THE U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
CENTERS FOR DISEASE CONTROL AND PREVENTION

NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH
WORLD TRADE CENTER HEALTH PROGRAM

TENTH MEETING

SCIENTIFIC/TECHNICAL ADVISORY

COMMITTEE (STAC) MEETING

March 1, 2018

The verbatim transcript of the

Meeting of the Scientific/Technical Advisory

Committee Meeting held on March 1, 2018, 9:00 a.m.

C O N T E N T S

March 1, 2018

P A R T I C I P A N T S

(alphabetically)

ROSEMARIE BOWLER, PhD - COMMITTEE MEMBER
EVELYN BROMET, PhD - PRESENTER
TANIA CARRÉON-VALENCIA, PhD - PRESENTER
KIMBERLY FLYNN - PUBLIC COMMENT
MRIDU GULATI, MD - COMMITTEE MEMBER
JOHN HOWARD, MD - PROGRAM ADMINISTRATOR
TRAVIS KUBALE, MD – PRESENTER
BENJAMIN LUFT, MD - PRESENTER
CATHERINE McVAY HUGHES - COMMITTEE MEMBER
VAYLATEENA JONES - COMMITTEE MEMBER
MICHAEL McCAWLEY, MD - COMMITTEE MEMBER
STEVEN MARKOWITZ, MD - COMMITTEE MEMBER
ANNYCE MAYER, PhD - COMMITTEE MEMBER
PAUL J. MIDDENDORF, PhD - DESIGNATED FEDERAL OFFICIAL
ALFREDO MORABIA, MD - PRESENTER
LILA NORDSTROM - COMMITTEE MEMBER
DAVID PREZANT, MD – PRESENTER
JOAN REIBMAN, MD - PRESENTER
DORI REISSMAN, MD - PRESENTER
WILLIAM ROM, MD - COMMITTEE MEMBER
MARGARET RYAN, MD - COMMITTEE MEMBER
MICKI SIEGEL DE HERNÁNDEZ - COMMITTEE MEMBER
GLENN TALASKA, PhD - COMMITTEE MEMBER
MIA WALLACE - PRESENTER
ELIZABETH WARD, PhD - COMMITTEE CHAIR-PERSON

WELCOME AND INTRODUCTION

DR. MIDDENDORF: Good morning, everyone. I am Paul Middendorf, as most of you already know. I am the Designated Federal Official for the World Trade Center Scientific/Technical Advisory Committee.

And we'll go through a number of administrative issues here on the front end, first to remind you that the exits are in the back and if we have an emergency, go through the set of double glass doors, turn immediately left down the hallway. There is a stairwell there that will take you down and out of the building. Restrooms are on this floor. Just keep going straight through the double glass doors and you'll find them on your right halfway down the hallway.

Just a reminder that food and beverages are not allowed to be consumed in this room. Water is fine but nothing else please. This is a great facility for us to come to and use—we really do appreciate it. We don't want them to kick us out for having coffee or spilling coffee or something.

It has been our tradition to spend a few moments at the beginning of each of our meetings in silence to remember those who were killed in the attacks on 9/11 and also those responders and survivors who have since died because of those attacks, as well as others who have been killed in or suffering from terrorist attacks around the world. Today I'd like to add one more person to our remembrances. Jim Melius, who was instrumental in so many ways to the Program, recently passed away. So please include him in your thoughts during these moments of silence.

[Moment of silence.]

Okay, thank you. I'd like to extend a warm welcome to each of our committee members, who have graciously agreed to share their time and thoughts with the Program to help improve it. We're looking forward to hearing everyone's thoughts and ideas. Also want to extend a warm welcome to the members of the public who are here with us or listening to us on the phone. We very much appreciate your interest in these proceedings. For those of you members of the public who have signed up to provide public comments, they are scheduled to begin at about 9:15 this morning; that's Eastern Time. Those of you here in the room please come up to the podium when I announce you. For our public commenters on the phone, when your turn comes, your phone line will be opened so we can hear you over the phones.

I guess I want to go into the roll call next and just say aye if you're present, and if you would also just address whether or not there have been any conflicts of interest, changes in conflict of interest, since you last filled out your forms. So Rosemarie Bowler?

DR. BOWLER: Yes. Good morning.

DR. MIDDENDORF: Good morning, and any changes in your conflict of interest?

DR. BOWLER: No changes. No conflicts.

DR. MIDDENDORF: Okay. Mridu Gulati?
DR. GULATI: Yes, and no changes.
DR. MIDDENDORF: So Catherine Hughes?
MS. HUGHES: Present, no changes.
DR. MIDDENDORF: Val Jones?
MS. JONES: Present. I retired.
DR. MIDDENDORF: Okay, congratulations. Steve Markowitz?
DR. MARKOWITZ: I'm here. No changes.
DR. MIDDENDORF: Annyce Mayer?
DR. MAYER: Aye. No changes.
DR. MIDDENDORF: Mike McCawley?
DR. McCAWLEY: I'm present. I did have one change. I am now serving on a National Academy of Sciences panel for NIOSH, so.
DR. MIDDENDORF: Okay, and what is that committee?
DR. McCAWLEY: It's on the coal workers, pneumoconiosis, the new regulations.
DR. MIDDENDORF: Coal worker, okay. Okay.
MS. HUGHES: Paul?
DR. MIDDENDORF: Yes.
MS. HUGHES: On here it says I'm Chair of Community Board 1. I'm no longer on Community Board 1 but on the papers that I filed, that was there. So I just want to make sure for the record.
DR. MIDDENDORF: Okay, where, which?
MS. HUGHES: It says "Chair, Manhattan Community Board 1". I'm no longer, I resigned from Community Board 1.
DR. MIDDENDORF: Is that the current roster? In that document—
MS. HUGHES: Yes, it says, the copy at our table.
DR. MIDDENDORF: Okay, so we need to get that—
MS. HUGHES: So I just want to make sure you're…
DR. MIDDENDORF: Okay, we'll get that changed.
MS. HUGHES: Because I filed that but I just saw it here. Thank you.
DR. MIDDENDORF: Okay, thank you. Lila Nordstrom?
MS. NORDSTROM: Yes, and no changes.
DR. MIDDENDORF: Bill Rom?
DR. ROM: Present on the telephone, no change.
DR. MIDDENDORF: Okay. Margaret Ryan?
DR. RYAN: I'm also present on the phone. No changes, sir.
DR. MIDDENDORF: Okay. Sheela Sathyanarayana? Okay, not present. Micki Siegel de Hernández?
MS. SIEGEL DE HERNÁNDEZ: Present and no changes.
DR. MIDDENDORF: Glenn Talaska?
DR. TALASKA: Present, no changes.
DR. MIDDENDORF: Liz Ward?

DR. WARD: Present, no changes.

DR. MIDDENDORF: And Marc Wilkenfeld? Okay. Okay, so we have one, two, three, four, five, six, seven, eight, nine, ten, eleven, twelve, thirteen members; that represents a quorum.

Okay. Before I turn this over to Liz, I just want to briefly go over the agenda. You should have copies of the agenda in the back. For those of you on the phone, they were sent out to you as well.

We'll begin with Dr. Howard as usual, who will give us our charge, and then we'll go on to public comments. After that, I will do a brief update on where we are with respect to peer review to lead into your discussion, and then later this morning, Dr. Carréon-Valencia will update us on the policy and procedures for adding non-cancer conditions to the list of covered conditions, and then she and Mia Wallace will provide an overview of the recently conducted public engagement on the Research to Care initiative. The afternoon is dedicated to World Trade Center research. Presentations there are intended to inform you about what is going on in World Trade Center funded research and that's an aid to you when you're asked to fill another role of the STAC, which is to provide the administrator consultation regarding research conducted or supported by the World Trade Center Health Program. At this point in time, there won't be any charge related to the research, but we wanted to make sure that you're up to date, up to speed with what's going on so that when you are asked, you have the opportunity to provide more informed thoughts and ideas for him.

So with that, Liz, I'll turn it over to you.

DR. WARD: Thank you, and I'd like to add my warm welcome to the committee members and the members of the public. In addition, I want to express my thanks to the staff of the, to the NIOSH staff and the World Trade Center Program staff who work so hard to put these meetings together and provide us such great background material, and also to the presenters who will be joining us today, and especially those who are presenting their research results.

So with that, I think we're ready to begin. And we'll start with John Howard.

CHARGE

DR. HOWARD: Good morning, everyone. This is the tenth meeting of the World Trade Center Health Program's Scientific/Technical Advisory Committee. I want to say, as I always do, (inaudible @ 00:07:55) very busy schedules to meet with us today. It's vital that the Program receive your input and the input of the public, so we appreciate the advice. I must say that, as a disclaimer, sometimes we don't take it all, but we listen to everything that you have to say, and consider it very carefully. Today, we fulfill one of our responsibilities under Title I of the James Zadroga 9/11 Health and Compensation Reauthorization Act, which is to develop a pool of potential peer reviewers with medical and scientific expertise that would help us in looking at the conditions that we propose to add. And we do this by requesting

recommendations from you all, either specifically oriented to individuals who you think might be helpful to us, or you know, processes that we can use to identify folks as we go through time. The last time we did this was November 3, 2016. We are required to do it every two years, so it's time; we're getting a head start, so you have plenty of time. Deadline is November of 2018. So we look forward to your recommendations for peer reviewers and we hope that you can provide those to us, with your vast knowledge of the fields that the Program covers.

Two other issues. One, as has already been mentioned, Dr. Melius passed away recently, and certainly there was no finer advocate for our program than Dr. Melius, not only during the early days of when the Program was a series of contracts to developing the James Zadroga 9/11 Health and Compensation Act of 2010, and then also the reauthorization for an almost unbelievable 75 years. Dr. Melius played really pivotal roles in accomplishing those tasks. He also chaired the Responder Steering Committee. We want to congratulate Micki for taking up that task and thank her for that. But Dr. Melius did so much for NIOSH, not only for this program but also for chairing our Advisory Board on Radiation and Worker Health, which is another program that NIOSH hosts. So we're going to miss him and his wise counsel, and that's why we need every one of you to help us out.

The other item I wanted to mention to you today is the President's fiscal year 2019 proposed budget. I would just like to emphasize the word "proposed". It is a budget for the period October 1, 2018 through September 30, 2019, and it was released to the public on February 12 of this year. It proposes to consolidate the activities of NIOSH within the National Institutes of Health, while the World Trade Center Health Program would continue to be administered by CDC. We always have to remember that the President's proposed budget marks the beginning of the annual congressional appropriations process, which in the case of fiscal year 2018, has stretched longer than any of us thought it would. And we're hopeful that the Appropriation Committees of the Senate and the House of Representatives will give thoughtful consideration to the President's budget. We have no indication at this time that these proposals relative to NIOSH or the World Trade Center Health Program would be executed in the absence of congressional approval. Meanwhile, NIOSH will continue to conduct our scientific research and our technical assistance that's aimed at protecting the safety and health of the nation's workers, and we will continue to provide the scientific and administrative support to the World Trade Center Health Program.

So thank you again for your time and your consideration. I want to thank Liz for continuing to chair the Committee and for all of you to help us, and all of you on the phone. Thank you very much for your effort, and we look forward to your advice.

DR. WARD: Thank you, Dr. Howard, and I'll turn it over to Paul for the public comments.

PUBLIC COMMENTS

DR. MIDDENDORF: Okay. Just as a reminder, what we'll do is, what I'd ask you to—announce that it's your turn please come up to the podium. You'll have five minutes to provide your comments. I just want to make sure that each of you is aware of the redaction policy for the public comments. The policy is in the Federal Register Notice and a copy of it is also in the back.

Our first public commenter is Kimberly Flynn, Kimberly, if you'd like to come up.

MS. FLYNN: Good morning, I am Kimberly Flynn, I chair the World Trade Center Health Program's Survivor Steering Committee, and I thank you for the opportunity to make these comments on the SSC's behalf.

I want to join Dr. Howard in acknowledging the enormous contribution made by Dr. Jim Melius, the person who would typically be preceding me to this mic to make comments on behalf of the Responder Steering Committee. Jim is missed here today, as he has been in every context in which he served. His immense knowledge, his long experience in worker health and safety struggles, his steadfast dedication to the cause of 9/11 health and compensation have made an immeasurable difference in the lives of responders and survivors alike, and will continue to do so for as long as the World Trade Center Health Program exists. Invariably, when I got up to make comments following Jim, I would start by stating that we endorsed everything he said, and I will cite his remarks at the last STAC meeting in my comments today.

As we know, the reauthorization of Zadroga mandates an independent peer review process for any decision by the World Trade Center Health Program's administrator to add new health conditions. Comments today are requested on the identification of peer reviewers with the potential to serve on an independent peer review panel constituted by the administrator and charged with peer reviewing additions to the list of WTC-related conditions and relevant supporting evidence. These peer reviews will have important consequences for the health and welfare of people whose health was directly affected by the 9/11 attacks, but also affected through being misled by their government that the air they breathed, the dust on the pile and in homes, schools and workplaces was safe, when it was in fact toxic. For the peer review process to gain the confidence of the public and of the 9/11 community, we believe it must be fully transparent from beginning to end.

So first point: we endorse the proposed open process in which the public's input as well as the STAC's input will be solicited through the Federal Register to identify peer reviewers for the World Trade Center Health Program. We also concur with the inclusive approach being taken to the issue of peer reviewers' respective expertises that would include, but not be limited, to occupational and environmental health, epidemiology, industrial hygiene, and clinical research expertise about specific conditions.

Two: as we understand it, NIOSH will use a robust conflict of interest policy used by the National Academy of Science. We did not have an opportunity to fully

examine the policy but if it is as robust as the policy being used by the STAC, we do believe it will minimize bias.

Three: once peer reviewers are selected by the administrator, they will only have 30 days in which to consider the quality of the evidence on which the decision to add a new condition is based. The NIOSH policy and procedures document refers peer reviewers to government sources for studies on the 9/11—on non-9/11-exposed populations, so we think this is a very important thing to flag for the STAC, because the STAC may be the best, the most feasible venue to bring in outside experts with specific subject matter expertise on the linkage between certain World Trade Center contaminants and illness outside of the 9/11 context. And to cite Jim Melius's remarks at the last meeting, he spoke specifically about silica, studies of silica, raising the risk for developing certain autoimmune diseases.

And four: we believe that the public's trust is best served by publishing peer reviewers' comments with attribution, and I'm going to quote Jim's remarks to the last STAC meeting. Quote: "I see no sound justification for secrecy. Scientists commenting on public policy generally expect that their names and their submitted comments will be public. Those that object based on personal preference may do so by not participating, but I know of no evidence that the lack of participation by the few individuals who might object to being identified would significantly limit the availability of qualified peer reviewers. Similar peer reviews conducted by NIOSH and by OSHA in their rule-making identified the peer reviewers and their comments." Close quote.

And now an update. Over the past years, the SSC has called on NIOSH to address the limitations of the Registry's child cohort by entering into negotiations with New York City Department of Education to gain their cooperation in creating a new cohort composed of people attending New York City public schools in the New York City disaster area from 2001 to 2003. After much effort by many players, there is agreement. There is even a tentative timetable. We owe thanks to Dori Reissman of NIOSH, Ben Chevat of 9/11 Health Watch, Ellie Engler of the United Federation of Teachers, the World Trade Center Health Registry, and of course the late Jim Melius. The challenges of this project to reach out to and enroll a population of rapidly dispersing young adults 17 years after 9/11 are daunting. It can only be accomplished through a collaboration with the SSC and its network of community stakeholders, including StuyHealth, which is why we call on NIOSH to commit to coordinating with us on outreach to build participation.

And I'm going to skip my comment on blood banking; it will be included in my written remarks, which I will submit to the docket.

Finally, I would like to say a word about NIOSH and the WTC administrator. In 2006, Dr. John Howard came to a meeting with more than 30 Lower Manhattan community representatives held in the closest residential building to Ground Zero.

He was the first Bush Administration official to meet with downtown residents, workers and school parents to discuss 9/11 health impacts to the community, and he and his Science Team spent nearly three hours in dialogue with us. Following the passage of Zadroga, we formed the Survivor Steering Committee to advise the World Trade Center Health Program's management team on how best to meet survivors' 9/11 health needs. We have appreciated their dedication and integrity, and benefited from their broad and deep competencies.
We are extremely concerned by the President's fiscal year '19 budget request to separate the World Trade Center Health Program from NIOSH and believe, after many years of working with NIOSH, that the loss of NIOSH leadership, expertise and close engagement with the two steering committees constitutes a serious threat to the World Trade Center Health Program, the standard of care it provides, and the wellbeing of responders and survivors who depend on it. As we speak, there are survivors and responders whose very lives depend on the good functioning of the World Trade Center Health Program. This proposal stands to do dramatic damage to the Program's ability to meet their needs and the needs of many thousands receiving care. SSC joins the calls of the New York congressional delegation and many, many other stakeholders for the proposal to be withdrawn. Thank you.

DR. MIDDENDORF: Thank you, Kimberly. Our next public commenter is Rachel Lidov. Rachel, are you on the phone? Let me ask the operator. Operator, is Rachel Lidov on the line?

OPERATOR: I do not believe she is on the line, sir.

DR. MIDDENDORF: Okay. And I'm assuming she's not here in the room. Okay. Those are the only public comments that we have then, so.

DR. WARD: The next topic on our agenda is the presentation by Paul Middendorf on the peer review report.

DR. MARKOWITZ: Steven Markowitz. I think as members of this committee, we—Paul, you may want to clarify this—we may be special government employees. If so, or even if not, what are the limits as to how we can interact with government officials, to Congress and the like, to express an opinion regarding the proposed changes in the organization of NIOSH and the WTC program?

DR. MIDDENDORF: The President's budget specifically is not part of the purview of the Scientific/Technical Advisory Committee so that is not something that we can discuss here. As special government employees, as I understand it, you are not allowed to lobby, in any way shape or form, congressional members on behalf of the Program. So as a member, you cannot. But in your individual personal life, you can engage with your congressional representatives.

DR. MARKOWITZ: Thank you.

DR. WARD: Thank you. Good question.

UPDATE ON PEER REVIEW

DR. MIDDENDORF: People on the internet, we seem to have lost our connection. We'll try and get it

back again. Let's see. As always, the technology seems to be a challenge when we come here. Just meshing two different technologies, organizations' technology seems to be difficult. Let's go ahead and get into it.

Since the administrator has given us the charge to address independent peer review, I thought it would be helpful to just spend a few minutes going back down memory lane, taking a look at where we've been, what we've done, and as kind of a prelude to your discussions on the topic.

And just as a reminder, under reauthorization, there were a number of new requirements for the Program, one of which, as Kimberly mentioned, was that prior to issuing a final rule to add a health condition to the list of covered conditions, the administrator is required to provide an independent peer review of the scientific and technical evidence that would be the basis for issuing that rule. In addition to that, there is a requirements that the STAC, within one year of reauthorization and at least two years after that, the administrator is required to seek recommendations from the STAC regarding identification of individuals to conduct the peer reviews that are required.

When the STAC addressed those back in 2016, it came up with two recommendations that specifically addressed identification of independent peer reviewers. One of those was that the administrator should develop and implement a process to solicit from the public recommendations of scientific experts to perform peer review, and the administrator responded to that, saying that he agrees with it and he will include a Federal Register Notice to solicit public input for consideration in the process of identifying potential peer reviewers for the World Trade Center Health Program, and that is the policy and procedures which the members should have a copy of, and we'll look at the specific wording of that in just a moment.

The second recommendation was that a pool of peer reviewers should be formed by NIOSH that can be drawn upon when a peer review is required. This could be done by an open solicitation by which persons could be nominated, a process that could be repeated periodically. And again, the administrator agreed with that and said that he would be putting out a notice to solicit public input for consideration.

If you look in the policy and procedures on page 11, you can see where that is actually in the policy and procedures under section 6(b), which says, "Independent Peer Review (1) Selection of peer reviewers." It states that at least every two years, the administrator will develop a pool of potential peer reviewers with medical and/or scientific expertise by requesting recommendations from the STAC regarding identification of potential independent peer reviewers, and by publishing a Federal Register Notice soliciting nominees for potential peer reviewers for the Program.

Back in March of 2017, in fact a notice was published in the Federal Registered—a Federal Register Notice was published, specifically requesting nominations for

peer reviewers. That solicitation is open through February of 2019, so anything that we receive can be put into the pool; any names that we receive can be put into the pool.

I will say that that solicitation has netted us a total of three peer reviewers, so not quite the pool that we were hoping for or looking for. So we're hoping to get some new thoughts and ideas on how to go about doing that, and that leads us to the administrator's current charge, which is to recommend specific individuals who may be expert in various types of health conditions, or make a recommendation about procedures that the Program should use to identify peer reviewers.

So that's where we are.

PEER REVIEW DISCUSSION

DR. WARD: So one quick question before I turn to the panel for questions. So beyond the Federal Register Notice, was the Federal Register Notice disseminated in any way, like through the NIOSH listserv or in other venues that could call it to people's attention? Because other—people don't review the Federal Register.

DR. MIDDENDORF: Yes, all too true. The Federal Register is not light reading; people don't generally get into it. There were some other efforts. It was put on the Committee's webpage soliciting for new members initially; I think that has been taken down. So we need to get that back up. But again, that's still not an area that people automatically go to. So finding other ways to publicize this. If I remember correctly, it was put out in eNews—NIOSH puts out an eNews, I think it was broadcast there, and there were some other things. We may need to repeat those things.

DR. WARD: Any questions for Paul from the panel? Yes, Micki.

MS. SIEGEL DE HERNÁNDEZ: Paul, can you clarify, once a pool is developed, is that peer review group, how long they are agreeing to be on that group, within that group, and is it just a two-year term or will you be asking if people will stay in that pool? And one of the reasons for asking is that as new research comes out, there may be a very good pool but then additional expertise needed for a particular condition, and a need to add to that group.

DR. MIDDENDORF: Yes, the intent is to keep the people in the pool as long as they're willing. So every few years, the intent was to send out another—an email or a notice to the individuals in the pool, asking them do you want to continue to be considered, so that we can keep the pool as long as possible. If people don't want to be in the pool, obviously we'll take them out. They also have the right, when a condition comes up and the administrator is looking for peer review and he comes to them, they have—and asks them to serve—they have the right at that point to say no, I don't want to serve, for whatever reason. So it is a voluntary thing. And then there was another aspect to your question if I remember correctly.

MS. SIEGEL DE HERNÁNDEZ: It was basically the timeframe.

DR. MIDDENDORF: Okay.

MS. SIEGEL DE HERNÁNDEZ: But I had two follow-ups maybe.

DR. WARD: Sure.

MS. SIEGEL DE HERNÁNDEZ: The other question is for a typical peer review for adding a new condition, what is the general size of the group that you would be looking for, and do you seek to fill each of—just like with the STAC, there are certain areas of expertise. Would you look for, to have those various areas of expertise for each peer review that's conducted?

DR. MIDDENDORF: Yes, I think the peer review, the administrator will look at the available members in the pool to see whether or not there are people with the appropriate knowledge/expertise to provide all the perspectives that are needed. Typically, the intent is for three people to serve as peer reviewers. I think that's a fairly typical, normal size for a peer review.

DR. WARD: Mridu?

DR. GULATI: For some of the subspecialties that may—for some of the areas of the subspecialties which intersect a little bit less commonly with occupational exposures, how—is requiring sort of, or not requiring, the need to have a significant background in occupational exposure sort of an impediment? Like so for example, I don't know rheumatology or something, something like that. Are those challenges for particular subspecialties and where do we, how do we actually seek reviewers in those areas?

DR. MIDDENDORF: Well, I think the administrator will look at the available peer reviewers, what the specific condition is, to see where the appropriate knowledge relative to exposures, relative to the medical condition, and make sure that he has the right people who know and understand the condition and hopefully the relationship between environmental exposures and that condition, so that he can get a fully informed—or as fully informed an opinion as possible about it.

DR. GULATI: I think some of the peer reviewers may have an understanding of the condition but may not have as much experience on the exposure side, and so in some situations, that might affect the availability of the pool, and is there a way to kind of work together if that's the pool that you're—that is available?

DR. MIDDENDORF: It would be very difficult to pull together a panel—

DR. GULATI: Yes.

DR. MIDDENDORF: And have the peer reviewers talk to each other, because that invokes FACA, and that would be a very long, involved process and one of the issues under the Zadroga Act is that there is a limited amount of time that the administrator has to respond. So it's finding that right balance between finding the right people, getting the information in, and being able to process it.

DR. WARD: I just want to make sure Micki asked all of her questions. I moved on—I'm just afraid I moved on prematurely, but you were done?

MS. SIEGEL DE HERNÁNDEZ: I have one more but I'll go after Steve.

DR. MARKOWITZ: No, no, you can finish your question.

MS. SIEGEL DE HERNÁNDEZ: Will this list of peer reviewers be published? Once you start populating

that group, will that—will we know who those peer reviewers are and their area of expertise? Areas. Because it also has bearing on outreach and who we might want to suggest for the group.

DR. MIDDENDORF: Yes, I don't think that question has been asked yet. I think it's something the Program will have to think about, consider whether or not it wants to make the whole list public. If we do, then we'd have to make sure that the peer reviewers know that the peer reviewers know that we're going to make it public, and that hasn't been expressed to them at this point, so that's a change we're going to have to make if we go that route. I don't think that's necessarily an impediment; it's just something we have to think through.

DR. MARKOWITZ: Steve Markowitz. So I was just trying to think about what entities have the most ready access to peer reviewers, and in fact one source—I don't know how quite you word it—but are the journals in the area and the field, in occupational medicine. There are a few journals in the US. I edit one of the journals and I have access to untold number of peer reviewers that are called upon, in their view all too frequently, but regardless. And that's true, I'm sure, of occupational and environmental medicine, *Journal of Occupational and Environmental Medicine*. I don't know how you do it, but those are the entities that day in, day out access relevant peer reviewers. I don't know if it's a question of reaching out to help them solicit, or at least note the need, or what exactly. But it is an untapped resource.

DR. TALASKA: Yes, those are published. I'm sorry.

DR. WARD: It's Glenn Talaska speaking.

DR. TALASKA: Thank you. The editorial boards of all of the occupational health journals have complete addresses of all the board members and that would be a—I think Steven's right—that's an excellent source of quality people.

DR. MARKOWITZ: Steve Markowitz. So, look, the boards are a dozen or two dozen large but the number of peer reviewers run into the hundreds and hundreds, and I'm looking around the room at people who have served as peer reviewers on various articles. So sometimes the names of the peer reviewers are published once a year as a thank you.

DR. TALASKA: Yes.

DR. MARKOWITZ: But to get full information, you'd need some cooperation from the journals.

DR. WARD: So I had a question, and this may be a little out of scope, but in the two years since we, you know, made the initial recommendation, has NIOSH had an occasion to convene a peer review and how has it been handled given that there were only three people in the pool?

DR. MIDDENDORF: Yes. No, nothing has been proposed to be added during that two-year period. The last things to have been added were acute traumatic injuries and new-onset COPD. If the administrator does not find the necessary knowledge/expertise he needs within the pool, he will have to go outside the pool. The critical thing here is to get good, quality peer reviewers who know the subject matter and can provide

the scientific and technical input that he needs to make a good, solid decision.

DR. WARD: Any other questions on this topic?

MS. SIEGEL DE HERNÁNDEZ: This is Micki. Not a question but in addition to the peer reviewers for various journals, in terms of outreach, you have universities, schools of public health, American Public Health Association, with professionals that regularly do research and also serve as peer reviewers. So I think there are many other opportunities besides the Federal Register Notice and professionally, to get the federal—to get the request out.

DR. WARD: Lila.

MS. NORDSTROM: Sorry, you just touched on this briefly but can I just ask what the process would be right now, given that we don't have a full panel of peer reviewers, if a condition came up for consideration?

DR. MIDDENDORF: Yes, the administrator would look at the three people that are in the pool to see whether or not they had the knowledge and expertise. If they don't, then he would go beyond and begin looking outside, away from NIOSH, away from CDC, to try and find people with the knowledge and the expertise, because we do want the independent peer review. That's what he's looking for. Independence is an important criteria.

DR. GULATI: So one more—sorry, one more question.

DR. WARD: Yes, Mridu.

DR. GULATI: Sorry, Mridu Gulati. Were there more reviewers recommended but not deemed appropriate to be in the pool, or…?

DR. MIDDENDORF: Yes. One of the recommendations from the STAC was that we not limit the pool. So any names that come in are put into the pool. So that's all we've had are three. Any selection would occur at the time at which there is a condition that the administrator is proposing to add. At that point, he would look at the knowledge/expertise of each of the individuals and decide whether or not they should serve as, or can serve, as a peer reviewer.

DR. WARD: So are there any questions from people on the phone, or comments? Okay, hearing none and not seeing any further hands in the room, I guess we'll move on to the next topic, which was to be a break, but I think it's rather early for the break so we will go on directly to the next presentation, which is from Tania Carréon-Valencia, an update on policy and procedures for adding noncancer health conditions to the list of World Trade Center-related health conditions. Tania.

UPDATE ON POLICIES AND PROCEDURES FOR ADDING CONDITIONS

DR. CARRÉON-VALENCIA: Good morning, everybody. It's my pleasure to be here to talk about the update of policy and procedures, which was last revised on February 14, 2017, following some of the recommendations that you made at your last meeting. And I'm going to wait for my slides to come up. I think we need to go back. Next one please.

So you all have in front of you a copy of policy and procedures for adding

noncancer health conditions, and in there, you can see that there are two pathways that the administrator follows to add a noncancer health condition to the list. One is that the administrator initiates the process at his discretion; or he initiates the process after receiving a valid petition. In either case, a health condition can only be added by rulemaking.

In the case that—next one please. So once the petition is received, we have specific policy and procedures for handling submissions. The policy coordinator evaluates that submission to determine if it meets the requirements of a valid petition. There are administrative requirements and there is also medical basis to determine that petition is valid. And the requirements and the terms of medical basis are that the petitioner will provide references to peer-reviewed published epidemiologic studies about the health condition among 9/11-exposed populations, or clinical case reports of health conditions in World Trade Center responders or survivors. In no case, however, firsthand accounts or anecdotal evidence may be, are sufficient to establish a medical basis. In both cases, whether the petition meets—if it's considered valid or not—the petitioner will be notified by the Program if this is the case or not, and if we proceed in the evaluation of the condition. Next one please.

So once it is determined that the condition—the petition is valid, the Science Team will evaluate the evidence to determine if it follows the requirements. And as suggested, as proposed by this committee, when necessary, the administrator will seek assistance from subject matter experts, both from the World Trade Center Health Program, NIOSH or other federal agencies to assist us in consultation on the definition of the health condition, analysis of scientific evidence, or assessment of the petition.

So once we have the information, we conduct a literature review of the scientific evidence to identify published, peer-reviewed epidemiologic studies of 9/11-exposed populations. And with that information, we evaluate the scientific evidence in terms of quality limitations such as assessment of confounding, selection bias, exposure assessment and other criteria. We also apply selected Bradford Hill criteria to establish causality, and we determine if the evidence represents exposures in 9/11 responders or survivor populations. Next slide please.

Once we have reviewed all the evidence, the Science Team provides a summary to the administrator, with recommendations on how to evaluate the—how we evaluate the evidence. There are four possible outcomes here to determine if the condition is substantially likely to be causally associated with 9/11 exposures. If the evidence supports the causal association, then the administrator will propose adding the health condition to the list. Two, if the evidence supports a high likelihood of a causal association, the administrator may direct the Science Team to consider additional highly relevant scientific evidence from sources other than

non-9/11-exposed populations. I'm going to come back to this one. If, number three, if the evidence is limited or inadequate, then the administrator will publish a notice of insufficient evidence in the Federal Register. And number four, if the evidence does not support the causal association, then the administrator will publish a notice of determination not to propose the condition to the list. Next one. Okay. As I mentioned before, I'm going back, when we have evidence that there is substantial likelihood of a causal association but it's not completely supportive of this association, then we identify additional evidence, looking at additional peer-reviewed scientific evidence from authoritative scientific sources published by the US government such as the toxicological profiles published by the Agency for Toxic Substances, and this is ATSDR—Disease Registry—or the Monograph by the National Toxicology Program, or the Human Health Risk Assessments by EPA. We will review—or the Science Team will review—this evidence and provide an evaluation and determine if there is a scientific basis for the determination. If the evidence that we review fills an important gap in establishing a causal association and if it mitigates the quality limitations found in studies in 9/11 populations. Also, the Science Team will evaluate the similarity of the exposure conditions in these studies and in 9/11—how similar they are to 9/11 conditions such as what is the route of exposure, the source of exposure, etc., and will review the source limitations that may impact the evaluation. Next slide please.
At the conclusion of the evaluation, then the administrator will have—he can have four actions. He can request a recommendation of the STAC if he determines that the expertise of the STAC will be helpful in making a determination whether to propose to add the condition or not, and I will come back again to this one. He could also publish a notice of proposed rulemaking to add the health condition if the evidence supports that it's substantially likely that it is causally associated with 9/11 exposures. Or he could publish a notice of determination not to propose to add a rule if the evidence supports it, that there's no evidence supporting adding the health condition; or a notice of insufficient evidence. Next one.
So in case the recommendation request or the administrator requests a recommendation from the STAC—next slide please—then he must make his request within 90 days of receiving the petition, and he convenes the STAC to help clarify the interpretations and determine if the evaluation is inconclusive or there is conflicting scientific evidence. In either case, the DFO will work with the STAC to schedule meetings and assemble the necessary information, and the STAC then will submit its recommendation within 90 days on whether to add the health condition, or by a date specified by the administrator, but it cannot exceed 180 days. After receiving the STAC recommendation, then the administrator evaluates this recommendation and within 90 days, he will publish a notice of proposed rulemaking proposing to add the condition, or a notice of determination not to propose the rule. Next slide please.

So the next steps summarize the rulemaking to add a health condition. There are four steps. First, there will be notice of proposed rulemaking if the administrator decides to propose adding the health condition to the list. This will be published in the Federal Register, and the administrator will solicit written public comments. Next step is an independent peer review, and next slide please.

I will move on to this stage and come back to the last two steps on rulemaking, and I will make the next two steps short since Paul has already discussed them. But as you know, there is a pool. The administrator will periodically develop the pool of potential peer reviewers, and when the health condition is being proposed to be added to the list, the administrator will select three subject matter experts from the pool, or if he cannot select from the pool, he will select at his discretion, as Paul has already discussed. The selection of peer reviewers will balance medical and/or scientific expertise, independence from NIOSH and CDC, and previous service as peer reviewers. Next slide please, Paul.

Also, in this case, the administrator will apply Federal (Science @ 00:51:55) Agency conflict or bias prevention methods to prevent or limit potential conflicts of interest, ensure that bias is minimized, achieve a high level of credibility, and balance extremes in scientific perspectives. Next slide please.

The charge to peer reviewers will be to review the assessment of the evidence, and they will be provided a list of questions they will need to answer when they evaluate the evidence. They will be asked to provide other available evidence that may not have been considered, if the requirements of the policy and procedures have been fulfilled, and is the evaluation or interpretation of the available evidence appropriate and if it did support the conclusion of adding the health condition to the list.

It is expected that the peer reviewers provide the report within 30 days, and it will be compiled and published in the NIOSH rulemaking docket. As mentioned by Kimberly before, and as suggested by you at your last meeting, peer reviewers will be identified without individual attribution to their comments. Last—next slide please, Paul.

Coming back to the steps in rulemaking, once the independent peer review is completed, there will be a public comment period, and it will remain open for 15 more days after comments from peer reviewers have been posted, to allow the public to add additional comments. At the end, the final rule, and after reviewing all public comments and peer reviews, they will be considered by the administrator and responded in the preamble. Then the administrator will consider all these comments and determine whether the evidence continues to support the addition of the health condition to the list and if so, he will publish the final rule. Following the publication of the final rule, then the Program will develop implementation procedures. It could be, for example, exposure clarifications or time intervals for diagnosis and/or symptom onset.

And this is all that I have this morning for you, I'd be happy to answer any questions.

DR. WARD: So I have one question. I noticed in your slides that when you define the identification of additional scientific evidence, and I guess this is invoked when the evidence from the 9/11 populations are inconclusive, that it appears from what I'm reading that you are restricting the scope of the evidence, you're looking at, to an authoritative scientific source published by the US government. And I understand from our previous discussions that this issue is a big concern to NIOSH because you know, you had to define the scope somehow, because it could be infinite, right?

DR. CARRÉON-VALENCIA: Exactly.

DR. WARD: But I do just want to reflect on the limitation that that means that if the government hasn't really—there may be quite a bit of literature, medical literature, scientific literature—but if the government hasn't published on it, then it wouldn't be considered.

DR. CARRÉON-VALENCIA: That's correct.

DR. WARD: Or if the government publication was issued ten years before and was really out-of-date, then it would be considered but it wouldn't be, it really wouldn't be timely and relevant. So do you have any—is there, can you react to that concern?

DR. CARRÉON-VALENCIA: Yes, and you are correct, and certain, for example, EPA documents are quite outdated, although—and the NTP Monographs are limited at this point. They are updated but quite limited. The strongest evidence probably will come from the ATSDR report, although there is some other evidence from public, from federal sources such as TOXNET that is much more current that we could possibly configure as well. But we are certainly aware of that limitation but as you know, also, we are limited in terms of time to respond, and we have a limited scope.

DR. WARD: Thank you. Questions or comments from the panel? Glenn Talaska.

DR. TALASKA: Thank you. And that limitation is not by statute; it is just because of the time scope, right? The second thing was on one slide you indicated you will balance medical and scientific expertise, independence from NIOSH and CDC, and previous service as a peer reviewer.

DR. CARRÉON-VALENCIA: That's correct.

DR. TALASKA: Does that indicate that persons who hold grants from NIOSH or CDC will not be eligible to serve as peer reviewers?

DR. MIDDENDORF: It isn't necessarily that they won't be eligible, but it is something that will be taken into consideration. I mean if we can find people, one who has a grant and one who doesn't have a grant, and they can provide similar perspective, knowledge and background, the preference would be to go to somebody who doesn't have the NIOSH—it doesn't mean to disqualify them, but it does mean that we would prefer somebody who doesn't have that connection.

DR. TALASKA: And then finally, I guess a question, can people on this panel, if they have

expertise, be identified as peer reviewers or is that a conflict?

DR. CARRÉON-VALENCIA: No, that is—the people on this panel won't be peer reviewers. That's my understanding, right?

DR. MIDDENDORF: Yes.

DR. CARRÉON-VALENCIA: We discussed that at the last meeting.

MS. HUGHES: What about prior panels?

DR. WARD: That was Catherine.

MS. HUGHES: Yes, sorry.

DR. CARRÉON-VALENCIA: Yes, that may well be, they could be considered if they were part of the panel before. But not currently serving. Is that correct?

DR. WARD: Mridu then Lila.

DR. GULATI: Okay. I just want to add, I'm also concerned about how much scientific and medical research information that you're excluding from the scientific evidence by it being published by the US government. I think that's a significant limitation.

MS. NORDSTROM: I have that concern as well but I also wanted to ask, do you have any specific criteria for handling submissions for groups that are likely to be underserved by the current clinical, sort of…the—I'm asking specifically about, because it seems, a large body of the research, because we have a full compendium of the research sitting in front of us that's been done on 9/11 populations, is done on responders. There's not nearly as many survivor populations and within those populations, there's very few specifically on pediatric populations, on women's health—

DR. CARRÉON-VALENCIA: Right.

MS. NORDSTROM: And specifically young women's health. So I'm wondering, because those populations are not able to be seen by the World Trade Center Health Program without having prior health conditions, so they're not just being broadly screened, and there's almost no research done on them through the World Trade Center Health Program. And because of that, they are very unlikely to meet the initial submission criteria that you lay out here. Are there any sort of, are there any—is there any criteria for underserved groups like that that you can talk about, or are they just going to be excluded from even the ability to submit for conditions?

DR. CARRÉON-VALENCIA: No. If they can provide some evidence, we will review it. I know I talked briefly about the current policy and procedures for handling submissions, so we're looking into that right now to—it's a big burden to ask the public to provide that published peer-reviewed epidemiologic study—

MS. NORDSTROM: Absolutely.

DR. CARRÉON-VALENCIA: In 9/11 populations. So (inaudible @ 01:00:33) that it's not just my personal information but something that is published, we are looking into that as well.

MS. NORDSTROM: Right. And for the submissions, do those also have to be from government sources if—?

DR. CARRÉON-VALENCIA: No.

MS. NORDSTROM: Okay, that's the second part of my—I'm done.
DR. WARD: Annyce?
DR. MAYER: Yes, Annyce Mayer. I'd like to add my concern, as has been already stated, about the requirement that the additional scientific evidence be something published by the US government. I fully understand the importance of time, and would ask could there be a deadline of a certain amount of time that people have to identify good other scientific evidence from other sources and if they identify it within that given timeline, that that could be considered as well?
DR. CARRÉON-VALENCIA: Well, during the public comment period, both the STAC if they are convened, or the public—or the peer reviewers, if they identify relevant information, we will consider that in our evaluation even though there—
DR. MAYER: Even if it's not published—
DR. CARRÉON-VALENCIA: And there is public comment period as well. So that will be part of the consideration.
DR. WARD: Before Glenn, I just wanted to ask a procedural question though. So if the evidence is limited or inadequate, the administrator published a notice, but there is no public comment period.
DR. CARRÉON-VALENCIA: Exactly.
DR. WARD: So in the case where—which is probably in many ways the most important case for more extensive input—really there is no opportunity. It's really the judgment call is made by the program staff, or the recommendation of the program staff to the administrator. So just wanted to clarify that.
DR. CARRÉON-VALENCIA: That's correct.
DR. WARD: Glenn?
DR. TALASKA: Annyce had another question.
DR. WARD: Oh, Annyce?
DR. MAYER: Another question. If the administrator decides that he would like the input from the STAC, the STAC will provide a recommendation. Does that include simply a yes or no, or is there a rationale that is provided in addition?
DR. CARRÉON-VALENCIA: Well, you can provide recommendations on to how information was evaluated, if it follows and it's our evaluation of the evidence supports the decision to add the condition or not. So it's more than just yes/no. We do also have a limited time to respond.
DR. MAYER: Sure, no, I understand. I guess that really got to my second question is if, for some reason, when the STAC gave their rationale, it helped answer some questions he had in his mind, but it actually leads him to a different conclusion than that of the STAC, is he allowed to make a decision against the STAC? Okay.
DR. CARRÉON-VALENCIA: Yes. So the administrator will consider both public comments and the recommendation from the STAC in making the final determination.
DR. MIDDENDORF: Yes, let me just clarify that the STAC provides advice to the administrator. He is the one who makes the decisions.

DR. WARD: Glenn?

DR. TALASKA: Yes, I guess my question would be if there would be any chance of, once number two is invoked by the administrator, which is the seeking outside, other scientific evidence from the Science Team, whether there would be a chance for people to provide maybe other sources. For example, international for cancer—and I know this is not an issue that we're talking about—we go for the literature at IARC at their meetings. There may be associations for endocrinology that are similar that people may be aware of and may recommend on an international basis that might be useful and may be more current.

DR. CARRÉON-VALENCIA: So if they are recommended by peer reviewers during the comment period, we will definitely take those into account.

DR. TALASKA: Okay.

DR. WARD: Steve?

DR. MARKOWITZ: Steve Markowitz. So Tania, when condition two exists—the evidence supports high likelihood of causal association—exactly how much time does the Science Team have to make a decision about that?

DR. CARRÉON-VALENCIA: Ninety days.

DR. MARKOWITZ: Ninety days.

DR. CARRÉON-VALENCIA: From the time of the decision to the publication of the Federal Register Notice.

DR. MARKOWITZ: And I also want to point out that it's not just Science Team that has that amount of time.

DR. CARRÉON-VALENCIA: Right.

DR. MARKOWITZ: It's all the administrative time, developing the Federal Register Notices and things of that nature, having those things reviewed within CDC and HHS that have to be included in that 90 days. Because typically, the Science Team has about 45 days.

DR. CARRÉON-VALENCIA: Yes, that's correct.

DR. WARD: Micki?

MS. SIEGEL DE HERNÁNDEZ: So two things. One, I think that this process would do very well to be translated into a flow chart because it's very hard to understand, even though you have, you spoke well slide by slide, it's very hard to understand what might happen concurrently and what the options are at each point. And I think to Lila's issues that she raised, there are some things that there seems to be no pathway actually and although you will, can take public comment, that's not something—everything can stop well ahead of that time. And I think for those of us trying to figure out how to provide some evidence and what might be necessary, I think it would be good to see that visually.

And then I would also like to add my concerns, more than concerns, about limiting those studies to the US government, and I have a question as to how that might be changed, because I think that understanding that there is a time limit, and of course you still need the time limit, but to within that time limit have very limited

sources that you can look at, again, it's kind of a barrier that goes up for moving many of these things forward. So is there a pathway for us to, for the STAC or by some other means, or for the Program staff, to change that?

DR. CARRÉON-VALENCIA: To extend the time?

MS. SIEGEL DE HERNÁNDEZ: No, no, not to extend the time. To not limit, on page 17, to the—

DR. CARRÉON-VALENCIA: To the government.

MS. SIEGEL DE HERNÁNDEZ: For the additional peer-reviewed studies, limiting it to the US government, which has all of the issues that have been made out already by yourself and others on the panel.

DR. MIDDENDORF: Some of the criteria that we were looking for when we met, was being contemplated, was we're looking for someone who is already—that we could leverage the work done by others, because these reviews take EPA, NIOSH, anybody can take many, many years to do a full systematic review to look at a situation or a condition. And obviously that's not going to be done within the 90 or 45 days that the Science Team has. So the intent was to try and find a source that we could leverage work that is already done. If the STAC had ideas on who else would have done that kind of work that it's already been done, that's an authoritative source, there's independence and peer review and all those other kinds of criteria, I'm sure the Program would be more than happy to listen to thoughts and ideas on how to expand that.

MS. SIEGEL DE HERNÁNDEZ: I mean, this isn't to say that a government source should not be used. If there is something that's appropriate to whatever the condition is, then it should be used. But to limit it and say nothing else, when there may be some other things that are very—that are more relevant—just seems…

DR. MIDDENDORF: And if the STAC can provide thoughts and (ideas @ 01:08:41), that the Program would be more than happy to listen.

DR. WARD: Catherine?

MS. HUGHES: I agree with the other people that are concerned about "published by the US government". Can we just modify that one clause at today's meeting?

DR. MIDDENDORF: That is not part of the charge today.

MS. HUGHES: Oh, so we can't say—

DR. MIDDENDORF: But you could talk about it. It can come up. The administrator is sitting here and I'm sure he will be more than happy to listen to thoughts.

MS. HUGHES: Okay, so you know, the fact that we were looking at the experts for, you know, that are on the journals, you know, top journal, medical journals. Why can't that also be tacked here? Because then it would be a lot more current.

DR. CARRÉON-VALENCIA: Remember we have limited time as well, so convening a panel of experts to help us review the evidence outside of 9/11, it's also adding considerable—may add a considerable amount of time.

MS. HUGHES: I guess I wasn't clear. I was just meaning like if there's research that's been published by peer reviews on that particular condition.

DR. CARRÉON-VALENCIA: Right.

MS. HUGHES: That that would be included, because it may not have made it through to a US government publication.

DR. CARRÉON-VALENCIA: Right, but that would imply for us to do a systematic review of all published scientific evidence outside of what is included in the government documents. So one solution, and that's what I was telling Dr. Ward, could be TOXNET, which is peer-reviewed and it's also current. That provides some source of evidence. But going beyond into a systematic review will had hundreds and potentially thousands of new publications that we will have to look into.

DR. WARD: Steve?

DR. MARKOWITZ: Yes, Steve Markowitz. So clearly there's a tradeoff between this 45-day period between the validity and feasibility, and I just wonder, realistically, the kinds of conditions that are going to come up, that is likely to be novel, relatively novel association—excuse me—meaning that actually the medical literature might be relatively limited and probably not covered by ATSDR, IRIS, NTP or the like, meaning that the decision might occur in a relative vacuum. And I just wonder whether, readily admitting that 45 days is a very limited period and confessing you're not going to do a systematic review, whether some limited review of peer-reviewed published sources wouldn't put you in a stronger position to make the right kind of decision. It would be an incomplete review, but an incomplete review is probably better than essentially no review of those other sources. So I understand the tradeoffs but in thinking about the conditions you're likely to have to rule on, I think it's likely that the relevant, highly relevant literature is going to be relatively limited and that you could accomplish much of that review in a 45-day period.

DR. WARD: Val, and then Mridu then Lila. We'll go this way, okay.

MS. JONES: Yes, I guess that's my concern also, that from looking at various reviews, let me advocate for the people of my community. My community very much is New York City housing, and one of the things that I remember at somebody's presentation was the fact that it was very difficult to get people to participate, and that it was very difficult—I think the person who presented their material was basically, they had to explain to people exactly how the material was going to be used, and they had to, I think, give something that showed, to people, something that was concrete as to this is what has been done with what you participated in. Because people are very concerned about participating when you live in public housing and people are looking at your income, etc. and people are feeling very uncomfortable that they want to move them out. Because my neighborhood is very much being gentrified and most people are very concerned that they want you out. So I would think that you want to try to find some kind of way to include that population. One of my reasons for participating is I have relatives who lived in Smith Houses and that wasn't included, and they had problems—asthma—that came up. So I would

think that we need to try to find a way to include various populations that I guess, as people said, underserved, especially Latinos and African Americans because that's very much who lives in public housing all along the East Side, and they very much were affected. So I would hope we find some kind of way to include, be inclusionary, and find ways that encourage people to participate. And I would also say that that I think that there's a portion that is immigrant and very much does not want to be documented for various things. So I would hope we find some kind of way to include those various populations that very often are not part of these studies or government study, etc. and I would say would probably not want to be in a government study, and especially with a government as now. Like no, do not want to be included. So I would just hope that we think about that and try to find ways to include that population, and I just don't think that when you said it has to be in a government type situation, that it would happen. But I would hope going forward, we look at ways to include those populations because they were definitely affected on the Lower East Side.

DR. WARD: Right. So Paul has suggested that we jump to the phone people and then we'll get back to Mridu and Lila. So does anyone on the phone have any questions or comments? Okay, we'll proceed with Mridu.

DR. GULATI: I'm sure I am also repeating everything that everybody else has said. You know, I think one of the issues with putting other peer-reviewed literature at equal footing, it's an issue to keep it as equal footing as public comments. And so even if maybe there could be, if you can't change the US government phrase, there could at least be a hierarchy of what information can actually be accepted, because if you lump all the peer-reviewed stuff with public comments, then you're lumping it in almost with anecdotal stories as well. And then I also want to echo that there is, there are assumptions being made that it is going to take a lot of time and that the literature is going to be huge, and I think while time is certainly an issue, validity and making sure you have the right information is more, I think the most important thing that we can all agree on as well.

DR. WARD: Lila?

MS. NORDSTROM: I wanted to go back to Steve's point for just a second because I—because sort of the ultimate mandate here is to provide evidence for health conditions that people are then going to need to seek treatment for. And as Vaylateena is talking about, these are health conditions that can become like an actual crisis even when they're not serious health conditions for a lot of the exposed populations. So I think it's important to get all of this done in a timely manner, but I also want, you know, I think it's important that we think about how inclusive we can be about, you know, studies that are actually kind of relevant to the populations that are affected and perhaps the least rigorous—or not the least rigorous—a less rigorous process is not as important as something that provides some basis for these determinations, because ultimately it's still like people's health that they're seeking

real treatment for in real-life situations.

DR. WARD: Glenn?

DR. TALASKA: Yes. Tania, I think the—this sort of language here, especially limiting it to federal sources, seems to limit the expertise of the Science Team as well. I mean, it limits what you can review, it sounds like, by statute. And I would suggest that perhaps we just indicate that where you'd be using authoritative sources including those of the US government, instead of saying just the US government because there may be—you guys are going to be experts on this. You're going to be aware of where things are and other things, and I'd hate to see you limited by what, just limited to US government sources when in fact you may know that there's something some place international, or some other source of things that you—because you're going to be looking. And so I'd just make a couple of minor changes and then not limit it to US government sources, if you're aware of them already, and you may be.

DR. WARD: Mike?

DR. McCAWLEY: Yes, so one of the things that I think you also need to consider in this is that we've been talking about this as if it's a bunch of separate diseases and somebody may have just one separate disease. You may also be talking about a syndrome, and in a syndrome, you'd have to look at a collection of information all put together. That may not be in some of the sources that you've been considering, and so you need to cast a broader net potentially to scientifically, medically be appropriate in what you're looking at here.

DR. WARD: Yes, and I guess a specific suggestion to at least think about—I know PubMed searches are tricky and you can go on and on with them forever, but maybe you could kind of define some kind of paradigm where you take the health condition and you just do a couple of searches, like health condition and "environmental exposures" or health condition and "disaster". You know, if you could define a set—and then really, I think it's just in general, it doesn't take a person who's knowledgeable in the field that long to scan the results of a PubMed search, and just see if there's any, like, really obvious information in the literature that's directly relevant to what you're reviewing. I mean, it does take a level of scientific expertise but it doesn't necessarily take that long if you have the right expert doing it. I realize you may miss something that way, because I always find more in PubMed if I then look at related articlesl—you can go on with PubMed forever, but just doing a very simple paradigm to try to get the very obvious literature that might directly pertain to your issue. It's really just a way of making sure that you're not missing something very important by restricting to the government publications.

DR. CARRÉON-VALENCIA: Thank you.

DR. WARD: Micki?

MS. SIEGEL DE HERNÁNDEZ: Tania, on the same slide that talked about studies published by the US

government, underneath the review of scientific evidence, one of the bullets is "Evaluation of the similarity of exposure conditions to 9/11 exposure conditions".

DR. CARRÉON-VALENCIA: Right.

MS. SIEGEL DE HERNÁNDEZ: And I just wonder if you could talk about that a little more, what you were thinking of, because there are very few exposure conditions that are similar to 9/11 exposure conditions, although there are exposure studies that may look at a contaminant—you know, occupational studies that look at a contaminant that was contained in World Trade Center exposures. So I'm just wondering where that—how you do that.

DR. CARRÉON-VALENCIA: For example the tox profiles published by ATSDR divide exposures by inhalation, ingestion and other routes of exposure. But if we know that the main source of exposure in this specific population is by inhalation, maybe we won't take a deeper look into the ingestion studies but focus more on the inhalation part of it. So we would look into that, the route of exposure, the type of exposure as well, because it's not the same as a study reports the agent in a liquid form when we know it was in dust or as particle matter. So we will have to also review the evidence in that respect.

MS. SIEGEL DE HERNÁNDEZ: Thank you.

DR. WARD: Mike, do you have a comment?

DR. McCAWLEY: No, no.

DR. WARD: Any other—oh, Annyce.

DR. MAYER: I was just going to ask, I totally agree you have to consider route of exposure. I would just ask in this particular case that ingestion be considered. With heavier exposures and also household exposures, ingestion was probably fairly common.

DR. WARD: Catherine?

MS. HUGHES: Yes, on that note, I think one area of ingestion is just being around because there was dust everywhere, and whether people cleaned their offices or their homes adequately, it just was overwhelming. But people also didn't look at water tanks and if dead birds can be found in water tanks, you're going to tell me that the dust being propelled at 70 miles an hour wasn't going to penetrate into water tanks either? So.

DR. WARD: Micki?

MS. SIEGEL DE HERNÁNDEZ: Just one more comment regarding the ingestion at Ground Zero in the restricted zone, people were not decontaminated at all really, and there were various locations set up where people would go and eat their food and conduct their business. So I think that that should be always a consideration, as well as clearly inhalation was a primary source.

DR. WARD: I just want to check with the people on the phone again, did you have any comments or questions? Okay, it looks like we've concluded our discussion on this topic.

DR. CARRÉON-VALENCIA: Thank you.

DR. WARD: And thank you very much for your presentation. And with that, we'll take a brief fifteen-minute break.

[Break.]

DR. MIDDENDORF: Just for the record, I want to note that the panel members are all here. Rosemarie, are you coming back, and Micki? Okay.

[Panel members return.]

DR. MIDDENDORF: Okay, let's go to the phone real quick. Let me see. Megan, are you on? Dr. Ryan?

DR. RYAN: Yes, sir. Yes.

DR. MIDDENDORF: Okay, thank you and Sheela, are you now on? I saw you joined us earlier; are you back on again? Sheela, did you say something? I'm seeing you on the website. If you're there, can you announce yourself, just say yes, I'm here, or something? Okay. All the panel members are at the table. Rosemarie, Mike, Micki, Catherine, Steven, Liz, Lila, Mridu, Annyce, Glenn and Val are all here.

DR. WARD: Thank you, and our next presentation is on Research to Care public engagement, and our speakers will be Mia Wallace and Tania Carréon-Valencia.

RESEARCH TO CARE PUBLIC ENGAGEMENT

MS. WALLACE: Okay, good morning, everybody. I will be presenting to you about the work of the Research to Care community engagement that we had on October 21 at NYU Langone Medical Center. Next slide please.

The purpose of the event was to distribute new developments on 9/11 health, provide knowledge on the latest research on health conditions associated with 9/11, improve access to the findings and research and its relevance to the care of the program members, and advise on maintaining good wellness for the community. There was no admission to attend—there was no admissions to attend the event, and it was open to everyone that was affected by 9/11. Next slide.

The event began at 8 p.m.—I mean 8 a.m. to 4 p.m. It was conducted in a community-friendly format, which included plain English research presentations and small group discussions on a variety of 9/11 health topics. To ensure that the information, presentations and materials were presented in plain English for the participants, NIOSH provided guidelines and templates to moderators, panel presenters and researchers. Guidelines and formats were provided to small group sessions and discussions. Okay, next slide.

The morning session consisted of two panels, the program researchers—of program researchers—that presented and discussed their current research on various health effects from 9/11 to participants. For this session, translation services, livestreaming and continuing education and continuing medical education credits were available. Translation services were available in Spanish, Mandarin and Polish. Livestreaming was conducted from 9 a.m. to noon on Facebook Live and live tweeting on Twitter. NIOSH collaborated with NYU's media team on the video production and streaming. So we would like to send a

special thank you to them.
To receive the CME and CE credits, individuals that participated in-person and online had to complete the post-test and score at least 80%. The online process was available until November 21—yes, the 21st, 2017. That, and they can also use the Facebook Live video to do the testing. There is a sheet available in your folders, the Research to Care folders that's on your table, that breaks down the CME and the CE credits that you can earn, and how much it was. And that's going to also be available online to the public. Next slide please.
The afternoon sessions were small breakouts groups based on five health topics. The five health topics were respiratory disease, children's health, cancer, mental health, and other chronic conditions. Participants had the option to choose two of the breakout groups of their choice and attend those sessions. The first session was from 1:30 to 2:10 p.m., and the second breakout session was from 2:15 to 2:55 p.m. NIOSH assigned program researchers and community partners to each health topic based on their expertise, to conduct these small group discussions with participants. This gave participants the opportunity to ask researchers how their findings impacted their health and any questions that may have—they may have on the 9/11 health effects. NIOSH staff was available to answer any questions in the breakout groups for the participants. Next slide please.
The wellness workshop consisted of a panel discussion with program researchers and community partners on maintaining wellness, and exhibits from the program's outreach and educational partners. The exhibits were displayed outside the auditorium and participants were able to have one-on-one time with the partners and receive valuable information, services and knowledge on what's available for the members of this program. Next slide please.
Okay, so the summary for the participants breaks down as to this. We had 160 people to attend. There were 46 walk-ins that registered in the morning session. We had 19 that walked in at the afternoon session. We had 175 people participate in the afternoon session and that total includes the 11 NIOSH staff that participated. There were 35 people who attended the cancer breakout group, 45 for the mental health breakout group, 10 for the children's health breakout group, 55 for the respiratory disease group, and there were 30 for the chronic conditions, the other chronic conditions breakout group. We had three individuals that used the Spanish translation service for that morning session. Next slide please.
Our live streaming data that is being presented today is based on the actual time that we went live from 9:00 a.m. to noon. So of the 1,958 video views on Facebook Live, this number included partial and repeated views and autoplays that any users had on their profiles. There were 17,934 Facebook users who displayed the video in their news feeds. The top location for Facebook Live views were New York, and the top audience was men that ranged, with the age range of 35-44. The program posted 18 live tweets on Twitter that—and they received 120

users that reacted or responded to those 18. Twitter inserted the event to 12,424 users' news feed. Next slide.

The research—the Research to Care resources that are available is we have a transcription for the morning session that will be available on our website, on the program's website. The program social media pages are active and live video available for viewing. We have the 13 summary factsheets that summarizes the research findings and the impact, and their impact on the community. The summary factsheets are translated in Spanish, Mandarin, Polish. All versions of the factsheets were available for the participants and will be available on the website.

I just wanted to say thank you to everyone who participated in the event.

DR. WARD: Thank you. Does the panel have any comments or questions?

MS. HUGHES: Yes, it's Catherine. First of all, thank you. I think this is an excellent summary of the event and the fact that it's—you've even seemed to reach more people outside of the people who actually attended the event is pretty amazing with those statistics. I was fortunate enough to spend most of the day there, and I thought there was a very friendly atmosphere and it was also very informative. But what was interesting for me was there were people I had never seen from the survivor population that actually made it there, people from my neighborhood around the World Trade Center, that lived there. So it was interesting that after all this time, that people still have a lot of questions, and there was also a lot of opportunity in the breakout sessions for individuals to ask their questions to human beings, which I think was really important. So just thank you very much.

MS. WALLACE: Yes.

DR. WARD: Micki then Steve.

MS. SIEGEL DE HERNÁNDEZ: Oh, Tania and Mia, one of the things—I was there that day and coordinated one of the sessions—that people were able to, that participants were able to do was to submit a question on a card. Some of those questions were answered during the afternoon sessions or were able to be asked to the morning panelists but not all of them. And I'm just wondering if there is—there was some talk about taking those questions and also putting together a Q&A, providing answers to people that were not able to be addressed during the Research to Care session.

DR. CARRÉON-VALENCIA: Yes, we are in the process of reviewing all those questions and putting them together in a list of FAQs, and as Mia mentioned, all those factsheets that you had on your folders are currently being translated into Spanish, Mandarin and Polish to also be put on the website. We have a long video of the morning session but it's being divided by individual presenter and being captioned to be (508 @ 01:54:32)-compliant. So that will also be on the website. The whole video is currently available for continuing education and CME credits, but it will be available for the public captioned as well. So yes. We will—you all have probably

on those folders the little index cards that we had, and there were ample opportunities to answer them but you were right, we couldn't just answer all of them there.

DR. WARD: Steve?

DR. MARKOWITZ: Steve Markowitz. So I was there that day, I thought it was a great event, and the audience looked exactly what the profile in your table demonstrates, a very diverse mix of responders, survivors, practitioners, researchers and the like. One of the only venues I can remember where that was achieved, so that was a nice thing.

If you go back two slides, you know, there's something interesting about the—one of the, the table you have where it shows the leading two groups who looked at the video were men 35-44 and then the second group was women who were younger, 25-34. So actually if you go back, if you dial back 15 years, that group of men who were looking at this, 35-44, were in their twenties. It was men who in 2001 were in their twenties, and in the women, it was women who were teenagers actually was the leading group. So I think it was an interesting thing.

DR. WARD: Let me just go to the phone and then we'll take more comments from the room. Anyone on the phone have a question or a comment? Okay, Lila?

MS. NORDSTROM: I also noticed what Steve was just talking about which I was going to bring up, but I also wanted to ask, do you have plans to do any events like this in the future or is this something that you'll be doing regularly? Because this seems like it was a great event.

DR. CARRÉON-VALENCIA: Well, there were many suggestions for us to do this on a yearly basis, but probably…it's a huge effort.

MS. WALLACE: Yes.

DR. CARRÉON-VALENCIA: So we, of course, we would like to do it regularly. We don't know right now how often, and as you can see, even though we had a nice attendance, if the rooms were bigger, we could have filmed the room, but the online presence was huge. So having the information available online is going to expand it, but we certainly hope to be able to repeat this in the future.

PARTICIPANT: Excellent.

MS. NORDSTROM: I had one sort of follow-up question to that, which I know that like in my cohort, a lot of people couldn't attend this event because it was during the day, and my cohort apparently was—it seems to be the women that were most interested in this information. So I'm wondering if there's any thoughts about doing maybe smaller evening events instead of just like full-day panel type things for community engagement stuff. Because I know it's a lot easier to get people to come after work, especially on the survivor end.

DR. CARRÉON-VALENCIA: Yes, we received comments as to some people liked the format, some people want it later. It's hard to—

MS. NORDSTROM: Please everyone, right.

DR. CARRÉON-VALENCIA: Please everyone, but certainly we are taking that into consideration. We have been also asked to have smaller community events within the community.
MS. NORDSTROM: Yes.
DR. WARD: Other comments, questions?
MS. HUGHES: I do.
DR. WARD: Yes, Catherine.
MS. HUGHES: It was on a Saturday; it wasn't a Monday to Friday, so that was actually helpful, but you were also competing, I believe, it was a phenomenal weather day.
DR. CARRÉON-VALENCIA: It was.
MS. HUGHES: And so you were competing in that situation with Mother Nature. And I just wanted to say something about the location. The facility is terrific but it's far away from public transportation and so I hope that you'll consider having another event, but you might want to try it in another location.
DR. CARRÉON-VALENCIA: Yes.
MS. HUGHES: Because I know a couple of downtown residents raised that with me. Thank you.
DR. WARD: Annyce.
DR. MAYER: I had a question. On that bottom slide on page 26, the left-hand graph there is bars in dark blue and then bars also in light blue, and I wasn't sure what dark blue and light blue meant.
MS. WALLACE: The light shade was the next option. So the dark blue one, I'm assuming it's that same slide that's showing up there?
DR. MIDDENDORF: Yes.
DR. MAYER: Yes. Yes.
MS. WALLACE: Okay. So if you look on the slide that has New York for the top location, so Virginia was the next location, so that's why it's shaded the light blue. So it's like the next, so it shows you what's number one, what's the top, and what's the next one that follows the top.
DR. MAYER: All right. I was just struck how many were in Virginia.
MS. WALLACE: Yes.
DR. WARD: Okay, it looks like there's no more comments or questions in the room. Any thoughts from those on the phone? Okay then, we'll close this part and I think we want to move on to the topic that we were going to start after lunch, since we are running early, and that's an update on the World Trade Center research portfolio by Travis Kubale.

RESEARCH PORTFOLIO UPDATE

DR. KUBALE: Well, good morning. Paul, how am I doing this? Am I, are you changing the slides?
DR. MIDDENDORF: Yes, I'll do it.
DR. KUBALE: What a team. That's why they never let me come and do things. While Paul is getting this very important presentation up for you, I want to thank all of you on the Committee for the work and the expertise that you provide, particularly the

research part of the program, and I want to talk with you and give you sort of an overview of some of the things that we are doing to make sure that our research is collected and analyzed in such a way that we can really track and make sure that we are continuing, and that we're continuing to progress, and that we're identifying gaps in areas that really need our attention.

I also want to special thanks—you'll hear later today, sort of see a continuation of the processes that I'll talk a little bit about in the presentation, but I want to special thanks to very busy researchers Dr. Luft, Dr. Prezant, Dr. Farfel, Dr. Reibman and Drs. Bromet and Morabia, who will be here later on, and give you a chance to really see from them in two of the key maturing areas of the portfolio—respiratory disease and mental health—what we've learned, what the researchers think the gaps are, and what really the future direction and needs of the research program pertaining to these two important focus areas are concerned.

So the first slide, Paul, is just, again, I just want to give you a brief—mine will be a pretty high-level just overview particularly of the program activities that pertain to how we are managing the research information and making sure that the research is moving forward. I do want to talk about two very important pieces that we put together, tools, that will also be available not just to World Trade Center staff but we want to make available to the STAC as well, which we hope will help increase the efficiency of the very important work that you all will be doing in the future.

And the first thing that we have done, and we will talk a little bit about, I'll talk a little bit about, is a publication database, and this is a database that we update every day. It contains over 1,300 publications, World Trade Center publications, and it also includes the publications that are in the compendium that I'll talk with you about as well. And then we'll talk a little bit about how that segues into the biannual research grantee meetings that we have, so how all of those are connected and again, how all of it keeps us on focus and task as far as knowing what we've done and where we need to be going. Next slide. Thank you.

Just a couple of brief things that I want to say. We, in case you don't know, the way that the Program operates is that we, since Zadroga, there is a special program announcement that is the research solicitation. And in that announcement, we have of course an agenda and a research scope, and we pay very special attention to that and want to make sure that as we're going along, that we're not stuck somewhere and just doing the same thing in every five-year cycle. And these are five-year cycles. They're all cooperative agreements, research cooperative agreements, and the important thing to remember about that is that these are what we're saying when we award those is that we know that these particular researchers have an expertise, an area of expertise and an area that we're interested in knowing more about. That's the announcement. And we are using their expertise to help us understand particular aspects about the

Program and people that we're treating that we think are important.
Again, the research impact is what we're going to focus a lot on today, and that's how we're essentially utilizing the research findings to make sure that we inform and keep current the research agenda, and that we improve the treatment, that it makes a difference in the lives of the people that were survivors and responders that were impacted by the disaster. Next, Paul.
One of the things that we felt that we needed to do first is that we needed a platform. We needed a really clear understanding of not just what has occurred as far as research is concerned since Zadroga, but really what started happening almost immediately after 9/11, and what the activities were and what work was involved, and what kinds of key pieces of information were written about, documented and then incorporated as we moved, you know, past post-Zadroga.
We also are going to talk a little bit about the grantee meetings and how those have now, with the maturing of the portfolio, moved into specialty workshops where we do really bring the work—the researchers who are doing the work—here to talk about specifically in an area what they think they are learning, what they think the remaining issues are and, more importantly, what they would recommend as far as future directions of the Program are concerned.
What we do with that information is that we communicate it as widely as we possibly can. We want to make sure that we use it appropriately to modify the research agenda, which can be and is often modified, the announcement, each year of the five-year cycle. And then of course what we want to do is that we want to make sure that we're using the latest research information in a way that improves the care of the people that we're concerned about. Next slide, Paul.
Just a little bit about the database and what I want to tell you is that as a member of the STAC committee, Paul as the DFO does have this database. So in the future, if you are interested in certain areas that pertain to your charge, you will have access to this database, it's searchable, and we have a variety of publications including not just the ones that are currently portfolio projects but we also go all the way back to, you know, late 2001. We also include special editions, so the *AJIM* special edition, those publications are also included. We have conference abstracts that are there as well.
We also segregate out in the database so you can see what data centers, each data center has produced since the very beginning, because they continue to do a superb job but early on, there was a tremendous amount of very good, important research, early research that was published in concert with the clinical centers through these data centers.
The Health Registry of course has been very prolific in their contribution. We have those publications that go all the way back to 2006 and those are listed also in the research compendium as well as the database. And we also have the research publications since Zadroga, which began with the eight research contracts that

were awarded in 2011. And so there are separate sections in both the database, the—in that database that we have, and in the compendium so that you can see how we've sorted through and tried to make sense out of what has been accomplished. Next slide.

Again, the compendium is, this is a—please look at this as it's a draft that we have. We will be finishing—we use the draft, we used the hard copy, it is basically our way to look at formatting and 508 compliance and those kinds of things. We will have shortly an electronic version that will be made available to Paul, that he can make available to the STAC members. It's searchable and the navigation is a lot easier and you can move around in the document much easier. We just wanted you to have something in front of you so you could get sort of an idea of how we were trying to put it together and how we were trying to present the information. Next slide.

Again, I won't—I've gone over some of this, but what was very important to us was in the Program, and for program staff, to have an understanding about all of the effort and the important work that happened prior to 2011, and there were some really important things that happened. You know, there was—you can see in the documentation how the clinicians were faced with massive number of symptoms from a tremendous number of people, and how they tried to make sense of that, how they tried to get that categorized into different disease categories, what was working, what was not working, lessons learned are in there. The first guidelines for—that were published about treatment for adults and children are also included in that section. And then the New York City Mayor's Working Group is essentially in that, included in the compendium because of the very important work that they did in laying the groundwork and providing the research foundation for the later post-Zadroga program that we're running right now. Next slide, Paul.

After Zadroga, we have had, like I've said, there have been a total of 66 projects. We've also continued the World Trade Center, the work with the World Trade Center Registry. All of our research from 2011 on had been cooperative, research cooperative agreements. We did have in 2011 eight research contracts that were three years, but there have been no research contracts since then, for various reasons. But one is that the cooperative agreement provides what we think, a lot more flexibility in working with the PIs and it's just been a better fit for the Program. Next slide.

I want to say just a little bit about where we're moving now, and you'll hear more about this this afternoon. Each year, twice a year, in June and in November—and we have been doing this since 2012—we bring all of the World Trade Center researchers together, and in the very beginning, the early stages, one of the major focuses of those meetings was really on progress, how are they doing, is there—are we having trouble somewhere, are we keeping all of the projects on schedule.

Those kinds of things.

As the portfolio has matured, there has been an increasing need for us to split the goal of those workshops, and one of the splits, one that we still monitor and we still look and we still track and we still collect—and we do provide that information to Paul to provide to the STAC, there's always, you know, a book that goes with each meeting that has the presentations and those kinds of things. But one of the things that we have started doing is that we have, beginning with respiratory disease and then followed by mental health, is that we have the researchers that are involved with those studies in the portfolio come in and they basically give—they take the day, and we have discussions from them about what it is they have learned, what it is they think the impact that they've learned has been on treatment, what the current research gaps are, and then we get their recommendations to the Program about what we need to be doing in that area that we may be not doing. There is a meeting transcript with those recommendations, and what we do in the off-time in between the meetings is that we look in the Program very closely at all of those, match them up with the research that we have, we look at their recommendations and we see overall where there may be gaps. And then when it comes time to select a project, we make sure that the secondary review committee that reviews for programmatic relevance has this information as they're beginning to make their decision and make a final recommendation to Dr. Howard.

So these are going to be a permanent fixture now that we are in that phase of the research, but it allows us to hear in a systematic way from the researchers, and it allows us to get the kind of information that we need to have from the researchers so that we know how to again move forward. Paul.

The workshops plan coming up, the next one in June is going to be the research needs really from the perspective of the CCE, the clinical directors. One of the things that we think is very important is to hear again from those individuals that are in the clinics and they're doing the work, what they think we need to be looking at and what they think, you know, is important.

The other thing that was going to be included in that is that we, the data centers have an annual report that they produce each year and we're going to be asking Dr. Prezant and his team that are putting this together to also give their thoughts on what they're finding in those early—you know, sometimes you'd see early trends or early signs and those kinds of things. So we'll be folding that over into this discussion as well. As the cancer research starts to mature, we're hoping to have a session on some of that work, if we can, in November; and then in June of '19, we'll have a children's research section; and then in November of '19, one from our emerging conditions section. So that's our tentative schedule. Next, Paul.

The next slide I will just start talking about while we are… So one of the things that I wanted to just point out in the compendium is that there is a section in the

compendium that is devoted to research that is done by the Registry. And there are several things that I sort of want to call your attention to. One of the things is that we collect a variety of pieces of information (inaudible @ 02:17:51).

One of the things that you see here is one of the graphs, and it's in the compendium, where you can get an idea of really what the scope of their—of that project is, and what they're involved with and what the activities are.

We also include, for the Registry, an update by specific aim. So also included in the packet that you have is an update of activities by those specific aims. So you can tell for instance, there are always probably between 20 and 25 research projects that the Registry is involved with in addition to the other activities that they have, and you can get a summary of those kinds of activities. All of their publications are included in the compendium as well.

One of the things that I want to point out is that the Registry—and I'll talk about our overall focus areas in the next slide—but the Registry mirrors also those focus areas. So when I'm talking about the individual cooperative agreement research, you need to also bear in mind—and I'll remind you—that the Registry for instance for respiratory disease has 35 or 36 publications as well. So when we're looking at what that research means, they are certainly involved in that discussion and those publications are included as well. So next.

This slide, what we have, this is the current, the 66 projects, cooperative agreements that we have deployed since 2011, and what you can see and how we track this and what we look at is that we want to make sure that we are certainly aware by area, are we getting the production that we need and the publications? The publications are key to area. If we don't have it written and documented, then if you're looking at particularly adding something to the discussion that you all just had, we have to have that kind of documentation. So we really do watch that, and as the PIs know, I talk with them often about areas where we need to boost that up a little bit.

Respiratory disease and mental health—I'll start with respiratory disease, just to say a couple of quick things. These are broad categories. So in these categories, you've got upper respiratory, studies looking at upper respiratory disease issues, lower respiratory disease. There is a variety of things, sleep apnea, asthma, that are included in these areas.

Again, one of the things that you'll learn this afternoon and you learn in the documentation is again, this is an area where one of the concerns that researchers are helping us with that we want to see in the Program is that there are people who over time are not getting better. And we want to know why, and we want to know what we can do about that. And so one of the things that you'll hear this afternoon is, you know, how meticulously they've been going through this. So you know, you may have individuals who have a normal lung function test, oscillometry is normal, but they still have symptoms. So what do we do about that

and what do we need to know, and what kind of research do we need to be promoting?

It's also very complicated with comorbid mental health issues, and you'll be hearing about that from Dr. Luft and his group this afternoon as well, and we need to be looking at how—you know, there are individuals, for instance, that we know in the portfolio over time, with PTSD, that haven't gotten better, and that haven't gotten better from visit to visit. We need to learn why that is and we need to see if there is some treatment modalities and things that we can do to impact that.

Cancer, I want to say just a couple of things. Those of you who have, you know, seen—and the concern has certainly been early on with excess thyroid and prostate—we have some very exciting things that are coming, and one of the things is that there is a multicenter study that has gotten started that involves the general responders, it involves the Registry, and it involves FDNY, and it's a cancer incidence and latency study. Another one is using NIOSH firefighter data in a cohort study that will, for the first time, look at and be able to look at pre-9/11 prevalence for certain things that we are very interested in, and we think that that study is going to do a tremendous amount as far as disaster research is concerned.

I will say one concern that we have about the cancer area and probably many of you all are already aware of this. There, particularly in Illinois, there are significant delays in getting access to cancer incidence data, and it has to do with a variety of things, but one is it's not just the lack of budget money, but there is a real crisis in getting access in these state agencies in order to certify registrars. And we have at least one study right now where we're still early, but we've already put in place, with the Grants Office in Atlanta, the administrative wheels to extend that project probably, we think it's probably going to have to be extended because it will be delayed for at least one year and possibly two years. So that worries me a little bit, and I want to just make sure we have made the Program aware of it, but we do have some real concerns about that struggle.

I'll move on to the next slide because I want to wrap up. I want to say this was—Kimberly Flynn talked about this today—and I want to first of all, in the compendium, we do keep notes and we have all of the STAC recommendations, and we pay attention to that. And one of the recommendations that had to do with children's research had to do with expanding the cohort, and we were having real difficulty, when you all did your review, doing that. There were some significant challenges in figuring out just how to open discussions with New York City Department of Education. So Dori Reissman, Dr. Reissman was key in that, Ben Chevat, who they talked about, the survivors' group, and also the Health Commissioner and staff at New York City Health Department. They opened the gates, and I am happy to report that there are ongoing talks with the Department. They are proceeding. We hope to have, actually by late summer or early fall, the

Registry database from the Department of Education. There are several steps that we have to do first, and that the Department of Health staff has been outstanding in helping us with, and that is creating a protocol that then leads to a notice. You have to have a Federal Registry Notice about how you want to use the data and who you want to access, if you want to call. And we hope to have, like I said, that in place by early summer.

We think that the potential—at least what we have seen so far, and the Department of Health has been able to ask some questions and get some ideas about the completeness of the data. We're not going to know the specifics of that until we actually get the dataset, but the early indications are good. The early indications were that the kind of information that we would need to expand the cohort, also expand the cohort to individual parents and students that were in non-exposed areas, and finding them, the early indications are that, you know, we're on the right track.

So the Department of Health staff, Dr. Farfel, they do keep both the responder and certainly the survivor steering committees updated on our progress, and we'll have hopefully more on that soon.

So the last slide. Just the research calendar I put in there because I just sort of wanted you all to have a brief sense and an understanding about what's occurring when. The progress reports for all current grants we put in there because again, those provide us with information that also guide us on what we need to be looking at for future research. So we pay really close attention to, you know, what we're learning and even if it's preliminary, that's important information for us to have as we go along.

There will be a scientific peer review meeting for this cycle, and that is April 11. We hope to have the new awards made by the 1 July. We also have our spring and summer research grantee meeting which is, Dr. Markowitz, it is June 13 and 14 which I think is on your calendar. And I would urge any of all of you all to attend. And then we have in November and December, we'll have application due dates again and also the autumn meeting, so.

So I think that's, Paul, I don't think I have anything else other than I put some websites on there, again, that I think might be helpful for you all, so questions if there are any.

DR. WARD: Thank you, Travis. I'd like to take questions from the folks on the phone first this time. Does anyone on the phone have any questions or comments? Okay, moving to the room, Glenn?

DR. TALASKA: Thank you, Travis. An issue that some of us have talked about off-camera before has been the interaction between certain environmental exposures and some of the exposures that occurred during 9/11. And, but looking at the research portfolio, I'm now looking at—I'm not seeing any animal studies that would test the interaction, say, between smoking and the impact of World Trade Center dust, or

that interaction between environmental exposures. Is there any intent to investigate that with this program?

DR. KUBALE: You know, it's interesting. We have had some, we've had some proposals over that that have not made it. We have one, as you've seen in there now, it's the cardiovascular, we've got the study that is looking at the World Trade Center dust, and I don't think there's a smoking component in that one. But as far as those kinds of studies, and I can't remember in the current round, I just don't recall if there are any applications.

DR. TALASKA: My thoughts are just that…

DR. KUBALE: Yes.

DR. TALASKA: As the infant and young adolescent population starts to grow, it may be a very good idea to prevent their—prevent them from starting smoking, if nothing else, and to advise them about what other environmental exposures, or occupational exposures, may interact with the exposure caused by the dust and the effects caused by the dust.

DR. KUBALE: There have been, in other parts of the portfolio, the FDNY has done this, Stony Brook. There have been looks at smoking cessation programs, particularly with, you know, the responder group and it's a very important component and I know there, you know, they're certainly looking at that. And there have been recent and I think current applications that further that part of the research. So that is certainly something that's on the, you know, being thought about. Yes.

DR. TALASKA: Thanks.

DR. WARD: Lila. Then, and then Mridu.

MS. NORDSTROM: I would second that point and also ask when is the next time the STAC will be able to weigh in on research priorities?

DR. KUBALE: You know, that's above my pay grade. Whenever Dr. Howard…

MS. NORDSTROM: Asking the room.

DR. KUBALE: Whenever Dr. Howard and Dr. Reissman say that, you know, you need to weigh in. And we anxiously await that day.

MS. NORDSTROM: Specifically as, you know, things—as things, as my cohort grows up and as we start to sort of see some of these situations emerge like, I think that would be—it would be important to check back with us about that kind of thing.

DR. KUBALE: Well, what I would say is I certainly, as you all know how the STAC works, so that's in… However, please come to the grantee meetings. You know, those are areas, all of the important, you know, key World Trade Center staff with the researchers, like Dr. Reissman. All of the, everybody's there. And I think that, you know, we want to hear what the concerns are and certainly look at, you know, the compendium and we want you to look at all of the information that you've had, if you think we've, one, if we've missed something, we want to know that. But as you're looking at it, we hope it makes it easier for you to sort of look through and tell from your viewpoint and vantage point what you think the gaps are. And you

know, that's the reason we want to do this. We really want to hear from you. It's important to us. So please do come.

DR. WARD: So we have a question, a comment from Mridu, then we want to hear from Dori, who had raised her hand that she'd like to speak, so Mridu, go ahead.

DR. GULATI: Just two questions. One, in terms of the research compendium, is there a way to actually look through it based on specific populations of interest? So I mean are you talking about children's population, I mean there are different age groups, race/ethnicity? Is there going to be a way to actually do that? That's one question. And then the second question I have is about the children's cohort expansion, sort of what factors are going into a feasibility assessment? Because I presume that we are trying to go back and find kids who were in that area so is it going to be we're going to try to get hold of this many people and if we can't, this is what's going to happen? Or I'm just trying to get a sense of what is going to go into that feasibility assessment.

DR. KUBALE: Sure, so let me take the first part of your question. We have a variety of things that sort, you know, the current portfolio from 2011 on. So there is a table by focus area and those kinds of things. So the compendium is a start. Where, for your question, where if you really want to look at more specific, you know, kinds of things and you want to do a more advanced search about what's been done, then the database is really a place to go for that. So you know, that's a place where you can go and you can search on keyword terms, you can—there are a variety of ways that you can do it. And then it will provide and you can produce from it a bibliography of those studies that relate to the particular area that you want to look at. So if you want to search prenatal studies, if you want to do it by age, if you want to do it by gender, that allows you to very quickly look at either segments of the whole 1,300 studies or the whole thing.

As far as the feasibility is concerned, yes. The first big key is they have the data that, you know, that's going to be meaningful, number one. And if they have it, can we get access to it, number two? And then once we get access to it, then it becomes a decision after the, you know, that phase of the feasibility for the Program to look at cost and what, you know, the Program will be able—and will be most beneficial to do.

So what we're doing right now is that we're just trying to collect all the information that we can about what's there and what shape it's in and what we can get access to, and then based on that, what are the kinds of things that you could potentially do to that that would move the children's research forward? And with each one of those, there's certainly a cost and you know, that will be included in that part of the proposal or the feasibility is one.

DR. WARD: Dori?

DR. REISSMAN: Thanks. I just wanted to comment a little bit to Dr. Talaska's request, and I just wanted to hear a little bit more if I can ask that, when you said how do we be

proactive in having those who were young when they were exposed as they're developing and growing up and entering adulthood as they have now, avoiding smoking is a little bit more obvious to many of us but from the perspective of avoiding other exposures, how would you suggest that we approach that? That's like a whole different arena I think than things that are happening in the survivor program right now.

DR. TALASKA: My thought would be that you would identify those things that are known to interact with those exposures and be they specific compounds or specific environments like occupations that are related, and just give people information, let them know that these are things that are known to interact and these are things you might want to consider avoiding if you can. That would maybe be how I would approach it, and if there was some research to back it up, that would be another thing, specifically for this exposure. But you know, talking about say asbestos, the asbestos that was in the dust, what sort of things are interacting with asbestos in the literature. You know, this is a thought that I just came up with ad hoc so it's…

DR. REISSMAN: Yes, and I heard it so I wanted to take advantage of the moment, and with Lila, you mentioned two different times today, you mentioned something about women's health and then sort of alluding to the same idea of people growing up and not sure when you can impact on the research agenda. While the STAC may be asked to do things in a certain schedule, it never stops you as an individual to send a letter. So if there's areas of interest, send it to me.

MS. NORDSTROM: Thank you.

DR. McCAWLEY: Dori? Yes, before you go...can I…?

DR. REISSMAN: Yes, go ahead.

DR. McCAWLEY: Can I add something?

DR. REISSMAN: Sure.

DR. McCAWLEY: So I think I've mentioned this to you before. One of the things that I've noticed in the list of symptoms now and the list of diseases that are coming up is these kind of reflect some work in areas that I've been doing, particularly with the mountaintop mining stuff that we're doing, but now also with fracking and communities who live around fracking, and we're seeing the same sets of diseases in particular orders. And we believe, in fact, that the common link here is probably an inflammatory process that's going on, and so if you're talking about what to avoid, avoid those kinds of exposures that are going to be very inflammatory. So for example—I can give you one very easy example, that would be diesel particulate. So, and if you live in New York City…

DR. REISSMAN: Yes. That's a tough one.

DR. McCAWLEY: Yes, it's a tough one, but it might also suggest some approaches also intervening in some of these diseases. So if we have an inflammatory process going on, there are things that could be done that are anti-inflammatory, and the diseases that I

think you're going to see, I'll make a public prediction on this, if you have—and in fact I know probably one of them you're starting with. So I think you're going to see the autoimmune diseases rise. Although you haven't got any papers yet out on cardiovascular disease, I think that will probably be a bigger problem than respiratory in this population if it follows along with what we've seen. And last but not least, neurodegenerative diseases. So I would be concerned about the rate of Alzheimer's in this population as well.

DR. REISSMAN: Thank you very much.

PARTICIPANT: I think a couple of those autoimmune disease and I think cardiovascular disease, I think some of you will hear some of that this afternoon, I think, so.

DR. WARD: So Steve, I think you had a question for Dori and then we'll—no? Val first, okay.

MS. JONES: No, no, he as opposed to—

DR. MARKOWITZ: No, I don't have a question for Dori so if you have a question for Dori…

DR. WARD: Okay, so first I'll take questions for Dori and then we'll move on to other questions.

MS. JONES: Okay. Okay.

DR. WARD: Just since she's there.

MS. JONES: Okay.

DR. WARD: So we have Lila and Catherine.

MS. HUGHES: Hi. As a downtown resident and mom, and one of the big issues seems to be air quality here in New York City, right now is the battle about congestion pricing. So we have vehicles going through our neighborhood, major trucks that are just avoiding tolls, crossing through our neighborhood. So I just want to put congestion pricing on how there could be a positive upside for the residents as well, and workers in the area.

DR. WARD: Lila?

MS. NORDSTROM: I have what might be a crazy question, I don't know. In hearing Michael talk about fracking, the effects of fracking, I know that in hearing echoes—in hearing all of these speeches I've been hearing around gun violence victims, I've been hearing a lot of echoes of things that we heard around Stuyvesant after 9/11, concerns that are likely related to PTSD about helicopters and things like that. And I was wondering, is there any system by which government agencies like this can combine research on—instead of just doing focused research on small populations that are affected in certain ways, doing larger studies about how, like, sort of larger issues affect pockets of populations that have similar exposures? Because it seems like they're, you know, as we're talking about, you know, the difficulty with getting a children's cohort set up and all, you know, we've been talking about this difficulty for a decade at least at this point. But there are a lot of ways in which exposures that other kinds of pop—other kinds of pediatric populations face might, in certain situations, around certain conditions, sort of have similar consequences.

So I'm wondering if there—I don't know if that's a thing that an organization like

NIOSH can accomplish but that's something I've been thinking about a lot as conversations around fracking have happened upstate, and I've heard just sort of from family and other connections upstate about a lot of the consequences being similar in nature to what we see in 9/11-exposed populations.

DR. REISSMAN: It's intriguing. Thank you for raising it.

DR. WARD: Okay, so I think we have Val and Steve who would like to comment but not necessarily to Dori.

MS. JONES: Yes, my question is simple. I see that you have here in several places that you want to look for the gaps. Can you identify any of the gaps now or is that just a question? What gaps did you find so far?

DR. KUBALE: Well, I think I would say a couple of things about that. Yeah, we have some ideas. We're still at the point where we are wanting to, you know, we are wanting to listen. I think this afternoon, you'll hear some recommendations from, specifically from the researchers. Again, you know, we're looking and where we're really concerned is that in several of these areas, in particular the research areas, there is some—there has been time, and so we have results—with respiratory disease and mental health is that there is a substantial number, we think, and it's not just responders, it's responders and survivors. You see it in the Registry studies, you see in the FDNY, and you see it with work that Bellevue has been doing is that there are people that aren't getting better and that are still, they still have symptoms, and they still have symptoms after 16 years. And you know, that's a concern, and the concern is is it inflammatory? I think some of the things that you were talking about. There is some evidence there. We want to make sure that we are exploring all avenues and that we're listening to what the researchers are telling us and what they're learning in the clinic so that we can hopefully improve that. But those are the things that, you know, that start to keep us up at night. It's, you know, the people that are there in the program and we're still seeing difficulties. Mental health is another area. Cancer, I think that that is an area where, you know, we need to do things that address latency and some of those issues that this group has talked about, and I think that we're in a good position to do that. I think that it's still early in that process. So that's what we're, you know, concerned about and that's where we're looking to make sure, do we have everything in those areas that we need?

DR. WARD: Steve?

DR. MARKOWITZ: Steven Markowitz. So I just want to recognize and really congratulate you on the level of structure and organization that you and your colleagues bring to this research program.

DR. KUBALE: Thank you.

DR. MARKOWITZ: Because it's really exemplary.

DR. KUBALE: Well, thank you.

DR. MARKOWITZ: Including this bible that you have created. I know—I still believe in the separation

of church and state so I understand you couldn't call it a bible, but this is incredibly useful. I think it's useful to the STAC because you know, one place, we can bring ourselves up to date. I think for the clinicians at the World Trade Center, you know, the clinical centers of excellence again, in one source, they can stay abreast of what's going on. It's not an easy thing to do. So I think it's incredibly useful.

I also want to point out that it's—you can read this on the subway given the size of it. Travis, your accent, I don't think you're from New York but you took the *New York Post* approach.

DR. KUBALE: I've been on the subway.

DR. MARKOWITZ: The *New York Post* approach to the size of this thing, so I think that's really great. Can you invite the STAC members to the specialty workshops so that the STAC members can, you know…?

DR. KUBALE: Yes.

DR. MARKOWITZ: Okay. One of the things I think about is the impact of World Trade Center work on, in the outside occupational medicine world and beyond, because the research and the clinical activities are all centered here, the researchers are mostly centered here, yet we learn a lot that ought to move and be learned by—outside of New York and outside of the occupational medicine world. Very hard to measure. The only way I can think of looking at it is the number of times that David Prezant goes to the American Thoracic Society meeting and presents this kind of work, or other researchers outside of occupational medicine, in the mainstream pulmonary world, psychiatry and the like. Actually, one could look at that, because you've tracked the presentations. It is a true benefit to the Program. I don't know whether you want to add that as a metric or not, but that, I consider that to be an important output.

And by the way, we've also, this World Trade Center activity has also managed to pull in researchers who otherwise wouldn't be involved with occupational concerns. I think one was (Nevsky @ 02:48:38) from Sinai. I think Alfredo Morabia from Queens, but others, smart, accomplished people who are spending part of their time focusing on World Trade Center issues. That's a good in occupational health, for not just World Trade Center but for the future.

So just one small suggestion. In this book, this bible, in the tabs you list—there's a tab, I'm looking for Ben Luft's publications and what I, I don't see Stony Brook listed anywhere. I don't see Rutgers. I don't see Northwell. What I see is the Icahn School, and I have an appointment at the Icahn School of Medicine so I confess that. But you may want to consider not referring to that cluster of studies as Icahn School-based studies because many of them are based at Stony Brook or the other institutions. So I don't know if they're sensitive to that issue but it's just a suggestion for the next version of the bible.

DR. KUBALE: Yes, well you know, that's very interesting. That's right, and I have struggled with

that, because the Stony Brook group, you're right, they're in there. I just want you to know they're in there.

DR. MARKOWITZ: No, I see that, I see that.

DR. KUBALE: Okay, I just want—you might not have gotten to that part of the bible but they're there.

DR. MARKOWITZ: Right.

DR. KUBALE: So here was the struggle, and it's not over yet, on how to organize this massive thing that we call World Trade Center research. And we certainly would love to hear these kind of suggestions, and how we did it at the first cut that made sense to us is that the CCEs sort of feed in to the data centers. And we used that feed as the way to organize it. So Ben and Stony Brook are going to be probably in the Mt. Sinai data center. So if there's another way to do that or if it looks better, we certainly can, you know, can work on that, so yes.

MS. SIEGEL DE HERNÁNDEZ: I think that other—you can subdivide it by the various centers, or that's part of the other responder program. So I think just referring to it as the other responder program.

DR. KUBALE: And not putting Mt. Sinai? Oh okay, okay.

MS. SIEGEL DE HERNÁNDEZ: Not putting, not—right, exactly. Not flagging it as Mt. Sinai.

DR. KUBALE: Oh okay, okay. Sure, sure. Like the general responder cohort.

MS. SIEGEL DE HERNÁNDEZ: Even though that's where the data center is located.

DR. KUBALE: Yes, okay.

MS. SIEGEL DE HERNÁNDEZ: That's really all the research that you're talking about.

DR. KUBALE: Okay.

DR. WARD: Catherine, did you have a comment?

MS. HUGHES: Yes. First of all, I agree this is an amazing compilation and it's, I think, thank you to all the researchers and all of your World Trade Center team for putting it together. Just two quick things I just want to point out is one, I think it's really important that the privacy of the participants in any of these studies remains private unless they want to go public with that information. And two, if for example there was a study that was beyond just the World Trade Center Health Registry, it's just really important that the people who volunteer to participate get to know the results of the study. Because I know in some situations, with the public studies, the people who took their time and who went through it may not know what the outcome—I know if they're at the workshops, it should be, the onus should be on that researcher outreaching to the participants in some way.

DR. KUBALE: Well, thank you, Catherine, for raising that. What I…so, that's part of any research project that we have in the portfolio, that's part of the terms and conditions. So we have ways where we think we're tracking it. If we're missing something, please let us know because that's really important to us, and it is a specific term and condition in every single cooperative agreement, every single study that we have is that, you know, the individuals that participate, certainly privacy is an issue but

also that those results, that they're communicated with directly by the researcher. So if that is not happening and we're missing somewhere, please do let, you know, communicate directly with Dori or me. We would really want to know. That's important, and we agree with you, yes.

DR. WARD: Yes, Val.

MS. JONES: Yes, I'm not sure how appropriate what I'm going to say is but you said a number of times that the people are not getting better. So I'm going to say something personal because it's…

DR. KUBALE: I'm sorry, I meant there is not general—there are parts that we're concerned about, yes.

MS. JONES: Okay. Okay, well, let me, let me—you know, so I'm going to say something personal. In preparing for something that I'm doing, one of the things that came up was the fact that sugar is very inflammatory, and every time I have orthopedic problems, they tell me my issue is arthritis, but I don't remember—oh, I think she was sitting over there this morning. Well, what did I have for breakfast this morning? A bacon, egg, cheese biscuit from McDonald's with a tall sweet tea. So what am I saying about inflammation here and my behavior?

And one of the things, and I'm just going to segue that, like I said, that one of the things I do in my neighborhood very often is do health fairs and like I said, my neighborhood is a lot of Latino people. And so one of the things I very often do is bring a plate with the quadrants, and I'll put the Spanish rice here, because this is like my neighborhood. We do Spanish rice and (baja lajo @ 02:54:51), this is what we eat. And the Spanish rice takes up like this little portion. If I was to tell you the number of people who have said to me, oh no, Val, I do a mountain of rice and then I put my chicken on top. I'm like oh, okay.

So I think that one of the things with research, or something that needs to be done with research is if there is any behavior associated with what people need to do, you have to look at behavior because I can say as a nurse, I used to talk to diabetics all the time and they clearly understood, you know, things about sugar and then I'd go in the kitchen on my job and Joe that I'd just finished talking to, that he'd clearly said he understood, is sitting there eating Rocky Road ice cream, chugging away. And so I just think that if we, in terms of research, I think one of the things that has to be looked at is behavior, because I think a lot of times, what we need to do that's healthy and what we do that's healthy is two different things. So I think that that has to be looked at, and that's why I started off with inflammation, and while I understand it, I was sitting there eating—you know, I drank my entire McDonald's sweet tea knowing it's inflammatory, and hopefully I'll be able to walk home tonight when we finish this. But I just think that that's one of the things that we, a lot of times, don't like to look at is that sometimes healthy behavior is uncomfortable behavior, it's not customary behavior, etc. So hopefully there is some research that looks at behavior associated because I think that's

one way that people continue to have the same health problem because they don't change certain behaviors, and I don't know if the research is looking at whether people are changing behaviors that may not be healthy.

DR. KUBALE: Thank you for that, and I think that that's an excellent segue into the afternoon.

MS. JONES: Oh, okay.

DR. KUBALE: I think that both Dr. Prezant, I think Dr. Bromet, Dr. Luft, they're all going to be talking about the complexity. And it certainly does speak to your point, and I think that there is a lot of emphasis on that, and a real struggle on sort of how to really examine it and how to tease out, you know, what is occurring and then what might be done to help.

DR. WARD: Thank you. So one last call for questions from the, from people on the phone, questions or comments. And in the room, Annyce has a question.

DR. MAYER: I was really glad to see the great efforts and some progress forward that had been made in expanding the children's cohort, which is great. And when I asked that question about the people in Virginia, that was kind of in my mind in that again, not quite understanding exactly what the graphs were showing, but there's a lot of people in that 35-44 previously later teens/early adults, and many people in Virginia, and the question that popped into my head was I think of people in New York still living in New York. Well, of course some people have moved elsewhere, and could all of these viewers in Virginia have been people who were children here and are now living there, and could that be another potential population source?

DR. KUBALE: Well, thank you, and it is one that, as we are looking and exploring, part of the information that we'll have, we hope, will help us identify where people have gone and how to contact them.

DR. MAYER: Has there been any thought to any kind of public outreach, either on the media, social media, for people to self-identify who are interested in participating in research?

DR. KUBALE: I think, you know, maybe this afternoon, I know the Registry has done, you know, targeted outreach. I know that the children's researchers have done targeted outreach. I can't recall off the top of my head if that reaches, how far that reaches. But I know there has been tracing, and there have been tracing efforts and those kinds of things to identify and to expand the cohort.

I will say, just one brief caveat that we have noticed that we were very concerned about, particularly with—that goes to part of your question, I think—particularly with Dr. Trasande's studies, early on we were very concerned about recruitment and about power. And he is finishing those, and I will tell you that we haven't had an issue with power. And so you know, the recruitment and the recruitment effort, and I think with several of those studies, the outreach that was done not only by the Registry, which was substantial, with particularly the Trasande studies, but also what's been done by the responder—survivor, I'm sorry, survivor groups—

has been really helpful. Is it, you know, exactly what we want as far as the size of the cohort? No. But it, so far, you know, the numbers have been robust and we are happy about that, so. I'll leave you with that.

DR. MAYER: No, no, that's great, and power is very important, but you know, to be sure that we're capturing representative sample of the population.

DR. KUBALE: Absolutely. Absolutely, absolutely. Yes. Yes?

DR. WARD: Lila, did you have a comment?

MS. NORDSTROM: Yes, I'm just—I'm going to identify myself as someone who specializes in outreach to that population and say that one of the things, there's been a sort of resurgence in outreach at the moment on, just on sort of like the World Trade Center Health Program side, but that has had a tremendous impact in our ability to help find people who will identify themselves publicly as being affected but not only that, participate in—or are expressing interest in participating in things like studies. So there is a big sort of like, there's a big relationship between outreach that's done more broadly to let people know about their healthcare options as 9/11 survivors and their willingness to self-identify as 9/11 survivors and then also participate in research surrounding 9/11. And there is a huge dispersed population nationally of young adults because anyone who was in high school at the time of 9/11 graduated into a recession and did not necessarily return to New York in huge numbers because of the cost. So that is definitely a concern.

DR. KUBALE: One thing I would just add to that is that in the compendium, there is a section on the—that I talked about earlier with the Registry, that talks about progress by specific aim. And there are a couple of things that I would just draw your attention to. One is the treatment and referral program, where there is a substantial outreach effort that is occurring and coordinated. The other thing is there is a section where they talk about the number of kids who are now adults, but they were kids in the original 3,000 cohort, and the follow-up efforts that, you know, they have that are ongoing to ensure that those individuals as adults are back in the—you know, are in the cohort and available for study. So I don't want to forget those efforts as well.

DR. WARD: Travis, I had one comment and then Catherine has a comment. I do want to mention that several times, you said that the members of the STAC are invited—or invited to the specialty workshops, but I think at this point, we don't receive notification when those workshops are occurring, and I understand that financial issues would preclude NIOSH supporting travel to come to the workshops but I think at the very least just having a direct notification to STAC members when the meetings are occurring would allow those in the area to avail themselves and those who might, you know, have opportunities to come in for the meetings. So I just wanted to just reflect on that and perhaps you could notify us. Yes.

DR. KUBALE: I'll make sure that that's, that that happens. The other thing that we'll also make sure that's available for the STAC, and Paul can distribute, is we have an initial

conference book that has all the, you know, the presentations, and those include updates that maybe aren't presented. So you can get sort of a sense of what's occurring in the portfolio. And then we send another one out after that occurs. And we'll make sure that the STAC not only has the meeting notices, but we also will make that information available as well.

The other thing that we're probably going to start doing soon, since we are, we get probably, in the portfolio, since the first of the year, we've gotten probably a publication a week. And probably what we'll start doing is we'll send abstracts of those out to the researchers, but we're also going, we'll include the STAC on that as well. But certainly we'll make sure that you have the information about the meetings, yes. We'd love for anybody on the STAC that can come to…

DR. WARD: Thank you. Catherine.

MS. HUGHES: Two quick things. I found out about some of those through the survivors' committee, thanks (inaudible @ 03:05:05), and when I've had the opportunity to come, they've been very helpful and informative, for me at least, being there visually and hearing the speaker talk is important. So thank you for getting that out.

But second, with the 25-year anniversary of the 1993 bombing, I do want to thank CDC because I did see some ads in the local papers talking about the outreach programs, so that was very important to hear about it from CDC versus a lawyer. So I just want to thank you.

DR. WARD: Okay, any last comments or questions on the phone? And none in the room, so I guess we're ready to adjourn for lunch. We'd like to take it one at—we'd like everyone to be back and ready to start at 1 o'clock.

DR. MIDDENDORF: For those of you on the STAC who ordered lunch, I think Mia is back. They were there, Mia? Yes, lunches are over in the break area over here.

DR. WARD: We can eat over there?

DR. MIDDENDORF: Yes, you can eat over there, not out here.

[Break.]

DR. MIDDENDORF: Okay, can we get the members to come back to the table please? And members on the phone. If you can prepare yourselves, we'll try and get started again.

Okay, just want to do a quick roll call before we start up again. Just looking around the table, all the members who were here earlier are here again. Members on the phone, if you'd like to speak up, just let me know you're there. Bill Rom, are you on?

DR. RYAN: Margaret Ryan.

DR. MIDDENDORF: And I'm not hearing from Bill. Margaret Ryan?

DR. RYAN: Yes. I'm here, sir.

DR. MIDDENDORF: Okay, thank you. Sheela, are you on? Okay, I'm not hearing anything from Sheela. Marc, you said you were going to join us at 1:00. Have you been able to join us? Okay. Not hearing. Okay, well, we still have a quorum, so we can move

on.

DR. WARD: Welcome back from lunch, everyone. Our first presenter is going to David Prezant and—or, presenters will be David Prezant and Joan Reibman talking about World Trade Center respiratory disease research findings and grantee recommendations. Dr. Prezant.

WORLD TRADE CENTER RESPIRATORY DISEASE RESEARCH FINDINGS AND GRANTEE RECOMMENDATIONS

DR. PREZANT: Thank you. True honor to be here and to see so many friends and so many interested people who are participating in helping us move forward with the World Trade Center Health Initiatives. Very much appreciated. You—Paul, are you going to be doing the slides, or...or I don't have a clicker. Thanks.

So I've been asked to talk about some of the findings and research priorities that we had highlighted in a previous June research meeting. And as such, I'm going to be concentrating on the non-mental health issues because Stony Brook is going to be representing that. So, and I'll be focusing mostly on the responders because Dr. Reibman will be talking about the non-responders right after my presentation.

As you well know, there were approximately 90,000 responders who were exposed to the toxic dust and organic matter, and we all are well aware that this toxic dust—next slide please—that this toxic dust contained silicates and Freon and PCBs and PVCs and dioxins and polyaromatic hydrocarbons of small amount, but a significant amount of asbestos. And to a large degree, pulverized concrete, which we feel is one of the major inflammatory mediators of this exposure.

The next slide. Our program for responders includes FDNY that I represent, which is predominantly FDNY firefighters and FDNY EMS workers. In total there are about 16,000 in the World Trade Center Health Program. And it also includes the other responders, or the non-FDNY general responders which are predominantly law enforcement, communication workers, construction workers, sanitation workers, other responders, other labor organizations and some volunteers.

Next slide. Concentrating for the moment on the FDNY health program demographics, as I said, we have nearly 16,000 people. But I'd like to highlight some very unique aspects of our program. We're the only group with pre-9/11 health data and that has allowed us to be able to make a large number of comparisons with pre-exposure health metrics. We're the only group where essentially everybody was enrolled prior to the onset of any benefits. We're the only group that had an early exam in 2001 through 2002. We started our first monitoring exam October, first week of October 2001, which allowed us to get some very early metrics right after the disaster.

We have the highest retention rate with greater than 80% of our cohort returning for exams. We have a growing but robust biobank, which I'll talk about later in this

presentation. And the reason why I highlight all of this, and these numbers here can substantiate a lot of it, the reason why I highlight this is because this, to me, is one of the greatest, if not the great success of the World Trade Center Health Program. In that, we have been able to forge a unified, completely committed partnership between labor, management, government, and healthcare. And that is incredibly unique after an exposure.

In fact, it's incredibly unique and I'm really honored and privileged. It's incredibly unique for an organization like the STAC to invite really FDNY. Normally, it would be an academic medical center that was up here.

Next slide. So we have 15% of our cohort who were present during the collapse of the two towers. Another 44% of our cohort was present in the afternoon during the collapse of one of the other towers. And then you can see that the rest of our cohort responded, and over 70% of our cohort was there in the first three days. Meaning that we had a massive acute exposure. And that is one thing, plus a more healthy worker effect that does reduce some of the generalizability from our cohort to others. Yet, nearly all of our findings have been reproduced in the other cohorts.

Next slide. Aha, it probably is a different color. Can you go to the next slide just to be certain? No, there it is. There it is. You just had it hidden in there.

PARTICIPANT: Yes, found it.

DR. PREZANT: So one of the benefits of our program, and the reason why we've been so productive and also so dynamic in being able to look at this so rapidly is that there's complete integration between our clinical center and our data center. And this slide, while not a perfect representation, tries to demonstrate this bidirectional nature of communication between our CCE and our DC. And it's in large part because we only have one CCE, one clinical center. But it's also because the leadership and all of the infrastructure is shared between our CCE and our data center. So that has made this marrying of all of this data and all of our applications and programs as really one and that is something that's often not understood by people looking at our data.

Next slide. The CCE is responsible for looking at patient information at the micro level but the data center is responsible for looking at patient information at the macro level. And again, it's this communication between the two, so our CCE doesn't download its information into our data center once a year through some VPN site and then waits another five years to get back some information. It's not that type of model, which works perfectly fine for multicenter national studies. It's not our model. We're communicating daily and weekly about what these results are showing.

Next slide. So now concentrating—next slide—on the respiratory aspects. This is a bronchial alveolar lavage from a firefighter that was brought into Bellevue Hospital. This was in the third week of September and our NYU associates, which

we have a very close collaboration with NYU, with Albert Einstein, and with several other of the medical schools, but NYU and Albert Einstein are our two closest collaborators. This firefighter was in acute respiratory distress. He was intubated, and he was bronchoscoped and lavaged. And the reason why I show this to you is it demonstrates a variety of things, but for this study it demonstrates that there was Word Trade Center dust down there. This is an uncoated asbestos fiber to the far left, which means it's an acute exposure. Fly ash particles, which is pulverized concrete, and fibrous glass.

Onto the next slide. So it demonstrates that these large particles were to get down into the small airways, it demonstrates the fact that scientific studies done before the World Trade Center are scientific studies. They aren't—mean what they were meant to mean, which is that if you constantly think that large particles don't get into the small airways, you're not reading all of those studies correctly.

Those studies are low density, low concentration exposures. They're studies that are very, very important for infectious disease, for manufacturing metered-dose inhalers for asthma medications. There the concentration is going to be very small. And what you find is that particles less than 10 microns in size don't get into the small airways, don't get to the alveoli. You can't apply that to the World Trade Center where the concentration was massive. It overwhelms the upper airway protective systems, gets down into the airways, gets down into the alveoli.

And on this slide, as you can see, creates inflammation that's visible on a CAT scan and creates inflammation that's visible on pathologic specimens. And if you were to look at this on a higher power you would see that this is a lot of the eosinophils.

Next slide. And what this led to was early pulmonary function loss. And you can see here that this is a dose response curve between our greatest exposure at FDNY, which is those people arriving on the morning of 9/11 versus lesser exposures as we progress from initial arrival time early on to several days later. What you see in the bottom on the sort of reddish color is the annual pulmonary function loss that occurs in this cohort. Not nationally, not in some scientific study, but in this cohort prior to 9/11. And what you see is that they drop by about 27 to 30 milliliters per year, which is typical for normal aging. But in this one-month period, essentially, though it was measured over 6 to 12 months, they dropped by, as you can see here, over 370 milliliters, which is more than 13 times of what you would expect. And those people who were most symptomatic, as I'll show you later, dropped far more than this.

So the next slide plots this a little bit differently and shows you that prior to that giant red arrow, they're dropping as you would expect for normal aging and then there's this huge drop that I just showed you. And what this study, which is published in *CHEST*, shows not only that drop, but it speculates on what the future will hold. And the future could have been any one of those three lines. It

could be that the normal reparative processes of the lung, which are huge, brings everybody back to normal. And that would mean that this was an acute problem, that it would last a certain period of time, and then it would all be over.
Alternatively, the middle of those lines with the question mark, is that this is a drop, it occurs, and people never recover, and they then continue to drop at the annual expected rate for aging.
And then the third line down below would be a tragic line, depending on its slope. Because that would imply that the drop now was accelerated. That because of this, not only was there an acute massive drop, but that thereafter there was something wrong, that combination of host and environmental interaction that created an accelerated decline. And that accelerated decline could become quite ominous, resulting in early death and the need for lung transplantation. So we did not know at that time, and this study was published in 2006.
Next slide. We have published data and similar data was published in the survivor cohort that Joan will go over, showing that the reduction in pulmonary function correlates with symptoms. Those people with the lowest pulmonary function with the greatest reduction had the greatest amount of symptomatology. Symptoms being wheeze and shortness of breath and cough.
Next slide. And as I said, this has been reproduced in both the general responder cohort and in the survivor cohort.
Next slide. The survivor cohort that Dr. Reibman will go through in more depth has also been looking at very important measurements of pulmonary function other than just barometry. They've been looking at oscillometry and shows that a lot of this airway inflammation and obstruction is occurring in the smallest airways right by the alveoli. Again, demonstrating that these particles did get down into the small airways and alveoli.
Why is that important? It's important because it shows one of the points of action for this respiratory abnormality. But it also shows that these particles and the chemicals that were coated to them have bioavailability. They're very close to the pulmonary vasculature. So that they're going to be absorbed and that these are true potential carcinogens and inflammatory inducers. Where, if it was occurring just in the upper airway, while that would still be possible, it would be less likely.
Next slide. And in this paper, we attempted answer the question that we raised in 2006, which is what will be the outcome of this gigantic drop in pulmonary function?
Next slide. And while this is a busy slide, the main thing to take from it is that this giant drop that occurred early on in time "zero" on this graph, which is the first months after 9/11, then leveled off. And depending on which group you look at, whether it's EMS, whether it's firefighter, whether it's the earliest arrival group or a later arrival group, you basically can see that on average, it's pretty much a straight line adjusting for aging. And that's telling you that luckily for the majority of

the cohort, they didn't continue to decline in an accelerated fashion. Unfortunately, they didn't recover, all right, but they didn't continue to decline in an accelerated fashion.

This, however, like all averages, is a misleading statement, because within the average are people that have improved and people that have gotten worse. One of our main goals is to try to understand those differences and to try to identify the people who are not staying stable and declining at an accelerated rate. And we'll show you that momentarily.

Next slide. Again, demonstrating that this was shown in the general responder group, as well.

Next slide. So they fell in terms of their lung function, and that firefighter that I initially showed you his bronchoscope alveolar lavage had what's called eosinophilic pneumonitis, and that's one of many interstitial lung diseases. It has a very good prognosis when it's diagnosed early and treated appropriately, and for him it was, thanks to our NYU and Bellevue partners. But one of the main questions in the middle of this time period, because we want to know how to treat this, is this going to be interstitial lung disease, which is very difficult to treat, has an ominous mortality, and really the only treatment for it is lung transplant. Is this going to be many of these people with interstitial lung disease as that first firefighter might have suggested? Or, is this going to be the more common of both lung diseases and occupational lung diseases, which is some type of obstructive airways disease. Some spectrum of asthma, chronic bronchitis, chronic obstructive pulmonary disease, and hopefully not severe emphysema.

So we embarked on a series of studies, and this is one of them, where we try to understand using pulmonary function tests, what is the underlying mechanism? Is it going to be interstitial or is it going to be obstructive? And luckily for the cohort, the majority of cases, this is obstructive airways disease. It's unclear whether it's pure asthma, pure chronic bronchitis, some mixture of the two which is COPD, and it probably varies from one person to the other, but really is, is obstructive airways disease for nearly all of them.

And this slide looks at that and it shows that those with the greatest decline in lung function were the ones most likely to have a bronchodilator response, i.e. obstructive airways disease, and were the most likely to have airway—I'm sorry—air-trapping or hyperinflation, which is the opposite of what you'd see in interstitial lung disease.

Next slide. And, again, our partners in the survivor group at Bellevue have also shown that while there are large numbers of people without airways obstruction, there are a large percentage with airway obstruction.

Next slide. Another way to look at obstructive airways disease, and in particular asthma, is to measure hyperreactivity. And we can measure hyperreactivity in a lot of different ways. The most common way in the United States is with

methacholine challenge testing, unlike spirometry, can't be done for the entire cohort. It's way too labor intensive. It's way too costly, and a variety other reasons. So we were able to do spirometry on everybody, but in terms of hyperreactivity studies, we look at either looking at the most symptomatic or doing some random polls, and we've done both. And what hyperreactivity is, is that when you're exposed to methacholine do you have a drop of more than 20% in lung function and is it occurring at very low doses of methacholine exposure? If it occurs at very high doses that's probably normal. But if it occurs at what's called a PC20 which is the measurement of the dose, if it occurs at a PC20 of less than 8 or less than 4, it's consistent with hyperreactivity. And one disease that's commonly synonymous with hyperreactivity is asthma, but certainly airway obstruction.

So this is graph of just a single person and what their methacholine challenge test would look like. But on the next slide is our results. And we actually have some very important results because, number one, not shown here is that on the people that we tested for hyperreactivity, 25% of them were hyperreactive and it was much more common to be hyperreactive if you were there early on during the first day or two. So that's not shown here, but we published that.

But what no one really has looked at, or, well, I should say what is very rarely looked at in any occupational setting is the long-term impact. So in this study, what we did is we brought people back 10 to 12 years later and we repeated their methacholine challenge testing. There are only two or so studies of repeating methacholine challenge tests more than five years after an occupational or environmental exposure, and those are non-World Trade Center.

So in this one, we actually, if you had an original test so we knew what you originally were after 9/11, shortly after 9/11 within the first year or two, we then brought you back 10 to 11 years later and repeated that methacholine challenge test. And what we found was that the baseline methacholine challenge test persisted in the majority of these patients. That hyperreactivity did not go away. You're actually going to see that shortly.

But on this slide, what you see is that a hyperreactivity, persistent hyperreactivity as shown in the blue, was more likely to be associated with persistent symptoms, which is somewhat obvious, but also more likely to be associated with an accelerated decline in FEV1 which is on the far-right bottom graph.

On the next slide—I'm sorry I'm going fast because I have limited time. On the next slide, you see what I had originally mentioned, which is that 10 to 11 years later, the majority of the people that were retested had continued to be hyper reactive. So just as the decline in lung function did not go away, neither did the hyper reactivity. And in many of these patients, this persistence of hyperreactivity occurred despite treatment. Many of these patients were treated for years with at the very least inhaled corticosteroids. And yet, the hyperreactivity remained when we took them off drugs to do this test.

Next slide. As Dr. Reibman will go through, her study also showed hyperreactivity in a select group.

Next slide. So now we come to really what I would say is a turning point. We've characterized the group. We've looked at the group as an overall cohort, but our goal is to do more than that. Our goal is to realize, as I said before, that an average is an illusion. All right? What is the standard deviation off of that average? Are there people buried in this group that are not doing well? And here you can see that this does exist.

So we have here three curves looking at them from time "zero" forward, and this was published recently. And what it shows is that there's about 1,200 people in this study—his study was a study of approximately 10,000—there's 1,200 people that you can see on the bottom line are declining faster than everyone else. We arbitrarily defined an accelerated decline in lung function as more than twice the average of the cohort. So before 9/11 the decline was about 27 to 30 milliliters. After 9/11, if you discount the initial drop of 370, after 9/11 for the cohort, it's about 34 milliliters. So twice that is what we defined as accelerated decline. So 64 or more milliliters per year, and that's demonstrated in this bottom line.

So this bottom line group of 1,200 individuals is not doing well. Now, that doesn't necessarily mean that they're more symptomatic. Some of them certainly are. We have a healthy worker effect. They started at a very high lung function to begin with so we're not talking about large numbers of people that are less than 60% of predicted. But these people certainly have greater (provocable @ 00:29:58) symptoms, more shortness of breath with exertion, with irritant exposures, etc. And if this decline was to continue at this rate, it could potentially be ominous, and therefore there's every reason both medically, scientifically, ethically to find out what's the difference, what's the reason that makes them different from these other two lines, from these other two groups, the group in the middle that's declining as you'd expect for age and the group above that's improving just a little bit, even recovering a little bit.

What's different about their genetics, about their environmental exposure, about how we may have treated them earlier or later, or not treated them at all, that makes them fit this accelerated decline? Because we have a responsibility to find them, to reach out to them and to help them. But also as scientists, to learn who they are, why they are, for the next disaster.

Next slide. And we've started on that path in studying these patients.

Next slide. And bronchodilator response, predicts the accelerated decline, so that argues that those people who have a true obstructive disease are the ones that might be most at risk for an accelerated decline. Now, the odds ratio here is 2.3. It's not 10, but it's significant. It's important.

Next slide. And we've looked at a variety of biomarkers of inflammation and of other issues and we found a host of them are associated and are predictive

because we drew this blood right after 9/11, are predictive of this accelerated decline, specifically Alpha-1 antitrypsin deficiency, which you know when it's a major deficiency is a predictor of emphysema. So far, we have seen a lot of emphysema. MMP-1, MMP-2, these are predictors of either lung function or MMP-2 of regaining lung function. Some of the metabolic inflammatory mediators—lipids, CRP—are predictive of decline. Triglycerides are predictive of decline. And then at the last one, which were going to highlight in a moment, eosinophils are predictive of a greater decline after 9/11.

I can get to the next slide if I can get it to the next slide. There, you see that when we control for aging and smoking and weight, that—well, here, we're not controlling, but we're adjusting for race here and arrival time. You can see that smoking is hugely predictive. The comments earlier this morning about how we can't take away the World Trade Center exposure, but we can take away smoking exposures. And we've been very aggressive with that. We used to have about 19% of our firefighter workforce were smokers on 9/11 and now it's down to about 6%. We've got a very active tobacco cessation program. We haven't done as well on our EMS side, but we're working at it.

So smoking's a huge predictor. Current smoking is the main problem. Weight is a small predictor. Weight gain is a predictor. But eosinophils are a predictor as well.

Next slide. And this just goes to show you that at every point in time, the group that has the accelerated decline has a higher eosinophil level and a higher neutrophil level.

Next slide. And the survivor cohort, they also have looked at eosinophils and have found that eosinophils too are associated with symptoms and airways obstruction.

Next slide. And this is now moving, while we're continuing this basic science initiative to understand what are predictors, we're also looking at removing those predictors so that we can reverse this. Now, some of this will be quite complicated, but this is complicated to achieve but easy to think about, and that is tobacco status. So this shows our cohort. It shows us, it shows our members, that it's never too late to stop smoking. And what you can see here is that in those people that stop smoking before 2008, their lung function declined, returned to the same slope, same rate as the never smoker. And we're now hoping that if we were to reproduce this study, that those people who stopped smoking after 2008 would show similar recovery. So smoking, while it does not define the people who have these diseases, these diseases affected smokers and nonsmokers. Getting rid of smoking can have a small role to play in your recovery and also, of course, a role to play in cancer prevention and other things.

Next slide. Here's showing that eosinophils are not just predicting lower airway disease, but they're predicting upper airway disease as well. Here, the endpoint is severe upper airway disease, which is sinus surgery. So the triangles are people who, despite aggressive medical treatment of their chronic World Trade Center

sinusitis kept doing poorly required surgery, and their eosinophils are elevated compared to the cohort.

One of things that I didn't make clear, but I wish to now, is none of these people have extremely high eosinophils compared to the normal population. What they have is high normal eosinophils. So within our cohort looked isolated alone, their eosinophils would be viewed as normal. But if you look at it compared to our entire cohort, their eosinophils are high. And that is yet another value of having a clinical center of excellence, all right? Where these patients are all being looked at and treated together. If these patients were disbursed over all of North America, being treated and evaluated in a fragmented way, none of those data would be known, all right? And even if it was known in some way, this wouldn't have been put together because their eosinophil levels are coming out as just high normal, but they're elevated compared to the average eosinophil level in our cohort.

Next slide. So understanding all of this—next slide—we came up with some recommendations, and I'm not certain these recommendations do all of the people justice. They're an attempt and they will be modified as we go forward and as we learn more and as we think about these things more and as data comes in. But this is at least a start now, 18 years later to say we've done a lot and now where should we be going?

So, Recommendation #1 is to analyze the trajectory of respiratory symptoms in pulmonary function over time. Yes, we've done that, but we can't stop doing that. Because you're only going to start seeing differences now, right, and we want to see what those differences are. But the underlying theme, which we'll see in all of these recommendations, is the second point. What are the genetic metabolic and biomarkers that can be measured yesterday, today, and going forward that define these subgroups? That define the groups that are the most vulnerable and the groups that are the most protected? All right, that's going to help us find those people that need treatment, it's going to help us be able to determine for the next disaster who would be most likely to have problems and less likely.

Next slide. And it's not just symptoms and pulmonary function that we want to study over time and continue to study over time, it's disease. Because some people will have symptoms and pulmonary function declines, and not actually have disease, and other people will. And you'll see that later when we talk about comorbidity.

Next slide. And this all leads to us conducting these etiologic genetic studies to determine what is causing this initial prevalence and then incidence, and the severity. We've talked a lot, and I direct this at my own program as well as all the others, we've spent 18 years looking at incidence and at declines and changes. We need to concentrate more on severity and quality of life. We've done some of that already. It hasn't gotten a lot of notice, but we have. But we have a lot of data on this and we need to explore this in greater depth. So that's why we're talking

about here is genetic studies. Not just on prevalence and incidence, but also on severity. And when we mean that, we mean developing a robust biobank.

Now, we developed an initial biobank immediately after 9/11. We drew blood on everyone and we got IRB consent, and I'll talk about that later on, on everyone. And everyone is never everyone, but we have it on, in a 16,000 cohort, we have it on about 12,000 people.

The CDC helped us draw this blood. It was very interesting. They were on, quote, vacation. Vacation was they had just come back from responding to an Ebola epidemic in 2001 in Africa. They found it to be just absolutely a vacation to draw blood on people without having to wear a Hazmat suit, and we were more than happy to entertain them. But they were very nice and they helped us draw the blood in the first six months. We stored it, but they helped us draw it.

We have refreshed this biobank with new blood that we started drawing in 2016. What we have not done is looked at nasal swabs, nasal washes, induced sputum at this point in time, breath condensates for micro RNA. All of these things are useful tools to expand how we look at the inflammatory response and to be able to study it both at the protein level and the genomic level. This would allow us better to define these patients and to ultimately treat these patients.

Recommendation #4 is to use this stuff to identify these patients. And this is all in a patient arena, so this is confidential medical information that should never be shared with the employer, it should never be used to make decisions about hiring and firing and promotion. It should never be shared with insurance companies. As we all know, these studies predict a group over time. They don't predict individual outcomes, but it helps us to explore greater monitoring and greater treatment for people who might be at risk, and then to let them make their choice, right, as to what they do. So that is Recommendation #4.

Number 5 is to then use this not only to impact on lung function, but also on respiratory symptoms and quality of life. We can't forget that it's not just the FEV1, the forced vital capacity, the diffusing capacity, that we're treating. Where actually, patients don't really care about that. What they care about is, does this make an impact on their daily life, on can they breathe, can they do the things that they want to be able to do?

And Recommendation #6 is why this is so complicated, and Dr. Luft is going to be getting into this in more detail later today, but this is not a single isolated disease. These are comorbidities, so people who are short of breath, some of them also have mental health issues. People who have asthma, some of them also have known triggers for worsening asthma, sinusitis, acid reflux. All of these things, it's unusual. This is why our questionnaires are so long. It's why our monitoring exam is so long. It's why our treatments need to be so diverse. This is an environmental exposure that did not affect just a single organ, and as Mike was saying, the mechanism for this is as I've shown you with these biomarkers, chronic

inflammation. It's affecting all, potentially all of the organs of our body. Which moves me on nicely—let's go a little bit quicker and skip a flew slides. And go to the next slide. Leads me nicely to the cancer research that we've done.
Next slide. So we at FDNY were the first to show an association between an increased incidence of cancer in our World Trade Center exposed group. It was a small increase with odds ratios of somewhere between 1.1 and 1.3, depending on how you look at it and how you statistically analyze it, but it was consistent and it was elevated. At the time in 2008, when we published this in 2011, but the study went on to 2008, that was only seven years. And to find this small but significant increase in seven years really made us worry about whether this would become an even larger increase over time. At that time, we didn't have enough data to talk about individual cancers, though there was seemingly signals for increased cancers in thyroid, prostate, colon, and some of the hematologic malignancies. And there was a signal for lower than expected lung cancer. And we think the lower than expected lung cancer was not because the World Trade Center protects you from getting lung cancer, we wish that would be the case, but rather the healthy worker effect. We have less cigarette smokers than the general United States population that we're comparing to, and lung cancer is a solid tumor so you wouldn't really expect to see an increase early on.
Next slide. This was substantiated in the other cohorts that have looked at this, the general responder cohort and etc.. And, again, concentrating, it seems that the consistent finding is—and this was also shown by the World Trade Center Health Registry—the consistent finding of thyroid and prostate, and probably some of the hematologic malignancies.
Next slide. So we've been trying to update our studies. The World Trade Center Health Registry already has one updated study, and what we've been concentrating on is our own cohort, but also a multicentered study as Dr. Kubale was talking about just before the lunch break. Where we have taken a lead with a lot of cooperation from the Registry and the general responder cohort, and from the New York State Tumor Registry to link all of our data, deidentify it, remove any of the duplicates, because there are about 3,000 firefighters in the World Trade Center Health Registry, and there's more duplication between the World Trade Center Health Registry and the general responder, so you don't want to double count people. But the New York State Tumor Registry has taken on that deidentification and removing of duplicates. They've already completed that work and now we're matching to all of the tumor registries that our members across all three cohorts might now be living in and trying to update this data. This is going to give us, A, an updated dataset for each cohort individually, and also be able to do it generally or for all three combined for responders only, and that should allow us to have power to look at individual cancers. So that's our goal. But this is just a brief snapshot of FDNY's own data through 2011. And this is a potentially

complicated slide to understand, so let me take you through it for a moment. The Y axis is the general U.S. population, age and gender matched. So 1 on the Y axis is your cancer incidence rate is no different than the general population. The difference between the blue and the red bars is the difference between FDNY exposed and FDNY non-exposed. And what you can see in the blue bars is that FDNY exposed by 2011 has had some substantial increases compared to the general U.S. population, especially in thyroid, colon, hematologic malignancies, those all have odds ratios greater than 1.25. And still has, thankfully, a lower than expected lung cancer rate.

For prostate cancer, while we're above the general population, it seems like that is true also for our non-World Trade Center exposed firefighters. We're going to learn more about this as we go forward in time, but also as we add the other three firefighter cities that NIOSH has worked so hard to define—Philadelphia, Chicago, and San Francisco. They have agreed to share their data with us so that we can take the lead, along with our NIOSH partners in following now four cities going forward. Being able to differentiate hopefully firefighting from the general population, and World Trade Center from the firefighting population.

Next slide. Next slide. And, next slide. Next slide. Sorry for the animation. Okay, I think that's it. So MGUS is a—go back one. So MGUS is a precursor for multiple myeloma. It's also a precursor for some autoimmune diseases, but it's mostly associated with being a precursor for multiple myeloma. And as I said to you, some of the hematologic malignancies seem to be increased. One of those that we're getting a signal for is multiple myeloma. So we collaborated with the National Cancer Institute and then with Sloan Kettering and with Albert Einstein with philanthropy money from the Jimmy V Foundation to get more blood on all of our firefighters and on a subsection of them, send them over to originally was going to go to the National Cancer Institute but that lead physician moved to Sloan Kettering, so it went to Sloan Kettering and he did the analyses.

Next slide. And this has just been accepted.

Next slide. I think I have animation. Next slide and hold it there. This has been accepted in JAMA oncology. And basically what this shows is that MGUS is a predictor for multiple myeloma, as we would know, but that this is occurring at an earlier age than in the general population. And not shown on this slide, the type of multiple myeloma that is being found in our group is light chain multiple myeloma. And light chain multiple myeloma is less common than heavy chain. It also has a far worse prognosis, and importantly, there's a scientific literature that shows that light chain is associated with various different exposures that have occurred, toxicologic exposures that have occurred in the past. So there's a lot of bio-plausibility for this, and this study moves to showing that.

Our next step is going to be reaching out to these people who are MGUS-positive and offering them a heightened surveillance for multiple myeloma. This is all

about what I've been saying, which is now from roughly 2017 forward, our focus at FDNY is not just to be able to characterize, but to be able to identify the vulnerable groups, all right, and offer them something necessary to hopefully deal with their vulnerability.

Next slide. So our cancer research recommendations are the same recommendations as for respiratory research. So that's an easy summary.

Next slide. I want to conclude with our autoimmune disease. And while dealing with what Mike was saying, these are all inflammatory outcomes.

But, next slide. But our first signal for autoimmune inflammatory outcome was sarcoidosis. And one can speculate on why we picked up sarcoid first, it's up to you to define what the real answer is. One possible answer is we've always had an interest in sarcoid, so we were following it before 9/11 and published an increase in sarcoid before 9/11. And as you can see from this slide, post 9/11 there's an even further increase in sarcoidosis in our firefighter population. There was no increase in our EMS population prior to 9/11, but after 9/11 there was as well. So that's probably the main reason why we picked up on this first and earliest.

I would like to say that, of course, sarcoidosis is an autoimmune disease that primary affects the lungs. It affects all organs, but it affects the lungs and therefore that's why we picked up on it, because the lungs are the most important organ system in the body. That's just a joke. Small joke, obviously.

Okay, so our next slide. Thank you. This has been duplicated in the general responder network and also not shown here, it's been duplicated in the World Trade Center Health Registry, that the incidents of sarcoidosis post-9/11 has increased. And sarcoidosis is covered by the World Trade Center Health Program because while it affects many organs in the body, the main organ that it affects is lung, so therefore NIOSH was able to consider this as an interstitial lung disease and therefore cover the treatment of sarcoidosis.

Next slide. You can see why this is very, very, very important. Because this slide talks about the clinical course of these patients with sarcoidosis. And as you may know, the majority of patients with sarcoidosis stay stable over their lifetime. There's a small number that develop severe problems with lung transplants, heart transplants, etc., but the majority do not. They might require intimate treatment, but they don't generate a terrible outcome.

In fact, 30% of patients with sarcoidosis have some form of spontaneous resolution. We're not seeing that in our cohort. And as you can see in this table, the middle column is what organs were involved at diagnosis. And the far-right column is what organs were involved at our follow-up study, which NIOSH funded as one of their research grants, our follow-up study done in 2011 and later. And what that shows in these 59 patients that participated in both data studies, that the lung findings either persisted or in many resolved did not get worse. We haven't

had any lung transplant requirements due to sarcoid. But the systemic autoimmune inflammatory consequences of this multisystem autoimmune disease have become more pronounced, not less pronounced. And we have a greater number of people, we've gone from 7% to 15% with rheumatologic findings. And we've had the development in some of neuro and cardiac findings. And this is of great importance. A, it demonstrates that a lung problem can have systemic effects, nothing new for sarcoid, but it demonstrates it very clearly in this cohort. But also, it's had treatment impact because our treatment has had to shift from stabilizing the lungs to stabilizing these other organ systems. And in contrast to what the literature has shown about rheumatologic sarcoid, the rheumatologic sarcoid in 9/11 exposed people is very significant and unresponsive to standard therapy. So if you pick up any textbook on rheumatologic sarcoid, they'll tell you response to Plaquenil, you don't even need steroids and just it's fine, wait three months and it'll get better. I'm slightly exaggerating.

We have had very few respond to that. All of our patients have had to accelerate to either Methotrexate or the majority, actually, to biologicals that you see advertised on TV. Why is that important? Because, A, they have a lot of side effects, and B, they're incredibly costly. So it's costing the same amount of money to treat rheumatologic sarcoid as essentially it costs to do chemotherapy for a cancer patient.

Those with heart sarcoid have required, some of them, about half of the six you see here, have required implantable auto defibrillators to protect them from sudden death. We are really making a difference in these people, all right? So these are the most vulnerable and we're making a difference.

Next slide. What about other autoimmune diseases? Well, we've seen an increase in several of them. We've published this now, I believe, in three papers, and rheumatoid arthritis is the highest incidence rate, but we've seen it in polymyositis, in lupus, in Sjogren's, and in several of the others.

Next slide. The problem is, there are no autoimmune registries. So as much as I'd like to see some improvement in the tumor registries, compared to everything else, they're leap years ahead. We've had to find a control group from the Mayo Clinic. It's not a perfect control group by any shape, but it's a control group, at least. It's not firefighters, but it is of similar ethnicity. And you can see here where the arrows are that there is an exposure effect and for some of the diseases there's an increase.

Next slide. So clearly in our opinion, World Trade Center exposure is associated with systemic autoimmune diseases. I think we've clearly shown that for sarcoid, for rheumatoid arthritis, and for polymyositis, and probably for lupus, as well. We need continued surveillance. The other cohorts are joining us in this effort, and I believe the World Trade Center Health Registry will shortly be coming out with their findings on this. We've shared our questionnaires and our medical record

review process, so we're hoping that we can find out whether this is reproduced in the other cohorts, and at least preliminary rumors are that that has. When that occurs, we will be coming back to NIOSH to ask for these autoimmune diseases to be added as World Trade Center covered conditions. We hope we will have the STAC support if the scientific evidence supports that, of course.

We did already go to NIOSH on this, but they ruled that they could not add it while they waited for the other cohorts to come up with their findings. As I said, this is critical. These treatments are very costly, and it's been shown that in the absence of these treatments there is joint destruction, so that if you don't start these treatments early on, especially in rheumatoid arthritis, you are increasing the chance for having to do joint replacement, and of course having a terrible quality of life. We have several patients with sarcoid who are covered, but we have several patients with especially rheumatoid arthritis that are not and are spending a tremendous amount. Yes, our cohort is lucky that they have health insurance, but they reach their deductibles and their copays and their lifetime caps very rapidly when you're having to spend $5,000 a month on medication.

Next slide. I'm going to finish up, then. Oh, next slide. Next slide. That we haven't stopped. We are listening. We are listening to our other partners, both at NIOSH and at the other clinical centers of excellence, and at the other data centers, at the World Trade Center health registry, and we're listening. We're listening that peripheral neuropathy is an issue of concern. We've added questions to our monitoring exam, and we are now hopefully going to start a focus on that. We are listening that cognitive capabilities may be diminishing. It's unclear whether that's due to aging, whether it's due to psychological comorbidities, but we're listening and we're deploying a series of cognitive questions to start our analysis of this.

As you can see, weight is a big issue. It's a big issue in terms of pulmonary function decline. It's a big issue that has been shown in non-World Trade Center studies for favoring inflammation. You talked about that, Ms. Jones, on your own about that. so it's a big issue. We've added a series of questions about whether people would be interested in participating in dietary studies.

Next slide. And then finally, lessons learned, and I've updated this slide and I will share it with you. But lessons learned I think are critically important to come away with. It's not just recommendations from the future, but it's lessons learned.

This is my last slide. I apologize for going over. Pre-disaster health baselines are critically important. The National Heart, Lung, Blood Institute says that large portions of our population should be getting spirometry as part of their exam, not just blood pressure and a cardiogram. Certainly, any responder should be getting pulmonary functions, as part of their exam should have a baseline chest x-ray updated at some interval as part of the exam. Without that, we would not have been able to show any of this because as I showed you, our pulmonary function was very high as a percent predicted because of the healthy worker effect. So if

we didn't have the baseline to compare to it would look like after the disaster everybody was 85% of predicted, and that's considered normal and nobody would have believed us. This is critical. It's also critical to identifying the most vulnerable, right, and getting them into more aggressive treatment programs.

You need to fully integrate monitoring, treatment, and research. Nobody wants to go to a monitoring program without treatment. Nobody wants to go to a treatment program without monitoring. And if you form a partnership and tell them that they're not going to be experimented on, that research is not experimentation, research is knowledge, knowledge that they can use to better themselves, then you can do all three. And it's labor management cooperation that realized that.

In that final point about research, I must say, you need IRB support. This country needs to change the way it does IRB for disasters. The national NIH has realized this. The Assistant Secretary for Preparedness and response has realized this. NIOSH has realized this. Translating that down at the ground level needs to happen. We were incredibly fortunate that our IRB was Montefiore Albert Einstein. They decided that this was a patriotic initiative and we received full IRB approval by the first week of October of 2001, all right? And every one of our subsequent IRB proposals, while of course it has required oversight, has been fast-tracked because they have fully committed to assisting in this national priority.

So I thank you very much. Nothing would be possible without your continued listening and support. And I know there's probably no time, which I did purposely, but I am available for questions.

DR. WARD: Well, thank you for that amazingly comprehensive presentation and all the great work that you all have done. Do you want to—I think it might be good to go ahead and take a few questions now because this is, you know, obviously before we move on, we should address the questions that people have about your presentation.

I'd like to start with anyone on the phone who has any questions or comments for Dr. Prezant. Okay, not hearing anyone.

DR. RYAN: This is—I don't know, can you hear me?

DR. WARD: Hi.

DR. RYAN: This is Dr. Ryan, Margaret Ryan in California. And just very impressive portfolio of research. Amazing, and appreciate you sharing all of it. I had a question about potential for infectious disease to add to the morbidity of these cohorts. So particularly like focused on Slide 25 where we have this trajectory of people who did worse. And of course, the airway hyperresponsiveness might make them vulnerable to infection. Infection, in turn, kind of creates vicious cycle. I'm wondering if there's any chance that these are, the ones that did worse, perhaps had the comorbidities over time of infection. I'm asking the question also because I also share your passion for wanting to do something and thinking about immunizations, not just classic like pneumococcal and influenza, but maybe even

some interesting ones like adenovirus that could potentially prevent some of this potential complicated morbidities.

DR. PREZANT: I think that's an excellent question and I think it pertains both to the lower respiratory system, as well as to the upper respiratory sinusitis issue. We have not had that as a focus of our research. We do have aggressive offering of the regular vaccines, pneumonia, flu, etc., but we have not had it as a focus of our research and I think it's an excellent question for us to think about.

DR. WARD: Any other questions from folks on the phone? Okay, Mridu.

DR. GULATI: I thank you for that wonderful presentation. I have a few questions, and I'm glad you brought up the diet piece on the longitudinal decline. I was curious if you were going to be doing anything in regards to the microbiome. But going on, I have sort of two other very separate questions. In terms of the pulmonary fibrosis and interstitial lung diseases, it seems that early on you seen a signal with sarcoid. I know there've been some reports in ILD. How are you going to incorporate screening for interstitial lung diseases and pulmonary fibrosis? And now they're actually some antifibrotic agents on the market.

DR. PREZANT: Right.

DR. GULATI: So it sort of—before, we couldn't really do anything, and so—

DR. PREZANT: Right, so we do offer pirfenidone. The World Trade Center Health Program is paying for that.

DR. GULATI: Okay.

DR. PREZANT: We have, I think, two or three patients, probably two on pirfenidone right now. Luckily, we have only a handful, 10 to 20 patients, that have significant pulmonary fibrosis. I wouldn't include the sarcoid patients in that because they really have not demonstrated that. Two of them went to lung transplant. They have subsequently died, one from cancer and the other from rejection and repeated infections. We don't currently have anyone at the transplant level. We have a few people who have reached that level but they're too old to qualify for transplants, and we have a few people that might be getting there, all right, but it's a real minority of our patients. How do we screen for it? We screen for it by looking for a decline in pulmonary function that then generates a full pulmonary function test with diffusing capacity, exercise test, chest CT scan, etc.. The regular population, if they're not showing that, they get chest x-rays every two years. If they're big-time smokers they get low dose chest CT.

DR. GULATI: The other question I had on the rheumatologic or autoimmune diseases, I assume there's specific diagnostic criteria for those.

DR. PREZANT: Yes.

DR. GULATI: And also, you're doing baseline serologies on everybody who comes in and then following them over time? I mean, is that part of it?

DR. PREZANT: Well, we are going to be doing basic serologies now that you have thankfully given us $1.2 million to do that. No, it is expensive. So we have not had the

funding to do baseline serologies. We are contemplating trying to figure out how to do that on a sort of random stratified group. We obviously do those serologies when someone is symptomatic, and that's what's part of our criteria for making the diagnosis. So these are all, when we're talking about in that study, 59 cases, and I think we have 60-something, 70-something cases. Now, we're talking about all of our sarcoid cases with the exception of two are biopsy proven, and all of our autoimmune rheumatologic cases are either serology positive or they've had a rheumatologic specialist start them on treatment consistent with seronegative autoimmune disease. So they're not just on nonsteroidals. They're all on either methotrexate or a biologic, or something, to convince us that a rheumatologist thought this was real.

DR. WARD: Sheela, we'd like to take your question now, or comments. We are having trouble hearing you on audio, I think. So you're not coming through by phone. Do you want to type your question in to Paul, or your comments?

DR. WARD: Okay, Glenn?

DR. MIDDENDORF: Thank you.

DR. TALASKA: Dr. Prezant, all I can say is wonderful job, well done. I'm sure the firefighters appreciate the effort that you have done and the rigor which you've—the studies that you've performed over the years.

DR. PREZANT: Thank you very much.

DR. TALASKA: But it's a whole group of people.

DR. PREZANT: I'm sure it is. I'm sure it is.

DR. TALASKA: Take that back home with you, then. Okay?

DR. PREZANT: Thank you very much.

DR. TALASKA: First thing, I wanted to mention to you that I'm not sure if you're aware of the studies that I'm not sure if you're aware of the studies of (Gerday, Madinski and Bond @ 01:11:29) who looked at lavage, lavage and particles of different sizes into animals years ago. And what they saw was that there was an inverse correlation between particle size and length until the material that was on the particles got absorbed—or desorbed from the particles and absorbed by the animal. To the point where with submicron particles—and I'm not going to be able to give you the numbers because it's in my head—

DR. PREZANT: Sure.

DR. TALASKA: —submicron particles, it was fractions of a second. For large sized particles, hundreds of microns, it was years.

DR. PREZANT: That's very important work. We'll look that up. Thank you.

DR. TALASKA: Yes, okay. The second thing was, am I reading this slide right, the one on lung function decline with the average and then the two extremes?

DR. PREZANT: Uh-huh.

DR. TALASKA: That the initial rate of change was much lower in the people who have steadily worsened than it was in the people who responded and then recovered.

DR. PREZANT: Right. Yes. Isn't that interesting?
DR. TALASKA: It is interesting.
DR. PREZANT: We don't know what to make of it. It's—
DR. TALASKA: But you're talking about predictions.
DR. PREZANT: Yes.
DR. TALASKA: Just the opposite of what you'd expect, right?
DR. PREZANT: Yes.
DR. TALASKA: Okay.
DR. PREZANT: And that's always a point of further research. But it was very unexpected.
DR. TALASKA: Got you.
PARTICIPANT: In terms of multiple myeloma, what exactly happens? Because you were saying that with multiple myeloma that the people with their copays and pay-downs, whatever, so what happens—
DR. PREZANT: No, I was talking more about autoimmune disease. But, I mean, this is true of all—I mean, it's true of cancer too, but cancer is covered by the World Trade Center Health Program. But the general, if you don't think about the World Trade Center Health Program and you just think about regular health in the United States, some people are very lucky to have insurance. But it's sometimes a misnomer because there are copays, there are deductibles. Even worse than that, many insurances—because people don't try to choose the least expensive—many insurances, if you reach a certain amount, you then don't get anything, all right? When you are dealing with very expensive therapy like chemotherapy for any of the cancers, or biologics for autoimmune disease you will reach those numbers very, very fast. So luckily cancer is covered by the World Trade Center Health Program, so starting in roughly 2013, we no longer had to deal with that problem, all right?
MS. JONES: Oh, okay.
DR. PREZANT: But we still have to deal with that problem for autoimmune disease.
MS. JONES: For what?
DR. PREZANT: Autoimmune diseases.
MS. JONES: For multiple myeloma?
DR. PREZANT: No, for rheumatologic arthritis, for—
MS. JONES: For autoimmune, okay.
DR. PREZANT: For Sjogren's, for lupus, polymyositis.
MS. JONES: Okay.
DR. PREZANT: Those are conditions. If you're lucky enough to respond to prednisone or methotrexate, it's like pennies. But if you require biologics, it's $3,000 to $7,000 per month, depending which one you need.
DR. WARD: Sheela, I understand your question has to do with childhood survivors, so we're going to hold it until after Dr. Reibman's presentation. We have one more question that we'll take from Steve Markowitz.

DR. MARKOWITZ: Thank you, David. I'd offer you more compliments, but I don't want your head to get too big,

DR. PREZANT: The team.

DR. MARKOWITZ: Here's my question. The firefighters get older, I would be the majority of the people who were at 9/11 probably don't even work for FDNY any more, or a large proportion.

DR. PREZANT: 35% still work for FDNY, right.

DR. MARKOWITZ: Okay. So the pre-9/11 comparison data is extremely useful for active firefighters, most aren't active any more. So NIOSH needs to give you money to figure out the reference group problem, because this is going to be an ongoing problem. Increasing problem in the future, and you're going to not be able to give people good answers unless you figure that out.

DR. PREZANT: And the Swiss bank account is...no. But yes, we acknowledge that. NIOSH has been very cooperative in supporting some of the ancillary studies we have going on to our data center to define those reference groups.

DR. WARD: Thank you. And one more question and we'll move on to Dr. Reibman.

MS. JONES: No, I just, that was really kind of what I was asking because it sounds like money would be an issue at some point with that population. So one of the answers would be through NIOSH. Okay.

PARTICIPANT: She has a question.

DR. WARD: Okay, one more question. I keep saying one more question.

DR. MAYER: I'll just have to echo the crowd, thank you for an excellent presentation and the excellent work that you and your group have done to date to really help us understand what health effects we are seeing and very well characterized in the lung. Just to echo the thoughts about the concern with interstitial lung disease. One of the things that we see developing 20, 30, 40 years down the road are things like silicosis, asbestosis that are largely related to the persistence of these fibers in the lung, and the inability of the body to clear it. And that is something that's observable years before we're going to see the clinical manifestations of that. And I didn't know if there's anything your group is doing, or potential. I've seen some cases of descriptions of things that appear to be clearing, but is there any work that's being done to characterize what may be remaining in the lungs?

DR. PREZANT: Right. So our group, while there've been very high retention rates, they're not interested in participating in bronchoscopic research studies. We've had no success with that. They are participating in our chest CT surveillance study. So through our low dose chest CT, based on the NCI recommendations of 30s pack-years, etc., we've got about 300-people-ish that qualify for that. But everybody who merits a CT through symptoms or decline in lung function is enrolled in the same study. And that means that we have approximately 5,000 people that we are doing sequential CT scans on. And that is going to be the population that we focus on to determine whether interstitial lung disease is occurring. Thank you.

DR. WARD: Thank you. Thank you, again. Dr. Reibman.

DR. REIBMAN: Thank you very much for inviting me to be here and to talk really on behalf of the survivors. I don't think that's my first slide, is that? And you've heard really a lot from David. It could be. Of course, I sent these—and let me just say that I sent slides a week ago but I actually changed them as of last night. so please relax and just watch what's going on and don't worry about what's going up—what you have in your thing. Yes, thank you very much.

So I'm really here today to talk really on behalf of the survivors and it's a very different population than what you've heard about from David. In fact, it's really the antithesis of that population. We did not have a preexisting medical program, and in fact, it became an issue just to document that. In fact, there were adverse health effects in this population, what we have. And I want to talk, if you can now give me—now that you've done that. Thank you very much.

And the next slide please. What I'd like to talk to you about today is really focused predominantly on respiratory, since I thought that's what I was going to be doing mostly today, and talk about respiratory symptoms in this population, what we've learned about location of lung injury, what we are learning about mechanisms of these lower respiratory symptoms. And in the context of doing that, talk about continuously what we think about in terms of this catastrophe, but also what can we learn from this catastrophe that pertains certainly to other catastrophes, to other exposures, to other illnesses. And then David covered a lot about what we learned and what we need to do next, and I'll touch on that briefly.

David showed a lot of what I'm going to talk about, but I want to do it in a little bit of a different perspective. So if I can have the next slide please, thank you.

First, I want to talk about exposures. And I think this becomes very important in this population, that we're talking about a very, very disparate group of local workers, officer workers, residents, commuters, teachers, students, and that these individuals had a variety of exposures which we now think about in retrospect. Of course, as we were doing this, we had a different perspective, but we're now beginning to understand that we can think about these in terms of an acute exposure, i.e., those from the dust clouds, and I show you a picture, once again, just again show you what we're talking about with this massive amount of dust that many people who are living, working, or just passing by were exposed to. And we call this now, for simplicity's sake, dust cloud exposure or acute exposure.

The next slide please. Thank you. We then also understand that many people returned to their work places, their homes, even their schools, starting really one week after the event. Many actually returned earlier. Many went back and forth. But again, for simplicity, many returned about one week later. And we call this chronic indoor and outdoor exposure, because we know that these individuals were exposed to resuspended dust that was outside, to resuspended dust from

incompletely cleaned indoor areas, to the fumes from the fires that burned, which I'm not really going to focus on. But this is more of a chronic exposure. And we know, if I can have the next slide please, that this dust included large and small sizes that I'll go back to in a minute. So the first issue we had in this population was to document respiratory symptoms in this community population.

Next slide please. And because we didn't have a preexisting group in which to really look at this, we actually did a very, very major collaborative study, and this is really quite impressive because we collaborated not within New York City Department of Health initially, but with the New York State Department of Health, with many, many, many local community members. And we did this as an academic center at that time with NYU with funding that we got from the Centers of Disease Control.

And this first study was a cross sectional study of individuals who were exposed, who lived around the World Trade Center compared to those who lived on the Upper West Side. Upper West Side is known for their activism. We thought they would participate more. They did. They told us our questionnaires were wrong. And this is important also because it's one of the few studies that in fact had a control population early on.

And as from this early study, if I can have the next slide please, the other thing we did is we didn't look for disease. We felt that disease was going to be biasing us in terms of what we were going to find. And so what we really asked for was symptoms. And again, we looked in this study for lower respiratory symptoms of cough, shortness of breath, wheeze, chest tightness, exertional dyspnea, or any of those. And we showed, in fact, that this residential population, there were new onset respiratory symptoms in this population that had started after 9/11. And because, in fact everybody is somewhat biased against symptoms.

Next slide please. We also documented that, in fact, these individuals had an increase in unplanned medical visits, an increase in prescriptions for fast relief medication use, that's albuterol, and an increase in control in medication use, so those were inhaled corticosteroids, many of the other things used for asthma.

Can I have the next slide please? Thank you. So this was the first study really documenting that there, in fact, were adverse health effects. Not only in the responders, but also in the local community, in this case the residential community. This took us a long time to publish. We were sent back from The Blue Journal because they told us this was a retrospective study. We told them thank you, it is. It would have been hard to do it prospectively. So, but just again, to illustrate the difficulties of working in a disaster with a very diverse and different type of population.

New York City Department of Health subsequently, and they're here in the audience today, went on and did a beautiful, developed a beautiful registry that you know about with many, many more participants and have done longitudinal

studies, and in fact have reinforced these findings. And I show you only two publications, but they have many, many more than that. but again, showing you again and supporting the findings, that there were adverse respiratory health effects in this what we now call the survivor population.

Next slide please. Thanks. And it's these studies that led to first an initial pilot program, so again, we did not have funding right away. We had a very small pilot program that was at Bellevue Hospital in collaboration with many community members. We eventually got philanthropic funds from the American Lung Association. New York City funds, and then eventually Federal funds. And we are now one of the clinical centers of excellence called the World Trade Center Environmental Health Center. A lot of centers here. For the survivor program, our term is now "survivors" which is developed when we were going after the Zadroga bill, and we're now under the James Zadroga 9/11 Health and Compensation Act. Again, it's very important for you to understand, our program is different than the responder programs. It's a highly regulated and monitored program. We do not, we are not allowed to just do general screening for a population. We have to have, people have to have a symptom to come into the program, and we have to certify that symptom for them to stay in the program. So I say that because that has huge implications for research for us, and it's very, very important to remember that as we go on.

Again, the certified conditions include aerodigestive disorders, mental health diagnoses, and cancers identical to the ones that are in the responder programs. But you can only stay in the program, or even get in the program, if you are already sick. We do not screen an un-symptomatic, or non-symptomatic population. By law, not by choice.

Next slide please. So the other thing to note about our population is that, again, it's a very different population from the responder population. This is from an old publication, but it's really identical to our data today of a much larger population. We are approximately 50% women. That's very different in the responder population. We are a very diverse race and ethnicity. We are almost 50% Hispanic. We have, as you heard, before different exposure categories. We can break them, slice them, or dice them in a variety of ways, but simplistically we, call people as local workers for potential exposure as a local worker, residents with potential for exposure through their residency, clean-up workers, and also others. Here, it's 40%. It's now about 50% of our population, reports having been caught in one of those initial dust clouds or having had this early massive exposure.

Next slide please. And despite all of this is again from an old paper, the point I want to make here is in a manner very similar, in part, because we asked for it, but also very similar to what you see in the responders, our patients have lower respiratory symptoms, cough, wheeze, dyspnea on exertion, upper respiratory symptoms, sinus and nasal issues, as well as GI symptoms. So if we look in

terms of the symptoms, we're seeing very, very similar to the responder program. Next slide please. And in fact, to date, with our expanding program, and this is the data now from about a year ago, the main diagnoses that we are certifying our patients for are aerodigestive diagnoses, lower respiratory symptoms, or what we call obstructive airways disease, and upper respiratory disorders, probably most likely rhinitis and sinusitis. We have smaller numbers of interstitial lung disease, smaller numbers of sarcoidosis. In contrast to David, we actually have what I would call a large population, over 15 to 20 people now who are on their way to transplant or have received transplant. But again, those are self-referred patients who are coming in.

Next slide please. So very early on, we were challenged about exposures and we had a lot of difficulty trying to figure out how to classify exposures in this population, and it comes up over and over, but this is a very important study that was done in collaboration with the New York City Department of Health. And what I want to say over and over again is what we have done over and over is collaborate. Collaborate with the New York City Department of Health. Collaborate across centers. Collaborate within our institution. That has been really one of the main and beautiful, I think, outcomes of a lot of these studies. But this was a collaboration with the New York City Department of Health. Carey Maslow and Steve Friedman working with us. And what this showed—and you can't really see, it doesn't matter—what I want to show you here is really that during a whole cluster analysis of different characterizing exposures in all different ways, what we were able to show is that both acute and chronic exposures were associated with lower respiratory symptoms. So again, this is important because it doesn't mean that just that initial exposure is what's key. It means both acute and chronic exposures were associated.

Can I have the next slide please? So I want to talk a little bit about location of injury, because this question certainly came up, and David showed some of these slides, but I want to show them in a little bit of a different reason here.

So if you come—if I can have the next slide please. Sorry to have you do this. Those of you who are toxicologists know this clearly better than me, but we understand if we're talking about particles that we're going to talk about size, PM10, that is 10 micrometer aerodynamic diameter, 2.5 ultrafine. And in pulmonary disease, this is very critical to us because we think about the large particles getting blocked in the upper, upper airway, and the smaller particles being able to be inhaled and reaching deeper into the lung. And so we think that size influences the site of damage in the airway.

So, can I have the next slide please? One of the things that, and I think this is the slide that David showed you previously. One of the early patients to come into Bellevue was this firefighter that David told you about. And this gentleman came in very, very short of breath and had an abnormal CAT scan. Oh, so let me—oh, I'm

sorry, if you can go back. So what we learned about the dust really from Paul Lioy, as well as others, is that in fact, there was a huge amount of building materials, that most of it was large. But again, he was sampling settled material.
There were very, very few samples of the airborne material, although we had some that we gave to him. but even though 90% of the particles were large, there were many, about 11,000 tons that were less than 2.5 micrometers in diameter. So these are small; it's still massive amounts. And that there were acute exposures from the mass of dust, but also chronic from the resuspended dust, and the indoor dust makeup was very similar, if anything, there were more smaller particles in the indoor dust. So the dust from the collapse of the buildings was composed of large and small particles.
Next slide please. Okay, so it's getting hung up on that slide. So this is the slide of this firefighter who came into Bellevue Hospital two weeks after the event. and he was very, very sick and was in our intensive care unit. And at that time, the chairman of our division was Bill Rom, whom some of you know. I think he was on this committee. And Bill Rom is very, very aggressive, and he said, "We got to bronchoscope this person." So he was bronchoscoped.
What you see there is his CAT scan which has some abnormalities, the white areas are abnormal. And the first thing that I want to point out about this is what David pointed out already. The next slide please. Thank you. Is that, there were particles that were washed out of his lungs. And those particles included asbestos fibers, fly ash, a variety of things that were not normal to be in the lungs. But importantly, these were very, very large particles that were deep in the lungs. So that is very important to understand because that meant that this was very different than our standard toxicologic learning where we thought small particles, not large particles, but only small particles could get deep in the lung.
So the next slide please. The second thing I want to show you, again, David showed you this, but this is we published a series of biopsies of fairly large biopsies on patients in our program who had undergone video-assisted thoracoscopic surgery for abnormal lung findings. Actually, their CAT scans were pretty normal, so it comes back to that interstitial lung disease issue. Their lung function was abnormal, but their CAT scans were pretty normal. And what we found in here was very, very interesting, and I don't want to go through the histology, other than to say that what we found was really destruction of the air spaces themselves. These airways were in fact quite normal. They did not look like asthma airways, but the air spaces themselves were quite destroyed.
But the point for today that I want to make is, we found particles in there, and those particles, first of all, were lit up under polarizing like microscopy, but also had abnormal material in them. So we didn't know for sure, but we presumed that these materials could be World Trade Center origination. The point I want to make about this is that these were done many, many, many years after their

exposure. So it comes back to the point that was made earlier about these materials staying in the lung and not getting cleared rapidly.

Next slide please. So we learned from this that in massive exposures, large particles are able to access deep in the lung, and that large and small particles persisted in the lung. And I think these are two very important concepts to think about. Certainly, as you start thinking about David's recommendations, future and certainly in terms of what was raised earlier.

So the next slide please. So that made us think early on about where is the location of damage in these airways, and how can we measure it, and was there small airway or distal lung involvement associated with these lower respiratory symptoms? Unfortunately, there's not a real good way to measure this noninvasively.

Next slide please. And so, the standard measure that we were all doing a screening with spirometry, this is the standard that's used throughout the world for looking at lung function. But spirometry may not detect small airway abnormalities, and in fact, you wouldn't necessarily expect it to be abnormal. For those of us in the asthma world, we expect to see normal lung function, unless somebody has remodeled. So you wouldn't really expect to see changes, necessarily, in spirometry. So at that early, when we started these studies, forced oscillation techniques called impulse oscillometry were just sort of coming. There was just a new machine used that you could, in fact, use commercially as opposed to one that you made up yourself. And these were just coming out and we thought that these could detect subtle changes in airway function, not identified necessarily by spirometry. And so we set out to ask whether patients with lower respiratory symptoms had small airway abnormalities that would be participating in their symptoms.

Next slide please. And so very early on in our World Trade Center program, our initial pilot program and then our Red Cross program, and then our federal funded program, we actually did routinely forced oscillation in all our patients. And in fact, as David told you, as we've seen in many other programs, have seen most of our patients, in fact, had normal spirometry. But most of those patients had abnormal oscillometry measures, but we couldn't interpret this without a control population. And we didn't really have a controlled population and so we didn't really know we were looking at.

The next slide please. And so again, we collaborated. This time, again, with the New York City Department of Health, World Trade Center Registry, and we did a field study of World Trade Center Registry participants in participants who had persistent symptoms in their first and in their second questionnaires and compared those to participants who had no symptoms, either in their first or in their subsequent questionnaires. And we compared lung function, spirometry, and forced oscillation measures between these symptomatic cases and controls.

Next slide please. So this gave us a very beautiful control group. And what you can see here is in blue that both in our controls and in our symptomatic cases, most people, in fact, had normal spirometry. And this didn't surprise us. It's what we had seen in all our other studies and it was consistent with that. and even our symptomatic cases, there were a few who had abnormal spirometry, but most of them had normal spirometry.

Next slide please. But if you looked at forced oscillation measurements or impulse oscillometry measurements, what you can see in yellow are those who now have abnormal measurements. And you can see that although there are some certainly in the control group who are abnormal, and this is not surprising, in part because some of these may be due to obesity, which is confounded when you do these measurements, but in the symptomatic cases that many, many of these had abnormal oscillation measures, even though they had normal spirometry. So this was really, we thought, very, very important because it suggested that these patients who had symptoms, but normal spirometry had abnormal measures of small airway function, suggesting that this could be a site of entry in this population.

Next slide please. And indeed, we went on in other studies, and I really want to give credit to these two, Ken Berger and Roberta Goldring in our physiology lab for all of this. But we went on, and we were able to show, in fact, that as you did these measurements, so the higher you get with these measurements the worse off you are, we can see a trend with an increase in these measurements with an increase in severity here. The symptom I'm using is wheeze, but as you have more severe wheezing or more frequent wheezing, there is a trend for an increase in these measurements. So again, there's an association with symptoms with abnormalities.

Next slide please. So we thought this was very important for a number of reasons. First, it showed that in our symptomatic population, we had an objective measure of abnormalities and even in those who had normal screening spirometry, that it showed—suggested that they were abnormalities within a small airway that were associated with exposure. And I didn't show you that data, but we've shown an association with exposure and with these abnormalities. Again, worked with Steve Friedman and Carey Maslow. And that these small airway abnormalities are associated with the severity of lower respiratory symptoms. So we think this is important for this group. We also think it has larger implications because this was, in fact, the first use of forced oscillation techniques or impulse oscillometry to assess environmental injury in the lung. You have to look at these data carefully. There are things that can confound your reading, such as BMI, but it still is important, I think. It's a very important noninvasive tool; we did this in the field. So I think that's an important thing to think about for future studies. Particularly, when we're looking at other future exposures of all sorts of environmental issues.

Next slide please. So we also have tried to focus on mechanisms of injury, again, within the context of our funding limitations and our program. But we really wanted to understand what are the symptoms, lower respiratory symptoms. Can I? Yes. And if I can have the next slide please. So I show you this as overall diagram of how we think about asthma currently. And the point to make about this is the mechanisms of asthma, if that's what we're talking about, are very, very complicated. There are lots of different stimuli. There are lots of different pathways. All my students' eyes glaze over with this slide. There are redundant pathways. In fact, you can see many pathways can give you a final endpoint from all different directions. And if we think about asthma, not all asthma is the same. Not all asthma includes all of these pathways. So this makes thinking about these illnesses very, very complicated.

Next slide please. But what we are learning, to some extent, is one pathway which we call a Type 2 inflammation, or a T2 pathway, ends up, through a variety of different redundant pathways, to a final common inflammatory cell, which is the eosinophil, which is the cell that you heard David talk about.

So, can I have the next slide please? Thank you. So that led us to ask will pollutants or particulate matter activate this Type 2 pathway? And in fact, there's a good amount of work showing that various pollutants can, in fact, do this. But the question was, were we going to see this in a World Trade Center population?

Next slide please. And if you come back to this firefighter, again, what David showed you, if you looked at the cellular profile of this firefighter, if I can have the next slide please, what you can see here is that, in fact, this firefighter had a lot of eosinophils in his bronchial alveolar lavage, so when we washed out his lung there were, in fact, a huge number of eosinophils in his lung. And so we thought early on that's a great clue, we're going to be seeing eosinophilic lung disease in these patients, and that's, in fact, what we went to look for.

Next slide please. And so one of the first studies we did was to look at eosinophils using blood measures of eosinophils, which is not the same as lung, but is an okay surrogate. And what we found, in fact, is that if we looked, if we dichotomized accounts into patients who had high eosinophils compared to low eosinophils, in fact, very few of them had high eosinophils. And I think you're hearing that from David, too. And in fact, in our Department of Health study we saw the same thing. Very few had high eosinophils, but when they did have high eosinophils, it was a risk for having obstructive lung disease. I.e., the findings, the spirometry findings we would see in classic asthma. So some of them did, but most of them did not have high eosinophils, and most of them did not have an obstructive lung pattern.

Next slide please. So this suggested, again, that there's heterogeneity in this population in terms of their mechanisms, and that, in fact, we could have involvement of this Type 2 pathway but clearly also had something else going on.

What I'll call a non-Type 2 pathway, which could be neutrophils, could be other cells. We really didn't know.

Next slide please. So as David showed you, he has been extraordinary lucky to have blood samples very early on, we did not have those. And we could only take blood as patients were coming into our program. And we actually had some young physicians come in who were budding cardiologists and they said C-reactive protein is really important, can't we measure that? And we really couldn't measure that, but we decided that we would call it a clinical marker and so we routinely measured it in a series of our patients coming into the program.

And what we found out, in fact, was that we could find an association of, again, dichotomizing CRP level. So C-reactive protein is an inflammatory pathway that is a very different pathway than an eosinophil pathway. We found that, in fact, that there was an association of elevated CRP levels, with again, our symptoms—cough, wheezing, dyspnea, chest tightness. And again, this is not completely surprising. We have seen this association in other lung diseases, but it was important to find it in this population.

Next slide please. Interestingly, what we saw is that these levels were not associated with the classic asthma obstructive pathway. But what they were associated with, was the group who had lower forced vital capacity, lower lung volumes. Again, suggesting that this might be something different in these lungs and may be associated with small airway abnormalities. And in fact, I'm not showing you here, but we did find an association with abnormal measures of our forced oscillation technique. So this suggested that, and it comes back to David's concept, that there are different—that there's heterogeneity in this population. That they have different mechanisms and different abnormalities and lung function, and that those can be due to different pathways of inflammation.

Next slide please. You can't see this very well, but I want to show this because I think this becomes important, particularly for the subsequent talks when we talk about pathways of inflammation here. And what this is, we had our mental health group working, again, with our biostatistical group, and this is a study done by Rebecca Rosen and her team. And we asked, are there going to be associations with C-reactive protein with mental health scores?

And in fact, what we showed was that there was an association of elevated CRP levels with our scores for PTSD. Not particularly for depression or anxiety, but with our scores for PTSD. And the next slide, we went on to look at this a little more closely using clustering for PTSD, so we now know that not all—that PTSD can be broken down into components. And it turns out that these CRP levels were more associated with different components of PTSD. So not every component of PTSD. And I think that that's going to be very important and very provocative, particularly as we move forward with steps forward of trying to understand are there underlying pathways that are involved in both the lung diseases or systemic

diseases and in mental health diseases.

So next slide please. So this, so far, has opened up questions that there are multiple types of inflammation associated with lower respiratory symptoms. Certainly, there are classic Type 2 inflammatory pathways that are involved in the lung, and as David showed you, also in the upper or sinuses, that there's non-eosinophilic inflammation. That these different types of inflammation are associated with different patterns of lung function, probably different areas or types of damage. And that at least the systemic inflammatory markers, CRPs associated with both lower respiratory symptoms and mental health symptoms.

Next slide please. So we have not as long longitudinal work as David has, but some. And we found something somewhat different, which is that if we looked at longitudinal change in lung function in our program, we began to see, in fact, improvement in lung function. We didn't see improvement in all parameters that I'm not showing you here. We saw a different improvement in different populations, with the least improvement in local workers. And those who had abnormal lung function at baseline did not become normal. And actually, we're looking at our impulse oscillometry data now, which I'm not showing you because that doesn't seem to change that much.

However—next slide please—despite these changes in improvement in lung function, if we looked at our reports of symptoms there were certainly patients who got better. And if we look at each individual symptoms shown on the right, we have improvement in each of the individual symptoms. But if you look on the left, many, many, many patients continued to complain of very frequent lower respiratory symptoms.

Next slide please. And again, I'm not showing you, and David showed you, so thank you, David for showing me that, that most of these patients, but not all, but many of them, had normal lung function. So I just want to show you this really as a final area, just to sort of provoke some thoughts. We were funded by the CDC to do a study in uncontrolled lower respiratory symptoms. And when we first proposed this, we were turned down and then we were told we needed to do methacholine and prove that these patients had asthma. And since we didn't actually believe they had asthma we were sort of mad. But we went back, and we submitted, and we said we will look at every hyperresponsiveness. And what we asked was whether adherence to high dose inhaled corticosteroids and long-acting beta agonist therapy would improve these lower respiratory symptoms. And what were the characteristics in these patients who had persistent uncontrolled lower respiratory symptoms despite having taken high does inhaled corticosteroids. So what I'm saying here is, we know, all of us who practice medicine in asthma and respiratory disease, we know that we prescribe patients these medications and very few of them take it. And so when someone remains symptomatic, our first thought is always they're just not taking their medication. So

what we did here was, in fact, we had large arguments. Should we take them off medication to look at this, or keep them on? But we felt we couldn't really take them off medication if they're still so symptomatic, so we said we really have to characterize these patients.

So next slide please. So the way we designed the study was actually to enroll patients who had lower respiratory symptoms at their initial visit who had normal spirometry and uncontrolled lower respiratory symptoms at monitoring. We were going to do a run-in for three months to confirm, in fact, they were taking these medications. We were then—we presumed to find a group who had controlled symptoms and a group who had uncontrolled symptoms and we were going to do a whole series of characterizations, including lung function, airway hyperresponsiveness, vocal cord evaluations, blood samples, and compare these two. And I don't want to go over the whole study, I just want to show you two very important things.

So the next slide please. So first of all, when we did our—

[Intercom interruption.]

So our first finding was that, in fact, despite compliance with high dose inhaled corticosteroids and long-acting beta agonists, our standard asthma therapy, few, if any, of these patients got control in their symptoms. So this wasn't just—this wasn't an issue of adherence. This was an issue of maybe we weren't targeting this correctly. So we had to modify our study and we therefore enrolled people who had symptoms initially but at the time of the study were no longer symptomatic as our control population, which was difficult.

So next slide please. So this is a difficult population to work with. They don't get paid for time off for their exams. They don't get paid for time off to do the study. They don't really like doing clinical studies. This was a really hard patient group to recruit, but we did recruit 73 patients for the study. They looked very similar to our usual clinical patients in terms of age. We had a lot of women. Our BMI's 30, which is our standard BMI, and 50% had been in the dust cloud.

Next slide please. And what we found, and again, by definition, they had predominantly normal lung function, their forced viral capacity was normal, their FEV1 was normal, the ratio for their age was normal. Their oscillometry here shown as R5 and R5-20 was slightly elevated, but we have to adjust that for BMI, so this was not particularly revealing.

Next slide please. Importantly, when we looked at markers of Type 2 inflammation, which include FENO, or exhaled NO, eosinophils, or total ITE, they were low. So these were not our classic Type 2 asthma kind of group, which is what we had already suspected, given our earlier information. So I told you that we were sort of forced to look for hyperresponsiveness in this population because we were challenged to say, "Did they have asthma?" and we really didn't really think they had asthma, but we felt we had to do this. So what we did was we did

what is called a methacholine challenge study on these patients on medications, and also look for irritant induced vocal cord dysfunction.

Next slide please. And what you can see on the next slide, thank you, is again, very early on as a group, over 50% of them had positive methacholine challenge. So they were hyper responsive. So over 50% did have airway hyperresponsiveness or twitchy airways, which was not what we thought we would see. It did not differentiate between uncontrolled symptoms and controlled symptoms.

Next slide please. And over 50% also had paradoxical vocal cord movement. I.e., if you looked at that upper airway and you triggered it with an irritant, or something, you could see abnormal movement.

And finally, the next slide, over 70% had either airway hyperresponsiveness or vocal cord hyperresponsiveness. So this suggested that there's something going on in all of these patients. It's not really differentiating symptoms at this time, but that they all have very, very high rates of twitchiness in their airway. First in their vocal cords or in their lower airways. And they are just sort of hyper responsive. And I think this is important because we're seeing this in the absence of this Type 2 inflammation. We're seeing it from a different pathway, probably.

Next slide please. So most patients with persistent uncontrolled lower respiratory symptoms had symptoms despite good adherence to high dose medications. They had high rates of airway hyperresponsiveness and paradoxical vocal cord movement, despite therapy. We could not differentiate the rates of these with the symptoms, and few had evidence of Type 2 inflammation.

Next slide please. So this really leads us into future questions, and I think David illustrated these very, very well. I'll say them again in a little bit differently, which is that we really need to understand the underlying mechanisms for these persistent lower respiratory symptoms and for the hyperresponsiveness. We think, in fact, many of these inflammatory pathways may have changed over time. People might have started with, for example, eosinophilic process but as time has gone on, there's something else going on. So we really need to look at these pathways over time. We need to ask, even, are these inflammatory pathways involved, or is it a different process? And one of the things that we're concerned about, is there something for activation of irritant neuropathways, which would be consistent with the findings that we're having. What is the role of systemic inflammation and the interaction with comorbid conditions. Again, something that was discussed earlier.

Next slide please. And clearly, we need further studies to understand mechanisms. And I say that because it's so important that we move on from just describing lung function. We move on to trying to understand what are the pathways that are going on and what's the heterogeneity among patients. These are not all the same. We need biologic samples. Certainly, we need blood. I think one of the biggest lessons to have learned from this whole project is that the

firefighters had early blood. It was critical. The rest of us could not get blood samples. And so, even now, we can't predict disease based on any biomarkers, but it doesn't mean we can't do it now in terms of understanding biomarkers for persistent disease in terms of predicting future diseases such as cancers. So I would say even though we made a huge mistake early on, we should not accept that mistake and we really need biobanks or biomarkers now.

We need other samples, as well, so we have a future—a current study we're doing now looking at induced sputum. We've done induced sputum in asthma looking at cellular responses. We have a small study now in our survivors. We really need clinical trials to identify appropriate therapy. We have everybody on high dose inhaled corticosteroids and long-acting beta agonists and we don't even know whether we're doing the right thing any more. So we really need clinical trials to understand is that the appropriate? Should we be using other agents? And clearly, we should be now using biomarkers for more precise targeted therapy, just like we're doing in asthma.

We need to understand the interaction with comorbidities, which you'll hear more about, and again, we need longitudinal studies to identify those that improve with those who have persistent symptoms.

Next slide please. And these are critical because we need to understand mechanisms that can promote improved treatment for the World Trade Center populations, that includes targeting therapy. For example, if it's small airways, should we be targeting those airways? Targeting pathways precision medicine. Targeting multiple comorbid conditions for—or common pathways. And we hope that these studies will provide information that can enhance our understanding of this injury but also of future injuries.

So I'm going to stop here. I just want to say three other quick things. Since David touched on other projects, and I'm really not focusing on those, I just want to say we are also, in fact, however, looking at peripheral neuropathy and have an ongoing study in our population. We were, in fact, doing biopsies to really identify whether they're small peripheral nerve damage.

We are very different in our ability to look at cancer. We are a self-referred population so we have tons of cancer patients coming in, so we clearly can't do prevalence. But what we are looking at is really building a comprehensive database that has all the biomarkers we can think of because we really believe that one of the things we're finding is that there is a whole diversity of cancers. And so the question is, are there going to be similarities or contrasts within the markers and genetic abnormalities we're seeing in these cancers, which I think is going to be very important. So this is one of our very, very large endeavors that we're doing, again, with support of the Centers for Disease Control.

And I think at that point, I'm going to stop. Thank you very much.

DR. WARD: Thank you, Dr. Reibman. I think as everyone realizes we are running very late. I

would like to allow just two questions for Dr. Reibman, one of which is the one that came in earlier from a telephone caller. And then we'll move on to the last speaker. We not taking our scheduled breaks. If anyone on the panel needs to step out, feel free to do so. But Paul, do you want to—

DR. MIDDENDORF: Obviously if Sheela can—

DR. WARD: Sheela, can you ask your question? I think we're still having technical difficulties.

DR. MIDDENDORF: She was wondering about the pediatric outcomes.

DR. WARD: With respect to respiratory disease? Yes, so she was interested in learning—one of our panel members who is on the phone—was interested in learning whether you have any information on pediatric outcomes related, I guess, specifically to respiratory diseases?

DR. REIBMAN: So I don't really want to—so our program, per se, initially we actually had a huge attempt to recruit pediatric patients and we were not very, very successful. There is, however, one of our collaborators at NYU, Leo Trasande, has published on lung function in children. And the spirometry, again, seems normal but there are some other abnormalities, and he's looking at biomarkers of exposure in this population and has published on that. There was another group at Columbia who is, in fact, doing a lot of mental health and now also trying to do physical health. I think it's a major gap in our—it's major gap. And again, if there's lessons learned, I think one of those is that we really, really need to focus on the children and I think we didn't focus well enough. Many of those kids are now aging out and our coming into our program. Although we have a pediatric program, it's not really been that big.

DR. WARD: Thank you. Is there one more pressing question, shall we move on to the next speaker? One more pressing question.

DR. GULATI: I'm sorry. Thank you. I know it's so hard to enroll these patients. You're doing an amazing job. A question about, just on the small airways disease. Are there correlates with—I mean, I think I saw one CT scan in there, looking at air trapping on CAT scan. Are you looking at that in terms of correlations with other physiologic parameters of air trapping?

DR. REIBMAN: So de la Hoz from Mt. Sinai published a beautiful paper in the responders showing air trapping. We do see air trapping in many of these patients, but we haven't published that.

DR. WARD: Thank you so much, Dr. Reibman. Sorry we had to cut questions short. We appreciate your presentation. For the transcript, the last question was from Mridu. Okay, so now we'll move on to the last presentation which is on mental/physical comorbidity research findings, and we have three speakers listed. I don't know who's planning to give the presentation, but we're ready for it.

DR. LUFT: We all are.

DR. WARD: Okay, great. And again, I apologize to all of you for cutting your time short. We've had such great informative presentations this afternoon.

MENTAL/PHYSICAL COMORBIDITY RESEARCH FINDINGS

DR. BROMET: So let me start at the outset by saying that there are three of us who are going to make some very short remarks. We interpreted our task completely differently. We'd love to come back and tell you about the enormous amount of mental health research we've been doing at Stony Brook. But our interpretation of today's task was to summarize the November meeting where we asked some of the key people doing mental health research in different populations affected by the World Trade Center to summarize their main points. And that today we would basically give you a very short synopsis of what took place in November. And then conclude with our recommendations that really came out of six and a half hours of presentation.

So this is going to be completely different, so we're shifting gears. Not just in terms of mental health, but also in terms of the whole style of what we're going to be doing, okay? And I'm going to go through this fairly quickly because you have the transcript, which tells you each person's story basically in their own words, apart from the editing that some of us did with their own words. But, and I think it's much clearer than what I'm going to do, sort of second-hand taking you through quickly what other people have done.

Okay. So we had the opportunity in November to pull together the wealth of mental health research on World Trade Center populations. And the speakers were selected from across the programs because they've done some rather outstanding mental health studies.

So we can go to the next slide. And then the next slide. We also included a couple of non-World Trade Center PTSD researchers because we really wanted to get a reaction to what our little world has produced from people outside of the World Trade Center mental health research. Not that we don't get it when we submit papers, because obviously we get it through reviews of our papers. But it was very interesting to have them as discussed in our meeting talking about what they just heard about the World Trade Center.

So next slide. The first person on our program was Robert Brackbill from the Registry. And one of the things I sked him to do, although he's not a PTSD researcher, is to give a little background on PTSD, post-traumatic stress disorder, which is the sort of bread and butter issue that's been studied after lots of disasters since it was codified by the diagnostic and statistical manual, the DSM bible of psychiatry in 1980. So while there were beautiful descriptions of PTSD in high-risk populations, World War I, World War II, Civil War soldiers, even, after special disasters and Holocaust survivors, the formal diagnosis didn't actually take place until 1980. And that diagnosis has been refined a bit over time in subsequent iterations, but the core features of it are still there. And they involve not just sort of classic symptoms that you know about, like flashback and so on, but also impairment in functioning. So it's both symptoms and impairment, and

that's one of the limitations of what you're going to hear about because the symptom part of it has been nailed down in all the studies, but the impairment part, not so much.

So Robert talked a little bit about the prevalence of PTSD in epidemiologic studies, the prevalence of PTSD in disaster studies. I think we can go to the next slide. And the risk factors that people find across the board, whether it's a disaster study or an epidemiologic study that that looks up various kinds of traumas that people experience. And the major ones are whether you've had a traumatic experience before, whether you're had psychopathology predating this event, and being female. I mean, those are really the three most powerful explanatory variables for whether this next trauma is going to affect you in such a powerful way.

The literature on PTSD is a chronic mental health problem. It is not something that people get and recover from very easily, and it's comorbid with a lot of psychiatric conditions, it's also comorbid with a lot of medical conditions, which is part of the chronicity. And the epidemiologic data has also shown that PTSD in people who've never had chronic disease before is a risk factor for new onset chronic illness. And that's important to understand as we go through the literature on the World Trade Center responders because they're high risk, they were healthy, they've developed PTSD, and subsequent to their PTSD, they've developed a range of medical problems, and also cognitive impairment, which is what I'm going to conclude my part with, and cardiovascular disease, which Alfredo is going to talk a little bit about his research on that because it's terribly important.

Okay, so the next slide is sort of a bubble slide that Dr. Brackbill put together just to show you that the work on mental health, particularly PTSD after 9/11 actually began with some phone interviews that I think the City Health Department paid for. And then later after the World Trade Center Health Program was in effect, there were some systematic studies of PTSD that were done.

I want to make one other interesting comment about the fact that the World Trade Center Health Program and the fire department now has such a big emphasis on PTSD, as well as medical conditions that you would be worried about in relation to the exposures. Up until then, I couldn't find a single example of a health surveillance program that included mental health, including Chernobyl, and I was on the scientific advisory board for the thyroid research for Chernobyl. And I couldn't convince anybody to combine mental health with looking at thyroid disease because there was no interest in it. I mean, it was really amazing to me. But things changed with the World Trade Center. And partly, they changed because people like David Prezant and Ben Luft, and others, were down there and they experienced the mental health components themselves, so they understood that this was not a simple disaster situation that wasn't going to have

a very complicated set of health risks, including mental health—

[Intercom interruption.]

Yay. And one last little comment before I—

[Intercom interruption.]

So one last comment about the fact that both mental health and physical health are being studied in the World Trade Center. It's not that surveillance studies after disasters are any different from how epidemiology has been done over the last hundred years. So there are studies of chronic disease—medical diseases, there are studies of mental health, but there are very few examples where both were studied well. So there are examples like the National Health Survey where there may be a screening measure for a mental health problem, but there are very few examples where people said to themselves mental and physical health are two sides of the same coin and if we're going to do studies of health, we need to understand both sides adequately. Just hasn't happened.

So the two risk groups that Robert talked about are in the next two slides. So one, my distance vision isn't good enough to see that, but one are the area residents and the tower survivors as one of the high-risk groups for PTSD, and the other which is shown on this slide, actually, are the nontraditional responders. The construction workers and all these people who went down there, doing the right thing with no experience and no even realistic anticipation of what they were going to experience in terms of finding body parts, seeing the dead bodies, losing their own colleagues, and so on. So for them, without any experience and any training, the mental health component has been huge and long-lasting.

So the next slide circles the tower survivors and the people from Lower Manhattan.

The next slide was Robert's attempt to put together the three levels of risk factors for PTSD in the Registry tower survivors and Lower Manhattan residents. And they were pre-event risk factors. And what's important about that is that it's absolutely consistent with the rest of the literature on other disasters, so that was good.

Peri-event factors, in other words, disaster severity kinds of experiences, and he added a slide showing there was a dose response relationship with disaster severity. And then he emphasized something that I think has been neglected, which is that as a result of 9/11, a lot of people have lost their jobs. They've had low social support. They've lost family members and that set up a cascade of other stressful life events in their lives. And so in many ways, although we think of that as separate from the World Trade Center, it's very much connected to the World Trade Center.

The last slide from Robert's presentation, which was very interesting, and this has been done with several other populations, is the trajectory analysis. Which essentially shows as all these trajectory analyses after disasters tend to show, the

majority of people function very well. They're resilient, they bounce back and you don't even see a little bump in their mental health scores. And they're the ones at the bottom, and that's something like three-quarters of the sample.

But then there's a group of people who start high and stay high or start moderately high and stay high. And another group of people who actually are getting worse over time. And they're the ones who are hardest to understand. And in the tower survivor in Lower Manhattan sample, that's 16% at the end. That's a lot of people all those years out whose lives were turned upside down in terms of their mental health from the World Trade Center.

So then we had a really interesting talk—next slide—about mental health and responders. And the initial trajectory work was actually done with the police and nontraditional responders. And you can see that for the police responders, there's only a very small group who were high to begin with, and then their scores, the instrument that's been used in all these studies called the PCL, the post-traumatic checklist, are creeping up a little bit. Why they're creeping up is really hard to understand. But the vast majority of the police responders who were trained, not that they were trained for what they experienced, but at least they were trained, and there may have been other reasons why they didn't want to talk about their mental health in the monitoring visits. Anyway, they—basically three-quarters of them were asymptomatic.

So if you can skip the next slide and go to the one after that, these are the nontraditional responders. And as opposed to that 16% of the tower survivors in Lower Manhattan folks, it's 36% of the nontraditional responders who are really having the hardest time in terms of PTSD symptoms.

So jump two slides, if you don't mind. Thank you. We then had a really—yes, you can skip that one. I thought we showed that one. Okay, you can skip that one. And one more. I'm sorry. I love to do this myself, actually. I'm sorry you're having to sit there and do this.

So we then had a really interesting talk from Jennifer Yip who is with the FDNY, and I'm sure David had a lot to do with this talk, so I'll thank him in advance for that. They started their first mental health assessment in 2007, so that's six years later and they used the same metric. And then they looked back at when people arrived, so retrospective and six years later. And I actually found this, the left-side of this graph quite astounding. So the right side of the graph shows the most recent mental health assessment, and nothing has changed. Basically, the people who got there really early were the ones who had the toughest time. They probably were the ones who sustained the most losses of their colleagues, who had the most health problems, and so on.

The next slide that is also from Jennifer's talk, and it's actually very classic, which is that PTSD is high comorbid, as I mentioned earlier with other mental health problems, and with alcoholism. And in fact, when PTSD first came about in 1980,

the VA were very disdainful of it because it was going to cost money to take care of people with PTSD. And they said they're all alcoholics who are just now claiming that they have PTSD. And time has proven them absolutely wrong, and the VA has really gone the extra mile to develop programs for PTSD to try and prevent chronic PTSD, to try to intervene with suicidality among PTSD patients. They've been fabulous. So this is really classic kind of circle slide showing that there is a lot of overlap.

So the next set of slides are from the comorbidity work—which is the title of this talk, I'm not sure why—at Stony Brook on lower respiratory symptoms. That's where we started. And we started by analyzing the cohort data from Mt. Sinai on the relationship, the cross-sectional relationship which was striking then and is still striking now. And in the next slide, you can see the longitudinal relationship. What's interesting about the longitudinal relationship, and I didn't believe it, I've finally been forced to believe it, is that PTSD temporally precedes lower respiratory symptoms and it doesn't work the other way around, no matter how you analyze the data.

So let's skip the next slide and go to the final slide that Roman Kotov gave on lower respiratory symptoms and PTSD. Because after doing that study, we did a formal study where we got a diagnosis of PTSD using a diagnostic assessment on about 3,600 people and looked very carefully at that relationship between PTSD as a diagnosis and people's trajectories of lower respiratory symptoms. In his theory that it was mental health driving lower respiratory symptoms just kept being proven over and over again and so I'm starting to be a believer. What he's doing now is very different and very interesting. He is having people fill out questionnaires three times a day over the course of a week, his ecological momentary assessment method. And taking their blood pressure, and asking them about vegetative symptoms, and asking them about depression symptoms and measuring other physiological things over the course of the week. And he's in the process of analyzing that data and looking at moderators and so on. But that same temporal sequence is happening on a daily basis. So if you're upset with PTSD symptoms on Day 1, on Day 2 you're likely to be starting to report more lower respiratory symptoms, and it doesn't work the other way around. Not as strongly, anyway.

So the next talk that we had, and I'm going to go through this quickly because I'm not a neuroscientist, and the next two talks are basically neuroscience talks. Mt. Sinai, with Rachel Yehuda's guidance, and she was one of the experts who was at our meeting, but she's one of the people who basically got PTSD off the ground in the early days with her studies of Holocaust survivors. So they've been looking at sort of links between trauma exposure and PTSD and how genetic factors influence that link.

The long-term hope of all of this work is that we're going to end up finding

something really critical and be able to develop more personalized treatments for people. There haven't been any new treatments for PTSD in at least a decade. And the treatments that are typically provided for PTSD are not unique to PTSD, they're the same as their antidepressants, basically, for medication treatment and cognitive behavioral therapy. So it's our great hope that the World Trade Center research programs that are going on, ours included, are going to end up identifying very strong genetic markers or other biological markers that are really going to improve down the road the treatment because it's a chronic debilitating condition for people who have it.

So I'm going to, I think, skip the next couple of slides only to say that they're taking this in a very serious way. They're looking at childhood trauma. They're looking at World Trade Center trauma, and they're looking at PTSD with a really excellent diagnostic interview to get a handle on how all these genetic markers really work. And as you can see on this slide, their hope is to come up with biological subtypes. Again, with this really important goal that I hope I live long enough to see, but I think it's going to be slow-going.

So in our program, next slide, we're also looking at genetics but we're looking at gene expression in particular. And we started looking at epigenetic issues. Epigenetic patterns that are subsequent to PTSD since we didn't have data on people before they became ill. And now we're looking at gene expression. And there've been 100 genes that were found by a really excellent statistician who joined Stony Brook a few years ago. She had been doing cancer research before, so this mind switch to PTSD was not an easy thing for her and she's really done beautiful work. And as you can see, the people who never had PTSD who are in blue, are less likely to have the FKBP5 gene than the people who currently have PTSD. And the people who remitted, and we had people who remitted, are sort of in the middle. I have a symptom, but I don't have a disease, to quote David's earlier talk.

And the next slide shows that she used the machine learning to create a prediction model for PTSD. And it turned out the model not only predicted PTSD and had an AUC of 0.76, which was really great, but it also predicted lower respiratory symptoms because the two are highly correlated. So that was really nice to see.

The last part of what I'm going to talk about before I turn this over to Alfredo is the work that we're doing at Stony Brook that I think you know about and I think there's a lot of angst about, which is cognitive impairment that is happening. So the background to this is that Ben and I had, Ben Luft and I had a discussion about four or five years ago that the monitoring program was created in 2001 and '02 when the average age of the responders was 39, and now they're heading into their fifties. And in your fifties is when chronic diseases of aging start happening, and they include changes in your physical functioning, at least they have for me,

changes in your cognitive functioning. I like to think that's not true of me, but it probably is, and cardiovascular disease.

So around that time that the program in public health at Stony Brook hired an epidemiologist, a life course epidemiologist. Thank God, because this is a life course issue we're talking about, named Sean Clouston, who was analyzing epidemiologic data sets on cognitive impairment. So this was his field. So we started assessing cognitive impairment along with our monitoring visit, and then I heard this amazing talk by a guy named Jack Guralnik on the physical functioning measure that's used in studies of the elderly, which is very simple. Chair stands, gait, balance were the basic things that younger people can do that get more and more challenging as you get older. And it's one of those measures that like cognitive impairment that makes people nervous to fill out the questionnaire or to be asked these questions. Nobody minds being asked to stand up from a chair ten times and to stand with one foot in front of the other. I do, but other people don't.

But anyway, so we stated doing this. And Sean started analyzing the data. And the next slide shows that shockingly enough, the top group are people from a primary care clinic. The bottom group are people from a neurology clinic. A lower score on this measure, this is the MoCA. This is what President Trump said he wanted to have, he probably studied the answers ahead of time. You can go on the Internet and find it. I shouldn't have said that here. Sorry.

PARTICIPANT: But it's not so highly educated people.

PARTICIPANT: You can (inaudible @ 02:27:33).

DR. BROMET: Right. The World Trade Center responders, who were a health population to begin with, are smack in the middle. And that was pretty shocking to us.

The next slide shows that the World Trade Center responders who are most likely to have low scores.

If you could go to the next one. Next slide. Yes, right. So that lighter colored bar, those are the World Trade Center responders with PTSD. And you can see that across the board, at different ages. They're the ones that are—they have a larger—they're more likely to score lower on this MoCA that President Trump had. And we've also used another measure, which is a computer-based measure of cognitive impairment, and it shows basically the same thing so we got really concerned about this. Sean is also looking at incidence data, so among the people who look absolutely normal on the MoCA, when they come back for their next visit we have people who are starting slide, and that too is related to be PTSD.

So the next slide, this is Sean's title on this side: "Many Responders Have Real Troubles". It's very difficult to get through life when you're cognitively impaired. So it's well-known that PTSD is associated with certain cognitive dysfunctions. But this issue of it preceding and predicting the onset of cognitive impairment, not

other aspects of neuro-psyche dysfunction, is really of great concern.

So if you could skip the next slide and go to the imaging slide. All of that led us to a guy named Sam Gandy, who's an expert on Alzheimer's disease at Mt. Sinai. And Mt. Sinai, as you know, has a big World Trade Center program with some—a lot of active research. And we said we need to understand what's going on in the brains of people who are severely cognitively impaired in our sample, and they're in their fifties, because it just doesn't make sense. And to start labeling them now with some kind of dementia, frankly is something that makes me very nervous because it just doesn't fit with their age. But maybe I'm being overly conservative, cautious, and old.

But anyway, so we started a study. The early results, which are very early on the first 15 or 20 cases, they look more like people who have Alzheimer's and they look like normal brains. So it's a 2-by-2 design: PTSD, yes, no, and cognitive impairment, yes, no. Because we're interested in that comorbidity and we're recruiting, we're in the process of recruiting, a sample of occupationally and demographically matched controls from Long Island from the same unions who didn't go down to the World Trade Center. So when the study is done, we're going to have some very interesting and maybe some very worrisome findings.

So I'm going to skip the next slide and turn this over to Alfredo. Do you want this? You have better long-distance vision than I do.

DR. MORABIA: Good afternoon. I have five minutes. I will show you the results of this world trade center heart cohort study. So as you can see, the title is important because it says male and female first responder. And as of now, this is the only study that actually has assessed the association between PTSD and cardiovascular disease in both men and women. I mean, all the available evidence is in male Veterans and in the nurses' health study.

So this essentially, this study essentially confirms what was suspected but does it in a very novel way. So next slide. So the study is a cohort study. So we recruited 6,500 participants of the World Trade Center Health Program at Mt. Sinai and in Queens. And we assessed at baseline their risk factor for cardiovascular diseases. We actually measured those factors with both the equipment at Mt. Sinai and at Queens so that they could be standardized for the measurement of blood pressure, for the weight and height. And we also assessed whether they had had previous MI or stroke before entering the cohort.

And then we started to follow them, and we followed them actively. That is, we contacted them every year, all of them, and asked them whether they had had an MI or a stroke. And when they said yes, we asked them where and when, and we retrieved their medical charts. And so we were able to validate the event they were reporting.

And what we also were able to link the cohort with a New York State Registry of Hospitalization called SPARCS, so that we were also able to know all the

hospitalizations that the cohort had had during the four years of follow-up. After four years of follow up, we had still 92% of the cohort that was being followed.
So next slide. This is what I essentially said. There were 10,000 people during the two years, one year and a half during which we did the recruitment that went to the program, and 6,500 of them were entered into the study. It was not an issue of refusal, but just that we were not there at the time that they went to their visits.
So next slide. This slide shows you the hazard ratio, so the rate ratios of MI or stroke in men and women. The results were very, very similar in men and women, and for someone else has actually grouped them. And this is quite an interesting slide because it shows that except for smoking, none of the traditional cardiovascular risk factors are associated with cardiovascular disease in this cohort. And what does this say, it means that it's not that cholesterol or BMI or hypertension are not risk factors for each individual in this cohort, but the cohort is extremely homogeneous. They're all more or less blue collared, and there's not an insufficient diversity in terms of exposure to these factors for them to come out as determinants of heart attacks or stroke.
And so because the cohort is homogenous like that, and young, so at very low risk of heart diseases, it gives us very good conditions to actually assess the effect of PTSD, which was quite prevalent in the cohort, as you know. 20% in men and 25% in women. So we have that situation where the traditional risk factor, besides smoking, don't show—don't come out as determinant.
So next slide. These are the cumulative risks. It's called Kaplan -Meier type of analysis. The blues are about 20, 25% of the cohort who had PTSD at baseline, and the reds are those who didn't. And as you see, the hazard, so the rate of MI in this case in men, I'm showing you the data in men. They are very similar for women, even though the numbers are smaller and the power is smaller too. What you see is that the risk starts to accumulate immediately after the beginning of follow-up and the two lines get separated progressively over time. So the accumulation over time of the event was much higher among the people who PTSD than among those who didn't have PTSD.
So this is for MI. Next slide. And this is for stroke. And as you see, similar, there is almost no accumulation among the red line, the people without PTSD, whereas there is a progressive increase among the people who had PTSD.
So this is the—what we observed. Then we did some analysis in which we adjusted for the cardiovascular risk factors and it's in the next slide. And what you see in this slide is the result of the active follow-up. So those, you don't have this under your—yes, yes. Yes, it's here.
So the active follow-up of the participants, where we assess whether they had MI or stroke over the next four years, and so it was a phone call and then followed by, again, retrieval of their medical charts, shows that it's again for men. There is for MI alone in the multi-varied analysis, so adjusted for all the cardiovascular risk

factor, there is a 2.2-fold increase in the rate of MI among men. There is a 2.8-fold increase in stroke. and if you pull them both, because actually the etiological—I mean, the hypothetical pathways that would relate PTSD to cardiovascular is very similar for stroke and MI. So you can pull them, and you get 2.5 hazard ratio. And they're all statistically significant.

In women, we find the same thing in terms of magnitude, but they're not statistically significant. When we move to the hospitalization, which it was very a big advantage to have the hospitalization because the hospitalization is, of course, not self-reported, the quality is not as good because you don't validate. There may be some of the diagnoses, discharge diagnoses that are invalid (and current @ 02:39:38). But on the other hand, there is no self-report. Whereas we had better quality in terms of validity of the diagnosis, but they were also self-reporting.

So if you look at the hospitalization, you see almost exactly the same thing. A little bit stronger effect because there were also more hospitalizations for MI and stroke than they were self-reported. We missed some of them in the follow-up. but you see that the men have 3-times more rate of MI, 3-times more rate of stroke, and 2.8-times more rates of stroke or MI if they had PTSD, compared to people who didn't have PTSD at baseline.

Interestingly, among women, this result, when you pull MI and stroke, and I think in this case it's absolutely possible to do that because the associations are really very, very similar and the Kaplan-Meier analysis is very similar. In women, it statistically significant. And showing that actually the long-term effect of the World Trade Center exposure would translate into PTSD and increases the risk of heart attack is similar in men and women. And again, this was a question open in the literature, which this data, at least after confirming what was expected from under study can solve.

So these are our results at that stage. It's a very young cohort. They were 55 when they entered the cohort. They are still in their fifties. You would expect no MI or stroke among women of that age, and still we find that statistically significant association. The risk of MI and stroke was very low, so we are able to identify very neatly, very clearly the specific effect of PTSD.

And I want to conclude by saying that these results are valid for this cohort, but they probably also are valid for the mass of first responders that are now going to other types of disasters. I mean, we saw last year with the hurricanes, etc., there will be more and more of these disasters. There won't be many more opportunities to study the impact, the long-term impact of this type of disaster on cardiovascular health. So these results may also be useful for other first responders and first responders to come.

That's it. Thank you.

DR. MIDDENDORF: Thank you.

DR. LUFT: So my name is Ben Luft. I'm from the Stony Brook program. I think Evelyn

mentioned to you, we try to give you a summary of our meeting, which was almost a seven-hour symposium or colloquium that we had, and at the end of which, where we had the leaders of the program all involved. And by the end of the program we solicited everyone's recommendations and came up with a consensus of recommendations, and this is what we really wanted to spend or what we envisioned spending time with this body, which is such body in terms of your advisory capacity. And I think you have that in front of you, the summary. But I just wanted to make a comment. After 9/11 in 2001, we had a national emergency which we all knew. It became very clear to us all. But at that time, I don't think we really recognized that we had a public health emergency and we were slow in our response, slow in our development of our program, slow in eventually making it into the program that we have today.

But for a variety of reasons, we're now at the precipice, perhaps, of another public health emergency. Part of it having to do with the fact that our population is no longer a young population. Even though they were injured in 2001, they had a lot of reserve just by the fact of their youth and that they had the healthy worker effect.

We now have a population that is now coming to the age of on the average or age of 55. That's kind of almost a magic number when a variety of different conditions become manifest normally. Conditions like cognitive impairment and Alzheimer's disease, cardiovascular disease. And so you have that, the act of aging occurring. You have the act of chronic inflammation as the result of the World Trade Center exposures. You have the fact of PTSD, which initially we had all thought of as a psychiatric illness, and now we all know it's more, it has a lot of the characteristics of a systemic illness. There's a lot of outpouring of a lot of different neurotransmitters and neuropeptides, and there's the spicing up or the charging up of the immune system as well. And we have a lot of data. We haven't shown you all of our data because we try to keep this to a 45-minute presentation.

So we came up with a variety of recommendations, and these recommendations are based on the data that we've accumulated. Earlier in our program, there was a prediction made and I said your prediction is only going to last a few hours, that's how far you are ahead of the curve. And you can see that a few hours later, you heard the talk from Alfredo, you heard the talk from Evelyn, and actually we have more, over 60 different individuals who've undergone neuroimaging, and they show very similar patterns. So I think there's real data. We'll be very happy, once we go through a peer review process, to be able to share that data with you, as well. We were somewhat limited. I wish we could have had this as a closed session.

So what are our recommendations? And I wanted to go through this with you because this is the most important part of this presentation. We feel that the monitoring program has to be expanded, and probably the monitoring and

treatment program, to include a broader array of lifetime risk factors and other traumatic experiences which may have an impact on the current situation. And I think that those are things that we could include very easily into our monitoring exam, but it wouldn't really—but it would give a much fuller picture of these patients and perhaps a much fuller picture of the risk factors they each have in regard to psychiatric condition.

We also feel that the monitoring program should be expanded. The screen for cognitive and physical impairment indicative of accelerated aging, as well as cardiovascular disease. My personal feeling is that it shouldn't be just the monitoring program, but it should be the treatment program as well. And I would implore you to consider this much more quickly, whatever data you need you should try to get that as quickly as possible. If there are further studies that need to be done, if there are confirmatory studies that need to be done, the beauty of this program is we have multiple centers, multiple cohorts and we could easily confirm these things from cohort to cohort. And why do I say this? Because I think that there are even—one, is that we don't fully understand the pathogenesis of the disease, or when you talk about these diseases such as cardiovascular disease, stroke, even cognitive impairment, there are things that can be done.

We could be doing a lot more in terms of cholesterol and diabetes, and all of the other risk factors that are associated with these conditions, and so this should really be part of our monitoring and treatment program, because we can make an impact. And quite frankly, we don't really know what the pathogenesis is.

Everything in the World Trade Center is unique to the world trade center. It may be that there are different types of initiatives and different strategies that we could use, and I'll get into that a little bit later.

We should take a formal review of the quality of our mental health treatment interventions in the World Trade Center program as the first step in understanding the persistence of PTS symptoms in responders receiving treatment. And I think that this is important. I think we have to be self-reflective. We shouldn't shy away from these types of things.

This has happened—when Evelyn chose a statistic, the 36% or as many as 36% of a sub-cohort continued to suffer from a disease, we really have to examine why that has occurred. It may be that everything was right and it may be that there was—that everything was done appropriately or all the therapies were available. But we can't just take that for granted. I mean, there is a lot of people that continued to suffer, and we need to continuously reexamine ourselves and re-see what is working and what is not working and come up with a new strategy to be able to take care of that.

We should start focus on certain statistical analyses, the links between exposure, PTSD and systemic conditions to determine whether these conditions could be classified as World Trade Center related conditions. We should expand the model

of PTSD to incorporate the trajectories and psychosocial determinants, any ensuing disabilities. And we should do some real-time biological measurement. And we've talked about this whole idea of having a biological bank. At Stony Brook, we have over 100,000 biological specimen that we've collected over the last seven years, or so. So we have almost every one of our patients that are involved in research, they give us serum, plasma, RNA, DNA cells. This should be really something that's done across the entire program, and resources should be given for this.

We have a very good relationship with our institution, but we wanted to start this. They supported us and we're in a very strong position to do some very fundamental type of research. But this is the type of thing that needs to be done. We should increase the support of research on the biologic links between PTSD and the earlier and unexpected onset of age-related conditions, such as cardiovascular disease, autoimmune diseases, and cognitive impairment. We should develop a biomedical model of disease that pulls together the multiple impacts of PTSD on medical and psychological outcomes, as well as biologic, physiologic, and endocrinology changes that occur concurrently. That basically is what we call in the scientific problems, we need to do more of a network analysis. We need to put everything in.

Right now, you have—we've been a very—I'm an infectious disease specialist, I'm a molecular biologist. I got involved with the psychologists and the psychiatrists. We need to have more of that interactive and collaborative type of arrangements. We have to kind of see that there's no such of thing as mind and body, but there's actually—they interact with one another, and we really need to be able to bring together the model to understand that.

We should really be looking at neuroimaging a lot more. We are very involved. I think Evelyn mentioned to you that in a program for neuroimaging. Most of our program revolves around functional MRIs, but I think we should be doing a lot more with molecular markers, such as amyloid, tau inflammation. We just have preliminary or pilot-type studies going, but I think that that's the way we should be classifying our population.

Last thing, or one of the last things, next to the last, was the whole area of doing randomized control trials. I mean, I think that this is such a strong, strong program. We have such a variety of different centers that are involved. We have real illnesses and real issues. We have a captured population who are loyal, who are interested, who are engaged. And we have to be able to start offering them alternatives because the same-old isn't working for them.

And so the only way that we could do that is by really developing a randomized control, doing randomized controls, trials. Very similar to the AIDS clinical trial group. And I think we should really be starting to think about that and be very serious about that. we might have to go and look for different areas of support

besides the government, maybe to team up with the pharmaceutical firms, or whether it's to team up with the new bio ventures, and things of that sort. There's a lot of interest out there, but we really need to start solving these problems. And I think we can do that. And I think we have a great opportunity to do that. We have a—you have a great group of physicians. I mean, you have—everything is in place, we really should do that.

And like I said, the last thing is developing the biobanks. I think that those are very important. We've done that. Patients have no problem in providing us with materials. They're very interested, and it's lead to a whole host of opportunities for us. Things that we've now studied. Things that when we started the biobank, we really didn't know what we were going to use it for. But now we're seeing that people are cognitively impaired. We're doing some studies on cancers. We do some studies on autoimmune disease. We want to see what genes are being turned on and turned off. We now have the capability of doing that. And I think that we really have to start thinking that this is a problem, it's going to be before us for a long time and we have to kind of look toward the horizon.

So I want to take any questions and maybe open it up for discussion. We have like three minutes. We have a few minutes.

DR. WARD: Yes. I think we can go a little late. I know some people have to leave because they have flights that they have to get to, or other reasons to leave. I did want to just thank you, the last three speakers for your very thoughtful presentations. As you know, your audience is not just the staff members, but the Program directly. And I think you've laid out your research so clearly and compellingly, and articulated your recommendations so well that it will be taken very seriously, both by the Program and by the STAC if we're asked to come up, you know, to deliberate further on research recommendations to the Program. So we very much appreciate, it's clear the time and effort that was made to really bring this together. I'm not an expert in any of these fields and I came away with a huge, a lot more knowledge than I came into the room with. So I very much appreciate it.

DR. LUFT: And we're available for any questions, any interrogatories that come up in terms of more information, more to drill down or specificity, and we'll keep you informed. As, like I said, if this was closed session we would be able to present to you a lot more compelling data, but a lot material is in review. And I think it's something we just—I wanted, I think it's important for you to be aware of and I think that these are things that will be coming down the pipe.

DR. WARD: Steve had a question.

DR. MARKOWITZ: Steve Markowitz. I have a couple questions. One for Ben, and one for Alfredo. So are there interventions with regard to PTSD that are ripe for clinical trials? Has any been proposed to NIOSH that you know, and NIOSH has or has not been accepted—

DR. LUFT: No, I don't think—I think that this is, one is that I don't know of that. I know that,

for instance, I could talk a little bit about the neurocognitive things because I've been thinking about that a lot, for instance. One is that we really don't know what the pathogenesis is of the neurocognitive issue. Whether it has to do with amyloid deposition, or tau, or whether it's similar to the concussive brain injury, or whether it's due to neuroinflammation, which is now becoming a more, a hotter topic. And all those three areas are being examined. The point is, is that once we begin to understand that, there may not be therapeutics that may be currently available, but it may be something that will be—that people think may be available. It's just, it's like I said, I made this analogous with that particular condition, to what is going on with the, for instance, with the AIDS clinical trial. But you begin to do this, you begin to examine it, you begin to focus your energy and your research. I don't say that I have any answers for anything. I do think that we should be opening up these question, not only to our small world of the World Trade Center program, but to the larger world for them to start giving us input and for new approaches, new strategies, new tactics. And that's all I'm saying.

And in regard to being able to look at, you know, for us to do a review of how we've been doing and whether we've been successful or not, I don't know whether that's going to be—I have no idea why the police are at about 4% in one study for PTSD, and the nontraditional responders are at 66%. Whether they got the same therapy. Whether they didn't get the same therapy. Whether or not they're the same risk. I have no idea, Steve. If I had an idea about that, I would have published it

DR. MARKOWITZ: Thank you. Alfredo, Evelyn presented a slide on the trajectories of PTSD over time and I'm just wondering whether maybe you don't—there are not enough events in your group so far? Maybe in the future there'll be more. But were able to look at, or could you in the future look at how the trajectories of PTSD and their evolution relate to cardiovascular risk?

DR. MORABIA: May I answer your previous question too? Because there's an excellent randomized trial that could be done. I mean, it's actually, at this point, observational studies won't show much more about PTSD and cardiovascular disease. But a randomized trial which would randomize treatment for PTSD and see whether this reduces the incidents of cardiovascular outcome later in time, would be a great trial. I think that that's the next step in the field.

DR. MARKOWITZ: Yes. Actually, if you look back at one of those slides, the Feder et al study, they're showing improvement over time in the police responders and some of the nontraditional responders within particular groups. And so you could conceivably look at cardiovascular or pulmonary, or something like that in those groups. It suggests its own kind of trial, where you wouldn't have to—where you wouldn't necessarily have the other variable of the treatment method where these groups are improving already.

DR. MORABIA: Yes, there could be alternatives, but the clearest way to show it and to put the

final point to that question of whether PTSD causes cardiovascular disease would be that trial, I think. And I think we are in very good condition because of the high prevalence of PTSD in this cohort, etc. But there are other observational indirect—

DR. McCAWLEY: My concern would be whether the treatment is, in fact, effective. Because it sounds like you're assuming that the treatment would be effective in that particular case, and I don't know that it would be. I know of some treatments that are being done for PTSD that have some promise right now. They're mostly surgical though.

DR. MORABIA: Yes. So if there was no—I thought there was a treatment and people are using it. But if you say there is no treatment, then there's no trial.

DR. McCAWLEY: Well, there are treat—I think there are treatments, but the success rate of those treatments is—

PARTICIPANT: Questionable.

DR. McCAWLEY: Is quite questionable.

DR. MORABIA: I see.

DR. McCAWLEY: So you'd have that extra variability in your trial.

DR. MORABIA: That's a good point.

DR. LUFT: I just want to make a comment about that. One of the things that we looked at with these biomarkers, and I think Evelyn showed you some of them, it really depends on how you define success, and it also depends on what you think is driving the actual disease process. It's not the same what's happening necessarily psychologically, it might not be necessarily what's driving the process physically in the heart or in the—or cognitively. So for instance, we had one gene called the FKBP5, which is elevated, and this has been associated with a variety of cancers as well as a variety of other conditions. It may be that the strategy has to be to get down the level of FKBP5, or one of these other neuro hormones, or something of that sort.

So it's not—that's what I meant. But because it's, you know, it depends on what your endpoint is and what your—the reason for doing that. And it may be that you—the patients continue to have the flashback or may be paranoid, but that doesn't mean that necessarily you can't control some of these other side effects that might be impacting other disease processes.

DR. McCAWLEY: Exactly.

DR. LUFT: But the only way we know that is by doing the studies and by—that's why we're doing it.

DR. McCAWLEY: Yes.

DR. WARD: Catherine?

MS. HUGHES: Yes, I have a short little comment or question. So, I'm looking at page 105 at your slide at the graph at the top about nontraditional responders.

DR. LUFT: Yes.

MS. HUGHES: And you have a timeframe year since 9/11, and approximately around year '08,

that was the economic collapse. So leading up to that and around that period, that would definitely be a factor of stress. And I believe we've talked about that before.

DR. LUFT: Right.

MS. HUGHES: So I want to find out how you've isolated that. And then about year '12, guess what happened then? Superstorm Sandy. We had seven feet of water here at the South Street Seaport, and a lot of the first responders waded low lying areas and were flooded. So I would not—I would say those are two other major shockers to people's system.

DR. LUFT: Right.

MS. HUGHES: And if you're—

DR. LUFT: Yes, there's no doubt.

MS. HUGHES: And that has been taken out of your analysis?

DR. LUFT: No doubt, no doubt.

MS. HUGHES: Okay.

DR. LUFT: I think we've tried to put that in the other aspects of really looking at these different life events. and I think it's also a little bit in trying to understand PTSD, here again, you're talking to an infectious disease specialist, so telling you about the PTSD. But, so PTSD is really an accumulation of a variety of different stresses that occur. Some of it, a lot of the predisposition to PTSD occurs during childhood, and you may become predisposed toward the development of PTSD. And that was the work of Rachel Yehuda. So it's not a matter that—and we've done these studies on superstorm Sandy and what's its impact was, and it did worsen the PTSD symptoms in patients who had preexisting PTSD, it made it worse. And so there's no doubt that these things do occur over time.

MS. HUGHES: Like If you were a firefighter—

DR. LUFT: No, in a case—

MS. HUGHES: And your houses were destroyed during superstorm Sandy that could be devastating.

DR. LUFT: So what we found was that—so we found that during the superstorm Sandy that patients who had PTSD, their symptoms came up and then they came down again, but they were still elevated. But that's not the point. The point is that if you look at—so I'm not saying that these are—what we're saying is that in the normal population in general, there's about 4% of people that have PTSD symptoms. In this population, we have 36% of people that have PTS symptoms. So that's basically what you're dealing with. And in the police population, this is work that was done by the people at—Pietrzak at Yale. Again, it was around 4%, so it's actually his—what he was saying was that the police who had this training and were perhaps more resilient because of their training and because of—they're basically pretty close to normal. What you would expect in the normal population. But in this population, it was up to 36%. Other people don't have 36%, they have 22%, 20%. But it's still, with Brackbill, he still had very high percentage. But it's

very high percentage, especially in the nontraditional responder. And I think Evelyn mentioned the people who are the tower survivors and the people who are living in that area. So I think that those are—so it's not to say that they were, I mean, it's high, it's high. Whether it's 20 or whether it's 36 or whether it's 24, or whatever. It's high. That's all.

MS. HUGHES: And just one more comment on tower survivors—

DR. MORABIA: Can I add something about that?

MS. HUGHES: Yes.

DR. MORABIA: Because it's a question. We could not separate the people according to that trajectory, but since you cannot fix a specific moment for the initiation of PTSD, we have looked at all the data we had about past PTSD. And in most of the cases, they had already PTSD several years before. We didn't see anything like a recent increase in PTSD just before we started baseline. So to answer whether it's long-term, I mean since 2001 or more recent, it looks like it's still the same phenomenon.

MS. HUGHES: And just one point with the tower survivors, the tower survivors. The towers were gone, which then meant a lot of those companies closed permanently or relocated. So you could have been doubly compounded by the loss of your friends, your colleagues and your job. And a lot of those jobs don't even exist in this marketplace 16 years later, whether you're in the financial services or insurance. Everything has changed in 16 years in the marketplace.

PARTICIPANT: I think that was—

PARTICIPANT: That was his point.

DR. WARD: That was his point.

MS. HUGHES: Okay.

DR. WARD: Yes.

PARTICIPANT: Yes, that was Robert Brackbill's point, the risk factors.

ADMINISTRATIVE ISSUES

DR. WARD: So thank you, everyone, for the discussion. I think Paul has indicated that we really need to close the formal part of the meeting as we're over time and he would like to wrap it up. If anyone wants to stay and talk further, I think they're welcome to stay until 5 o'clock, at which point the building will put you out.

DR. MIDDENDORF: As always, I really very much appreciate all the thoughts and ideas and discussion. It's always very, very helpful. Very much appreciate all the presenters and their time and effort to come here to present on the information. In the long-term it will be very, very helpful for the committee.

Just to wrap it up, thinking back to this morning where we started out. We started out with a charge on independent peer reviewers and there was a lot of good discussion around that. There was specific recommendations were made and voted on, but there were a lot of thoughts and ideas that were floated, and the Program will certainly take those ideas and work with them and try to improve the

pool of independent peer reviewers.
Also on the policy and procedures, the committee identified a number of soft spots that the Program already knew about but has struggled with. So there was a lot of good discussion around that as well. And I'm sure that there will be some continued, thinking about how to improve those areas. So we very much appreciate everybody's thoughts and ideas and wish you a very safe trip home.

DR. WARD: You too.

PARTICIPANT: Yes, you too.

[END MEETING]

G L O S S A R Y

ATSDR	Agency for Toxic Substances and Disease Registry
CCE	Clinical Center of Excellence
CDC	United States Centers for Disease Control and Prevention
CDC-INFO	Centers for Disease Control and Prevention National Contact Center (1-800-CDC-INFO)
CME	Continuing Medical Education
COPD	Chronic Obstructive Pulmonary Disease
CRP	C-Reactive Protein
CUNY	City University of New York
DOE	Department of Energy
DOL	Department of Labor
EEOICPA	Energy Employees Occupational Illness Compensation Program Act
EPA	Environmental Protection Agency
ERHMS	Emergency Responder Health Management System
FACA	Federal Advisory Committee Act
FDNY	Fire Department, City of New York
FEMA	Federal Emergency Management Agency
FeNO	Fractional Exhaled Nitric Oxide
GERD	Gastroesophageal Reflux Disease
HHC	New York City Health and Hospitals Corporation
IRB	Institutional Review Board
LHI	Logistics Health Incorporated
MoCA	Montreal Cognitive Assessment
NHANES	National Health and Nutrition Examination Survey
NIH	National Institutes of Health
NIMS	National Incident Management Systems
NIOSH	National Institute for Occupational Safety and Health
NPN	Nationwide Provider Network

NYPD	New York Police Department
ODAR	Office of Disability Adjudication and Review
PTSD	Post-Traumatic Stress Disorder
STAC	Scientific/Technical Advisory Committee
SUNY	State University of New York
VCF	Victim Compensation Fund
WTC	World Trade Center
WTCHP	World Trade Center Health Program

I hereby certify that, to the best of my knowledge, the transcript of the March 1, 2018 meeting of the Scientific/Technical Advisory Committee is accurate and complete.