



Presidential Commission  
*for the Study of Bioethical Issues*

## TRANSCRIPT

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## Roundtable Discussion

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DR. GUTMANN: Other -- we're going to move on to Ebola, from the brain to Ebola. Okay? Okay.

So, we had a great set of meetings on a very important topic. And we focused on the more directed topic that we will do a relatively short report on, the United States's engagement, and the global response to the current Ebola epidemic. And, throughout all these discussions, we keep coming back to the same theme, that major infectious disease epidemics are a matter of United States and global concern for both ethical and prudential reasons, and the importance of doing what can be done to prepare for an effective response, the importance of doing what can be done to educate ourselves and the public, what the best ethical and prudential ways of responding are.

So, public health emergencies often occur. They occur unpredictably, but it's predictable that they will occur. And they have the most devastating impact in countries and communities that are least equipped to manage and control them.

For example, we heard yesterday that Western African countries most affected by the current Ebola epidemic face numerous societal and health challenges, including a high burden of endemic diseases, such as malaria and other neglected tropical diseases, as well as inadequate health infrastructure, economic and political challenges, while they have many sources, are also often perpetuated by inequitable global policies that make it difficult to build and sustain health infrastructure on both humanitarian and global justice grounds. Acute health crises like the Ebola epidemic ethically demand a robust global response.

But, given the capacity of infectious diseases to travel easily in our interconnected world, or to destabilize regions or countries, it's also prudent to address epidemics at their source. And the only sure way to prevent Ebola or similar infectious

diseases from traveling to previously unaffected places is to stem the disease in highly affected areas.

Therefore, while we, as a bioethics commission, of course focus on the ethical impetus of our actions, there are also very practical and U.S.-centric rationale for our engagement in such public health emergencies.

I, myself, do not draw a bright line between the ethical and the prudential reasons. I think ethics is a practical consideration in our lives when -- we said it before. When scientists have, on occasion -- and it's the minority, small minority -- stepped in an ethical land mine, what it blasts up is a very -- has very practical effects. So you know, I think it's really important, in the context of a public health emergency, the nature of the response is extraordinarily important, from a practical and ethical perspective.

So, we have many times returned to the concept of regulatory parsimony, holding that restrictive measures taken to protect the public health and health care workers be grounded in the best available scientific evidence and restrict individual and community liberties only so much as is necessary. Such parsimony is justified in response to infectious disease outbreaks, because it respects and protects individual and community needs, interests, and liberties.

It is justified because it gives those most critical to fighting the disease at its source health care workers and other emergency personnel the support and respect necessary for them to work safely and effectively.

These concerns, be they regarding the whether or the how of global public engagement, these concerns are rooted also in transparency and come out of the -- we need -- the transparency and public deliberations are necessary to anticipate and react in

appropriate ways to high-stake decisions and justifications. We need to have kind of transparency in our public deliberations about this.

We've engaged in a kind of democratic deliberation. It's particularly well suited to public health emergencies, because public health emergencies gain everybody's attention. And it's really important to be prepared for those deliberations, because, otherwise, the loudest voices get out there first, and there isn't an organized public democratically-rooted response to these.

So, we've strived to set an example of such deliberations over our meetings. But particularly over this topic, over the past two sessions, it's really helpful to have the range of reasonable voices. And in this context, I'd like to propose, as a first overarching recommendation, that in such an interconnected world, the U.S. Government has a responsibility and stake in actively participating in coordinated global responses to public health emergencies, wherever they arise, for ethical reasons, and to protect national interests.

In addition, integrating ethical inputs into public health preparedness planning is critical to ensure justifiable responses to acute events and their longer-term health concerns.

And Anita isn't here, but I just want to know. Is there any further discussion of this? John?

DR. ARRAS: Yeah. Thank you, Amy. I think this is fine, but I -- we might want to think about adding an element to this regarding post-emergency planning, as well as preparedness planning. You know, because some of the testimony we got yesterday from people in West Africa, especially Sierra Leone, indicated that the public health infrastructure had been completely devastated, and it should also be, I think, a

matter of concern to us, as helpers in the process of development rebuilding, that we really assist in the building up of sustainable communities after these epidemics are over.

DR. GUTMANN: So, one of -- I agree. And we want to word it as specifically as we can. One of the admirable responses to date -- and we want to make sure it continues -- is that there are now health workers who have a sustained commitment to remaining in these countries, and there is a funding for them to improve the preparedness of these countries in the future, without being -- this is not going to transform three extremely poor and not, you know, entirely stable countries into, you know, any kind of, you know, total transformation. But it is going to, if there is a stick-to-it-ness about it, make a significant difference in preparedness.

DR. ARRAS: I agree.

DR. GUTMANN: Any other -- we will work again on as clear wording as possible. Nelson?

COL MICHAEL: No, I would only add, when you read this recommendation, there were a couple of clauses that were different than the piece of paper I have in front of me. But I think -- but I liked them. And I think --

DR. GUTMANN: Well, I have made revisions on the fly.

COL MICHAEL: I like them.

DR. GUTMANN: Yeah. So I hoped --

COL MICHAEL: So can I tell you the one I really liked?

DR. GUTMANN: Yeah.

COL MICHAEL: You used the term "national interests."

DR. GUTMANN: Yeah.

COL MICHAEL: And I think that's critical, when we're talking -- you know, we're pushing this up, obviously, to the top level of the executive branch. And getting to your point, John, when you talk about what's in our national interest, it is in our national interest to have post-emergency responsiveness. It is in our national interest to spend resources on developing these capabilities, either domestically or globally. So, I think that's a potent two words.

DR. GUTMANN: Christine?

DR. GRADY: Yeah, just a thought. I mean I think this -- I agree with this idea of recommending that the United States has a responsibility to respond to public health emergencies. But what's missing for me is building capacity for future public health emergencies.

Somewhere, making a recommendation that we have some responsibility sort of persists beyond the immediate response --

DR. GUTMANN: That's the next recommendation, really: "The United States should strengthen key elements of its global response capacity." And we're not trying to -- this is just the first --

DR. GRADY: Okay.

DR. GUTMANN: -- recommendation, and I think it's important we not pack everything --

DR. GRADY: So, I mean, I know you didn't get to it yet, but I don't see the idea of sort of a long-term commitment to other places, building capacity in other places. Maybe we don't want to say that, but we don't say it.

DR. GUTMANN: Well, I thought John --

DR. ARRAS: That's what I was getting at.

DR. GUTMANN: I thought John said that --

DR. ARRAS: Building sustainable communities, or helping to build --

DR. SULMASY: Yeah, I took that to be the strength of John's amendment to the first one, to make sure that, once the epidemic wanes, whatever it is, and people start pulling out, that we don't just sort of pull everything out, but help to build up an infrastructure that will help the -- even the -- as we heard yesterday, actually, you and I, afterwards, the same epidemic from recurring, because people are going back to hospitals where they got infected before, because we hadn't done anything but, you know, build acute Ebola treatment centers.

So, I think that's what John was saying, and I think that's what you're suggesting, is going in as a second part of recommendation one --

DR. GUTMANN: So, here --

DR. SULMASY: -- which is different than -- from recommendation two, which is our capacity to respond. So --

DR. GUTMANN: So we have to -- we do need -- let me pose this -- what John was saying was, in recommendation one, we should talk not only about the preparedness, but the stick-to-it-ness afterwards. That's more specific than a more global recommendation, which I don't know whether we want to do. But it's not as if we know that the next epidemic is going to break out in these three countries, right?

So, it is beyond Ebola, way beyond Ebola, to call for -- and way beyond public health preparedness, to call for the United States to support the Millennial Development Goals, which are directed at building -- you know, the Millennial Development Goals are directed at overcoming acute forms of poverty in all the poorest countries in the world and among the poorest -- you know, for example, one of the

Millennial Development Goals is to get everybody up to -- you know, what is it, a dollar a day.

So that's way beyond Ebola. But if you go any further than we've gone with John's suggestion, it's really taking it into the territory of building the capacity of all countries to resist in the -- the worst forms of disaster. And they're not just public health emergencies, they're all kinds of -- they're famines, if you read -- the vulnerability to famine is directly correlated with the poverty of countries.

DR. ARRAS: Yeah. Thank you for those comments. I want to go back to a comment that Raju made yesterday about how, you know, we're not really able to predict exactly what's going to happen in what country, which is absolutely true.

So, I think that the best response to that is to say that we should try to build capacity for kind of all-purpose public health infrastructure, you know, that will be flexible, and be able to respond in a way that Nigeria responded. Namely, you know, they had this whole system geared up for polio, and they just were able to deftly switch over to Ebola when the time came.

So, that's what I'm referring to here, is a kind of all-purpose public health infrastructure, so that they won't have their pants down the next time some kind of major catastrophic public health emergency happens.

DR. GUTMANN: Let me go on to the next -- and in an interconnected world, the U.S. -- well, we just did that, right? Okay.

So, next one. The United States should strengthen key elements of its domestic and global health emergency response capacity. These include: 1) identify and empowering a single health official accountable for all public health emergency response activities; and, 2) strengthening the readiness of the existing public health

workforce -- for example, the U.S. Public Health Service -- to respond to public health emergencies in different contexts.

In addition, the United States should contribute to strengthening the capacity of the World Health Organization to respond to global health emergencies in a coordinated fashion, including through the provision of increased funding.

This came directly out of yesterday's deliberations. Nelson?

COL MICHAEL: Yes. So, just to paraphrase what the intent -- at least as I saw it, since I read this on the Metro coming down here -- was that we should strengthen U.S. federal capabilities. I would like the term "capabilities," instead of "capacities," because I think it actually means that you're actually able to do something with it. Not that you have the ability --

DR. GUTMANN: Friendly word change.

COL MICHAEL: But to respond to domestic and global public health emergencies. I think -- so, in a sentence, I think that's the intent.

To implement, I saw three parts of this, that we need unity of command or control for the U.S. federal health crisis response.

Two, you needed -- and I changed the wording here. I kind of went right to the heart of the issue. I said you need to strengthen the expeditionary arm of the federal health workforce with U.S. Public Health Service Commission Corps, because, you know, I mean, obviously, the military has a very, very large and vibrant and very expeditionary health force. But it is geared towards a different mission. Sometimes we get those missions to help in global health crises, but that is not the prime mission of the Department of Defense. So, that's why I wanted to concentrate on that.

And, third, I think the intent was to provide federal funding to strengthen

the operational capability of the World Health Organization to respond to public health crises. What we heard yesterday was that, back in the day, you know, Geneva had operational control of the regional offices. They do not any more. So you have linked responsibility, which -- it's in Geneva, and the authority to execute, which -- it's elsewhere. And I will tell you that -- certainly in my agency, that never works.

DR. GUTMANN: And we should say -- so let me just, you know -- we should say that in the report, exactly what Nelson said. And we don't have to use the exact words. Nobody will understand, otherwise, why we're calling for what we're calling for.

COL MICHAEL: Right.

DR. GUTMANN: What we heard and what we read in the news and heard from people and -- is that there wasn't an ability to respond as --

COL MICHAEL: Right.

DR. GUTMANN: -- quickly as was needed, because of this organizational problem.

COL MICHAEL: So, I was able to come up with some changes to the draft recommendation, which I will send out. But it would just take a second to read them.

DR. GUTMANN: Sure.

COL MICHAEL: So, I only made a single change in the first sentence. I said, "The United States should strengthen key elements of its domestic and global health emergency response capabilities." I think that, of those three parts, the first one is going to be the hardest, because it's kind of wonky, in terms of how the U.S. Government works.

But I said that we should -- they include identifying and empowering a single health official accountable for all federal public health emergency response activities. So I changed a single word, but I do think that -- and I can give you some examples from the Ebola wars --

DR. GUTMANN: No, that's okay.

COL MICHAEL: -- will tell you why it's difficult.

DR. GUTMANN: We're not going to fully wordsmith it here, but go --

COL MICHAEL: But I think we should provide this --

DR. GUTMANN: But why don't you go --

COL MICHAEL: And this is where I get to the meat of the matter, "Providing the Surgeon General of the U.S. Public Health Service direct-line authority over all commissioned corps officers to strengthen the core's expeditionary capability for public health response."

But, right now, the PHS has --

DR. GUTMANN: Yeah.

COL MICHAEL: -- has capabilities in place that they can't use, unless a lot of other people give consent. Because the PHS distributes its people down to agencies, okay? I sent a PHS officer for one of those deployments, PHS called me, an army officer, to say, "Is it okay?" I could have said no. That shouldn't be.

DR. GUTMANN: Yeah.

COL MICHAEL: She should just go without anyone else's consent, other than the Surgeon General.

And, lastly, "Strengthening the capacity of the WHO to respond to global health emergencies through the provision of increased funding, and interoperability with

federal emergency response capabilities." So I think that captures what we get, in terms of a bang for the buck. If we're going to spend federal money, and it goes outside our borders, then we should have the ability to work with that normative body.

DR. GUTMANN: Good, good. So, turning now to our three in-context examples, I would like to bring up, first, the use of quarantine and restriction of movement provisions. We've talked about all of these. I think what we've heard, time and again, from our speakers on this topic, with not a dissenting voice, is that government and public health organizations need to put serious thought into what are the least restrictive means necessary, informed by the best available science for the implementation of these restrictions.

And the government and public health organizations should employ the least restrictive means necessary, based on the best available scientific evidence and the implementation of restrictive public health measures, such as quarantines, intending to control the spread of infectious diseases.

Barbara, you want to say something on this?

DR. ATKINSON: Yes. We've spent a lot of time talking about this one at multiple meetings. And I think the descriptive pieces that go with this talk about all the pieces that are important, the balance between personal rights and the public good. And it really was the Ebola episode in the fall, and the way that restrictions were handled, or handled poorly, that really triggered all this. So I think that's all good in the discussion.

I think the piece of the discussion on science and the -- how science defines the particular organism -- because there is one thing to talk about what the restrictions for Ebola would be, but because of the spread of measles a different way, being very clear that it depends on the organism, what you would put for -- and how the

organism is spread, what you would put for the restrictions is important.

DR. GUTMANN: So, could -- just to be clear, the principle is one should use the least restrictive means necessary.

DR. ATKINSON: For a particular organism.

DR. GUTMANN: What -- for a particular organism. Then, what the consequences of that are for the application, depends on the best scientific knowledge and evidence about what the threat of the organism entails.

DR. ATKINSON: Right. And I think that's said very well in this recommendation.

The one thing that I would have a word change is it says, "Based on the best available scientific evidence, and the implementation of restrictive public health measures, such as quarantines," and I think I'd at least put "quarantines and restrictions." It's not really just quarantines.

DR. GUTMANN: Right. I -- that jumped out at me, too. It's -- and whether quarantines, self-monitoring, monitoring --

DR. ATKINSON: Yes.

DR. GUTMANN: Account -- you know, we have a set -- right.

DR. ATKINSON: But quarantine, what most people think of as setting the person totally aside, and that's a little different than the restrictions --

DR. GUTMANN: And I wouldn't even try to pack it all into one sentence. I would say the least implementation of restrictive health measures intended to control the spread of infectious diseases, these might -- you know, there is a -- "these range from," and put some of the range.

DR. WAGNER: The words that we were given yesterday were

"monitoring," "restrictions," "quarantine," and "isolation." Of course, "isolation" doesn't belong in this recommendation. But those were the grades, if you will, the gradation of reaction.

DR. ATKINSON: And the one concept that's not in the recommendation, and I'm not sure it's quite as well worded in the text as it might be, is about the stigma that comes -- unintended consequences that come from being too restrictive of the personal rights. I think the unintended consequence part is in the description.

But talking about the stigma to health care workers and people that live in countries that are involved, like Africa, or the particular countries, I think -- I don't know if we want anything in the recommendation, but I think it at least needs to be fleshed a little more out in the discussion text.

DR. WAGNER: You know, I think it's -- in the discussion text, that would be great. I think, as part of the recommendation, it is more of a rationale.

What I thought about, the only thing you -- one way it could be addressed, if you are insisting on doing it here, but we should employ the least restrictive and least stigmatizing ways to -- and then you could have it built in there.

DR. GUTMANN: Yeah. The other part of this recommendation that's absent that we may want to add in here is that government and public health organizations and their representatives should also prepare to communicate these -- the rationale for their restrictions publicly, to optimize public understanding of why those restrictions are necessary and sufficient.

Because the preparation for communication is extremely important, right up front, to minimize public fear moving into panic. And so, it's not enough just to know what the necessary least-restrictive means are. It's also important to be able to be

prepared to communicate it.

And we do -- you know, public organizations go through all kinds of scenario exercises ahead of time. Nelson is very familiar with this in the military, but outside the military this is true. All big institutions do it. It's important to have the communication plan with the -- so should we add?

DR. ATKINSON: I think we should --

DR. GUTMANN: -- a sentence to that effect?

DR. ATKINSON: Add, or it's almost a separate recommendation.

Because, you know, Ebola had been around a long time. Somebody could have prepared what they thought the rationale would have been several years ago, when the first Ebola episode happened. And so, maybe in the broadest sense, that preparation should happen ahead for any --

DR. GUTMANN: So I don't have a strong view of whether it needs to be its own -- or, you know -- but there are two things that are needed to go together. One is that the least restrictive means should be -- least restrictive and least stigmatizing means should be used. And, secondly, we need -- those public officials need to be prepared, ready to communicate the rationale for the means they're recommending in a publicly accessible way.

Yes?

DR. SULMASY: Yeah, it seems to me maybe that raises the question of whether we don't want to add another, you know, recommendation, just overall, about communication. Because that's part of it, but there is also the part about communicating risk, et cetera.

DR. GUTMANN: Yeah.

DR. SULMASY: And we heard so much about that, that it might be best to have a separate recommendation about, you know, preparedness for communication about this.

DR. GUTMANN: My worry about not -- I agree with the broader recommendation. But my worry about not being specific about communication in this recommendation is that the best -- you know, most well-intended effort by public officials who want the least restrictive means possible to implement it, will fail if they don't communicate up front why this is an adequately restrictive means.

That's -- you know, so this -- to put it differently, if I read this recommendation from a commission that I was not on, the first thing I would say, "Well, that's well and good, but it will never work unless you communicate why you don't need a quarantine." So I would like to have this recommendation have that part of it on, and we may still want a broader recommendation about communication. Okay?

So, now I turn to the very compelling discussion we had yesterday regarding the use of placebo-controlled clinical trials. And I think we've learned, and I think we likely agreed, that the trial designs, whether or not they use a placebo, should be methodologically rigorous, and capable of generating results that are clearly interpretable, acceptable to the host communities, and minimize delays. Active engagement with stakeholders will, of course, be critical to designing such a trial.

I did want to make sure that we also continue our discussion from yesterday regarding providing best available supportive care in both arms. During our 2011 Moral Science Report we talked a lot about researchers not necessarily having to use best-proven standard of care in the control arm of a trial, especially when there is uncertainty about whether such a standard would be best for the local population under

study.

However, I believe that the Ebola context is unique, in that these trials are not comparing a treatment or a vaccine intervention with one we already know works. Therefore, if we are going to recommend that control arms use best-available support of care in this context, we should specify what we mean. For example, whether we mean best available in the country, where the trial is being conducted. That was what was recommended to us yesterday, and I believe that is the only way of moving forward quickly with -- and I believe, ethically, with seeing whether there can be a -- you know, a vaccine developed.

So, I would ask you whether we agree that what we're asking for is the best available in the country where the trial is being conducted. So the proposed recommendation -- and, John, I'm going to ask you -- is research during the Ebola epidemic should provide all participants with best-available supportive care. Trial designs, whether or not they use a placebo, should be methodologically rigorous and capable of generating results that are clearly interpretable, acceptable to the host communities, and, to the extent possible, minimize delays to completing the research. Research teams should actively engage with stakeholders during research to determine the trial design that best reflects these requirements.

DR. ARRAS: Okay. So, I think this is a good start. Christine and I had a long conversation about this paragraph, and we came to similar conclusions about where it -- what directions it might need to go.

One Amy just talked about, which is the question of supportive care, right? This is ambiguous, right? This doesn't really indicate whether we -- you know, what level of care we think is morally required, whether it's the best-available

supportive care in the region, or in the country, versus best available anywhere in the world. So we need to clear up that ambiguity here.

DR. GUTMANN: So I just proposed -- is that the clarification you support?

DR. ARRAS: Yeah, it is.

DR. GUTMANN: Okay.

DR. ARRAS: It is.

DR. GUTMANN: Okay.

DR. ARRAS: Yeah, yeah. But this is important, I think, because, like, Paul Farmer published an article in the newspaper not long ago. He's a very respected voice on these kinds of problems. And Paul Farmer came out and said, "Hey, we already know what really works here," and that's really, you know, excellent supportive care of the sort that, you know, Doctors Without Borders provides.

So, that's something to think about. Okay? Now --

DR. GUTMANN: No, he argued that -- he's in a battle with -- yeah.

DR. GUTMANN: It's a very big public fight that they're in.

PARTICIPANT: Yeah, big-time.

DR. ARRAS: Okay. I sensed that there was some disagreement, you know, between the -- but I got the impression that he was -- now, maybe I just misread the article.

COL MICHAEL: No, his point was that you provide good intensive care support, to include dialysis-intense monitoring of blood, of other blood infections, that you will have a better clinical outcome. And --

DR. ARRAS: Yeah.

COL MICHAEL: -- argues that's not sustainable, in the long term.

DR. ARRAS: Okay. So he's really more --

DR. GRADY: It's not even dialysis. It's intravenous fluids.

DR. ARRAS: Yeah. Yeah, so he's really more on the side of best available anywhere.

DR. GUTMANN: Correct, correct.

DR. ARRAS: Got it. Okay, yeah, yeah. Okay, so -- right.

DR. GUTMANN: And the providers on the ground have said, in no uncertain terms, that --

DR. ARRAS: Ain't going to happen.

DR. GUTMANN: -- that will prevent --

DR. ARRAS: Okay. Got it, okay.

DR. GUTMANN: -- from actually helping people survive.

DR. ARRAS: Okay, good.

DR. GUTMANN: The best ability possible on...

DR. ARRAS: Okay. So -- yeah. So, Amy, I would go with your interpretation. And I am just sort of demonstrating for you the kind of confusion we should try to avoid.

DR. GUTMANN: It's good that you brought it up, because I think people get very confused --

DR. ARRAS: See, I read these things too quickly, you know? It's a great help to get these press clippings from the staff, but -- okay.

The other thing that we might need to incorporate here is the distinction between research on vaccines and treatment. Nancy Kass made some cogent remarks

on that subject. Because, you know, the ethical treatment of those two issues in terms of design of trials might be important and relevant.

I guess, for me -- and I'm not really speaking for Christine here, but for me, the big problem that I have with this paragraph is that it's really mom and apple pie, in a way, and I don't really see it responding to the ferment in the field, you know. There is a serious debate going on about research design in this country, and the kinds of designs we should deploy overseas. Big debate.

But the kinds of proposals that we advance here are pretty tame. And they're proposals that just about anybody would agree to. Okay?

DR. GUTMANN: So you just -- your example of Paul Farmer is a prime example -- not everybody will agree with this. And we heard quite compelling arguments yesterday --

DR. ARRAS: Oh, yeah.

DR. GUTMANN: -- in support of this. I think we should make clear in the text that there is a controversy here, and we support this --

DR. ARRAS: No, Amy, I'm totally on board with that.

DR. GUTMANN: Okay. Good. That's all I wanted to know.

DR. ARRAS: Totally. Okay, but, you know, when we say that it should be acceptable to the host country, interpretable, minimize delays, I think those are all things that just about everybody would agree to. Okay?

So, here is my thought for my recommendation for the group.

DR. GUTMANN: You don't like everybody agreeing?

DR. ARRAS: Philosopher -- as you know, our job, as philosophers, is to make life harder for people. You know?

(Laughter.)

DR. GUTMANN: I don't agree with that, but that's okay --

DR. ARRAS: Yeah, okay. That's my mission in life. You know?

So, here is the -- and I'm not advocating anything specific here. Okay?

But I am suggesting this. If there is a big debate about clinical trial design out there, we need to ask ourselves, "Do we want to join that fray, and at what level of specificity do we want to join it?"

Okay? In other words, do we want to say that we think that, you know, that a standard brand -- gold standard, randomized clinical trial is the only way to go? Do we want to agree that adaptive trials are ethically acceptable? Do we want to say, with Nancy Kass and Dan, you know, from yesterday, that, really, a more creative design would be a kind of phase-one study at the start, and then go to a adaptive randomization design?

These are all just questions, Amy. Okay?

DR. GUTMANN: Yeah, I got it.

DR. ARRAS: But I think that if we don't -- I mean the worry that I have is that, if we don't at least in some way enter this fray, people are going to look at this and just shrug their shoulders and say --

DR. GUTMANN: The nice thing is, John, we are in this fray, and you feel we're not. So --

DR. ARRAS: At least here. At least here, yes.

DR. GUTMANN: We have --

DR. ARRAS: I mean in the text I think we are.

DR. GUTMANN: We have not -- yeah. We have not only entered it, but

my -- from yesterday, my sense is -- and Dan led this -- that we are in agreement on a position that is not universally accepted, but I think has the -- you know, has strong evidence and reasoning.

DR. ARRAS: Which position?

DR. GUTMANN: And I'm going to let Dan pick it up, and -- Raju after Dan. Okay?

DR. SULMASY: I think we could, you know, easily adjust the first sentence to say, you know, "Best supportive care available in the host country," something like that.

DR. ARRAS: Right, right.

DR. SULMASY: It would be -- and then, secondly, I think in the next sentence we could drop the "whether or not used placebo" part, and then put in a full sentence at the end that says something like this: "Properly designed placebo-controlled trials can meet these conditions, and innovative designs such as adaptive randomization or step wedge protocols ought to be considered as means of addressing these ethical research goals." A sentence like that gives it more specificity, more teeth.

I don't think in the recommendation we can get into vaccine trials versus drugs. We can get that into the text, we could get -- you know, whether or not there might be conditions for doing a sort of, you know, quick phase one into adaptive randomization considerations, depending on the circumstances in the text, if we want. But here, in the recommendation, just a sentence like that I think would help give more specificity to what I think we agree with.

DR. ARRAS: Yeah, I would approve of that. Sure.

DR. GUTMANN: Let me just go down. Raju?

DR. KUCHERLAPATI: A couple of things. One is I suggest that we take out "Ebola" in this first -- in this sentence, because we're not just talking about Ebola, but you're talking about any kind of epidemic that -- research during the Ebola epidemic, I said take out -- the "Ebola" out.

The second issue with regard to what John is talking about, it is the mandate for the Food and Drug Administration to approve the drugs, based on safety and efficacy. All right?

The third component that is not in the mandate is the time that it takes to be able to get -- you know, determine safety and efficacy. So this is the reason why the FDA began to think about these adaptive trials, so that you don't waste a lot of time, and to be able to get to the end point a little bit faster, if that is possible to be able to do.

So, I don't think that you need to be able to say, you know, whether adaptive trials are the right thing to do or not. That's not -- the ethical issue, really, is that you want to be able to have a drug, you know, that is available in a timely fashion. And that -- the goal -- but how to get there is based upon safety and efficacy, how we get there.

So, that's the ethical issue. We don't have to talk about, you know, the controversy that you're alluding to, which is whether placebo trials are ethical or unethical. That's not the issue here, I don't think.

DR. ARRAS: I think it is an issue. And certainly, in our report on Moral Science, we spent a whole chapter on that.

DR. GUTMANN: So, just on the first sentence, we have to say something that this is research during an epidemic like Ebola, such as Ebola.

Okay. Christine? So --

DR. GRADY: So I think there is a risk in being too specific, because some of the -- each trial is different, you know, what the drugs are, what the vaccines are. The candidates make a difference, how much you know about them make a difference.

And one of the things that occurred to me after the discussion yesterday that might be worth saying is that there are no different ethical principles that guide research in this context, that the same principles apply, and that -- you know, so the idea of, you know, finding the right design for the question that's being asked, making it as rigorous as possible, you engage in the community -- the things that we say are the principles that should apply all the time, and that these apply here, as well.

DR. GUTMANN: Yeah. But we do need -- we -- I agree on doing that. But we also need to be specific. This is a report about response of the Ebola epidemic. And I don't want to go from the frying pan into the fire. So the same principles apply. But if all we did, as a commission, is reiterate our principles, nobody except for us and a group of small very group of philosophers would understand what in the world are the implications of these principles for real-life situations.

So, I think we ought to be specific, because it makes a difference to know. The principles are only as powerful as we can get some kind of agreement on their practical application.

DR. GRADY: So then I'm not sure what we're being specific about. I don't really --

DR. WAGNER: I think what is very effective --

DR. GUTMANN: What Nancy and others were --

DR. WAGNER: But Dan's statement, I thought, was very good, because

it -- it has a foot in both places. It specifically says that RCT, restricting things to RCT, is something we don't necessarily endorse, that there should be additional flexibility. It doesn't say you must use one of -- it's not so specific as to try to prescribe some other protocol approach.

But if you would read that again, the net intent of that is to say we would not restrict -- we do not think it would be ethically appropriate to restrict studies only to RCT in these -- under these -- please read that again one more time, if you would.

DR. SULMASY: Yeah, I tried, Christine, to put my feet in both camps. So it says, again, "Properly designed placebo-controlled trials can meet these conditions," right, of being ethical and scientifically valid, et cetera. And, "Innovative designs such as adaptive randomization or stepped wedge protocols ought to be considered" -- right -- "as means of addressing these research goals."

So, maybe it's -- you know, I don't know -- there are other designs, certainly, that could be used. But I wanted to get some sense that we have heard that there are designs that are, other than the standard randomized control trial, that could be used in these settings, and that they -- those are things people ought to think about.

DR. GUTMANN: Nelson?

COL MICHAEL: Just one point, because I think yesterday, just from a purely technical standpoint, we've gotten hooked on this adaptive trial design. There is nothing about that that is ethically funky. It is a RCT.

And so, drop the adaptive language. There is nothing about that that's unusual. It just isn't done that often, because, operationally, you don't usually have two products that are ready to go at the same time, full stop.

So, stepped wedge is way different. But a randomized control trial with

an adaptive or conventional design are essentially the same thing, from an ethical standpoint.

DR. SULMASY: But I'm just saying it's innovative, that --

COL MICHAEL: Well, it's not that innovative, it's using cancer oncology --

DR. GUTMANN: Yeah, but --

COL MICHAEL: -- all the time.

DR. GUTMANN: -- four people in --

COL MICHAEL: The issue is placebo. I could tell you two days at the World Health Organization, sitting next to Lu Borio in Geneva in September, and that was the whole issue, is placebo, yes/no. Not adaptive RCTs versus regular RCTs. And stepped wedge and other ring-backs -- there are other ways to do it. But I just think we should lose our fascination with the adaptive design --

DR. GUTMANN: We're not fascinated by it, it's just that it is a term out there, and --

COL MICHAEL: It is. It's an RCT.

DR. GUTMANN: -- it does modify the way standard RCTs were done. And it's now --

COL MICHAEL: Yeah, but I can tell you the debate is placebo. That's where the rub is.

DR. GUTMANN: Yeah. Christine?

DR. GRADY: So I'm going to disagree with Nelson, believe it or not, because I think adaptive actually encompasses a lot more than just, you know, three arms. There is a lot of other adaptations that people use. And adapting the standard

randomized clinical trial, I think, is the right way to go.

I would argue, actually, we shouldn't keep stepped wedge in there, because I don't think people know enough about it.

DR. GUTMANN: Yeah, I agree with that. I think you actually introduced it yesterday, or Nelson did. I think we don't -- I think we can agree that we should keep adaptive, not claiming it's something tremendously novel, but it does modify the way in which a lot of people think about the rigidity of randomized control trials. And it opens people's minds to the fact, and it is a fact that there are many different ways of running these. And the issue is the placebo-controlled trials.

And I believe we have agreement that if a home run isn't achieved in, you know, a safety study, that you go to adaptive placebo control trials. And I think this is not -- and very little in this report is -- we're not aiming to be provocative here. We're aiming to really be sensible, and help move forward in emergency situations that are life-saving, you know, whether there are lives at stake, and without hitting, you know, what we believe are ethical land mines.

DR. WAGNER: I have a question.

DR. GUTMANN: Could I go to Steve, and then to Jim?

DR. WAGNER: Okay. Mine is a confusion --

DR. GUTMANN: Okay, Jim.

DR. WAGNER: -- rather than a statement.

DR. GUTMANN: Okay.

DR. WAGNER: And I hope maybe it's this half of the room that can help me.

DR. GUTMANN: Sure.

DR. WAGNER: They're in heated agreement, maybe.

DR. GUTMANN: Maybe. The question is about, as you just said, that if the home run is discovered in a phase one trial, that, you know, things might be accelerated.

My question is, if under those circumstances -- and I don't think it's that far-fetched -- we might -- and I thought this subject came up yesterday -- we might imagine re-purposing an already-approved drug that -- you know, an off-label use, if you will, of an already-approved drug, presumably, since it's already been approved, it's already had its phase one study, and we wouldn't have the option of another phase one study in order to discover if there is a home run there. Is that -- am I understanding that correctly?

DR. GUTMANN: I think Dan wants to take you up --

DR. SULMASY: Yeah. Christine and I spoke a little bit about that yesterday. And it is, you know, again, complicated. And there may be, you know, disagreement here, but my sense would be this depends, to some extent, on community engagement. Right?

So, if this has never -- if drug has never been used before for this virus, or whatever the infection might be in other epidemics, then -- but it has been proven safe --

PARTICIPANT: Safe, yeah.

DR. SULMASY: -- one still might -- I would be willing, if the demand for treatment up front was significant enough, to go through, if you will, an unnecessary, you know, repeat phase one of about 40 patients, to see whether it's a home run or not for that -- in that case, even if we know that it's safe, and that maybe, you know, that there is the odd chance that it might be terribly toxic in this particular

setting, but largely just to see whether it's a home run or not before proceeding. And I would be comfortable with that much of a delay in going to the randomization with placebo. But I think others might disagree with that.

DR. GUTMANN: Steve?

DR. HAUSER: Well, just to pick up on this, there was a report in the press yesterday of an antiviral that may have hit a single or a double -- not a home run -- in a non-placebo-control trial, but using another population's placebo experience, as a comparator. And that happened through a pre-planned interim analysis. And I think this highlights the complexity --

DR. GUTMANN: Yeah.

DR. HAUSER: -- of all of this, and why we have to be broad, as well as specific, I think.

I think the idea of a sense of urgency during an epidemic is important. Another antiviral was stopped because the population that could have received the drug was petering out, and the trial could no longer happen. So I do think that we are -- we do have urgency for everything we do but the trial has to be finished, or it can never be finished, with --

DR. GUTMANN: I think that's extremely helpful. I think here is what we need to say here, and I'm not going to try to draft it. But I think it takes into account everything that we've said.

The same principles apply to research in an epidemic as normal. However, there is a heightened sense of urgency of moving forward with testing. In these circumstances, the full range of adaptive design -- RCT, right -- need to be considered. And then you go on with what we say.

I think that captures, and it actually also communicates why there is such a focus on figuring out what are you going to do, rather than arguing about it to move forward. Okay?

Could we move on? We have two more we have to do. So -- and then come back?

DR. GRADY: Very quick?

DR. GUTMANN: Sure.

DR. GRADY: Sorry. I would love to say in the text somewhere something that I heard strongly yesterday, and that is we can't forget research on other things. Not just the drugs and the vaccines, but the --

DR. GUTMANN: Yes.

DR. GRADY: -- natural history, the psychological effects, all of those things.

DR. GUTMANN: Well taken. A friendly addition well taken.

DR. SULMASY: What supportive care means.

DR. GUTMANN: I have to -- we have to, and, therefore, I have to -- get us through two recommendations before we adjourn, and we have a hard stop at 11:15.

The plan for a fifth recommendation -- thank you very much, this was extraordinarily helpful -- the plan for a fifth recommendation is to focus on the use and sharing of biospecimens internationally for research, in particular the importance of U.S. Government facilitation of the ethical acquisition of biospecimens, including addressing the challenges of obtaining consent during a public health emergency, and ensuring adequate privacy protections, and access to the benefits that result from related research. These types of assurances will clearly require ongoing dialogue with global

partners, requiring effective strategies for enactment.

Christine, you have put a lot of thought into this topic. You want to start us off? I have effectively summarized the recommendation -- or, ineffectively, as the case may be.

DR. GRADY: Well, I will say there is a lot packed into this. But I think that, you know, in this setting of an epidemic, obtaining consent for something that we spend hours debating about obtaining consent for in other situations is tricky, and we have to be cognizant of that.

Other things, like assuring adequacy -- adequate privacy protections, I think, are pretty standard, and we should continue to do that in this setting.

And I think the other -- the piece that's probably more -- not controversial, but more expansive than some is the recommendation about access to the benefits that, you know, benefits that are -- that derive from research done with specimens, et cetera, should be available to the broadest group of people possible.

I mean, I think that's right, but there are people who might contest that.

DR. GUTMANN: Raju?

DR. KUCHERLAPATI: There is something implicit about this that's very good that's not explicit, and that is actually -- you know, there are certain countries that have restrictions on transferring biospecimens outside their borders.

And what we are saying here is that -- you know, that is counterproductive, at least in certain circumstances, that it's important to be able to share, so that research can really progress well beyond. And that's a very good point. And it's not explicit, but it's in it, and I like that.

DR. GUTMANN: Yeah. I do -- again, we're not wordsmithing now, but

just for -- you know, just since we're trying -- we're going to try to get this out as quickly as we can, let's try to -- the ethical acquisition of -- what does that mean? I mean "acquisition," what does that mean? What are we -- should facilitate the sharing -- biospecimens -- yeah. Yeah.

DR. WAGNER: You're right, you're on to something.

DR. GUTMANN: And --

DR. WAGNER: Let our wordsmiths do that.

DR. GUTMANN: Yeah. So we could say another thing here about -- there are two things packed into the first sentence. One is the widespread sharing of biospecimens, and the good that that will do over time. And the other is the obtaining of consent during a public health emergency. And there, do we agree the same thing holds? The same principle for obtaining consent during an individual emergency, you bring somebody to -- you rush somebody in an ambulance to the emergency room. It's the same principle and, you know, and some version of the practice that that holds.

DR. WAGNER: Why wouldn't we just use language to the effect that we want to ensure consent, as we have also used in that phrase, "ensuring privacy"? Why not --

DR. GRADY: Well, there are some really particular challenges here, and one is that some of the people from whom we are obtaining biospecimens won't be able to give consent. And the other is that international sharing of biospecimens has a lot of meaning to certain people, and some people object to it.

So, there are reasons to be very careful about how you get permission to obtain samples and send them across the world.

DR. WAGNER: Yeah. I guess what I was saying, in the context of the sentence of what the U.S. Government should facilitate --

DR. GRADY: Yeah.

DR. WAGNER: -- I wish they would facilitate consent, and I wish they would facilitate transport, and facilitate sharing.

DR. GUTMANN: So, do we have -- is there a --

DR. GRADY: Stronger words, you mean. Strong words -- yeah.

DR. WAGNER: As far as they can facilitate it, right?

DR. GUTMANN: Is there international -- something analogous to international law in the area of what it -- is required, what are the standards for obtaining consent and sharing? And, if there isn't, do we need to call for understanding across societies for how we're going to share -- be able to get to the point of sharing biospecimens and obtain consent?

DR. GRADY: So, there is an agreement that was negotiated by the World Health Organization for pandemic influenza in this context of sharing specimens across --

DR. GUTMANN: And is it a best practice?

DR. GRADY: It's a relatively new agreement. It took years to come up with. And it's been -- it's been worded in a way that it's very specific to pandemic influenza. And it does leave room for negotiations between parties.

So, I think it is -- it's something that we do allude to in our draft report, and talk about, and talk about, you know, that maybe it's a good place to start. But I don't know that there is enough experience with it to say that it's the best practice. Is that fair?

DR. GUTMANN: Raju?

DR. KUCHERLAPATI: Just an explanation. You know, there are several countries like, you know, France and China and India, for example, that they prohibit sending DNA outside.

DR. GUTMANN: Right, right.

DR. KUCHERLAPATI: And part of the reason they do that is that they consider that as a national resource. And, therefore, they don't want to share that resource with others which might be competing.

And so, I think it may be very difficult to call for an international agreement to say that --

DR. GUTMANN: Yeah. No, I wasn't asking for -- I was just wondering what in this area the -- yeah. What do -- this is a very general call, and the more we discuss it, the more general that -- we don't have in mind how this is going to happen.

DR. SULMASY: I think we have to be careful with the first sentence, because I think there -- if we're going to put "sharing" in there -- because there are two different ethical questions, right?

One is the ethical acquisition, which could be either informed consent from a subject who is capable of giving consent, or other ways that the patient is not, right? But we want to make sure that that's done ethically. And we want to also facilitate the sharing across borders. And I think trying to put those into one sentence may be complicated.

DR. GUTMANN: And, in the same sentence is the challenges of obtaining consent --

DR. SULMASY: Consent, right.

DR. GUTMANN: -- and we're talking about individual consent, and not just the governmental consent --

DR. SULMASY: Right, right. So it's --

DR. GUTMANN: -- to this.

DR. SULMASY: So I think that they may be two sentences that need to be done for those, or something like that.

DR. GUTMANN: There is no disagreement about the desirability --

DR. SULMASY: Correct, correct.

DR. GUTMANN: -- of getting here. I think we're going to need to work -- so there is no disagreement among the Commission. That just would be good to get to. I think we need to work on how specific can we be in this recommendation, because there is a lot in it that's very general.

DR. SULMASY: And then just another question that I have about how much of this sharing that's desired by the scientific community is of the genome sequences of the subjects, versus the genomes of the virus, and et cetera.

So, it might be important to emphasize that in the report, because --

DR. GUTMANN: It's the virus.

DR. SULMASY: -- the privacy concerns are much less there, in terms of that.

DR. GUTMANN: Right. Good, good. That's very helpful. I think we can move on with that, because we don't -- it's out there, and we just have to refine it.

DR. SULMASY: Right.

DR. GUTMANN: For our last recommendation, I'd like to highlight the importance of ethical perspectives, like the ones we heard today being integrated into

public health decision-making processes early and often. This would require some sort of an advisory body or other public health consultant -- ethics consultant to be readily available to identify those considerations, ethical considerations relevant to public health emergencies and responses, in light of real-time available evidence.

So, Anita, I believe that this closing recommendation fell under your bailiwick. As well, if you would like to start us off, I will just read it. "Ethical perspectives should be integrated into timely and agile public health decision-making processes employed in response to rapidly-unfolding epidemics. An advisory body, or other qualified public health ethics consultant should be readily available to identify ethical considerations relevant to public health emergencies and responses in light of real-time available evidence.

I would just say, in light of our first recommendation, that there be a clear person identified for response. We should be more specific here, because it ought to be part of that person's oversight to bring -- and that way this will make this recommendation much more specific, to bring those ethical considerations to the floor in the official federal government response to an epidemic.

DR. ALLEN: Yeah, I would totally agree with that, that we -- there should be some specificity there.

DR. GUTMANN: Yeah.

DR. ALLEN: Just a couple of thoughts. One is that the draft guideline which you read makes reference to ethical perspectives being integrated, and I wondered whether we need to say something a bit stronger, like ethical perspectives and guidelines in order to open the possibility that what we're asking for is both sort of informal -- community perspectives, but also any professional or institutional guidelines

that normally would govern such a situation should be brought in, as well.

So, I was thinking that maybe --

DR. GUTMANN: Yeah, I would much rather use "ethical principles," "ethical standards" --

DR. ALLEN: Yes, yes.

DR. GUTMANN: I mean it's not, you know --

DR. ALLEN: Yeah, yeah. So we could either take out the word "perspectives," and substitute "principles" or "guidelines" --

DR. GUTMANN: There is a rigor to bringing ethics to bear in -- at the level of a public response.

DR. ALLEN: Good, good. So we're agreed on that.

And then, I take it that the -- that one of the purposes of this recommendation is to -- and to just underscore that ethics should be -- does not become irrelevant in moments of emergencies, we have, in this room, in the last couple of days, emphasized and questioned about what role do ethics play when suddenly you're in an emergency. And I think we agree that they don't become irrelevant, nor do they -- we have to invent a totally different perspective.

But in any event, this recommendation seems to underscore the notion that ethics are relevant, they should be integrated, as we've often emphasized --

DR. GUTMANN: Use "principles," instead of "perspectives."

DR. ALLEN: Yeah. Good. Right. And then the question becomes, well, whose decision-making are we interested in? And I think it might be an improvement -- although wordier -- to say something like "into timely and agile public-health decision-making by local state and federal officials in response to rapidly

unfolding epidemics."

DR. GUTMANN: I like that.

DR. ALLEN: Yeah. Okay, good. And then, when it comes to the nature of the entity that -- entity or entities that we've consulted, it did strike me that we might want to say something a bit fuller, like an ad hoc or standing public health ethics body should be consulted throughout an epidemic to help officials identify ethical considerations pertinent to public health emergencies, in the light of real-time available evidence.

That is to say I think that the current draft language, in terms of an advisory body or other qualified public health ethics consultant, to me, is a little bit less specific and less clear cut.

DR. GUTMANN: So --

DR. ALLEN: I mean we want to use language that, I think, ties into how we already think about the kinds of entities that are available for ethics consultation.

DR. GUTMANN: I would just suggest, if -- as a friendly amendment to that, that, given that we're calling up front, this is a nice book end of -- first and final recommendation. Given that we're calling up front for there to be an integrated public response to these emergencies, I think we should also call for ethical principles to be integrated into that organizational response at all levels.

I don't think we should call for a separate ethics advisory committee, as if ethics stands outside, and is wagging its finger at -- I mean too late, usually, right?

DR. ALLEN: Yeah.

DR. GUTMANN: I think we should call for an integrated -- for that -- the first recommendation and the last recommendation, to make sure that ethics is

integrated, ethical principles are integrated through every level of governmental response.

So -- and that includes --

DR. ALLEN: -- wonder whether we even need this last sentence --

DR. GUTMANN: -- that when governors and -- you know, governors and all public officials take a position in a public health emergency, they should have taken into account the ethics of what they're arguing for.

DR. WAGNER: Change "should" to "must."

DR. GUTMANN: Must.

COL MICHAEL: Yeah, it must --

DR. GUTMANN: Are remiss if they do not, yeah.

Yeah. They can, they should, they must.

(Laughter.)

DR. ALLEN: Must be integrated.

PARTICIPANT: Must be integrated.

DR. ALLEN: Yeah.

DR. GUTMANN: Okay?

DR. SULMASY: Yeah, and then --

DR. GUTMANN: I'm going to wrap up.

DR. SULMASY: Well, I just would make the recommendation, again, that we consider a separate recommendation on communication, because we heard so much about that yesterday --

DR. GUTMANN: I took that as a suggestion well taken, and we will draft it. But, for the public record, we will have a recommendation on how important

communication, through education proactively to communicate, and communication throughout.

And I would add in that -- and I love -- you can never repeat it too often. It's -- when you're a scholar -- and this goes back to something -- when you're a scholar, there is a negative to repeating the same thing over and over again. We want to be original, as scholars. When you're a public official and have the public responsibility to do the right thing, there is something that needs to be done, one has to communicate it early and often.

COL MICHAEL: That's also what army officers do.

(Laughter.)

DR. GUTMANN: Say no more. Okay. Let me close by thanking everyone. I will begin by thanking our vice chair, Jim Wagner, our Commission members, and, above all, our staff, who works full time on this, and works so well.

I want to reiterate that we invite everyone -- speakers, those in our audience, those of you watching on our webcast, or who will watch the webcast -- to write us with any comments. And there is an urgency about getting this report out, so write us early, and submit your comments on our website, [bioethics.gov](http://bioethics.gov).

And, with that, I will ask Jim, would you like to say any closing words?

DR. WAGNER: Just thanks to this great group and to our staff, as well. Thanks to you, Amy. Amazingly productive two days, wonderful two days. Thanks, and safe travels.

DR. GUTMANN: Safe travels, everyone.

(Applause.)

(Whereupon, at 11:15 a.m., the meeting was concluded.)

