



Presidential Commission *for the* Study of Bioethical Issues

TRANSCRIPT

Incidental Findings in the Direct-to-Consumer Context

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SESSION 7: ROUNDTABLE DISCUSSION

DR. WAGNER: We want to do in our final session, Roundtable Session today, what we always afford folks. And those of you that were here this morning saw the drill, so you won't be surprised at the question that begins our conversation. And that is to run down the table and ask you in your particular areas in the sessions that we had this afternoon on both education and direct-to-consumer issues regarding incidental findings, that one thing you would want to be certain that our Commission takes into consideration as we prepare the report.

So since Tom just put some in his mouth, I'll start at the other end.

DR. GUTMANN: Start in the middle.

DR. WAGNER: Start in the middle and go out? Carol, let's start with you. I can keep track of this.

MS. KRUCOFF: Thank you. One thing: As the representative of the patients, keep the patients in mind. Remember. These are people we are talking about and their lives, and do communicate with us honestly and compassionately. And give us some help through someone trained who can communicate well, because not every physician knows how to communicate well. Thank you.

DR. MORREIM: Can I do one from this morning? Leftovers?

DR. WAGNER: Sure.

DR. MORREIM: Okay. Thank you. It occurred to me that in the research setting, when you talk about seeing something that's on sort of a low

quality imaging study, and so forth, well, gosh. You know. It looks kind of funny, and should we follow it up? It occurred to me that within the usual parameters of the contract undergirding a research grant, it could potentially be actually or just this side of fraudulent to spend research funds on just what amounts to basic patient care. And it occurred to me that just as we now expect these contracts to describe, one way or the other, are you going to handle or pay for research related harms? Okay.

That's kind of, maybe, to consider whether or not these contracts should include something one way or the other. Are you going to put forward any money for at least initial follow-up of research-related, incidental findings? It's kind of pointing in the opposite direction, but something to think about, because I think we need to be very careful to expect researchers to use grant money that is circumscribed by contract to follow-up something that amounts to frankly ordinary patient care.

DR. WAGNER: Good point. Danielle?

DR. OFRI: Someone earlier this morning said that clinicians were well-trained in only ordering tests for specific reasons. I would disagree with that, and I'd want to put the eggs in my basket in terms of educating our future physicians about accurately ordering tests, thinking about consequences before ordering, and the appropriate use of clinical judgment. And then I would add from the patient and doctor point of view that nothing is incidental.

DR. WAGNER: Interesting!

DR. GREEN: And my second piece of advice is for us all to step a

little bit away from the fear that information will be overly traumatizing. We did hear that information can cause anxiety, but we also heard she wouldn't have necessarily have wanted it differently. And while there certainly are people who would say I wish I hadn't learned that, our experience, I think, is growing that they are few. Real autonomy starts with information, having a choice means knowing what your options are, and that's not easily -- it doesn't easily occur if you don't have information.

DR. WAGNER: Interesting. Tom?

DR. DONALDSON: Well, the question, as I understand it, is what's one thing I hope will be in the report. And I think I want to echo something I said earlier.

With respect to the private sector, it seems to me important, not only to talk about regulation, which is critical, but also cooperation at an industry level. So competition is the byword for private industry, and competition can overwhelm even good minds at point. In the animal kingdom, as you may know, even very competitive males often cooperate at key junctures.

And if we stop and think about, for example, the issue of direct-to-market sales, I would love to see that industry get together and talk about handling, say, false paternity findings or talk about -- perhaps even create -- joint arms and create a proscription on selling after-market services. We've just found out that you have a propensity to baldness, and we have a product for you. That's a mistake, and the idea, of course, is only inside the industry can some of these things be known as well as they can outside the industry, and we also live in a

global world.

DR. WAGNER: Gail?

DR. JAVITT: I'd like to echo that. I think standards are particularly important here, because DTC genetic testing is moving much faster than the existing laws and doesn't fit neatly into our understanding; whereas, the practice of medicine, we kind of know what that means. There's clinical guidelines, all sorts of standards. There's state laws that have gone up around that. DTC genetic testing doesn't quite fit. So perhaps voluntary standards can fill that role.

In terms of sort of the take-home message, I think it would be to expand the definition or modify the definition of incidental so that it adequately captures the DTC situation. I mean one way in which DTC is very different is who's starting the process. So when you're in a coma and somebody orders a test, you're passive. And then somebody says, "By the way, here's what we found." With DTC there's a consumer saying "I want this," but the consumer needs to know enough to really make that decision, and then needs to know what it means and what it doesn't mean. And, again, in the context of clinical care, there are guidelines and standards that have developed in terms of sort of the minimum package one must do that have not yet developed around DTC. Thanks.

DR. WAGNER: Danielle, if I could just follow-up very quickly on your comment, being in the education business, when you talk about educating our future physicians, the distinction between the kinds of data that are available now, and we imagine more of this being available that's more prescriptive as opposed to just diagnostic of a complaint or a concern, how do you imagine educating for

that? Our current educational construct is very much not about incidental findings, if you know what I'm referring to.

DR. OFRI: Well, I think there's two components. One is the actual curriculum that we tell our students, and the other is the hidden curriculum, what we show our students. And I think when our medical students and house staff see our defensive medicine practiced, they get a different message than when will we actually say to them. So I think part of demonstrating that, you can, for example, diagnose something with your physical exam and history and not necessarily embark on a million-dollar workup, is something we need to show, rather than just give lip service to.

DR. WAGNER: Thank you. I was just corrected by my Chair. When I said earlier I could certainly start in the middle and get everybody included, I failed to include Joanna.

DR. MOUNTAIN: I was just waiting. I knew I'd get my chance. So thinking about the future with whole genome sequencing being readily available, I think what 23andMe can offer now is at least an understanding that there are ways to communicate the implications of this information even to lay people, but it takes a tremendous amount of effort and curation of the scientific literature and thoughtfulness around how you present the information.

It's expensive to return the information in a responsible way. In fact, 23andMe's entire mission is to do that. So I do feel uncomfortable asking, having been an academic researcher. If I had been asked to fully explain genetic information -- the kind of information I handle now to the participants in my

research -- I would have spent my whole time doing that, instead of actually doing the calculations. And, also, to give people -- we give people choices in what they look at, and that's expensive, too, anytime you build a system that allows people to make choices.

And, yet, that is valuable too, because in a clinical setting, that may not be the time when you want to hear the news, the additional news. Maybe you'll be ready to hear that later, and so we built a system where people can choose at any time they're ready to get a particular piece of information. So these kind of systems are very expensive to build, and I think it can be done. And so we built a system where nothing is quite incidental, because we prepare people and we get them used to the whole idea of genetic information, the whole idea of research. But it's a major enterprise to do that.

DR. GUTMANN: Could I just ask anybody here -- that follows on a lot of what you've said -- are we being unrealistic if we're seeking a set of deliverables, findings that are delivered to people who are at risk for certain disease, and we are expecting non-anxiety, non-trauma? I'm thinking it's fine, Joanna, for a lot of what you deliver, but if you have a choice as a woman to click on the entry to BRCA I or II, and you just in a moment of strength or weakness -- I don't want to bias it -- click on, and you find out you are positive, I don't care whether you're clicking on 23andMe or sitting with your clinician or having a researcher tell you, that is going to be for most people a traumatic moment.

And the question for us is do women need to be somehow fully prepared for that, and what does that mean. Or is it good that there are multiple

ways of finding this out, some of which are incidental to what -- in the case of 23andMe -- what most people sign up for it for? I look to the physician that I have an ongoing relationship with and I am fortunate enough to have a wonderful doctor who knows me well, and I can sit down. And I don't think I'm being unusual.

I mean I think I'm probably in the majority of women who would prefer to learn it from somebody who knows me well, who can tell me, answer my questions, tell me all my options, rather than learn it on a website. Not everyone has that luxury. I mean I think it shouldn't be a luxury, but, so that's just a set of observations with the question for anyone to ask what standards should we be setting for how prepared individual people are for learning something that is by its very nature likely to be traumatic to learn about yourself.

DR. MORREIM: I'm sort of thinking back to the days when we first got HIV testing; and, at that time -- and I'm not recommending anything in particular. I'm just sort of remembering that in a lot of states it was required that you get pre-test as well as post-test counseling, because the information was inherently so deeply troubling.

DR. GUTMANN: At one time, it was deeply troubling, because there were no treatments. It was stigmatized. That's changed.

MS. MORREIM: That's right.

DR. GUTMANN: But that doesn't mean when there aren't treatments, things that were once more traumatic become less. But as Ruth Cowan was the first to say, contexts change; and, we'll have to take that into account.

DR. WAGNER: But we need to be a little careful. Right? I think it's a good question to follow-up on, but just because something is traumatic doesn't mean it's incidental. The HIV test is, I think, falls outside, although it's a direct-to-consumer product, if you will. It falls outside.

PARTICIPANT: No.

DR. WAGNER: Well, it is now. It is now. But it falls outside of incidental finding. It's a direct finding. It's binary. The answer is yes or no; and that's quite separates from --

DR. GUTMANN: I take it the comparison was trauma, wasn't incidental. There are some things that when you learn -- at one point in history, at one point learning you have any kind of cancer, the C word in my mother's generation, it was. And now there are counselors that by the very nature of having a cancer, they're curable. BRCA I and II has a different diagnosis right now. It's also curable if you have a double mastectomy.

DR. MOUNTAIN: This is not an issue we can solve here, but language is really important. The words "tumor," "cancer," and "mutation," even, can be very alarming, just on their own, and a "benign growth," maybe. We find our customers react to the way we present the information. And Robert Green has spent years finding out how people react to the ApoE, E4 news, related to Alzheimers.

Our customers, they read a statistic that says they are maybe 14% at risk through age 80, versus the average being 7%. This to them is not a death sentence. And they're much more open than we might have anticipated being the

scientists who have this sort of mythology around a particular mutation, which is, I think, a very healthy thing. It's partly because this is a new area.

DR. GUTMANN: But I would like anyone to answer. Getting information that is traumatic, isn't in and of itself a bad thing. There is some information that by its very nature is going to be when you get it traumatic, and you are going to have to work through it. And I think the question is who gives it to you, and how do they present it, and are you adequately supported in dealing with it. For all the talk of autonomy, there are other values besides -- and I believe we ought to be treated as people who can make choices for ourselves, but we also ought to be treated as people who need caregivers.

DR. MORREIM: Well, I certainly think so, and I think that's exactly why our recommendations asked for these results to come back through your clinician, though we recognize this is imperfect, because clinicians aren't always prepared, and because not everybody has the clinician scenario. But the other point you're making is that bad probabilities happened to people in all arenas, not just genetics. And we really have exceptionalized genetics in a fundamental way, in part because Huntington's Disease was the first genetic test that we had; and, in part, because it was a set aside from NHGRI to support ethicists to work in genetics that no other domain of medicine had. So, you know. These are historical, more. I mean I'm serious.

DR. GUTMANN: I don't think we're traumatizing forces.

(Laughter.)

DR. GUTMANN: We don't intend to be. That's incidental.

(Laughter.)

DR. GREEN: I think the world's going to look completely different in five years when there are so many inexpensive ways to get your genome and to have a sequence through your doctor, through the Internet, through a tertiary company that you have all sorts of choices. And this false scarcity that we have now has actually disappeared. So some of what we're talking about -- not all of it -- some of it I believe is really a transient problem.

DR. KUCHERLAPATI: I want it to be a little provocative here and ask you the question. You know. Despite the fact that they charged us, the Commission, to look at incidental findings across a broad spectrum of things, much of the focus really has been on genomics. And are we overreacting to all of these issues about the possible harms that could come from finding incidental findings and reporting them to the patients?

I mean with regard to imaging, imaging has been around for a long period of time, and lots of people get chest X-rays every day, and they find all kinds of things. And the doctors will report back to them. The society as a whole, I mean, we're okay. So what is it about genetics? Are we sort of thinking that genetic exceptionalism, this is somehow different than other types of information? Or what is the real problem? I'm trying to get at that.

DR. GUTMANN: But, could I just say, Raju, just in representing the Commission, we are not specifying genetics as something different, that if you have an FMRI.

DR. KUCHERLAPATI: All right.

DR. GUTMANN: Okay. Just say we understand that we're going into this and we specifically decided to go into this as something that's broader than genetic.

DR. KUCHERLAPATI: I recognize that. I'm saying that much of the discussions has been focused.

DR. JAVITT: May I just clarify? I think it's tempting to sort of go down the genetic exceptionalism rift, so I'm not going to do that. We should realize that most diagnostic tests have not historically been available direct-to-consumer. You know. People are pointing to HIV and whole body scanning, because I can't think of any other examples. And, as we talked about HIV testing went through many, many hoops, and I don't know enough about whole body scanning to know how many people really are accessing it and what they're finding. But I can't go get

DR. GUTMANN: The most common direct-to-consumer that was pregnancy testing.

DR. KUCHERLAPATI: Yeah.

DR. JAVITT: Which has been around, which is the reason they amended the Food and Drug Act back in the day was to specifically cover that device.

DR. WAGNER: But even eMedicine, you know, WebMD, is in that category as well, probably less precise -- not probably -- definitely less precise than --

DR. JAVITT: Yeah. So I think part of the struggle is what manner

of beast is this. Right? So, if you look at the disclaimers on the websites, they're saying this is not medical. Talk to your doctor. But, yet, unlike WebMD, you're getting an individualized result. So it sort of walks and quacks like medicine in some ways, but, yet we don't think of it as covered by the practice of medicine statutes, although maybe somebody might argue that it is. It doesn't fit, and I think that's part of why people are anxious. Yes, historically, to that extent it has been big and scary. I feel like that subset anxiety is subsiding a bit, and it's really about the fact that it's not fitting into our neatly understood ways of conveying medical information.

DR. WAGNER: Dr. Ofri?

DR. OFRI: From an internist point of view, to me, the difference of genomics, whole genomics testing versus the chest X-ray, is diagnosis versus screening. They are not the same at all. When we order chest X-ray for a cardiac complaint and then find incidental lung exam, that's entirely different than just taking a genomic screen of everything you have.

And our screening tests, we try to apply evidence-based medicine. We don't do mammograms on 18-year-olds, because the evidence doesn't support it; but, yet, we do genomics for anyone who asks for it. So that's a very different thing. So, while I agree we should look at incidental findings, I see a reason why there's more anxiety, because you are screening with an enormous net with no evidence to back it up, and that's quite different than noticing the mole next to the rash, which is diagnosis.

DR. GRADY: I have two questions. One is I was intrigued by both

of you commenting about creating industry standards, and I guess I have a couple questions about that. One is who would create them? Were you suggesting that maybe the Commission should recommend what some of them are, or just recommend that there are some; and, would it be a voluntary thing whether or not industry's decided to follow them or not?

That's one set of questions. And then the other question I have for anybody, actually, or everybody, in the debates that I'm aware of that have been going on for a long time with respect to research responsibilities related to incidental findings, there's always this comparison to clinical. You know. Here's what we're doing in clinical. Maybe we should do this in research. So I find myself thinking why. Why aren't we doing it more like this consumer model? Why aren't we saying, here's the researcher, here are the things that I'm planning to do. The rest of the things I could do I'm not going to do because I can't validate them, or I don't have the time or the money. And it's up to you. If you want to do it, this is what I'll give you and nothing more. So is there a reason that that wouldn't work for the research environment?

MS. MORREIM: I might actually. I see some reasons to encourage that, because the more we have -- for example, it was proposed maybe have a clinician involved, and so forth, as a clinician. The more we are inviting the therapeutic misconception, not just in the people who sign up to be research volunteers, but particularly in those who conduct the research, we're doing this because it's good for you, and because we're out for your best interest, which is fundamentally confused and can lead to serious mischief. So, in a way, I kind of

see virtue in the idea of compartmentalizing research in some important ways.

DR. GREEN: I would say I agree with that idea very much as well, but I would harken back to Joanna's comments about how much work it would take for any given researchers or bio bank to try to construct that. Now, Zack Kohani at Gene Partnership at Children's Hospital has put forward a model of a sort of you tune it yourself. There's information that flows out to the research participants, and they can pick and choose at any point in time which of them they want to get. And I think that's a brilliant model, perhaps modeled after what you were suggesting; but, I'm on the ICOB of that, the Informed Consent Oversight Board, and it's moving along but it's a tremendous amount of work. So it's a hard task.

DR. DONALDSON: I thought I might respond just briefly to the issue of industry standards, and your question was who does it. And I think the best template is probably successes in the past of industry cooperation; and, typically, those have involved a combination of industry members with especially industry leaders. We might have an industry leader here in the DTC context with 23andMe, trade associations, and sometimes, the industry, so new that it doesn't really have those, and the government.

In the Canadian Chemical manufacturers initiative, the government played a very important role and participated in some of the discussions, but especially in DTC with genomics and the issues we've been talking about. It's an industry ripe for this kind of cooperation. First of all, it says, clearly, this is not an anything goes competitive game, and you want to set that marker very early as the

industry and the innovation evolves; and, also, the stakes are just very high.

DR. GRADY: It seems like it would be true for whole body scanning industry. Right? Same kind of stakes are high?

DR. DONALDSON: Yes, absolutely. Yeah.

DR. JAVITT: And just to add to that, in thinking about standards which I think is a good idea, it's worthwhile considering the extent to which existing standards in the medical context can and should be transferred to the DTC context. So, for example, if ACOG recommends a certain panel for a certain ethnicity, is it appropriate to require or at least expect direct-to-consumer companies offering the same type of testing to adhere to those standards?

DR. WAGNER: I mean just back to you guys really quickly, are we talking standards of data quality? Are we talking standards of the responsibility of data delivery?

DR. DONALDSON: All of the above.

DR. WAGNER: All of the above.

DR. JAVITT: Yeah.

DR. ALLEN: Could I ask a follow-up, just of Ms. Mountain? Has 23andMe, as was suggested, taken a leadership role in trying to organize the industry as you define it around standards that might preclude the need for strong government intervention, or that might be collaborative with government regulation? I'm sort of wondering whether you've already begun to do this.

DR. MOUNTAIN: There are two pieces to the answer there. One is we have in the past had discussions with other company representatives of other

companies about just such standards. Those companies are no longer active in this DTC genome space. It is a small number of companies. That's on the health side.

In terms of presenting ancestry information to get back to a point you had mentioned, I am involved with a very large group of representatives from NIH, from academic geneticists and bioethicists, as well as representatives of other companies. We have been talking for about a year now, where we will be meeting in September here in D.C. to discuss analytical validity, basically the interpretations of genetic information around ancestry.

And there are many more companies in that space, so there's more opportunity for kind of coming together, and maybe more need right now in the sense there's a lot of variation between the companies. So we are involved in that, and certainly open to discussions and thinking about standards with other companies, thinking about the health interpretations of genetic information.

DR. WAGNER: Now, Dan. I think you're up.

DR. SULMASY: Yeah. This follows on that. I was going to say that in some ways all of you in each of the spheres, kind of, it seems to me, wants some kind of guidelines. You know, clinical practice guidelines or best business practices, or I think you were aiming to our best research practices. And it's true that we ought to, I think if that's the case, be careful, also, about the limits of trying to do it alone within our own groups. And there's a great quote from Tim Geithner that self regulation is to regulation what self-importance is to importance.

(Laughter.)

DR. SULMASY: And, that we ought to be sure that there are other

people who are taking part in that, and that may be a role, perhaps, that you may want to carve out for us, because I don't think we could do the guidelines. But, is the task that you would see for us to develop sort of the ethical principles that would guide the structuring of clinical practice guidelines, best industry practices, best research practices. Is that the role you see for us?

DR. DONALDSON: I mean, of course, it depends on what you come up with, but I think the authority of this body could be a significant lever encouraging some of the progressive activities, inter industry activities that we've talked about.

DR. WAGNER: Let me put a question in. Unless it's a direct follow-up on this, let me put a question in. Ruth Cowan is still with us and has a question for the panel. We talked a little about education of our physicians, healthcare providers, but this question raises the concern that with the amount of information that is available growing faster than our understanding of it, what should be doing and should we be recommending ways to educate the public.

She notes, for example, one could get an incidental finding if they are a carrier of some sort of genetic -- carrier of Tay-Sachs for example, or the fact that you are a highly increased risk for breast cancer. These are two, different kinds of messages to get from incidental findings. And, I believe her question is is there a way, and how do you imagine, that we could better help the general populace understand, and is there a recommendation that needs to be made about education of the patient-subject-consumer and responsibility for each of those groups?

DR. OFRI: I think looking at that more broadly, there's an idea in general population that more information is better. Why don't we screen for everything? Patients will come and say, Oh, Doc, test me for everything. And it's a big job to explain that there aren't tests for everything, that many tests are poor tests.

The PSA question; that can be a half an hour discussion right there with the patient. And I put a little bit of onus on the news media who spend a lot of time promoting lots of the new, greatest and latest technologies that are then misinterpreted by the general public who come in for these tests and the idea they'll know more. And so I think societal orientation that holds with both our medical trainees, but society as a whole, that more information isn't always better.

The idea that doing a mammogram every two years might be better than every year is very counter intuitive, but we do have to educate in a larger role, and I think sometimes when recommendation comes from a government body like the U.S. Preventive Services Task force can be very helpful to see that your experts can show that during the PSA test at a certain age for a certain group is actually counter productive is very helpful in educating patients in general population.

DR. WAGNER: We may want to be saying something. I'm sorry.

DR. JAVITT: I want to follow-up on that. I think another, perhaps, useful distinction in DTC specifically is tests that are traditionally offered in the healthcare setting, and this is another way of getting them; or tests that have never been traditionally offered in the healthcare setting, such as the predictive panels,

which are for better and worse, and I'm being neutral on that. But they're not part of what we think of is the standard of care, And each of them raises different concerns.

But it is useful to look at -- and don't let me be repeating myself -- when you're talking about moving the setting, there may be good reasons or not good reasons why, for example, with the PSA or other types of tests, they have been limited to specific contexts in the clinic setting. And, thinking about whether is this the kind of test that it makes sense -- that it is in the best interest of an individual to access in this new way -- is a useful question to ask, or to come up with principles to think about how would we make that decision about whether it is useful to have it in this new context.

DR. KUCHERLAPATI: I wanted to ask a question about how to act on research results. This came up both this morning and this afternoon, and this is a real dilemma. And that is that whenever a researcher gets a patient enrolled in a clinical trial or clinical testing that the expectation is the results will not be given back to the patients. But, let us say there is a patient with a cancer and that individual has consented to give their tumor for analysis; and I did a whole genome analysis on that tumor, and I found a mutation in that particular patient's tumor. And there is a life-saving drug that is available and that potentially that patient could be treated.

What is my obligation as a researcher, and to say my contract with the patient is to not return the results, and just not to do that? Or is there a bigger, moral issue here that I'm obligated, absolutely obligated, to somehow be able to

get this information back to the patient and the doctor so that they would be able to get this life-saving treatment?

DR. OFRI: It's hard for me to say whether they need debate that. To me, that falls under your -- this seems obvious to me, if it has a clinical import to a patient, it's 100% obligatory to discuss it. I don't see any reason why you would --

DR. GUTMANN: As a legal matter or an ethical matter?

DR. KUCHERLAPATI: These have got that straight forward. You know. Many of these kinds of things that I'm talking about --

DR. GUTMANN: As an ethical matter.

DR. KUCHERLAPATI: It is not a clinical. I'll give you a specific example. Let us say that we have a good drug for -- maybe this was breast cancer, has an RB2 amplification. Right? And I'm looking at lung cancer patients.

That lung cancer patient have the same genetic change. There is no approved drug for that, but potentially that patient could be saved if you treat them or get them into clinical trial with that drug. So it is not so simple, black and white, and be able to say, yes, that is a clinically actionable thing, but there is a significant -- you can potentially have a significant impact on the health of the patient.

DR. GREEN: Isn't this a little bit like torturing the terrorist who's with the nuclear bomb taking down kind of scenario? It's not necessarily a very real life scenario. What would happen in that situation would be if clinical practice recognized there was a life-saving drug for different tumors, then clinicians would be immediately testing those tumors for -- and if it wasn't clear,

then it would be definition be part of research where it was being sorted out. The two are mutually exclusive.

DR. KUCHERLAPATI: No. No. I think --

DR. FARAHANY: What if the person isn't going in to see a physician. I mean they're part of a research study.

DR. KUCHERLAPATI: Yes.

DR. FARAHANY: But they don't have regular care from somebody else.

DR. GUTMANN: This is just the opposite of the terrorist example. This is a case where whether you're a researcher or a "schmeesearcher". It doesn't matter who you are, if you're a person. Raju's got it just right. If you are a human being and you find out something which at very low cost to yourself -- and I don't mean just financial cost, just personal cost to yourself -- you don't have to be a hero to do this.

All you have to do is contact the person and say I found out something about you in the course of perfectly legitimate research that you should know, because knowing this, it's the first step in a life-saving treatment. I can't give you the treatment, but it's available. You have to do it. Whether you have to do it legally, I doubt. I doubt if there's a legal requirement, but I'm sure there's an ethical requirement to do it; and, I'm sure if you don't do it, you're being an unethical person.

DR. MOUNTAIN: If you don't know how the situation for lung cancer, how can you -- nobody's demonstrated it.

DR. GUTMANN: I'm not saying if there's not a known. This was Raju's first example. You come across something --

DR. MOUNTAIN: You're a cancer patient and you're not in the medical system. Is that the situation we're in? So you know you have cancer somehow, but you're not getting any medical care.

DR. GUTMANN: I feel like we need to think about more realistic cases scenarios

DR. KUCHERLAPATI: This is actually a real case that I illustrated for you; that there is a drug that is project to a specific genetic change in the tumor, that is approved in one tumor type, and that exact same genetic change is found in a different tumor type. And so there is a likelihood, and no certainty, right.

In life there is no certainty. But there is a likelihood that that patient could benefit from the drug; and, I'm asking, and I don't know the answer. I'm asking everybody the question. Are we then obligated to be able to somehow inform the patient and the physician, or we should not?

MS. MORREIM: I think there is a theme here, though, I'm sort of seeing. It has to do with defaults and exceptions, rebuttable presumptions, if you will, that in the research setting your defaults are going to be a bit different than they are in the clinical setting, but in every case you're looking for legitimate exceptions.

The default in the research setting is you generally are not going to, but clear exceptions you have to leave room for them. I'm a little worried about your case, because if the only thing you know for sure is that the drug works in

this type of tumor, then we don't know that it's life saving in a completely different cancer.

I am reminded of back to the 90s. I guess I'm living there right now, for whatever reasons. But back in the 90s we had high dose chemo and autologous bone marrow transplant for advanced breast cancer. It was a cash cow for hospitals. It kept some of them afloat, and it made it much more difficult, once we had politics in the works; whereby, either litigation or legislation forced a lot of health plans to cover it.

There was never a shred of evidence, good quality evidence, that it worked. It made it very difficult to complete good quality research trials until finally in 1999, finally, the NIH trials were able to enroll enough subjects to get the trial completed. And it turned out to be no better than standard chemo.

DR. GUTMANN: That's a totally different case, though. I mean all Raju, I believe, is asking is if you come across a finding in the course of your research that you have some reasons to believe the person whose finding it is, could find life-saving treatment by knowing it, do you have an obligation to tell the person?

MS. MORREIM: I think that's part of your default.

DR. GUTMANN: It's called just basic, ethical decency. You may be wrong, in which case you were acting on misinformation; but, if it was to the best of your knowledge, again, it's not because you're a researcher. It's because you're a human being with that information that you should do it.

DR. GREEN: But do you know how many researchers believe that

what they're working on is life-saving? And they passionately believe in this.

And I'm not doubting that there are such --

DR. GUTMANN: Sometimes people, or often people believe the wrong thing. They shouldn't act on it.

DR. DONALDSON: No, but I'm saying --

DR. GUTMANN: You have to stop a clinical trial, if you have the evidence that you found that the control group could be life-saving. Then you have to stop the clinical trial, but there are standards of evidence for that.

DR. FARAHANY: Amy, I agree with you that I think it is pretty clear to me that there is an ethical duty in the circumstances where there is an actionable finding that you come across, that you have an ethical duty to do something about it. I think, though, that if we think there is such an ethical duty that that creates significant gray area for expectations by patients and by subjects. Because if I believe that by being in a research study, that if there's an actionable result, the person will tell me about it.

That may lead me to think that the person has a duty to investigate it, that they will investigate it, and that they will uncover certain types of incidental findings. So, for example, I did an FMRI study where I was in the scanner for about two hours on something utterly unrelated about memory, recognition, something or other. And, you know, my expectation is if there was something actionable that researchers saw who have no clinical training whatsoever, that they probably would have told me about it.

But that may be a misinformed expectation, because they're not

trained to do so. And, so, the difficulty is while I think it's clear that there's an ethical duty, if you come across something to report it, I worry about the expectations that that creates for the research subject, and what that means for the duties to investigate by the researchers and by clinicians and how we manage the expectations between both parties.

DR. GRADY: I think there's a further complication, and that is there's disagreement about what's actionable. I mean actionable is the word a lot of people are using, but the case that you presented, Raju, you may or may not be actionable depending on who you ask. It sounds like you think it is, but I think a lot of people debate what is actionable.

And then there's a second part of that, and that is once there's some confidence that it is actionable and there is an action to be taken, then what happens. And so Amy said you would call up the person and tell them. Well, there should be a process. There should be a process, if Raju's in the lab looking at the sample, you know, there should be a process back to the people who are taking care of the patient who can give the information.

DR. GUTMANN: He means to suggest you get on the phone and call the person like that, but you have to think about how you get the information back.

DR. GRADY: Sure. And then it also raises, I think, an important question that was discussed this morning, and that is if we, in research anyway, give people the option of not knowing results, that can't be an absolute. You know; that there needs to be -- if there's an actionable finding that's serious

enough -- whether you want to know it or not, we'll tell you what it is. I mean I think not everybody agrees with what I just said, but that's the way I think about it.

DR. WAGNER: Anything else we need to hear from you before we do that? Then I'll let our Chair close us out.

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CLOSING REMARKS

DR. GUTMANN: This has been extremely edifying and we have a lot to think about; but, before we set to work thinking about this, which will be after the end of this meeting, we have a lot of things to give to all of our panelists. So thank you all very, very much.

(Applause.)

DR. GUTMANN: I have one other announcement, and that is for our speakers, for our audience, for anybody watching this on webcast, we welcome additional comments and we have a web address, Bioethics.gov. And everything you send there we will read.

So, once again, thank you. And I do want to thank our Commission members and also Lisa Lee, our Executive Director and our wonderful staff for organizing this meeting and carrying us beyond it. We look forward to doing our report. We are by no means ready to write the report now. We have more to think about, and we will meet again, next, in August.

Jim, would you like to say anything?

DR. WAGNER: We've just come to the end of another session where we've done a great round of thank yous and one more time failed to thank you. So, thank you, our Chair. And I add my thanks to everyone else's and so much appreciate everyone's contributions. Look forward to working through this problem.

(Whereupon, at 4:38 p.m., the meeting was adjourned.)

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