause and prevention of disease." Now, I'd like to be able to attribute that to Will or Charlie Mayo, but indeed that quotation is attributed to Thomas Edison.

And I use that quotation in a number of my talks when I talk about personalized medicine to highlight the fact that this allure of tailoring medical care to the needs of people who are healthy instead of responding to the needs of those individuals that are sick is a very old appeal. It goes back for generations. None of us want to be sick. All of us want to take the sorts of steps that we should take in order to prevent illness and disease.

This is, I think, part of human nature to want to avoid those sorts of tragedies in our lives. And that deep-seated interest in trying to avoid becoming sick, at the end of the day, is one of the primary drivers of the emergence of personalized medicine.

So what is personalized or individualized medicine? Many folks have defined this in different ways, but the definition that I like is that the promise of individualized medicine is to develop better diagnoses, earlier interventions, and more efficient drug therapies and customized treatment plans. Individualized medicine hopes to provide a genomic blueprint that can be used to determine each individual patient and person's unique disease susceptibility with the goal of designing preventive measures to address that unique individualized genetic composition.

As I mentioned a moment ago, heretofore this really hadn't been a vision that anybody could see operationalizing in any realistic way. So if you think back to the Human Genome Project and the cost of conducting that very first genetic analysis of all the genomic material in one of our cells, that took 15 years to complete at a cost of roughly $2.8 billion. That's a pretty sizable investment.

I think it was a worthwhile investment, personally, because it's enabled so many other advances. But if we wanted to make the case to our finance people here at Mayo Clinic that we should be doing that for every individual patient, we're never going to have much success.

And as you look back to the state of the art in 2002 and 2004, it was still just prohibitively expensive to consider doing a genomic analysis at the level of an individual patient. What we've seen though-- again, with the advances in these Next-Generation technologies-- is a remarkable decline in the cost, where today if you are looking at doing whole exome sequencing in batch situations, we're talking about costs that might be below $1,000 per individual and turnaround times that are now not years but weeks. And again, it's that trajectory that you see on a slide like this that really is part of the enthusiasm that's generating the interest in individualized medicine.

Lots and lots of our peer institutions have begun to take up these technologies and to utilize them in various clinical contexts. Here you can see a slide that includes a number of those leaders around the country. The personalized medicine coalition is a not-for-profit advocacy organization that is lobbying on behalf of organizations that are interested in new forms of individualized medicine. This is a short list of institutions that are affiliated with that organization. But it gives you some sense of what the landscape looks like with regard to other organizations that are pursuing similar initiatives. And you'll see here many of those leading institutions in medicine.

Many health care organizations have also begun to market themselves as innovators in this space. And I think this is an important part of what's happening now in terms of the emergence of individualized medicine, is that it's seen as a differentiator, as something that can distinguish the care that you might receive at a place like Mayo Clinic from the care that you might receive elsewhere. The idea being that this special opportunity to have the care that you received delivered on the basis of your unique personal genomic profile is part of the marketing of individualized medicine as well.

Here you can see a slide-- and this could be one of dozens and dozens of news stories that appear month to month. You can see a number of states that are beginning to mobilize and to invest into this area as well. Here a recent story from last month about the New York State Legislature pouring $100 million into investments into genomic medicine.

So why is this so attractive to institutions, to state funders, to the national government, and so forth? Why are people excited about this? Again, there's the appeal I mentioned a moment ago, wanting to avoid illness. But there's more to it. And I actually find it helpful to talk about the buzz around individualized medicine in terms of the 4Ps of personalized medicine, being predictive, preventive, participatory, and personalized.

Now, the first of those is probably the one that many of you are more familiar with, and this is the idea that you might send in a blood sample or a swab of the cells that are in the inside of your cheek to a company, and they might analyze that genetic material and send you back a risk profile that describes how likely it is that you might develop cardiovascular disease or various cancers or what-have-you over the course of your lifetime.

These are, in many ways, still aspirational products. OK? There are not well-developed, well-established data that support the idea that the results that have been produced through genome-wide association studies can be utilized in these types of settings to provide accurate risk assessments for individuals. They're promising technologies, but these are not things that people are using routinely in patient care settings.

Despite that, these are products that have been marketed directly to consumers, and the FDA has voiced a lot of concern about the marketing of these products. But they are still available in many segments of America today.

Just to give you a sense of the market reach and scope of some of these products, one of the largest of the companies involved in providing direct-to-consumer genomic risk profiling is a company called 23andMe. Many of you I can see nodding around the room. Many of you may be clients of 23andMe, perhaps.

23andMe has announced that they have now over 350,000 clients in their database. So these are 350,000 individuals here in America, largely, who have paid anywhere from $99 to $399 for the purpose of purchasing one of these tests. That's one of the things that's driving interest in personalized medicine, is the recognition that there is an enormous market sitting here. People want to know. They want to know how likely they are to develop these illnesses over the course of their lifetime.

The other P has to do with prediction of drug response. I'm going to be very brief on this one because many of you in the room are far more expert about these matters than I am, but certainly we know that there are many different genetic variants that have a strong connection to the metabolism of various antibiotics including drugs, and so that those are relationships that are far better understood.

The idea here though is to routinely evaluate patients who might be seen in facilities like Mayo Clinic with an eye toward putting those results into patients' electronic health records so that when a physician goes to prescribe that drug, she knows that there may be a particular susceptibility to an adverse event that that patient has. And thereby be in a better position to avoid that event happening.

And then the last P that I want to talk about in this context is one that you might not think of as specific to individualized medicine, but I think it's equally important in terms of understanding the attraction here. And that's a variety of movements that we might lump under the title of participatory medicine.

And this is the idea that we're using various forms of social media to a greater degree today to encourage patients to take ownership over their health care, to take ownership over their well-being. And so, for example, we utilize patient portals to get information to patients sooner so that they can prepare for their office visits and ask better questions and retain that information that's shared in that context to a greater degree.

More than that though, we're seeing patients reaching out to each other to better understand the illnesses that they have and the treatment options that might be available through various social networking functions. A website that I think is a particularly interesting one is the web site PatientsLikeMe, which has done an enormous job of connecting patients with each other and has had, I think, a number of very positive but also very negative implications in terms of helping some patients to better understand their condition, but also disseminating certain types of misunderstandings about disease as well.

The power here though for the emergence of individualized medicine is that we can equip patients with information about their unique susceptibilities so that they can go out there, if they're interested, and tap into some of these social resources. They can take advantage of this, and they can learn more about what's unique to their biology that might be driving their health risks over time.

So it's this perfect storm, if you will, that's coming together around individualized medicine and is making this movement so appealing to many. It's the perfect storm that you might think of as a movement away from providing care based upon best-available generalized evidence to something that's far more personalized. No longer a "one size fits all" model.

So what we're talking about, in my opinion, when we're talking about the movement toward individualized medicine, is not just utilizing genetic testing services to a greater degree, but really a shift in the way in which we deliver care. A shift from more traditional modes of engaging patients, which is largely passive and receptive-- Patients come to us in the hospital when they're ill. They come to us periodically-- to something that would be more participatory and proactive, and going out to them and saying, these are the risks that you have. We want to work with you to develop a plan that ultimately is going to address those problems before they occur.

And if you think about it in these terms, what we're talking about is a major shift in the way in which medicine and medical care is delivered. So this is, in my opinion, what individualized medicine is all about. And when you step up to this 30,000-foot level and think about these changes, I think it gives you a better sense of why there is the disruptive potential that many of us see in this movement. This is a change to the very way in which we deliver medical care, and so it wouldn't be surprising that it would be disruptive and potentially raise a number of ethical and social issues as well.

So we can look at that shift and ask a couple of very foundational questions. It sounds like a good thing. Should we be excited about this? Should we have concerns? And even though this idea of trying to prevent disease is a little bit like apple pie and babies-- right? I mean, who could possibly be against preventing people from getting sick?

On the other hand, we do know historically that many patients for whom genetic testing was medically an appropriate option have chosen to forego that testing. They've chosen not to pursue genetic testing for fears that they may suffer discrimination, or for fears that they might encounter burdens that they wouldn't know how to manage very well, or for concerns about the implications that knowing that information would have in terms of their relationship with others in their families. So there's lots of reasons to suspect that, in fact, many patients will not be receptive to these changes taking place.

Similarly, we know from previous empirical studies that many physicians don't report feeling well-prepared for these changes that are happening. So I think we need to anticipate that, in this context, as the scale of genomic testing changes from looking at individual genetic tests to looking at multiplexed and hundreds and potentially thousands of genes simultaneously, that the educational needs of those physicians is also going to expand dramatically as well.

So there's reason to think that there will be a number of disruptive waves coming out of this individualized medicine movement. And it's through that lens that I want to talk a little bit about the work happening through the Center for Individualized Medicine, which is facilitating conversations around many of these issues here at Mayo Clinic.

I know that Dr. Farrugia and Dr. Lazaridis has presented to this group before, so I'll be very brief. But the Center for Individualized Medicine is supporting a number of infrastructural programs that are meant to facilitate the emergence of new forms of individualized medicine. The goals of the Center for Individualized Medicine are to discover and then integrate into clinical practice the latest developments in genetic molecular and clinical sciences related to individualize medicine.

And for those of you who are interested in learning more, I would refer you back to a paper that really launched some of these ideas that Dr. [INAUDIBLE] wrote several years ago, as well as a more recent paper that's authored by Dr. Lazaridis in which he describes some of those programs in greater depth.

But currently there are two major clinical service lines that are offered through the Center for Individualized Medicine, one focused on meeting the needs of patients with advanced cancers, and another focused on meeting the needs of patients that are on what is commonly referred to as a "diagnostic odyssey," patients who are believed to have some sort of genetic feature that's contributing to their unique disease phenotype, but for whom that particular genetic cause hasn't yet been identified. So there are two major service lines that already exist within the Center for Individualized Medicine, and plans to develop several others in the years ahead.

As I said, the center has a three-fold mission to discover opportunities for individualizing patient care, to translate those discoveries into test tools and treatments and then evaluate them in practice, and also to apply to patient care those tests that are proven most effective.

Part of the challenge in really integrating genomic technologies into patient care is purely an informatics challenge. The volume of information that's produced through a genomic test is just so large that even being able to store on servers that information and then have access to it in real time can be a challenge. So if you think about the volume of data that you might have on your hard drive-- I have no idea how big common hard drives are today, but let's say they're 500 gigabytes. I don't know if that's accurate or not. I can see people looking out there like maybe I'm coming out of another generation of folks here. But let's imagine that that's how big they are today. We're talking about teragigs of data that would be associated with this kind of test.

And so how do you actually upload that volume of data into a patient's health record? The systems we have can't accommodate that sort of thing. Or how do we provide access to that through some type of filtering process that clinicians would actually be able to query and utilize in real time?

So one of the biggest challenges around utilizing these tools is really a challenge of managing the enormous volume of data that's produced. In addition, by looking at everything, you're guaranteed to find something. Right? And I think this is one of the paradoxes of individualized medicine, is that any genomic analysis is going to reveal a lot of information that you can't anticipate at the time you order the test. And that each of those possibilities that you may find-- that a patient is a carrier for a gene associated with some rare genetic condition, for example, each of those possibilities and all the different genes that might be analyzed can't really be discussed in-depth with patients at the time the test is ordered.

And so many ethicists-- I don't myself fall under this category, but many ethicists have said that that possibility that we can't walk through the gene list with patients in advance and put them in a position to know all of these different possibilities means that we can't actually get informed consent, and that talking about getting informed consent doesn't make sense in this context.

Even if you don't go that far in terms of your analysis, clearly you can see the challenge here. How do we position patients to make informed decisions about the many things that we can't anticipate and don't know in advance? So what sort of counseling is appropriate?

That's part of what we're trying to sort through within that sub-program within the Center for Individualized Medicine that is the bioethics program. That, and other related questions.

So our focus in the biomedical ethics program there within the Center for Individualized Medicine is providing specialized forms of ethics consultation, placing the needs of patients at the center of some of these developments in individualized medicine by bringing to the surface some of the values and assumptions that will guide patients' decision making about whether to utilize these new tests or not. We're also interested in engaging people outside of the hospital as well to see if they have concerns about these technologies as well.

And so I want to talk to you about some specific initiatives we have in this space and share some of the research studies that we're doing related to elucidating patients' values and clinicians' values. But in this particular context-- there are lots of values that we might attribute to bioethics research, but in this particular context I think one of the real things that bioethics research can contribute is it can identify potential discrepancies between what patients expect from these technologies and what clinicians expect from these technologies. And so in the next part of my remarks I want to walk you through some data that we have that I think nicely highlights the potential for there to be some divergence between these expectations.

So I want to share with you a study that I began before coming here to Mayo Clinic that was really meant to try to clarify clinician and specialist attitudes about genetic testing, and had as its aim to develop practical suggestions for counseling patients about the return of diagnostic results from genomic tests. There were several different arms of this study that was supported by the NIH, but the one that I want to share with you today was the arm that involved going around to leading institutions in genetics and establishing work groups.

So what sort of drove this study was the idea that, at roughly a dozen institutions three or four years ago you could look at those institutions and say, these are clearly institutions that are vanguard institutions. Right? These are institutions that are at that leading edge of medicine, and these are going to be some of the places in which the expectations around these technologies are going to be developed.

So if you went, for example, to the University of Pennsylvania or the Johns Hopkins University and so forth you would see those universities in that time beginning to experiment with using whole exome sequencing in various patient care settings. And we thought, we should go there and ask those folks, how are they thinking through these practical challenges? How are they thinking through these ethical challenges as they're coming up? And what plans do they have in terms of managing those issues?

We knew the issues that we wanted to explore were really complicated ones, and that it wouldn't make sense to do interviewing or surveying or anything like that. And so the methodology we adopted was that we identified a site contact there and we said, we know you're rolling these things out. Who's in the room when you're having conversations about the types of clinical services that your institution wants to offer? Who are your go-to people for the purpose of establishing these service lines?

And then from there we identified small groups of roughly 8 to 12 people who were considered experts within these leading institutions in areas related to individualize medicine. We then invited them to participate not just in one meeting, but a series of meetings so that we could keep going back to them and we could explore to them how their thinking about these issues were changing over time.

So we did 24 two-hour plus sessions at these six different sites that are listed here. This was the project that really got me in trouble at home with my wife and kids, as a matter of fact, as you might imagine. But the airlines loved me because of this project. So I literally got on the plane every couple weeks and would go to one of these sites and sit down with this group and talk with them about what was happening in the field of individualized medicine. It was an incredibly rich and interesting experience to have.

What we did at each of these meetings is, we would come to the folks that were in the room with an anonymized patient description. And these were, in many cases, real patients whose medical information we had de-identified and so forth. And we also brought to them laboratory reports from multiplexed and genetic tests as well.

And so we sat this in front of them, walked them through the patient's history and story, and said, imagine that tomorrow you're seeing this patient in your clinic. You're a genetic counselor, a medical geneticist. How are you going to start that conversation? What are you thinking about in terms of what information you want to prioritize? How do you want to structure the conversation? And so forth. And because of that, I think we ended up with a very rich data set from these conversations.

So I want to share what we learned from going to these experts. And I want to set this up by saying that I always found it quite surprising that, even at these places in which they were launching individualized medicine programs, there was enormous skepticism about whether this was going to work or not.

These genetic professionals that we spoke with had concerns about when you would actually order a genomic test. They were worried that they wouldn't be able to meet the practical demands in the real world of going through all of that data and being able to provide a comprehensible report to their patients. They were worried about the same issue that I mentioned a moment ago about whether it would really be possible to get informed consent. And they were worried about the volume of data from a different point of view, namely that they thought this might require hours and hours of counseling after a test was ordered.

And so I want to walk you through some of those major findings and share with you some of the quotes and some of the words that came out of these sessions to give you a sense of those conversations and how these expert clinicians flagged these issues. So, as I mentioned, they had concerns about when you would actually order this type of test. What's the purpose of this? What's the need? What's the clinical indication? If there's a diagnostic question then you want to order the test that answers that diagnostic question, and I think that's the way we're used to thinking about it clinically.

And so among these medical geneticists they worried that they weren't doing their job, in a certain way, if they were going to evaluate somebody using a genomic test. That what they should be doing instead is sitting down with that patient and looking at that individual and saying, this is the particular test that you need, instead of looking at the whole genome together.

Many of them used very strong language that would suggest that they really felt that, as medical geneticists-- and this is particularly true for that group-- they really thought that that was what defined them as professionals. That's what made them unique, was their ability to apply these tools and come up with a definitive diagnosis in situations that are really, really hard. And so they thought that they were abdicating their responsibilities in some ways if they were to simply use these tests without better forethought.

They also had very limited enthusiasm for using genomic testing as part of a patient wellness program. Now, this was a series of discussions we had several years ago, so some of these attitudes may have changed as other institutions have gained experience with this type of program. But here they said, so it's great to have that technical capacity, but I can't envision a clinical scenario where that's the test I would want to order or I would recommend a doctor order.

Now, as we went further in these discussions and some time had passed, the working groups that we had began to become more receptive to this as what they referred to as "a test of last resort." So thinking about the two clinical service lines that I mentioned a moment ago, I think that that type of service line associated with the Center for Individualized Medicine would be a good example of the type of clinical testing situation that these clinicians would have been more comfortable with. But this idea of using these technologies without greater specificity with regard to the goals was seen as very problematic.

They then highlighted a number of interpretive challenges related to trying to understand the significance of all the different variants that would be revealed. They said, quote, "we currently only know how to interpret the test results in the context of a disease. We don't know how to interpret test results in the absence of disease."

And here's, I think, to give you a real strong feel of the really strong visceral reaction that folks had to some of these scenarios. Quote, "I think this is our nightmare right now, of having patients walk in with these types of reports and saying, help me out here. You know? You know, obviously they're looking at differences, but what are you really measuring?" And this was really a concern that was consistent across all the different groups that we went to.

And I want to remind you, these are leading genetic professionals at the leading institutions doing genetic research and providing clinical services in the United States. If these folks were concerned that they didn't have the capacity to interpret the results, I think we should all be concerned about the capacity of other institutions to manage this. So going back to something I had mentioned a moment ago, this really brought to light for me the needs and interpretive needs that I think many clinicians are going to have in the context of utilizing these tools.

Lastly, just a couple of other quotes here to give you a sense of some of this negativity that was expressed. They were concerned about how to handle what we might think of as "incidental findings," findings that wouldn't be immediately relevant to that patient's care but would be relevant to other risks that they may have, risks associated with reproduction or later-onset diseases and so forth. They said, "what's going to happen in a couple of years when you know whole genome sequencing on people? I mean, there will be all sorts of incidental findings." And, quote, "you don't order a test with a plan to ignore half of it."

Again, just finishing the thought here. You can see here some of the negativity. "Even for a genetics expert this is going to be a challenging situation. It's a counseling nightmare. It's not focused at all. The geneticist is going to become your patient's new best friend because they're going to be coming to see you every week." Et cetera, Et cetera. You can just see the tone of these discussions and how concerned these medical geneticists were about the impact of these technologies and their disruptive potential.

Also a lot of concern about who would be ordering these tests and, in particular, what happens if primary care physicians, among others, begin to utilize these tests with greater amounts of frequency? You didn't order this test." As a medical geneticist, quote. "You didn't think it was a good idea, but you're left holding the bag and the patient is there in your office asking you to explain it, and so you have to do your best to take care of it."

As the costs get lower and lower, I think if we were to go and do these same meetings again today we'd see this concern to a lot greater degree. Right? If for $1,000 you can order a whole exome, then that's going to mean that many institutions and many individual physicians are going to be more willing to do that than when the cost was $10,000 or $15,000 for doing that.

And here's probably my favorite quote that comes out of this. Many people referenced the idea of cleaning up garbage, but as one person said, "in this context you are the genetics garbage man, where you're cleaning up what someone else has started."

So again, to go back to our major findings here. Strong negative reactions to the emergence of these technologies, particularly associated with their use outside of specialized medical genetics clinics. The biggest concerns being, how are we going to deal with all the information? How are we going to find the time to counsel people about all the different results? And how are we going to be able to accurately and meaningfully communicate all these results when they do come back?

So to go back to our second question here, how does this compare to how patients might see these same technologies? In that regard I'm happy to be able to share some preliminary work that's been generated by my colleague in biomedical ethics, Dr. Jennifer McCormick. And Dr. McCormick has been working with the teams here at Mayo Clinic to conduct interviews with patients that are going through this experience of having their entire genomic sequence analyzed. And in that context she's actually interviewed them to ascertain what hopes and concerns those patients may have, with an eye toward how we might improve the consent process and ultimately improve the experiences of those patients.

So at this point this is still very preliminary work. It hasn't yet been published, and so I do appreciate Dr. McCormick's willingness to share this with us today. And it's a relatively small study here to date, consisted of just 51 interviews. But I think it's still informative and interesting to look at.

So our experience here at Mayo has been that patients often desire maximal amounts of information. And in many ways this interest really is directly in opposition to what I was just sharing with you in terms of physicians' concerns. And here is an example, "I think information is power. It affects your family, your home, your children. I mean, it affects everything. The more you know, the better off you're going to be." So this idea that they would like to get whatever information is revealed returned to them was part of their motivation for pursuing some form of genomic analysis.

Another quotation here. "I know there's some like the neurological dementias that they won't even tell you that if they find it. They won't tell you if you have it, which bugs me. I would like to know because I think it's better to prepare my family, better to prepare my children for the years ahead. And I don't like surprises." OK? So even if it is an incidental finding, you can see evidence here, among other pieces of evidence, that patients still want to know even if it's not immediately relevant to their care. They want to know this information oftentimes.

And this type of finding is consistent with many others that have been done nationally. I don't think it's unique to the patients that come to Mayo Clinic for their care. They also want choices about what information they receive. Here's another quote to illustrate that. "I think this is the Individualized Medicine Program for a reason. Everything has to be on a case by case basis because this is serious information and there are many patients who could not handle that information. I think the patient should always have the choice under the proper instruction of a medical geneticist. I would never want someone else to decide that for me."

So these are patients that are not entirely willing to say, I trust my physician to decide what I can and can't handle, or what I shouldn't or should not receive. They would rather have a conversation with their physician to help to calibrate what gets returned to what they think they personally can handle. So again, this idea of individualizing not just care to patients' interests but perhaps even individualizing the types of information that people receive based on what they feel that they can handle seems implicit in a statement like that.

Another quote here. "I absolutely believe this is all about choice. And I don't want to imply that I wish this choice wasn't available, but it may tell me more than I'm comfortable knowing right now. So I think it is absolutely a choice, and it's all about the choice." Again, stressing this again and again. In these interviews that I've been able to review portions of consistently make statements along these lines.

Here again expressing concern. "Why should you get to pick what I have to deal with? For us, the family, this information is actionable." Knowledge is power, might be another way to paraphrase the primary message that is coming out of these interviews. The idea that even if it's not something that resolves a diagnostic paradox, even if it's not something that is immediately the cause for the development of some new medical management plan, people want to know. They want to know what's in their genes. And they don't want that information filtered. They want to have-- many of them don't want that filtered. They want to have access to that information themselves.

So from Dr. McCormick's study some of the major findings have been that patients are consistent in expressing a very strong preference for being given choices about the types of information, genetic information they receive, and they often desire more information beyond just what might be medically actionable. The views of patients regarding the potential benefits and risks of knowing genetic information are highly personal. Many people do also report that they have some concerns about not being fully prepared to handle some of that information. And patients want health care providers to collaborate with them in interpreting findings, including findings that might not have implications for their care.

And so now you can really see this gap, this chasm, if you will, that exists between those perspectives of clinicians and those perspectives that we're seeing from patients. Physicians are expressing concerns. I don't have the ability, I don't have the capacity potentially to deliver all this information in a meaningful and helpful way. Patients are saying, we want it. We want all of that information. How do we bridge that chasm? How do we bring those things in closer connection to each other? Because it's clear that there is a potential discrepancy here between the ability of providers to meet what are clearly patients' goals.

This is a challenge, I think, that is going to continue on and perhaps become even more difficult as we think about integrating genomic testing, in particular whole exome sequencing, into new forms of wellness initiatives, new wellness initiatives and forms of predictive genomics. And here I think the challenge for us, and certainly one of the major activities that we'll be undertaking over the next several years in the bioethics program as part of the Center for Individualized Medicine, will be finding the best ways to give patients options about what types of results they receive.

So, for example, how to counsel patients about whether they would like to receive carrier screening results or pharmacogenomic results, and potentially putting them in a position where they can pick and choose among those different testing options before those tests are ordered so that we're not dealing with the problem of how to manage incidental findings, but we're calibrating the ordering of tests based upon clearly knowing what those patients are most interested in learning. And so that's something that we're working actively to try to develop our tools for calibrating the ordering of tests to individual patients' preferences, working closely with many of the clinicians in the Center for Individualized Medicine.

And the other thing that we're spending a lot of time on in our group is thinking about other ways in which we engage not just patient communities but the public around discussions related to individualized medicine. And in that regard one of the things that we're expanding this year is our relationship with the communities in Arizona and in Florida. And we currently have a community advisory board that's been constituted around the Mayo Clinic Biobank. And many of you in this room have no doubt contributed to this collection at a personal level, or are aware of it, potentially have used materials from the Biobank.

But just to be thorough here, this is a collection of now more than 40,000 samples that exist here at Mayo Clinic that provide an opportunity for researchers to link biological materials, primarily blood samples, to that patient's health record. And to do that in a way that lets you stay current about the medical care that that patient is receiving.

It's a remarkable resource in terms of enabling new types of research. But the challenge in terms of thinking about getting consent from patients in a collection like that is very much analogous to the challenge of counseling patients about participation in things like genomic analysis. Right? We know at the time you get the blood sample that there's a lot of new things that are going to happen scientifically over the next few years that we may not be able to anticipate, and a lot of uses of those materials three or four years from now are going to involve technologies that we don't even know exist right now. And so how do you counsel patients about things that are so unknown?

And so what we've done to help to meet that need in the context of the Biobank is we've created a community advisory board that meets every other month and discusses some of these developments that are happening in genetics. This advisory board reports up to the Biospecimen Trust and Oversight Group, and ultimately has the ability to influence the ways in which the Institutional Review Board evaluates uses of those samples and materials in the collection.

This advisory group meets regularly, as I mentioned, and helps us with a variety of different things, everything from developing new educational materials and content for the general public to looking at particular proposals to use materials or to establish new types of collections. And I think that, as these areas of research expand and people are starting to utilize individualized medicine in other contexts, these types of community engagement exercises are going to become even more important.

It's a way in which we can connect to patients outside of the hospital and get their perspectives on what they're excited about and what they're concerned about. It's also a way to disseminate those deliberations to individuals that are in the collection. So we summarize the content of these meetings that we have, oftentimes. We share them in newsletters, and sometimes that will generate additional contacts with folks in the community as well.

So I'm happy that we've been able to allow some time for questions. And let me just recap a couple of broad ideas that I was hoping to convince you about while I was giving my talk today. Looking ahead, I think we should anticipate that genomic medicine is going to be one of these disruptive technologies. It's going to change the ways in which people think about medical care. It's going to change the ways in which doctors and patients interact with each other.

This is not just a passing fad. It's not something that's one technology that's going to be easily integrated into the delivery of other health care services. This is one of those technologies like the electronic health record, that's going to have ramifications for the delivery of care for decades to come. This is something that I think that we should all be mindful about.

Looking ahead, we should work to establish realistic expectations about what that type of testing can provide now, when we are in an era where there are so many uncertainties about the significance of various genetic test results. We should aim to develop clinical support tools, recognizing that more and more physicians will be able to utilize these tools given that the cost barriers have gone away and that more people are going to be experimenting with utilizing genomic tests in their practices.

And we should create an infrastructure for managing and interpreting whole genome sequence data. And I would add to that, an infrastructure that really is designed to allow for flexibility in responding to patients' needs at various points in their care. So an individual that gets a genomic tests done when they're 22 years old because they're curious about maybe their ancestry or maybe they're curious about whether they happen to have a very specific familial risk that they know about-- that individual's interest in getting incidental findings may look very different from that same individual's interest in those findings when they're 32 years old and are now planning a family. And so how do we make sure that we have an infrastructure that allows us to go back to those patients over time and adjust the information that they receive based upon the changes in their life and changes in their medical needs.

And in that regard I think that bioethics does have a role to play in helping with that translational process and the emergence of individualized medicine. Two last slides here. One, I want to thank several of the people that are in the room for their assistance, and again Dr. McCormick in particular for allowing me to utilize her data in this particular talk. And the remarkable support staff that we have in our group, all of whom are wonderful folks.

And also want to put in a small plug for an October conference that the Center for Individualized Medicine is hosting. And you can learn more about that on the web site. This is a very, very large conference. At least it was last year, and we hope that it will be again this year. There are roughly 750 people who attend this, and if you're interested in learning more-- not just at this high level about what's happening in terms of advances in individualized medicine, but what's happening on the ground-- this is an excellent conference to attend because it really will provide that kind of currency.

So with that, let me just thank you again for the chance to speak and answer any questions.

[APPLAUSE]