Q&A and Discussion of Pharmacogenomics: The Public Health Perspective

DR. WINN-DEEN: So I want to thank you for being extremely responsive to our charge of please tell us what the issues are and things that we could potentially consider as a committee for areas where we could maybe make some real task force kind of recommendations.

Are there questions from the committee for Dr. Davis?

Ed?

DR. McCABE: What you designed for us was an infrastructure which doesn't exist at this time. The first speaker mentioned that there's the likelihood that this may be driven by litigation, and I teach about pharmacogenetics to our medical students, and I maintain that the diagnostics will be driven by litigation. So that's going to happen much more rapidly, I think, than we will have time to develop the infrastructure that you've discussed.

So how would you develop a rapid response when the medical legal industry recognizes that there is a large vein of gold out there that they hadn't recognized before and now create the new cottage industry against this?

DR. DAVIS: That's a great question. I think there are two things that can happen. One is there is this Pharmacogenetics Research Network. I think I've gotten the name close enough. That's a wonderful network, one that I'm actually very jealous about. But what really sort of struck me is that there is no network like that for what I was just describing.

There is a network for what I was just describing for vaccines, and it was created because in the late '80s there were only three vaccine companies still left in the United States producing vaccines, and the liability that they were facing in the court system, the total dollar amount actually exceeded their total net assets for all the vaccine companies. In response, the CDC actually formed the Vaccine Safety Data Link process that actually now does exactly -- not exactly but pretty much what I've shown you on 5 percent of the United States.

So we have shown the capability of setting up these networks. We have something in response to these litigation concerns. The CERT networks were formed, I believe, in a joint effort by the FDA and AHRQ specifically to look at issues of patient safety, and I think that to a large extent they actually have the researchers and the networks that would be able to address many of these issues.

Why aren't we doing it? Honestly, it's a matter of money. I think there needs to be a substantial allocation of resources. How about if I stop there? I don't want to start moaning about the small amount of funding that we're able to get for some of these studies. But they are substantially less than the amount we need to actually do this in a systematic way.

DR. WINN-DEEN: I wanted to sort of follow up on that question. You described a system of large population-based clinical trials. I really enjoyed your outline, but as I started to think about if you had to make 100,000-patient clinical trial to answer every pharmacogenetic question that might be posed, what the cost of that is to the health care system. I'm not going to say which part of the system, whether it's the U.S. government or private that should pay for that, but how do we even begin to grapple with the thought of doing that for all of the drugs that are out there? Do you have any thoughts on how one might prioritize which things you would start with?

DR. DAVIS: Would no suffice?

(Laughter.)

DR. DAVIS: That was the honest answer, but you flew me up here. So just simply to say that I think what I see coming is genetic testing and pharmacogenomics is two things. One is it's really caught the public's imagination, and these sorts of things are being offered to patients already; and it has sort of the stunning ability to bankrupt the system, to either bankrupt the system or to dramatically improve health care. I think if you look at it that way, then actually the cost of these studies is not as much as one might think.

I think a lot of the cost is setting up the infrastructure. I mean, most of these patients in the large clinical trials are being seen already and they are being prescribed medication already. The technology to run their gene chips and to collect the information is already there. It's a matter of plugging those pieces together and funding that network to exist, and you then have to actually set up a group of people who are far wiser and far more experienced than I to prioritize that.

I say that with my pediatric heart shrinking, because who gets left out in those priority-setting committees? The priority is usually driven by either morbidity and mortality or cost. Those are usually middle-aged to elderly people who are beginning to die of congestive heart failure, stroke, heart attacks, and those are the things where the need is the greatest to do the studies. But I think the priority setting needs to also look at gender-specific effects, look at pediatrics, the very elderly, and whatnot. I should have just stopped with no. How's that?

DR. WINN-DEEN: Is there some agency within the government that you would see taking the lead in trying to develop such an overarching plan?

DR. DAVIS: I've actually wondered about that a lot because we don't really have a single agency that sort of has public health as its mantle. I think there is a very clear role for the FDA, a very clear role for AHRQ, and actually for what I'm talking about there's a very clear role for the CDC, although this would expand its mandate, and there's obviously the conflict of interest I have in saying that, where I'm doing my sabbatical. I think NHGRI and NIH could play a very strong role as well. I think there actually needs to be an amalgamation of those efforts.

DR. WINN-DEEN: Ed?

DR. McCABE: So I'll follow up with a question to Tim, because I think one of the expenses is the sequencing. If we can get the testing down, if we can get sequencing down and its cost -- I know there was an RFA to decrease the price of sequencing, and I was wondering what the anticipated trajectory is to get us to the thousand-dollar genome, knowing that it's a guess.

MR. LESHAN: Right. We're looking at the next 10 years as our focus and we're trying to get it down to that level. Whether or not we'll be able to will really depend on how well we can develop that technology. Based on the progress that we've made over the last 10 years, we think we can get there, but there's still a whole lot of work to be done in order to do that. I think you're right, that if we can reduce that cost, that will greatly enhance this.

But there's also the issue about people's receptivity to this. I think the public is very interested in it. But at the same time, I think we do have this problem, an issue that's been around for a long time that Dr. Weinshilboum talked about, how do we break the barrier within the academic and

the physician community to make sure that this is something that people really want to invest in and will participate in.

DR. McCABE: And a question to Sherrie, then, in follow-up. It would seem that VA would have a population in which to begin to pilot this. Is there any discussion of this in the VA population?

DR. HANS: Yes.

(Laughter.)

DR. HANS: You're absolutely correct that at the conceptual level the VA has the necessary patient population, has the necessary information technology infrastructure, has the necessary research infrastructure and delivery system to be able to do something like that. It is a matter of the additional costs of running such a large-scale research program under current budgets.

DR. DAVIS: Could I just follow up, if I might. One of the things I've really noticed is that there's a lot of people really beginning to talk about this seriously because they understand, I think, the costs of continuing to do not only business as usual but that the perceived business as usual within five years will be even magnified dramatically. So I've been really heartened to see people at CMS and the VA and the managed care organizations trying to climb on board the train. Unfortunately, we have train cars scattered around. We just haven't hooked them up and gotten them going yet.

I was up at AHIP not too long ago, America's Health Insurance Plans. They're very interested in these concepts. So I think there are a lot of very interested partners. It's just a matter of putting people together in the proper context.

DR. WINN-DEEN: We're going to take two more questions, and then we're going to go to break. First Julio, and then Francis.

DR. LICINIO: One question related to what you presented, which was very interesting, about large studies that you need to validate this. The issue is who is going to fund those? Because if you go to a more naturalistic setting, like a health care organization or something out there in the real world, the patients are on multiple drugs, and if you're trying to look at the effect of one drug, you really have to get more of a research type of study. Ideally for what you're proposing, it should be for drugs that are established, not trying to look at new drugs that are just coming to the market.

So the drug companies are usually not willing to go to the expense to do this kind of study for a drug that's already out there and is selling well and possibly at the end of patent. NIH was the exception, or NIGMS. The categorical institutes should then be a little reluctant to do this kind of large study just for pharmacogenetics because the cost is very high and they don't see the sample collection being worth the cost of several R01s.

So do you have any ideas for this kind of a conundrum?

DR. DAVIS: Well, I agree with you. I think there are a lot of reasons why people won't participate. In terms of who you mentioned, I think this work is going to have to come from people who are already paying the bill -- i.e., CMS and other insurers -- where they're actually

currently picking up the cost, and there's really no good evidence that certain of these medications work in the diverse situations. It is that the medications are actually being used.

So I think that it's kind of a perverse incentive, but it's one that's very real and very recognized. So I think in reality that's what we're looking for. What we're looking at now, can we align other things to make that more palatable. I think in terms of some statutory requirements and legislation that would require some of these studies to be done, and the cost could be shared a little bit, I think it's somewhat naive for me to say it but I think that's actually a realistic and probably a fairly, in the long term, beneficial thought.

DR. WINN-DEEN: Francis?

DR. CHESLEY: Thanks. I just wanted to amplify the dialogue we're having around cost and suggest that I believe that the tipping point here will likely occur when a strong business case can be made. As you've related, we really need infrastructure for the research, and a key component of that research is really going to be cost-effectiveness research, as well as the effectiveness research to be able to demonstrate to those who pay that there's a business case to be made, and therefore it makes sound business sense to take this approach. I think at that point, all the various players will come together, federal and non-federal as well.

DR. DAVIS: You know, could I just respond real quick, which is that a lot of times we think of these cost-effectiveness studies as being a home run. But, in fact, I think what they will actually show is that there's a tremendous amount of waste, and that's not nearly as sexy, but I think that's actually what we're dealing with, and that's the business case that needs to be made.

DR. WINN-DEEN: Sam?

DR. SHEKAR: Just one quick point. There's another trend that's going on in health care, as we know, which is the tremendous growth in the electronic health infrastructure, the underpinnings of health care delivery. Since so much of what you have discussed relies upon fairly immediate and fairly transparent transmission of data back and forth, the costs that are borne through an electronic health infrastructure underpinning may in fact be covered through that type of support. Therefore, as a suggestion for a future speaker, it may be interesting to know what's going on through the Department, through the Office of Dr. David Brailer and some of the work that's being done to support growth of electronic health infrastructure across the medical care industry and health care industry. I just made that as a suggestion.

DR. WINN-DEEN: On that theme this morning, as I was getting ready to come down here, there was an interview with Frist and Clinton on bipartisan support for the bill that is before Congress right now to get funding for this program, and I think it might be worth getting someone from the judicial side as well, or the Congressional side, to give us a briefing on where that is as well.

I think we'll stop here and take a 15-minute break and come back for the continuation of the session promptly at 10:20.

DR. WILLARD: At 10:20 to the minute.

(Recess.)