



Presidential Commission
for the Study of Bioethical Issues

TRANSCRIPT

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DR. WAGNER: Welcome back, Commissioners. We're about to commence on our final session and what we want to do is talk about a specific future topic, obviously there are many we could pursue, but as you will see, I think we have a special interest, if not obligation to be looking at a future topic on Incidental Findings.

Those are the findings discovered in the course of clinical care or research or for that matter in a customer/provider relationship. Findings that are discovered that are beyond the specific aims of that particular engagement, clinical test, research, but they have potential health importance.

In our history, we've heard presentations on a topic of Incidental Findings, a couple of years ago, we heard from several folks actually but Susan Wolf in particular stands out, she described the issue when we were talking specifically about genomic research as arguably in her words, "the most pressing issue in genetics today." And that is a quote.

Our own report, I'll remind you, on whole genome sequencing, privacy and progress, whole genome sequencing, we recognized and wrote that Incidental Findings raise important unsettled ethical issues. And we recommended those involved in whole genome sequencing discuss Incidental Findings as part of the informed consent process and that funders of WGS support studies to evaluate proposed framework for returning those Incidental Findings. And then we did this, we noted that a complete discussion of the topic was beyond the scope of that report, but we noted that we had plans to take up the issue of Incidental Findings in the future, so here we are exploring living into that commitment.

There were needs expressed from these experts for more definitive guidance about implications of Incidental Findings. Researchers and institutional review boards struggle with how to handle these kinds of things and they reach varying and sometimes inconsistent conclusions about what ought to be done with those findings. Clinicians have fiduciary duty to act in the best interest of the patients which may provide some guidance about how best to deal with the findings and there has thus far been only limited guidance about the possible contours of the ethical obligations to return Incidental Findings.

When I think of some of those and perhaps how we might begin our conversation for this session, I'm wondering if it would be helpful early on, in order to give some guidance to our staff as well between our meetings, if we have some conversation about the scope and context within which we might pursue Incidental Findings. There is several dimensions of scope along one dimension. We have those who are research subjects; those who are patients; those who are consumers, do we want to consider all those?

We have medical dimensions, for example, we could be talking about medical systems. We could be talking about genomics within the scope. We could be talking about imaging within

the scope of this. We could talk -- another dimension we could talk about is diagnostic modality. Is there -- do we make our contribution best by focusing on specific modalities?

Maybe the big question is do we imagine that we will discover generalizable ethical guidelines that could apply to the broad scope of everything in Incidental Findings? Or instead is there particular focus that we could identify in which our Commission deliberations could add value?

So, it is with those questions I'd like to open up a conversation. Hopefully you will agree, based on our history that, among many things, we should pursue since we made a commitment to do this. We ought to do this and that'd be the first thing to agree. And then something about scope. Amy?

DR. GUTMANN: So I'd like to make a virtue out of a necessity. The necessity is that we could not in the scope of whole genome sequencing report due justice to Incidental Findings and also maintain the focus of our report, which was on privacy. The virtue is that whole genome sequencing is just the tip of an iceberg of the issue of Incidental Findings. And, more and more, we're seeing that and most -- it is more the rule than the exception. That the tests that are now routinely given to people generate Incidental Findings and there isn't a clear sense of the ethics of how to deal with those and then, if you add on -- that is in the clinical setting -- If you add to the research setting, the issue of Incidental Findings and then if you add the direct to consumer aspects of this, there is, there is a set of issues that cross all of these domains. I don't think we have any predisposition as to whether the ethical rules, as opposed to principles, will apply to all these domain. But what actually in practice the ethics is, I think we would to dive into all the domains.

The one thing I would signal, which is really important here is that we focus not only on what happens after somebody gets a test, but what consumers, patients, research subjects are told before they enter in as to how Incidental Findings will be handled.

That is an important part of informed consent, whether in a regulatory standardized practice informed consent or it is part of the way consent, the ethics of consent in everyday life should be handled. So, I think it is a terrific topic for us to dive into and I think we should do it in this by looking at all of the domains and the different practices, whether it is an MRI or a genetics test or an X-ray that produces Incidental Findings; or direct to consumer practices and what -- it's always individuals whether it's a consumer or patient or research subject, what would be the ethics of what you should know and be told ahead of time about how Incidental Findings will be handled, what is done afterward and also there is or isn't counseling expertise because even when a doctor does a test, the doctor often isn't an expert at all the Incidental Findings that would come out of the test.

In the clinical practice, in some sense, it's the most straightforward, even though the -- the rules haven't been very well developed because you can bring a team in most clinical

settings, not all but most, you can bring a team together to interpret Incidental Findings. But I think it is terrific topic and I'd be interested in what other commission members think.

DR. WAGNER: Nita.

DR. FARAHANY: I agree, it's a great topic. I know we were disappointed we couldn't take it up earlier as part of the genomics study. It is an issue that is truly one of the most important across a number of fields from neuroscience to genomics to general research as well as in the clinical setting. So I strongly endorse us moving forward on it, focusing broadly both on what kinds of information people get before and after and I would just say that one context that could be a complicating feature for us, as we look to direct to consumer testing it raises complex issues about the role of direct to consumer testing in healthcare and in research and what the interaction is between individuals and the kinds of control they have about their own information. So, it is an issue I hope, as we get into, we're able to explore in some depth because I think it requires that we get into direct to consumer testing in a little more detail than we might otherwise get into just by looking at incidental findings.

DR. GRADY: One interesting way to think about it from my perspective is to think about what the obligations are or responsibilities are of healthcare providers and researchers and others to look for, identify, do something about. So there are lots of dimensions there. And what are the contour, what kind of constraints might there be on those obligations that are legitimate from an ethical perspective.

Like cost, for example, I mean one of the things that I've heard people say in the clinical environment is that a lot of potentially identifiable Incidental Findings are not looked for because they are focusing on the test that is going to be paid for and not looking beyond that. And so that is an interesting example.

DR. GUTMANN: I just ask because in many cases and, strictly speaking, Incidental Findings are things that you find willy-nilly by looking for something else.

DR. GRADY : Right.

DR. GUTMANN: So, and I could give from experience of-- from our medical system family friends a slew of examples where the clinician just finds something that wasn't the reason for having the test. That's what you just suggested is whether there is an obligation to look, not to report something that's found incidentally, but is there an obligation to look beyond and find something that you wouldn't otherwise find just incidentally.

DR. GRADY: I'm thinking of a more narrow report -- you can't report until you know what you're seeing and therefore when you find something, sometimes there's another test or another --

DR. GUTMANN: That's a different, oh, okay.

DR. FARAHANY: So, do you have to do that?

DR. WAGNER: Interesting.

DR. GUTMANN: Okay. So one of the things that just from a non-doctor perspective that makes this such an important and interesting topic to people is people differ, individuals differ greatly as to whether they want to know things that they can't easily act upon. So, while almost everybody would want to know a finding that the doctor could immediately deal with and remove the problem, people vary tremendously as to whether they want to know something in which there is no present cure or treatment from. Right?

Then there are Incidental Findings that don't necessarily affect the patient or person himself or herself, but others; that is where the genetic part comes in. But you find that not just in genetic testing, but in other kind of testing. And then there's the preparation of people for what might be found, because they are usually prepared for what the test is about and the question is if there is a clear probability that there could be Incidental Findings should they also be prepared by the professional for what might, you know, be found.

And then, I just want to do, to summarize, what Nita said in direct to consumer testing, which is a commercial enterprise. The people who are sponsoring that are not the medical professionals and the question arises what are their obligations and also what are the obligations outside of them for informing people about what these direct to consumer testing is or capable and not capable of doing.

DR. WAGNER: Dan, do you want to comment?

DR. SULMASY: Yeah, I think part of what is interesting about this relates to an aphorism of my mentor Edwin Pellegrino, who used to be fond of saying that great clinician practices with therapeutic parsimony and diagnostic elegance, and the era of diagnostic elegance is fast fading.

Just the sort of widespread nature of this, in a trivial ways, is that it is now cheaper to do 20 function comprehensive metabolic panel than to selectively ask for just a calcium and an albumin. So if I'm looking, if I want to look and see what somebody's calcium is and correct it for the albumin level I order the entire comprehensive metabolic panel and I'm under pressure to do so, right? Then I've done the shotgun and then the liver function test comes back 43 when the upper limit of normal is 42. So, do I -- at the least I repeat this and then it may be cascade of other tests that have cost implications, the question, it is a simple –

(inaudible)

Right; right. This is as simple as it is and then we get up to whole genome sequences where there could be thousands of different abnormalities, so it is incredibly pervasive. One

study we were given said radiology tests 40% of radiologic exam will find Incidental Findings of some sort, 40.

DR. GUTMANN: Yeah, that is why I think it's a virtue we didn't do it just with whole genome sequencing, because it is more prevalent in other tests and it affects people greatly. How it is handled.

DR. GARZA: So I agree with you Dan. Being the victim of incidental Findings in the Emergency Department. I have to deal with them quite frequently. But I think there's also gradations of the importance of what the Incidental Finding is. So, clearly and I think there is also legal implication, as well, so our -- are you legally obligated to go down this path, even though it wasn't what they came to the emergency department for in order to find an answer for them. And typically we rely on our friends in radiology and other things, is this an important finding? Do I need to do more testing to get it figured out? I admitted plenty of people who came in for a different reason and I found something else going on, so this happens not infrequently.

DR. GUTMANN: What do you do?

DR. GARZA: I admit them.

DR. GUTMANN: If you find something, yes.

DR. GARZA: It depends, Hey, this is Granuloma, they should really just get it checked out as an outpatient. I go and talk to them and say look, there is something on your X-ray, we don't think it is anything to be concerned about but you need follow-up. And they're happy with that.

If it's something more serious, looks like could be a tumor. Okay, that is a different story. Now we need to talk to them about that is always the long walk down the ER hall to tell somebody you just diagnosed them with something they completely did not expect when they came in to the emergency department. So there is varying degrees of what you need to do based on the findings. You know, the shotgun approach that you had just discussed, that happens quite frequently where you get one lab value out of norm and it's, okay, do I need to act on this or not? I tend to defer to treating the patient instead of the lab test, as we say. And so, but part of it is a little bit of art to be honest.

DR. WAGNER: Nelson, and Steve and Anita.

DR. MICHAEL: I'll join my other two clinician colleagues and say, I've had many similar experiences and will be doing so when I go back home tonight, thinking of my team. But I think some of the discussions we've had previously about this issue, and let's strictly talk about the clinical issues that have been raised, I'm not sure how often even myself I am mindful enough to tell a patient that we're going to get a CT examination of the chest, specifically because they came in with chest pain, yet you find there is a finite possibility we're going to find

something else that would necessitate that long walk down the corridor, as Alex alluded to. So, I do think there is merit in raising this issue even in clinical situations where I think we may think we have this well handled. I'm not so sure we do such a great job in setting expectations up now. We have more of a fishing expedition now in the way we practice medicine than in the past by our mentors. We don't aim laser beams; we do come in with shotguns and that is a marvelous part of the technology we have available to us but it does raise some ethical concerns in terms of what, really, the expectations were that we set with patients up front.

DR. GARZA: The difference between looking at the research side, if you were doing research on genomics and came up with Incidental Findings is a little different on the clinical side, where we can act on that Incidental Finding whereas – because we a relationship with that patient, you know, they are our patients. And so we have this duty to help them. Do you have the same duty on the research side and even less so, I think on the direct to consumer, where there is no relationship other than financial? And so I think there's multiple different categories.

DR. GUTMANN: One question to ask ourselves and I know how I would answer it, but I wonder what the Commission, is do we only want to talk about, and I'll say this in a way that is probably you can tell which way I'll come up, do we only want to talk about what you are ethically obligated to do or do we want to talk about what would be a good thing, ethically speaking, if people did, even if they weren't ethically obligated? I would come down on not just doing what ethical obligations are, but what would be good practice.

DR. WAGNER: Steve.

DR. HAUSER: Dan was speaking about judgment and we know that certainly for laboratory tests, they are gated so certain proportion of normals are above the upper limits or below the normal, the lower. Excuse me. But the other issue that I think is very interesting is, as we probe more deeply into information about all of us, we go beyond the traditional actionable and perhaps not actionable medically significant issue to these ideas of predispositions and probabilistic predictions about the future that even more so some of us want to know and some of us may not want to know and where that line is and where the boundaries change as we move and I think is fascinating.

DR. ALLEN: I just want to join others in saying I think it's a great topic to look at Incidental Findings in the context of research, clinical care, emergency care, direct to consumer and other commercial-type body scanning procedures.

I also want to add perhaps the context of autopsy to our list of context because in the post-mortem autopsy context. Things can be found out about a patient now deceased, a person deceased that the family might feel ethically, morally they have a right to know. It could be a condition such as cancer or tumor, but it could also be something more subtle. In any event, I wonder oftentimes what is it that the autopsy physician has an obligation to return to the family.

The other thing I want to say is that to me, something very profound is happening. I don't know quite how to articulate it. There was a simpler time when our bodies were our bodies and it was all exterior. And now we think of ourselves as an interior and an exterior and yet to some extent other people have more access to that interior self than we do. And I would love for our discussions about this topic to be perhaps a bit more philosophical than just, what should the regs be about research, because there is something profound going on here, changing perception of the self and how they bare on medical practice.

DR. WAGNER: (Inaudible) --

DR. FARAHANY: So, I want to echo what Anita just said and say that I'm quite interested in this topic from both perspectives, to Amy's point not only what is ethically required, but what would be good guidelines for practitioners, whether it's commercial clinicians, researchers, and it will likely vary by those different context. But also to Anita's point, looking at the individual and the rights of the individual, for use of that term quite loosely, in their self-interest in being able to learn about themselves, being able to have access to information and being able to not have access to information they would like to remain ignorant about particular type of predispositions or particular types of information. I want us to make sure we look at it sort of as a matrix which looking at the different context, the obligations and guidelines for individuals, but also the interest of the individual in receiving information and being able to learn as much as possible as they would like to know about themselves.

DR. GUTMANN: I'm wondering based on these comments, whether we ought to take at least part if not the whole report, a shift in the perspective. So, the report we're doing now is commissioned as advice to the Secretary of HHS and the President. I'm wondering, based on what this line of conversation is and I'm thinking, the intense interest of individuals and the public, if this could be a kind of guide to individual perspective patients, consumers of this, as to what you should know about present practices and what they do and don't tell you and kinds of questions you may want to ask ahead of time so you're prepared.

I think that given that this is a vast range of people who provide these services from clinicians who we could give some guidelines to, likely to take to researchers to direct to consumer, who we probably don't have very much -- that much influence over. But probably the greatest service we could do here is to give guidelines to members of the public as to what the present practices are, what you can expect and not expect, questions you might want to ask.

This is building basically on what Nita just said. I think it would be interesting and I think we have some expertise and ability to ask people to come and present, so we could actually do that in a report and so even if we had advice for new ethical guidelines that weren't taken, we could tell any individual who read the report what you should -- what you can and cannot expect and what you may want to ask for that would otherwise not be provided. I think that could be very -- I know I would find that useful and I know a lot of people who would find that useful.

DR. WAGNER: You know, I think the good news is, I agree with you 100%. I think the good news is, our prior reports often find that kind of use, as well. We even spun out educational materials from at least one of our reports. I think it should be a natural for that. Dan.

DR. SULMASY: I want to endorse something Anita said which could be folded into something that would be available to the public as well, and that's to sort of, maybe put this in the context of thinking about medicine and the sort of changes in medicine or broadly. In some ways, I think of it not as other people having better access to our insides than we do, but a kind of inverted Platonism, right? In which the shadows on the screen are the reality at which the gaze of both the clinician and the patient are concentrated when the concrete reality is what is casting those shadows. It's very odd the way in which we sort of begin to practice medicine and it's all of those shadows that we're interpreting that have taken on the reality and that's where the incidental findings occur, even if they have no even symptomatic, concrete consequence for the patient in his or her embodied life and never will. And that's, I think, the interesting context in which all this takes place.

DR. GUTMANN: Of course, sometimes we just have to -- sometimes they will have -- sometimes they are more real than what the patient thinks is real which is, I'm totally healthy and yet somebody has found turns out incidentally found a malignant tumor on my lung and by catching it early it's operable and I'm going to live, but I thought I was perfectly healthy before and this shadow tells me something that is truer than what I thought. It goes both ways and that is why it is very interesting and important, not just interesting, but important topic.

DR. HAUSER: Just one other little piece to this, we know that in medicine, often we do things that are at odds with the evidence at the moment and incident – an increased attention to Incidental Findings will also have economic and healthcare consequences that are very significant.

DR. WAGNER: Let me ask how we think we might be -- by the way, I will summarize briefly what I think are the questions that have been thrown out here and that will guide us, but where do we go for guidance? We heard, we're aware, I guess, that there are some communities looking at this more narrowly, the genomic community. I think our staff, it would be helpful to be able to be advised by those kind of activities as we go forward. Are there other templates or other processes that should -- that we should be looking toward to guide this conversation?

DR. ALLEN: Maybe some international standards. How are the Europeans, how are the Germans, how are British people, certain countries that we do look to sometime for comparative insight, how are they handling problems of Incidental Findings and return of research results.

DR. WAGNER: That's very good. Do you have one?

DR. GUTMANN: Jim, Robin Fiori, who is a Professor at the University of Miami, very helpful comment. "Please take up and hopefully take down the exceptionalism of Genetic information".

DR. WAGNER: Yeah.

DR. GUTMANN: I think you will get nods here. That is why I said we'll make a virtue out of necessity by do this in a broader context than just whole genome sequencing. We will take down the idea that genetic information is somehow different from other kinds of incidental findings. Sometimes it tells you something that is not just specific to you but to other people, but that is also true of other findings that could be Incidental Findings. So yes, very helpful suggestion and we will make sure we're explicit about that.

DR. WAGNER: Let me, so you can correct me, review where I think this discussion has gone. That in an era of change in medicine and health sciences, changing in part because we are more often less narrowly diagnostic and more exploratory would there'd be valuable contribution to prepare as a guide, a piece of work that addresses those changes and associated questions of access to self and who has access to self in internal privacy, looking at patients, research subjects, consumers of direct providers and for that matter, the deceased, with following kinds of questions: ethical questions, ethics on whether or not to look, what to do with those data that are discovered incidentally, how to judge the importance of those data. The obligation to follow-up and obligation beyond ethical obligation to do what is good, not just what is required. What constitutes good guidelines along those lines, expectations; what are the expectations of the patient, subject, consumer? Is there value and interest and value in knowing, and what is the interest in knowing and the ethical questions around that?

And then we suggested for our own benefit that we should look for those already going down this road in other areas. Specifically, the genomic community, but also looking for international activities and perhaps even discovering, looking for standards in conversations that have taken place. Is that a fair summary and does that prompt you to suggest some other questions we ought to throw into this before we turn our staff furiously to work on this? Christine, I'm sorry.

DR. GRADY: I know there's some guidance on neuroimaging , findings in neuroimaging.

DR. WAGNER: Neuroimaging, not just the genomic community but the neuroimaging community. Good point.

DR. GUTMANN: Taking stock of what guidance is out there and how well it is followed would be important. I just would, I think you intended to include that, but probably should be a little bit more explicit on what Steve said, there really is a challenge that Incidental Findings present to people who find them as to make a quick judgment as to how are they

important enough to follow up with and there is an implicit, if not explicit question, of whether this is so remote as to it's going to cost a tremendous amount of time and money to follow-up and the odds are tiny that this is going to amount to anything versus this is really important. And for us to point out that that has to happen, it is inevitable and to be called a form of, you know, rationing depends what you mean by rationing, but the fact is that we make those judgments day in and day out, even without Incidental Findings. But Incidental Findings make it impossible to avoid those judgments. I think that's a service that can be done just to say that this is -- there is no avoiding that.

DR. WAGNER: Other input on this? This should lead to some very meaty conversation and a long string of experts that can advise us I'm suspecting. Okay. Do you care to wrap us up Madam Chair?

DR. GUTMANN: I'd be happy to thank everybody. First and foremost my Vice Chair, for being so terrific in everything you've done, not just today, but since the beginning for our Commission. Our speakers were tremendously helpful. All the questions and comments we got, including the most recent, putting to rest genetic exceptionism have been very appreciated and helpful and of course my fellow Commission members who have been terrific in getting us to where we are and I expect to only be exceeded by getting -- moving us further to where we will be both on this report and on our next report on Incidental Findings and thank you all and safe travels.

DR. WAGNER: Safe travels and thank you, Amy.

(End of meeting)