28TH MEETING OF THE SECRETARY'S ADVISORY COMMITTEE ON HERITABLE DISORDERS IN NEWBORNS AND CHILDREN

Friday, September 14, 2012

AFTERNOON SESSION

1:30 p.m. - 2:30 p.m.

Humphrey Building

HHS Headquarters, Room 800

200 Independence Avenue, S.W.

Washington, D.C.

APPEARANCES

COMMITTEE MEMBERS:

JOSEPH A. BOCCHINI, JR., M.D.

JEFFREY BOTKIN, M.D., M.P.H.

CHARLES HOMER, M.D., M.P.H.

FRED LOREY, PH.D.

DIETRICH MATERN, PH.D.

STEPHEN MCDONOUGH, M.D.

ALEXIS THOMPSON, M.D.

CATHERINE A.L. WICKLUND, M.S., C.G.C.

EX-OFFICIO MEMBERS:

COLEEN BOYLE, PH.D., M.S.

CHRIS DEGRAW, M.D., M.P.H.

DENISE DOUGHERTY, PH.D.

KELLIE B. KELM, PH.D.

MELISSA PARISI, M.D., PH.D.

DESIGNATED FEDERAL OFFICIAL:

SARA COPELAND, M.D.

APPEARANCES (Continued)

ORGANIZATION REPRESENTATIVES:

NATASHA F. BONHOMME

FREDERICK M. CHEN, M.D., M.P.H., F.A.A.F.P.

JANE P. GETCHELL, DR.P.H., M.T. (ASCP)

CAROL GREENE, M.D.

MELISSA PUTNAM

BETH TARINI, M.D., M.S., F.A.A.P.

MICHAEL S. WATSON, PH.D., F.A.C.M.G.

MARY J.H. WILLIS, M.D., PH.D.

C O N T E N T S

P R O C E E D I N G S

CHAIRMAN BOCCHINI: All right. It's time to get started. So if everyone would take their seat?

(Pause.)

CHAIRMAN BOCCHINI: All right. Thank you.

All right. So for our after lunch presentations, we have two. The first is by Meredith Weaver, and this will be a discussion of

the carrier screening draft review.

Dr. Weaver is a board-certified genetic counselor and associate project manager at the American College of Medical Genetics and Genomics. In this capacity, she coordinated the implementation of ACMG's work unit study now in the analysis phase, oversaw the development of the genetic services directory, and is currently co-leading the expanded population-based carrier screening policy recommendations inquiry.

Dr. Weaver is also -- has also worked as a pediatric and adult genetic counselor at the University of Maryland in Baltimore, where she held a faculty appointment with the genetic counseling graduate program from 2006 through 2011, serving as a lecturer, clinical supervisor for genetic counseling and medical students, and a thesis adviser.

Her major research interest is patient decision-making during critical points in the sequence of management and treatment. So we welcome Dr. Weaver.

DR. WEAVER: Thank you. Thanks for having me for this talk, and thanks to everyone for coming back after lunch. I appreciate it.

So my talk is a little bit different from the title that's in the agenda. So instead of reviewing the draft, we're going to do the 30,000-foot view of the results. The draft report is actually 70 or 80 pages. So, hopefully, that will make you a little bit happier than going through that.

And the other thing I wanted to tell you is that my slides are significantly different from what's in your briefing book -- or electronic briefing book. So if we can focus on what's on the screen so that you don't get a little bit confused. Because I suffer from what I submit 2 weeks prior is not the same from what I do on the day of.

So just to reiterate, this is the charge from SACHDNC that was put forth in 2010, and to engage a multidisciplinary stakeholder group using the modified Delphi process to collect and document perspectives on public health, personal health, and

healthcare system readiness and needs for expanded population-based carrier screening for genetic conditions with the expected end product including an outline of recommendations and a road map of considerations.

So I put in my next slide just to really put side by side 2010 as well as today's reality because just in real life, projects change over time. So back in 2010, we were examining carrier screening issues and putting forth guidelines. Whereas, what has happened and what we have now is similar, but I just wanted to really hit home the points that we have points to consider when screening for a condition. And these are both general points to the screening process and condition specific. And I don't mean a particular condition, but in general when you're talking about positive predictive value, that refers to a condition.

And also what we have now is not currently intended to be used as a list of which conditions to screen for and when to screen. So it's not a yes/no

type of thing. It's, again, points to consider.

So the parameters that we used, the things that people were queried in the survey, there was four criteria, and they were asked about the desirability of an issue, the feasibility of an issue, the importance. And given those three criteria, what is their confidence in their judgments that they made?

There were five topic areas that the questions in the survey fell into, fell nicely into -- social issues, economic issues, psychological issues, education and communication issues, and then test issues.

Our definitions of consensus and nonconsensus, that's the part of the Delphi, was we were looking for -- we had what we called a "super majority." We were very conservative in what was considered consensus. So less than 20 percent disagreed with the majority opinion.

So, obviously, 51 percent could be considered consensus, but for our particular project, we started very conservatively. And

nonconsensus then was the flip side of more than 20 percent disagreed with the majority. So, again, 20 percent, we can either talk about that or not talk about that, but I recognize that that's very conservative.

So moving right into the results, and again, this is the 30,000-foot view. I'm going to start with the consensus results because this is what the majority of the results were. So most of the emphasis is on the consensus.

So the people who were queried in terms of social issues, they reached consensus around the desirability of the issues. And sometimes it was desirability and feasibility. So an example -- the three examples are including, but of course not limited to, just to refer back -- this is a long report. So I'm trying to give you the high-level kind of things that really jumped out at us.

So it was desirable to consider the level of detail of informed consent. People agreed that that -- we need to think about the level of detail. It was desirable to determine whether disparities

exist in insurance coverage. As one person said, we all know disparities exist.

It was desirable and feasible to disclose conflicts of interest. This shouldn't be a problem for people when we're talking about is a practitioner in conflict of interest with test development, for example.

The next topic areas is the economic issues. And again, the consensus centered around the desirability of issues. So some examples including, but not limited to, yes, it was desirable to consider the cost of screening to the individual. Yes, it was desirable to consider the costs of follow-up services. And yes, it's desirable to consider the cost-effectiveness of the screening to the healthcare delivery system.

So, again, this is what people were agreeing to. Agreeing with. Sorry.

So the third topic area was the psychological issues, and much like the economic issues, there was consensus around the desirability of certain things. So consensus that -- consensus

to determine whether psychological support is available.

That it's desirable to determine, that it's desirable to understand the psychological implications of carrier identification. That it's desirable to determine the potential harms and benefits, the positive implications as well as the negative things that happen to a person by being identified, having their carrier status identified.

More results. The fourth topic area was education and communication. Desirability again was where consensus fell down. It was desirable to educate the public and healthcare professionals about carrier screening. Our respondents thought it was desirable to provide comprehensive genetic counseling. It was desirable to engage in shared decision-making, and it's desirable to perform outreach activities.

The last topic area is test issues. This is a little bit different from the previous ones because there is consensus around desirability and importance. Importance is one of the criteria. And

I just separated these by a space because the first three are characteristics of a test, and the last three are characteristics of the testing, more characteristics of the testing procedure.

So robustness of the test. Yes, we want -- it's desirable and important to consider that. That the test is widely available. That it helps in reducing the cost. That it's desirable to think about reducing the cost of the testing.

In terms of testing process, it's desirable and important to consider preconception as the carrier screening timing, to understand the natural history of the disease before we're going forward with carrier screening, and to know from which population the frequency of the mutation was identified and is it a population that the person who's being tested belongs to?

So those, again, are the really high-level results of where consensus was found. The next slide is the nonconsensus. So, again, this is more than 20 percent disagreed with the majority opinion.

So, in general, this is around the issue

of feasibility. So people did not agree whether something was feasible or not. Kind of makes sense. Or it makes sense to me, I guess.

So was it feasible to determine individual perceptions of risk? Some people said yes. Some people said no. But it was not uniform.

Is it feasible to provide comprehensive genetic counseling? Some people in their comment section remarked what's comprehensive? What qualifies as comprehensive? So that could have contributed to the nonconsensus.

Is it feasible to have nonexclusive licensing of a test? Again, there was people on both sides of the fence.

The return, ownership, access, and storage of the results. The return, when should it happen? Who should it go to? Who owns the results? People listed multiple potential owners.

Determining is it feasible to determine the burden carrier screening puts on the healthcare system? Some people said yes. Some people said no.

Is it feasible to retest when new

information about a condition or a test becomes available? Again, people did not agree upon these.

So this is kind of my big slide. So the summary of the results, and this would be something akin of a portion of an executive summary. So the results are consistent with popular discourse on population-based carrier screening. So we saw similar issues and similar red flags.

In our report, it could be related to -- the issues are related to carrier screening in general or to specific individual hypothetical conditions. There was general agreement for the desirability and sometimes importance of issues, but conversely, there was little agreement regarding the feasibility of -- put in your verb of choice -- assessing, determining, considering, depending on which issue we're talking about.

So consensus on desirability and importance, nonconsensus on feasibility. That's the big take-home message.

So looking forward, so this is kind of the bad penny that keeps showing up. We were here in

May. We're here in September. We're going to come back in January. Hopefully, to have a report with recommendations about carrier screening in general and criteria for specific hypothetical conditions prior to the January 2013 meeting.

And this is just logistics in terms of the workgroup members are going to review the draft and then send it on to -- we'll send it on to the Advisory Committee meeting, the Advisory Committee to be discussed in the meeting.

So during 2013, it's anticipated there will be a vote. But of course, this depends on once people look at the draft if there's major issues, concerns, then the vote would be tabled. Determine the final disposition of the report. That still has to be determined. And ideally, use the report to inform subsequent discussions about population-based carrier screening.

So the next slide is a reminder of who's on the workgroup, and these people have done a lot of work for free and as volunteers. So we appreciate that. And then the last slide is just

let me know what you have questions about.

CHAIRMAN BOCCHINI: Thank you, Meredith, very much.

DR. WEAVER: Sure.

CHAIRMAN BOCCHINI: Are there any questions or comments? Freddy?

DR. CHEN: Thanks. A great presentation.

Has there been much -- I wonder sort of how the workgroup has been -- has discussed the distinction or if there is one between population-based and universal for carrier screening? How's that gone?

DR. WEAVER: Right. So we have -- we've had lots of discussion about what does carrier screening mean and what are people thinking of when they're responding to the term "carrier screening?" We haven't had as much discussion about those universal versus population-based words, but I think that kind of falls under the same umbrella of do we even know, are people responding in the same way when we're talking about carrier screening?

I should say that one of the impetuses for

this project was the coming onto the market of the different DTC companies. And so, we didn't query people specifically about universal screening and population-based carrier screening. So my answer is just that we mostly talked about what do you think of when you hear the word "carrier screening?"

So that issue in particular we didn't query. Were you looking for more?

DR. CHEN: No. It's just that one of the other important distinctions between it is sort of whether it becomes a public health mandated type thing versus a clinical population-based piece.

DR. WEAVER: Right. Right. Yes, and then that would be kind of a high-level introductory point. But we didn't query that.

CHAIRMAN BOCCHINI: Additional questions, comments?

(No response.)

CHAIRMAN BOCCHINI: If not, thank you very much. We look forward to the draft coming before the January meeting.

Thank you.

DR. WEAVER: Okay. Great.

CHAIRMAN BOCCHINI: All right. Next we have wrap-up here. Cathy Wicklund, a member of the committee, is going to discuss a summary, provide a summary of the IOM meeting on assessing the economics of genomic medicine. Cathy?

MS. WICKLUND: Thank you. And thank you all for staying until the bitter end.

I know economics of whole genome sequencing is riveting. It is to us. So I was asked by the committee to give a summary of a day and a half workshop that we did in July, and this was sponsored by the Institute of Medicine, translating genomic-based research into health.

And this is a group that's been meeting for about 5 years now. Several members are in the audience and were in attendance at this workshop, and we have several other workshop summaries.

In the past, we've looked at the value of genomic and genetic testing. We've also looked -- our last workshop that my subcommittee did was on integrating large amounts of genetic/genomic

information into clinical practice and how that's going to look.

So just to give you a little background on how we got this actual workshop, through these workshops, we try to build on our topics over time. And when we're talking about whole genome sequencing and integration into the clinical care, one of the things that keeps on coming up is the economic implications of this and the cost of this.

And certainly, we hear a lot of people discuss the actual cost of the technology and how it's dropping. But we also -- and we also hear talk about the interpretation and reinterpretation. But there's also much further downstream consequences of incorporating this information into the medical record. And that was where we were particularly interested in.

So we definitely agree that low-cost genome sequencing are being considered and being used for routine clinical use. And there really is a tension that exists between experts who feel that obtaining this information before having a clear

clinical picture could be premature and those who feel that the information could empower patients and providers to make decisions proactively rather than waiting until symptoms occur.

And we also wanted to kind of acknowledge that available sequencing data could also be used at point of care. So these were some of the discussion points that led us to where we were at, and we realized there's a lot of different issues surrounding this. But this particular workshop was really addressed at one particular issue of the debate, and that was, again, the economic issues that could arise in the course of integrating genomic information into healthcare.

We made several assumptions to go forward. One of the things we've learned about these workshops is the more we can kind of lay out ahead of time, perhaps the less debate we get in over some issue that we really don't want to spend our time debating about. So we try to do some assumptions.

One was that whole genome sequencing costs are acceptable and fixed, and this did not include

interpretation costs. That data storage costs are acceptable and fixed, but this did not assume that we could transport the data electronically. And that these tests are available in a healthcare encounter.

So just to give you a background on how the workshop was actually set up, what we wanted to do was follow one woman over about a 15-year period at three different points within her life span. And one point was preconception, so more of a well woman exam. The second point was at she presented to her physician with a deep vein thrombosis. And the last point in time was with lung cancer, non-small cell lung cancer.

And we ask a lot out of our panelists, too. I kind of feel sorry for them sometimes. If anybody's been there, they can appreciate this. We wanted them to think about three different models that they could apply to these clinical scenarios. One model being that routine standard of care right now. So targeted mutation analysis, which you would think about what is this person at risk for

preconception wise? I'm going to offer carrier testing, but not really go beyond that.

The second model we wanted them to apply was whole genome sequencing with the clinical data that was relevant to that particular situation, but also some actionable variants.

And then the third situation we wanted them to apply was whole genome sequencing. And as I think Greg Feero says, "the full Monty." So you're basically giving all the data relevant to the clinical situation, the actionable variants, and also significant secondary findings. And again, all of this really could include these variants of unknown significance, also things that have a lower effect size.

And then the second day of our workshop, we really wanted to identify research needs that arose and issues that came up during our discussion on day one. And so, we asked our panelists, we started out the day with realizing that if we're going to talk about economics and genomics that perhaps the people that are experts in genomics

might not be as knowledgeable about economics, and those that are experts in economics might not be as knowledgeable about genomics.

So we really asked -- we asked Dr. Jim Evans and Dr. David Veenstra to come and talk to us about those two particular things, which I think was a good idea. We even asked Dr. Veenstra to come back after lunch and to reemphasize some of the economic points for us because of our lack of knowledge of the nuances between even being an economist and a health economist. You know, that was different as well.

We had -- on each panel, we had a clinician, we had a futurist, and we had a patient or consumer. So we tried to get at different stakeholders. And then also we had several economists come and do a panel discussion after each one of these discussions. So it was a highly complex theatrical performance, I think, but we managed it.

Okay. So Dr. Evans started out with a great presentation about really thinking about what

the promise of genomic medicine held, but then also perhaps the reality through his eyes. And I have permission from him, by the way, to share some of these slides and from Dr. Veenstra as well.

And the promise of genomic medicine was that potential to shed light on genetic underpinnings of every disease. The assessing risk of common diseases -- heart disease, diabetes -- and actually do something about it.

A lot of promise about preemptive delineation of select pharmacogenomic variants. As an adjunct to newborn screening. And finding those relatively unusual individuals who are at a high risk of a preventable disease. And also enabling a variety of reproductive decisions.

And he did this nice -- you know, he went through each one of these and where we were at with each one of these. But he did this really nice scorecard that I'm just going to summarize for you and gave different utility to each one of these promises. He actually did checkmarks. I did stars and small stars and then Xs.

But he felt that, yes, it's going to be a power -- whole genome sequencing is going to be a powerful diagnostic tool for patients with primary genetic disorders. He also thought that it could improve treatment of cancer through genomic somatic analysis. He gave a big star to prevention of rare diseases through selective genomic discovery of highly penetrant mutations and also preconception screening to inform reproductive choice.

He gave a smaller star to perhaps the utility in newborn screening and gave some pretty big Xs to broad preemptive pharmacogenomic application, just given the number of really diagnostic -- DNA diagnostics we have in conjunction with therapeutics at this point in time. And also an X to this prevention of common disease through genomic risk assessment, given the low relative risk that's associated with some of the GWAS findings.

We then went on to talk a little bit about health economics. And I am not an economist. So if you have questions about this, is there one in the audience? Is Scott here? He can take those.

But basically, it was nice. We went through the different types of economic analysis -- cost minimization, cost benefit, cost effectiveness, and cost utility -- and really what things are taken into account when you do each one of these economic analyses.

And what Dr. Veenstra really wanted to emphasize to us was that health economics is truly about measuring value, and that cost-effective analysis evaluates not only cost, but also the benefits of a healthcare intervention to assist in decision-making. In other words, is the improved clinical outcome enough to justify the intervention? And it also tries to assess downstream consequences.

Most of the interventions that we talk about, a lot of them will fall into that upper right-hand quadrant that you see there where you see an increased cost and also an increased effectiveness. Where you would really like to be is in the bottom right-hand quadrant there, which is low cost with high effectiveness.

But the reality of the situation is that you're usually up in that right-hand quadrant. You definitely don't want to be in the upper left-hand quadrant. We shouldn't be doing those. However, we have. So that's what you want to try to avoid, though.

There are some simple misconceptions that he wanted us to recognize. One being that cost effective does not equal cost saving. Expensive interventions are not cost effective. Inexpensive interventions are cost effective. So he really wanted us to be aware of some of these misconceptions that we might have.

So, again, in summary, what he presented was an economic -- helping people to understand what's at stake, what's the decision is the point of this. Careful cost-effective analysis is about analyzing decisions, and you really have to clarify a lot of assumptions. You have to evaluate uncertainties, and it's not primarily about the cost, but about tradeoffs that you're making.

So the big question, of course, is next

generation sequencing cost effective? And I'll let you know I don't have an answer. Okay, I lied to Nancy Green and Coleen Boyle yesterday when I said that I had an answer. That was just to get them here.

(Laughter.)

MS. WICKLUND: Keep them to the end of the day. But we have lots of questions, as usual.

It's not as much about the cost, and this is, again, from Dr. Veenstra, as much about what is the outcome that we're actually trying to measure here? Are we measuring how many base pairs are sequenced? And is the technology cost effective?

Is it the number of variants that can be identified by this technology? Is it the number of diagnoses that we can make? Is it the clinical actions that we're going to take based on the results, or is it patient outcomes, reducing morbidity and mortality? And what are we comparing it to? You know, we have to think about what we're actually comparing it to.

So how do we determine the effect of

genomics on the healthcare system? And really, as we went through the day, again, this was a tough exercise, and I don't think our expectations were that somebody was going to be able to get up there and truly outline what the costs were of this.

What we really were trying to get at, if you're a clinician or a consumer and you're faced with these different models that we asked them to go through, what are you going to do differently? As a consumer, are you going to insist on different screening? As a provider, are you going to proactively do something?

With the first scenario that we gave in the prenatal setting and the preconception setting, the woman was a smoker as well. And really, that was the overriding issue. When it came down to everything else that was -- that she might have been at risk for, smoking was the big issue. And that was where the amount of time that that clinician was going to be spending, her try to behavior change was on the smoking because that had the largest impact on outcomes more than the other things that were

identified.

So we came up with a list of, well, first of all, how do we assess these needs? We definitely determined, obviously, this requires a spectrum of expertise and perspectives. We need economists. We need multiple stakeholders to try to answer these questions.

And some are strictly economic research, but a lot aren't. A lot of the questions that we need to answer in order to do the economic research has to do with outcomes, right? With patient-provider behavior. So a lot of it has to do with technology development, epidemiology, behavioral research, LC, education, and the health services.

And we only came up with 20 additional questions. That's not too bad. We did put them into different categories, and these aren't all questions that need to be answered, but I think that issues that have come up over and over or some of them over and over again in our discussions at the roundtable, you know, really about, for instance, with comparative effective to research. Every time

we have a roundtable, it's like I think a broken record where we come up and we talk about how to collect evidence and what is enough evidence and when we can -- and this meeting, too, it's an issue that we have in thinking about what to add to the newborn screen.

So we have a need for evidence-based development. We need a good infrastructure, and we need innovative approaches for prioritization. We need to determine if and how genomic sequence information modifies healthcare provision and patient outcomes. I mean, that's a big thing we don't know right now.

And most of the data has been more on direct-to-consumer studies. We're looking at populations that are usually early adopters, and we're trying to figure out where their behavior might be modified. But they're already doing a lot of things that they should be doing, and they're not always providing this information to their provider in the first place. And again, not at all generalizable to the population that we're looking

at.

The impact of increasing the accuracy of sequencing. So if we argue that the sequenced data will be stored and available at point of care, are you going to be able to really trust that sequenced data from 2 years ago, or has the accuracy of the sequenced data increased enough that we're going to want to resequence rather than rely on 2-year-old data?

The evaluation, we're still working on this, right? The evaluation and proper use of family history to guide medical decision-making and integrating that into the electronic infrastructure.

There's other health economic methods identified. We need better, quicker approaches and frameworks to performing health economic evaluations of genomic testing. We need evaluation of evidence thresholds for data in hand versus data that must be obtained and costs of further research.

Again, this is really getting at that issue of how much evidence is enough, and are we really going to be doing RCTs? What is the cost of

that? Are there other ways that we can get this information to help us make decisions in a quicker way?

The divergence of economic assessment models in public health clinical care and academics. It's one thing to do academic exercises or to implement something in a tertiary care institution, but to try to implement into the community we all know is very different, and how is that really going to play out?

And this was a big one. This was we heard a lot from leaders or individuals who head healthcare institutions or hospitals about how do you -- how are you going to integrate this in a zero-sum or negative-sum game? We have a shrinking pool of resources, and this obviously comes up in our discussions with the Department of Health, of trying to get that something new implemented where there's no funding to support that implementation, and you're doing more with less.

And really, the idea is what's going to be kicked out in order to try to integrate some of

these new things into the system. And really, has value been established that we should try to push forward integration into the system over some other? You know, we're all fighting for the same piece of the pie.

Lots of words on this one. When is genomic sequencing cost effective? Again, example, newborn screening scenario, we had considered using this with data being used over a life span. We need better education of genomic scientists regarding economic analysis. And also integration of economic analysis on ongoing studies, thinking about how can we incorporate this into the studies that we have going on at this time.

What are the methods, infrastructure, including informatics in health systems to follow downstream consequences providing sequenced data? So how can we follow this real time and be able to get a better assessment of what's being implemented?

Is cost reduction demonstrable? Demonstrable, right? Thank you. It's a long day.

Study of provider preferences by provision

of genomic medicine. Evaluation of barriers to implementation. Economic incentives for tests and evidence developed. We talked a lot about billing, reimbursement, CPT coding and the problems there. Determination of relative contribution of environmental setting on cost effectiveness as well.

And then the very last thing that we really spent time or the last thing on this list is patient-centered outcomes. Developing outcomes data on informed consent.

We don't have really good information right now on a lot of how information is being transmitted and communicated and the effectiveness of that and how are we going to consent people for whole genome sequencing. I know a lot of people are working on that.

Stakeholder engagement and increasing participation in clinical trials. Development of improved methods for assessing the value and personal utility. We talk a lot about personal utility. That ranges on what people feel that definition includes. And one of the things we

talked about was trying to get at that concept a little bit more deeply, and can we at least identify a set of shared values or shared ideas and maybe think about trying to get rid of some of the outliers?

But that's a tough one. Some people, the personal utility is "I want to know because I want to know." Other people, it's defined a little bit differently.

And of course, the other issue that came up over and over again was access issues and disparities. And really whether or not this information is going to be accessible to the population or is it going to be accessible to those who can afford to have this information and the looking at the minority and SES disadvantages.

So, again, these were just some of the main discussion points that we kind of came up with. Really no answers, just more questions. And I do want to acknowledge that, again, this is the work of the entire roundtable.

Greg Feero was the workshop chair, and I

was the co-chair on this. But it really was the work of the Clinical Practice and Public Health small group. And I also want to recognize all the work that Adam Berger, Dr. Adam Berger does -- he is the roundtable director in the audience today -- and the staff. And they're really the ones that kind of move all of this forward.

And I'd be happy to take any questions at this time.

CHAIRMAN BOCCHINI: Thank you, Cathy.

Questions? Jeff?

DR. BOTKIN: Well, sounds like a fascinating meeting. I guess in part what I'm not seeing here, I wonder how much conversation there was about the drivers of the process. It seems to me that so much of the issue now is being driven by test. And it seems to me that so much of the issue now is being driven by test vendors and estimates of cost per base pair, as opposed to the total cost of testing with analysis and follow-up and all of the downstream implications.

And so, this is a large system look, which

seems to make sense, but yet the people that are making the decisions aren't necessarily impacted by the system. They're sort of impacted by what they see as an early adopter of a technology that's being sold to them as the next best thing for their patients.

MS. WICKLUND: And I think, you know, that's what we were trying to do with this workshop was to shift the discussion from the cost of the technology, which is fine. Yes, we all get it. It's going to be cheap. To really the cost of what is it really going to -- what kind of burden is it going to place on the healthcare system?

And we were really trying to get at that. And to move the discussion away from the cost of sequencing towards this interpretation piece. And we talk a lot about interpretation, but that's just the tip of the iceberg, too, right? It's the reinterpretation. It's the storage.

But, and again, also do we burden a system with a lot of information that we don't particularly know what it means? And it is hard. This

technology is out there. It's being marketed and through direct-to-consumer, but also directly to providers.

And I do think one thing that we've learned over time and through our past workshops that providers also want to feel like, though, that there's value. There is a value or that it's going to change something about what we do with our patients, and it's going to change my clinical care.

And until you can tell me that it's going to do that, I'm not sure I'm going to utilize it. And we get that feedback through our roundtable meetings, and I'm also part of the eMERGE collaboration. And we get that feedback there, too, is that you want me to incorporate this GWAS data with a relative risk of 1.2, I don't really see how this is going to help me.

And part of it is trying to see is it a leverage point we can use for behavior change? Would that help? But again, I think there is also pushback from providers to say I don't have time to really implement this until it really can prove its

value.

DR. TARINI: Catherine, did the discussion focus across age groups, or did it focus more on pediatrics? The reason I ask is, and I'm one who will agree that the potential for creating more cost on the backend is a possibility.

But in my conversations, it's been often geneticists who see whole genome sequencing as a way to find etiologies for those children who walk around with a delay, for example, without an etiology. And they've already gone through like a $1,000 test. So what's another $1,000?

So the degree to which in pediatrics we're going to actually be using it to sort of help these -- find these rare cases, these enigmas and turn them into answers versus and then an extent to which you will suppress any other data raises a different issue of cost in pediatrics perhaps than it does in adult medicine.

MS. WICKLUND: I would say the focus really focused more on adult medicine because of our scenario that we gave with the well woman beginning

in her life span. I think because -- I mean, we're already, right, doing exome sequencing, whole genome sequencing in pediatric settings for kids. Perhaps we might be cherry-picking some of those, right? Looking at the kids who have been through multiple, multiple testing.

And the idea that over time, it would be cheaper just to go ahead and sequence that child in the first place or start with the idea of like a real sequencing panel of targeted genes versus a virtual where you're sequencing the whole genome, but you're only looking at those targeted genes.

But I think that that is more -- I think it's going. So we weren't focusing as much on that conversation.

DR. CHEN: Cathy, we were at the same meeting, but you actually took notes and did a great job. I do -- what I do remember taking away, though, from the meeting was that it was one of the first opportunities to really clarify this distinction in the field of genomics around what economists call some of the difference between micro

and macro economics.

And a lot of our discussions have always been around the micro level around the cost of the tests and sort of what that really means and what the clinical utility is and that kind of thing.

But the macro level, which we heard especially from leaders of health systems who were at this meeting and are critical to our discussions, the world of genomics doesn't live in a vacuum anymore, and it's not the same fee-for-service, insurance-based system that we are used to thinking about.

And sort of where genomics will be in a world of accountable care is a big piece, and this was one of the first times that we were able to try to draw that out.

MS. WICKLUND: Yes. Well put. I agree.

CHAIRMAN BOCCHINI: So what's the next step?

MS. WICKLUND: Just maybe one or two calls since we actually had this. I mean, there's another workshop being planned, and Adam can talk to you

about that one.

For our group, what we're trying to do is ask the speakers, moderators, like Freddy was a moderator, and some of the committee members to write some perspective pieces on some of the topics that came up here. So whether or not that will be like a white paper that we submit or just perspectives that are within the IOM.

And we have a Web site, the actual roundtable has. On the Web site, there is our roundtable with all the products. And all these workshops get summarized in books that are available to look at.

But we haven't really decided yet from a workshop point of view how to follow up on this. And I think as members of the roundtable, we are limited on some of the things that we can do. So sometimes the next steps happen not necessarily outside of the roundtable, but in trying to make perhaps recommendations, we need to take that beyond the roundtable.

So, Adam, I don't know if you want to

comment on the next workshop that's being planned?

DR. BERGER: Sure. Thanks, Cathy. That's a great summary of the meeting, by the way.

So we actually have a few workshops in the works at the moment. We've got a February 27th date set where we're going to be looking at co-development of molecular diagnostics and targeted therapeutics. Specifically, looking at this from the diagnostic standpoint, some of the issues that are evolving and being refined right now in terms of moving diagnostics forward in that space.

The second workshop that we're working on is going to be looking at drug repositioning and repurposing. The use of genomic and genetic information to help in that event, and that's going to be scheduled for June 24th.

CHAIRMAN BOCCHINI: Thank you.

Other questions or comments?

(No response.)

CHAIRMAN BOCCHINI: If not, again, Cathy, thanks for an excellent summary. It's great.

All right. I have one announcement. It's

been decided that our next meeting, our January meeting will be a teleconference. So we will be doing that in a virtual setting.

All the details have not been worked out, but that's the plan so we will not have to fight 6 to 12 inches of snow in coming here. We'll be in the warmth of our own offices, I guess. So you'll get more details about that as we get closer to the next meeting.

And lastly, I just want to thank first the staff for organization for the meeting. It's gone quite nicely. I want to thank everybody for their contributions around the table, committee members, liaisons, and then members of the audience. So we appreciate everything that you've contributed to make the meeting successful.

If there is no other business, we will adjourn. Thank you all very much.

(Whereupon, at 2:10 p.m., the meeting was adjourned.)