EXPERT PANEL/WORKSHOP ON CANCER AND MORTALITY STUDIES WITH WORLD TRADE CENTER- EXPOSED POPULATIONS

Friday- April 6, 2007

WORLD TRADE CENTER HEALTH REGISTRY

New York City Department of Health and Mental Hygiene

125 Worth Street, 2nd Floor Auditorium

New York, New York

- Introductions - Lorna Thorpe, Ph.D.
- World Trade Center (WTC) Exposure Assessment - John Dement, Ph.D., Professor of Occupational and Environmental Medicine, Duke University
- Mortality Study Methods - Jim Cone, MD, MPH, Medical Director, World Trade Center Health Registry (WTCHR)
- National Institute for Occupational Safety and Health (NIOSH) Life Table Analysis - Mary Shubauer-Bergan, Ph.D., Research Epidemiologist, Division of Surveillance, Hazard Evaluations and Field Studies, NIOSH
- WTC Responders Fatality Investigation Program - Dr. Kitty Gelberg, Director, Epidemiologic Surveillance & Occupational Health Clinic Network Section, New York State Department of Health
- Breakout Session- Mortality questions
- WTC Studies - Henry Sacks PH.D. Professor, Community And Preventive Medicine, Mt. Sinai School of Medicine; Joan Reibman, MD, Associate Professor of Medicine and Environmental Medicine, New York University; David Prezant, Chief Medical Officer, Office of Medical Affairs, New York City Fire Department

- Cancer Study Methods - Lih-Fang Chang, MD, MPH, Preventive Medicine Resident, New York City Department of Health and Mental Hygiene
- New York State (NYS) Cancer Registry - Maria Schymura, Ph.D., Director, NYS Cancer Registry.
- Survival Analysis - Sylvan Wallenstein, Associate Professor, Community And Preventive Medicine, Mt. Sinai School of Medicine (No Transcript)
- Breakout Session- Cancer Questions
- Coordination between monitoring and treatment programs and World Trade Center Health Registry - John Howard, M.D., M.P.H., J.D., LL.M, Director, NIOSH

DR. THORPE: We are going to get started. Welcome everyone to the New York City Department of Health and to the workshop that we have today on cancer and mortality assessment. My name is Lorna Thorpe, Deputy Commissioner of Epidemiology here at the Health Department. I'd like to welcome everyone here, particularly those from out of town. You all hopefully picked up a packet in the back which has an agenda in it. We have also circulated the agenda to you electronically.

As you see, it's a pretty full day, and, I think, an interesting day. Most people in this room have been dedicating some of their time, if not all of their time, to trying to understand and address the health needs of people affected by 9/11. Much of the focus on health impacts has been on respiratory and mental health conditions, and we know those to be probably the most prominent conditions people are experiencing today. There are concerns, and plausible ones, about the potentials for cancer risks and risks of death. We know individual cases have been cited, but population-based or scientific linkages have not yet been demonstrated for either cancer or mortality.

We need to be on the lookout and establish studies to assess whether this is a reality. We have had clinician and medical examiner assessments, but not findings from scientific studies that are the usual building blocks of causal linkages. I think that's what many programs are working on establishing now here in New York City. Several programs are stepping into this arena, from the Fire Department tracking the firefighters who responded, to the Mount Sinai Medical Monitoring Program and Bellevue, and ourselves here in the New York City Health Department with the World Trade Center Health Registry.

I think everyone who is working on this knows that it's very difficult to do these studies. There are a lot of challenges, there are a lot of limitations, there are a lot of logistics involved.

The purpose of today's workshop is to think together as candidly as possible about exactly what are the methods available to us. We know different programs may approach this differently, but it's very helpful to think through, in a scientific forum, what are the major issues that we need to think about as we establish these studies. Are there ways that we can mutually support each other? Linkages that we can make across different programs? What are the strengths of the different study approaches? What are the limitations? I think it's also important to think about how, as we move forward with findings five years after the event, 10 years after the event, 15 years after the event, how we translate this information to the public so it's understood. That's very difficult to do.

I really hope today is a day of candor, mutual support, and careful inquiry, sharing thoughts and sharing concerns. We have a lot to do. Before we begin with the agenda, I just want to point out a few housekeeping items that are important.

First, we are transcribing this workshop so that it will be made publicly available. We will send a draft to participants in advance for commment because our experience tells us that most transcripts are 95 percent correct and five percent incorrect. Names may be wrong or sentences aren't quite right, and we would like people to go through and correct what errors are put onto the transcript pertaining to their section. Once that process is done, we will finalize and post the transcript. That's what we did with the Expert Workshop held when we designed the Registry, as well.

For that purpose, if there's a discussion with the audience, and back and forth, it helps a lot before you go into your question or your comment to state your name; state it clearly so we can get it down on paper.

If there are issues that arise not directly relevant to the agenda (and I am sure many will that are important to discuss), we have left time at the end of the agenda between 4:00 and 5:00 to discuss a number of different topics. Maybe we can say "that's a really good afternoon discussion, let's talk about that in the afternoon," so we can focus on getting through all of the topics on the agenda today. Lunch will be served, I believe, at noon. And we'll have various breakout sessions throughout the day.

We originally planned to be in a warmer, more collaborative room, but we had such a large RSVP and attendance that we had to move to this room. It has nice historical aura in it, but it certainly puts this more into a lecture format. So we'll have to fight the ambiance in the room and get the discussion going even though it's in this presentation sort of set up.

Bathrooms for the men are out the door to the right. For the women, out the door, to the left, around the corner. I don't believe you need a code to get in. If you have any questions you can see myself, Jim Cone, Samantha Baras, (she's outside), Debra Walker,

Mark Farfel, or Laura DiGrande. There's a host of us here who would be happy to answer any questions.

I want to particularly thank the two people that worked the hardest to put this workshop together, Dr. Jim Cone and Samantha Baras. A lot of work went into preparing the logistics. If you've prepared workshops before you know that it's a lot of work.

I can answer one or two questions if there are any questions about the agenda. If not we'll move right into the first presenter. Any key questions? Once again, welcome to everybody.

Our first discussion is from John Dement from Duke University. Thank you, John. John will be focusing on World Trade Center exposure assessments.

DR. DEMENT: Thank you. It's a pleasure to be here discussing some very important issues for lots of people. Lots of dedicated work has gone into planning the Registry, as well as the work that will be done to use the Registry. One of the big challenges for these studies is, of course, the assessment of exposure. I think from the outset, it's fair to say that exposure assessments for these types of studies is both an art and science. It's driven by the desire to place individuals into relative exposure categories, also constrained by the data available to do so. So there are lots of decisions that are made along the way that I think will be important for us to discuss and document decisions that we have made to place individuals into categories. It's also fair to say that quantitative exposure assessment is probably not going to be the objective of this work. It will be semi-quantitative, I think, at best. And looking at relative exposure in many groups of individuals.

With that in mind, what I thought I'd do this morning is just briefly discuss some of the issues. I am not going to present detailed methods here. That comes with a lot of contention and discussion later. I will first briefly describe what's been done. A lot has been done, even with the lack of exposure data, certainly, early on in the event. I am going to talk some about the approaches. Some individuals have used different approaches in trying to quantify exposures among individuals, both workers and residents. And hopefully it will set the stage for some discussion.

This is a day that we all remember, it's one of those events that you know where you were, you know what you were doing and you know the details when we saw this horizon with the building collapses and resulting dust clouds. I think it's fair to say, this was extremely complex dust, both with regard to the components of the dust, fuel and combustion products; its dispersion, also, I think was fairly complex and non-uniform. As I said before, in the early hours, and perhaps days, very few exposure measurements were made beyond the typical air pollution monitoring stations that existed within the City. Nonetheless, some of these monitoring data have been used for exposure by Paul Lioy and have been used by others. A lot of work has been done in exposure modeling. Exposure modeling is not going to be that quantitative, it will be qualitative exposure assessment as I view it. Paul Lioy and others have done quite a lot of work in trying to describe the types of pollutants that were in the dust and fuel, both with regard to the physical and chemical properties, as well as variability with time and distance.

Again, this is a complex mixture. Although you may measure at one point in time and one distance from the source, things stratify downwind. You have differences in characteristics both with regard to things like particle size, and also with regard to the organic components. The exposure path of interest to us is obviously inhalation, but I wouldn't rule out the issue of ingestion, particularly with regard to some of the exposures such as metals like lead. Proximity is a great factor, as well as the manner in which the

pollutants were dispersed. Speaking with Jim Cone last evening about the Registry, it sounds like some data have been collected that will allow some approximation of proximity and duration. I think these are key variables to take into account. Of course major dust and pollutants resulted from the fact that buildings were pulverized, an event unprecedented with regard to exposure assessment. I happen to have been in the World Trade Center and looked at the asbestos issues in the building about five years prior to the event. It's fair to say most asbestos had been removed. There still were some issues with regard to phased removal as renovations had been done.

The major dusts were gypsum and concrete, wood and paper, and manmade fiber. Manmade fiber had been largely substituted for asbestos for insulation. Chrysotile was up to about three percent in dust collected, and it was very pulverized chrysotile. With regard to particle size, that also varied greatly, by proximity and time. With regard to mass, the dust consisted largely of coarse particles with largely upper airway deposition. I think Paul Lioy pointed out that glass fibers, even though they are relatively large in length, nonetheless, would tend to deposit more deeply in the lung, not because of their length, but largely because of their diameter. The alkaline PH of this dust is largely due to concrete and other components. This may have contributed to the airway lung diseases observed in the clean-up workers and rescue workers.

The organic compounds were largely the PAH, or polycyclic aromatic hydrocarbons. The lesser components were phthalates. Certainly, there were incomplete combustion products, both with regard to the event and the fire that continued to burn for quite a number of days later. Much lesser, and probably not as great a concern were some PCBs, and polybrominated diphenyl ethers. Even dioxins and furans. I'd say those are low in concentration but may be of interest if we are going to talk about cancer and cancer outcomes. Diesel emissions were of concern, certainly with regard to the workers at the

clean-up sites and residents who happened to be in and around the clean-up sites. Those were and continue to be some sources of longer term exposure.

There were no real measurements of that horrendous dust cloud. As a guestimate, I'd say exposure may have been in excess of 100,000 micrograms of dust per cubic meter of air. It was almost impossible to measure accurately. Looking at the data with regard to dispersion, it certainly affected most of Manhattan. The winds tended to disperse the dust and gases, mostly to the east and southeast. And I think Paul Lioy described five specific post-exposure categories. I think that is what's useful as we look at exposure assessments and certainly assessments for groups of people. I will describe those in a little bit and talk about how they might be used. This is an interesting series of photographs in the article by Phil Landrigan in 2004. Dust portion with regard to the dust has been mapped by satellites and certainly some NASA satellites have provided I think useful relative dispersal information. Again, these are not quantitative estimates but at least they will allow some estimation with regard to the directions of dispersement of the pollutants, and perhaps in conjunction with some modeling of deposition, how those particles and gases might be deposited. It's one of the tools I think we should keep in mind as we move forward in exposure assessment.

This slide shows a conceptual framework prepared by Paul Lioy, which has to do with the outdoor exposure. It describes the exposure scenario with regard to time, key events that occurred at the time, and post-exposure. And there are different categories of individuals who were involved with each one of these. The characteristics of the dust and fumes vary in each one of these categories to some extent. Obviously, the relative strength of exposure is one at the time zero, that's the horrendous dust clouds, and it decreased very quickly over the next 10, 12 hours. Then we had burning jet fuel. We had lots of coarse particles. Some fine particles, and then the burning fires that were in place for a number of days. The rain events actually did help to wash away particles,

remove particles from the air, and probably more importantly, help in preventing further re-suspension of those particles. I think this is a useful time frame and perhaps some categories to consider for placing individuals, and to work in residential circumstances. Category Five is the indoor exposures. That is, I think, actually much more difficult in some ways to assess. Obviously, the initial dust cloud was, as I said, coarse particles, mostly capable of upper airway deposition. But not exclusively. There were fine particles in those dusts, as well. Smoldering fires generated a lot of PAH that we have seen connected with the dust.

Re-suspended dust is a major concern. Looking at the data, variable building-related issues with regard to the magnitude of exposure and frequency of exposure indoors has to do with the design, whether or not the windows were open or closed, and Heating Ventilation and Air Conditioning system status. That's a tough one to look at with any degree of confidence, without taking into account the variability. I think I mentioned before diesel emissions during clean-up, and also we have all been involved in the discussion and debate about the degree of clean-up prior to re-occupancy. I think that is a major issue to take into account, at least qualitatively, as we look at indoor exposures down the road.

These are just some of the data that I mentioned before, which has to do with pretty routine air pollution monitoring stations that look at PM2.5 levels. Shown here is the small particle fraction of the airborne dust. What you see are a couple of things, you see a lot of variability depending on where you were. That's understandable, given the dispersion of plume, but you also see lots of peaks and valleys. Those have to do with activities in some ways at the site, and also driven, as I mentioned before, by environmental conditions - particularly a couple of major rains that occurred during this time period. Nonetheless, I think these data are potentially of use in exposure assessments down the road. One of the challenges I think is to pull together all the data

that exists from these sources that were actively collecting samples at the site. NIOSH did a lot of work at the site, and EPA did a lot of monitoring.

These data need to be assembled in a manner that will allow sort of an overall look at the data, with the idea of using the strengths of each of the data to put individuals into exposure categories. PAH levels certainly decreased very quickly when the fires were finally put out. Considerations for the exposure assessment design are going to be largely driven by the studies that come from this workshop and the discussions. With regard to exposure assessment, you can really invest the same amount of resources with regard to population based exposure assessments. Or you can back up and invest those resources in a case-control mode down the road that would allow you to spend a lot of time individually in reconstructing exposures. But that is going to be an issue driven by the outcomes of interest and the study designs. With that being said, obviously there are populations of WTC site workers in two categories - emergency response and clean-up and recovery - and those are clearly individuals that have high degrees of initial exposure and continuing exposure. And also, they are eligible to be enrolled in the medical monitoring programs and have had some more detailed questions with regard to their actual work. Regardig residents and other individuals exposed near Ground Zero, including people who came back after some clean-up, I think perhaps the approach might in fact be a bit different than it would be for the active workers at the site. Subject to discussion today, of course, is what's going to be really looked at, what are the long term goals of the project?

I mentioned before that the categories of exposure with regard to time and events as Lioy proposed could be modified - a good initial starting point for how we might consider both the time course, the characteristics of exposure, as well as the types of groups of people who are exposed. The last category - primary exposure groups. This represents a pretty good summary of the types of challenges posed by the exposure assessment process.

Talking with Jim Cone last night, it's clear that the individuals who are part of this Registry comprise pretty much the whole constellation of individuals with regard to these exposure groups. This is a complex mixture. You can't measure all the components of a complex mixture. What you can do, hopefully, is try to find types of exposures that act as surrogates, that at least reasonably predict the great mass of exposure. There may be more than one surrogate.

Remember, we have PAHs, we have organic compounds, dust, coarse and fine. So we certainly are going to be dealing with likely exposure surrogates for placing groups within exposure categories. This is going to be a qualitative exposure assessment. Hopefully, we can move to semi-quantitative for some individuals. Ranking of exposure by groups is going to be expert judgement. This will be a starting point for that: groups, intensity groups, actually modified by the actual data. There are good tools for exposure assessment that are being used that allow combinations of sort of dust, descriptive information, and quantitative information in arriving at categorization of exposures. Sort of a base approach to how do you approach the exposure assessment more globally, relying less on the numerical data. Allows individual judgments to be used in the process, individual level reconstruction. We are certainly interested in intensity. This exposure modeling is going to be really of a lot of use. I would say exposure modeling taken in context with the actual measured data modeling, to me, provides a good initial starting point to be modulated or validated, if you will, by data that actually exists. Duration is going to be important, and I think Mary Wolf did a pretty good study looking at pregnant women at the time and trying to look at duration from diaries that were kept. Certainly, residential data is going to be key. I understand that's certainly a big part of what's being collected.

Looking through the semi-quantitative exposure approach that Mary uses, it provides a reasonable framework, at least, at that level. Questionnaires and activity logs provide

information with regard to time spent indoors and outdoors. Those two are quite different with regard to characteristics of exposure. These are geocoded into zones using available software. The dispersion models were within use to predict eight hour relative concentrations over some exposure zones that were created over calendar time. The data were then combined to arrive at an individual daily exposure index. It's an index, it's relative to each other. These are the zones that were used by Mary, and the number of different zip codes. This is probably a more useful approach for some of the assessments, as well. These are certainly different with regard to the magnitude of exposure.

I will show you the next slide. Zones one, two and three in the data were more to the east and southeast and had the higher exposure levels. I think that's also an important issue to consider. Also, one of the issues is with regard to prevailing winds - that's what they are, they are prevailing. This doesn't mean that things don't happen. This is an especially complex situation with regard to a city where you have all kinds of redirection of air, to not exclude possibility of exposure. Sort of in an upwind direction, if you will, relative to prevailing winds. Actually, there are some pretty good models that have modeled such effects within cities. Exposure assessment approaches, again, involve the geographical assignments with regard to zones and groups, I think how you tie those together and establish exposure zones would indicate a relative intensity. Your histories and activity logs, whatever is going to be collected, will allow the individuals to be placed into groups. As I said before, they are pretty good analytical tools, and they are just that, tools, not necessarily approaches.

This can be used to look at the data, to look at the variability which is important to look at within the groups and between the groups. The objective of exposure assessment is to put people into groups that are really homogenous with regard to their exposures; but to maximize, if you will, the differences between groups so that if there are health effects

related to exposure, it will be more likely to actually see them in your analysis of the data.

We always have exposure misclassification, no matter how hard you work. Even the best studies with actual exposure data still have misclassification of exposure. As we all know, it's usually random and hopefully random, which in most cases will not bias your effect, means you will not see an effect, not always, but most of the time. I think you want to avoid bias in exposure categorization, such as may occur with systematic misclassification into higher or lower intensity levels. With regard to the exposure assessment, evaluation of the effects of misclassification bias with simulations are useful so that as the data are put together and as we have the ability to test out the algorithms, we'll develop algorithms placing individuals into groups. And we will test the algorithms to see how well they really work. That ends my formal presentation. I will be glad to try to address questions.

DR. THORPE: Questions?

DR. BRACKBILL: Robert Brackbill, Founding Principal Investigator, World Trade Center Health Registry. My question is, I have always thought one approach might be to actually take the material in the building, in the buildings themselves, the glass, computers, all that sort of thing, and then try to work backwards to see what was available, especially during the dust cloud, during the collapse, and then I guess as the fire burned. Because for the early couple of days we don't know what the actual by-products of the fires were, what the actual composition of the dust was, really what the intensity was just by visual sort of historical measurement.

DR. DEMENT: That would be an interesting approach, I agree. Quantification of the amount of dust within residences could also be useful as an input variable to exposure

assessment algorithms. There are lots of factors that predict re-suspension and exposure to settled dusts. For example, routine cleaning activities are going to be important with regard to exposure. So, in addition to some quantification of the amount of settled dusts by location, questionnaires concerning the performance of activities that have the potential to re-suspend these dusts could be useful as inputs to qualitative exposure estimates. Additionally, these data could be used to help validate some of the dispersion models that are being used to predict exposures.

DR. MOLINE: Jacqueline Moline. One of the pollutants of interest to all of us, and there have been no measurements that I am aware of, you mentioned briefly but didn't specify, is benzene. I mention that particularly because there's certainly a lot of concern about hematologic malignancies. Benzene is the carcinogen that may have been present in many ways. I don't think we had PH measurements until September 22, anyway. That is something that may not have gone down with the fires. The toxins got washed away but the fires continued in various pockets until mid-December. So the question is, at some point there's going to be a question of how much benzene or other organics were there. And what are the modalities in terms of exposure assessment? What models exist? Or an important question to frame as we go forward is to just to think about the toxins which we can have models for and we know, and measurements at various parts of the City. We know what the air patterns were and things like that.

DR. DEMENT: Those are reasonable questions to address. With regard to the benzene, there was probably more than one source of benzene. Certainly the burning fires are a source. The PAH compounds and organic compounds from the burning fires are very complex exposures resulting from complex mixtures, and I would expect that benzene would be at least a component.Then you have the diesel equipment that moved in for rescue and clean-up and certainly benzene is a component of diesel emissions. It's going to be very difficult to quantify the actual exposure levels for individuals. Some benzene

exposure data are available from NIOSH and EPA, and these data support much higher than background benzene exposures for site personnel.

For qualitative exposure estimates, you will likely need to look for some surrogates. Surrogates that predict exposures include the time and intensity of the burning fires and proximity of individuals to the fires and smoke plume. These same variables are of interest for the diesel exposures. I don't know of another way to actually do much more than that. Benzene is not going to be present in settled dust to any great extent due to its volatility. If you look at the data Paul Lioy has published concerning the presence of semi-volatiles compounds in settled dusts, little benzene was present.

DR. MOLINE: Any characteristics of dispersion of benzene that one may want to take into account?

DR. DEMENT: You can use models for dispersion of gases or vapors. The characteristics of the compounds are used to predict dispersion, as well.

DR. MIRER: Frank Mirer, from Hunter College. I have just one comment on the presentation. All the air sampling data that you have included are collected by a standard method which deliberately excludes the large particle fraction. In many occupational environments, probably three-quarters of the mass that's up in the air is in this large particle fraction –which could be part of the inhalable fraction given the high levels present in the initial cloud of dust from the building collapses. Clearly, the dispersion around the city would have included a lot of large particles which were never measured either by OSHA or by EPA. So that has to be taken into account both from an exposure assessment point of view, but also from trying to look at human health effects and whether there are systemic health effects from this large particle deposition in the upper airway. Which by the way, we all experience every day when you start sneezing and your

nose starts to run - all the other systemic effects we experience ourselves are coming from that large particle fraction.

DR. DEMENT: This has truly never been mentioned because the PM-10 doesn't go there either. PM-10 are still, relative to the particles you're discussing, small. Really there has not been a process for looking at that as a system. There are some PM-10 data, but much spottier than PM2.5, as I understand it.

DR. STAYNER: Leslie Stayner, University of Illinois, Chicago. I have two questions. One, is it a presumption that the rescue workers were wearing respirators and could that possibly have protected them more than some of the residents in the area? And the other question is, I wonder if we can assess overall exposure - high versus low - or is there really a hope of doing speciation where you can say in answer to the earlier question, this is a high benzene exposure or high asbestos exposure? It seems like it's all going to be highly correlated and very difficult to separate.

DR. DEMENT: I agree with you, Leslie. I think separation is going to be very difficult, at least in a quantitative way. With regard to the assessments that rescue workers and clean-up workers had high exposure, I think you have to take into account use of respiratory protection. My experience regarding respiratory protection in an environment such as this, you take very little into account because it's typically not as effective as you think it is with regard to the actual protection factor achieved. I think it's important to at least take into account the factor of having a respirator present. We all remember those early days when nobody had a respirator, or very few did. So some of those early exposures were certainly horrendous. And horrendous with regard to what Frank pointed out, too. Large particles. There was upper airway deposition. We don't actually know what the systemic effects are. We know those provoke airway responses but we don't

know what the systemic effects are. A lot of those would have been swallowed. Yet another exposure.

DR. HOWARD: I have a question. Dust cloud exposure. We wanted to find temporal and special patterns, but dusts have to be two categories. I think it was the Wolf paper that had the figure where they defined heavy dust and degrees of exposure, I think, 300 feet north of Zone Two.

DR. DEMENT: I think that's right.

DR. MOLINE: So from the area that would be somewhere between Reade and Duane, the people who were south of that location say, what would you say, up until eleven o'clock on the morning of 9/11/01 with the people who had that exposure? I remember at an EPA panel meeting Dr. Grayson explained to us, on the question of larger particles, in that kind of very intense exposure, those larger particles would get past the normal protections and would deposit in the lower airways. So are those people, that category of dust cloud exposure, significantly different from the people who may have been somewhat north of there or within the next five hours? And when people are looking at health effects, could that be a completely different disease process?

DR. DEMENT: These are all great questions and issues to discuss. I think a couple of comments with regard to these artificial boundaries - they are that, they are artificial boundaries. We know there's going to be a gradient with regard to levels, if you will, and characteristics, as well, of the dust - relative proportion of coarse versus fine particles. The fact that you have organics and particles mixed together, you have a great vehicle, if you will, for taking the organics deeper into the lung based on the fact they are attached to particles. It's a very complex situation. I think the ability to take that complexity into account is largely data driven in what we have, we can ask individuals with regard to

their own experience. We have to find ways of placing individuals for these studies at least into some relative categories, realizing there always is going to be some misclassification. Just because I lived one block above the dividing line for a zone that says I was on the low exposure or high exposure category doesn't mean that's true for me, individually. So the objective is to look collectively at groups realizing there's always going to be some misclassification in there. You try to minimize that as much as you can. But there's no way to avoid some.

DR. THORPE: What I'd like to do now is thank Dr. Dement who came from Duke University for this presentation. We have a brief break. We can still use this break to discuss. But for those who would like to get some coffee, water, refreshments, perhaps we can have a more informal continued discussion.

VOICE: To ask the question this way, we can try to assess the exposure of members of the cohort, or we can try to select members of the cohort based on their exposure. So if you use Mary Wolf's five region exposure assessment from high to essentially little, the question now would be, do we have sufficient members in the cohort from each of those exposures? Because if we don't, we are going to have trouble both with the cohort analysis, the case control analysis, and assessment case analysis. If you can comment and pass it back to the experts. It's an interesting question you raise, what is the practical question you're trying to answer? Are you trying to answer what is the health outcome of this range of individuals, X years after the event? Or are you trying to say, what are the exposures of individuals who are sick? What exposures made people sick or what happened to people exposed. They are very simple questions with the methodology entirely different depending what you're asking.

DR. DEMENT: I think it's an excellent point, unless your populations, which we have, are big enough that you're not going to see what you're trying to see. Which really points

to, I think, the importance of exposure assessment working hand in hand with the studies themselves to make sure that doesn't happen, and we do in fact have that contrast of exposures.

DR. PREZANT: Thanks very much for the presentation. Certainly many of us appreciate the difficulty in distinguishing clearly with confidence the variety of exposure populations. I think clearly what's going to happen, clearly a concern, is that the difficulty in establishing exposure populations means that we have to place an increased reliance on medical surveillance over time. And that will become both a technical and political issue.

DR. THORPE: Good point. For example, the Occupational Lung Disease Registry in New York State. We all know there's under-reporting of occupational lung diseases even before an event like 9/11. How do we try to enhance the reporting of these conditions so that they can be looked at more systematically?

DR GILLIO: Dr. Rob Gillio, pulmonologist, Lancaster, Pennsylvania. I was a volunteer in the early days with the NYPD. Looking at this time-wise, were they there when the building fell? Were they there within the first six hours? Were they there within the next 24? The next week? Or the next month? Were they inside of Zone One? Also looking at what activity, digging in the dust versus working at the perimeter fence being a guard? I encourage us to think in terms of multi-variable analysis with registrants thinking of time, location and activities. And when you are talking about time, the duration of time. From my experience - I observed and participated with people when they finally had masks - people did not know how to wear them. Especially the NYPD had no previous training or clue about using respirators. They wore them loosely, probably creating a higher velocity of air pulling things deeper into their lungs.

DR. DEMENT: I think what you point out is at least some of the issues with regard to exposure assessment. Certainly, within each of these zones, if you want to call them, we can construct it any way we wish, but within each of those, certainly time and task and duration, those are going to be key predictors. I think you're right. Ultimately, it's a complex exposure. You have to have a multi-variable modeling approach, more or less, to take those into account. Again, with the idea of placing people into relative groups. I think as far as the medical surveillance, that's going to be an important ongoing issue. Exposure assessment is never going to be a tool to say that individuals should not be part of a medical surveillance program. There's actually a lot to be learned down the road from the outcomes of that if we analyze the data in an aggregate way and place those individuals within sort of exposure categories themselves. That, too, forms how we categorize individuals.

DR. THORPE: I think we have more confirmed information about cancers that have been diagnosed because of the stringent laws with respect to reporting. It is more difficult with respiratory disease, even more difficult further when you are talking about mental health conditions. Dave?

DR. PREZANT: Very nice presentation. How can I say this respectfully to not just you but all the scientists in the audience, all the people that are concerned about this and we all are. I think at some point in time we have to really move past the concept of a perfect scientific exposure analysis. I think we are searching for that to be able to validate the diseases. Because clearly what we learned in occupational environmental medicine is that if there's a dose response gradient you have in a large sense validated the disease process. I think we have already done that for many of the diseases in question. I think we have done that based on the arrival time exposure and have found statistically significant correlations with a variety of mental health and respiratory outcomes. FDNY used it, others used it (WTC Health Registry, Mt. Sinai, etc.) and have also found

significant correlations. I think that we need to understand, as you have said and as other people have said, all of the faults in a World Trade Center exposure analysis. The fact that cumulative data was not properly taken by any of the employers down there. The fact that diaries are frequently inaccurate. The fact that exposure variability even as short distances from the WTC ground zero site are hard to analyze based on the multiplicative exposures that were there. Obviously, the sedimentation of large particles is completely different than the small particles. The same even more true for gases which are diluted so rapidly in the air. All of those things provide for problems and would force an extremely complicated and controversial weighted data analysis.

We need to remember three things. First, really, it's going to be diseases way above the background incidence that determines causal relationships. Number two, the fact that we need to realize all of the faults as I have just detailed, but also understand that these faults are not unique to the World Trade Center. Politicians and other people should not be saying to us, you don't have a perfect exposure index, therefore not relevant. Because in even single exposures such as asbestos, there are all sorts of variables, and they are only dealing with a single element. And thirdly, what I don't see being done is, and Paul Lioy and I wrote an article about this - but it will take a lifetime to achieve any change - what I don't see being done is the fact that we have learned from the World Trade Center more so than any other exposure, that these exposure - disease models often don't work, that they are hard to figure out. And we need for the next disaster, which is surely going to come, we need to institute changes so that we are not in this situation again. We need to get the EPA to measure things that are much larger in size than PM2.5 and PM10. We need to have volatile compounds measured, as well. And we need to have strict site control whether with barcoding or whatever mechanism, we are electronically measuring worker location and times of exposure, which is a very simple thing to do in this current use of technology and will become simpler and cheaper as time goes on. And then we need to take that information and limit worker exposure.

DR. THORPE: I think most organizations that are doing these cancer and mortality assessments are doing exactly that, moving into “let's proactively work on identification as soon as possible to help outcomes.” The question of exposure assessment, as imperfect as it is, I believe we have two options we want to veer away from. One option is to be stagnated in the effort to try to find a perfect assessment. I think that's very clear. That's productive to no one. The other is to say we have what we have, let's just keep it, use the same methods or same measuring bar and not have this ongoing dialogue. The better we can fine-tune the work we are publishing, fine-tune the information that's being disseminated, maybe the earlier we can identify the health outcomes that are associated. So really a good point, and I think today's discussion will help us know this is an ongoing process of inquiry.

DR. MASLOW: Carey Maslow, with the Registry, and I am part of the team that's doing a study of respiratory effects among the area residents and the building workers. One of the things that we are grappling with, to say the least, struggling with, tearing our hair out, is how is this matter of the exposure assessment, which I realize will never be perfect, but we do have an opportunity to interview people in depth. We are getting input from the community members. But what to ask them about not just levels of measurements of dust and particles, but behaviors, activities of daily living. In addition to time spent indoors and outdoors and getting diaries which are notoriously, as somebody said, imperfect, what are the questions to ask? I have searched the literature and found lots of suggestions but I was wondering if you can point me in the right direction for ways to measure individual levels of exposure which I think have drastically given the same levels of dust, et cetera.

DR. DEMENT: No one said the assessment was a science. You're asking questions and just wearing the hat of an industrial hygienist. The exposures of concern indoors are

certainly driven by the presence of re-suspendible material, so the dust is important. Largely task oriented. There are few studies that have looked at tasks. In part, one of the issues has been studying asbestos indoors and what happens when you do things like dust and vacuum and cleaning, those things that re-suspend dust. So there is some guidance that is out there, as to the questions you might put on the questionnaire.

DR. THORPE: The next session focuses specifically on mortality, and we'll be having three presentations, then breakout sessions for each group. Jim Cone will walk us through the process for breakout sessions.

DR. CONE: We look forward to your input. We are certainly at the beginning of the process, we expect to go on for another 15 years probably, understanding at least the beginnings of the longer term health effects of this exposure. Today, I want to give a little background for those of you who are new to the World Trade Center Health Registry. For those of you new to the Registry, I will briefly review what the Registry was set up to do. We all realize when we talk about exposure, exposure is very complex in the sense that it not only includes physical exposure but also circumstances that caused physical injury. Witnessing traumatic events may have been the most severe exposure, in terms of mental health. Dust and smoke we have talked about. And other exposures less appreciated are indoor and outdoor dusts that have plagued lower Manhattan since the event. The World Trade Center Health Registry itself was conceived shortly after September 11 by some of the people in this room. We were launched in 2002 beginning with funding from federal Agency for Toxic Substances and Disease Registry (ATSDR), Federal Emergency Management Agency (FEMA), and other agencies that came offering New York City assistance in developing something that was going to be groundbreaking. We realize this is a difficult undertaking. We became the largest effort so far in the U.S. to try to track health effects of a single event. We reached 71,473 persons who all spent at least a half hour talking to us either on the phone or in personal interviews. We then

most recently in the last six months have received augmented funding, that allows both the study that Carey Maslow and Steve Freidman are leading, looking in depth at respiratory effects, but also to look at the chronic health effects, cancer and mortality. Part of the reason for today's workshop is to kick off that new initiative that was funded through the Mayor's World Trade Center Initiative.

The Registry, itself, we think of as mainly a platform for exposure assessment and outcome assessment. It's a surveillance system involving surveys every two to three years, or in the case of the current follow-up survey, a Web based, paper or phone interview survey. We'll be doing sub-studies - we have already had at least five academic centers and others working with the Registry to develop various studies that will look at subsets of survivors. Robyn Gershon did a major study looking at the health effects and exposure of those who actually escaped the towers themselves.

Also, responding to mental health needs, we're doing more in depth analysis of the baseline survey looking at mental health outcomes. In addition, in a lot of ways, we are interacting with the community. I think one of the strengths of the Registry is the Advisory Committee system that's been formed. The Community Advisory Committee and labor advisors who have helped us are both critical for what we are doing, keeping us aware of what the community issues are. Cancer and mortality certainly are uppermost in the community's mind about what are the potential outcomes of this disaster, and the Registry is one of the ways that hopefully can be used to answer some of the questions that are being asked.

Eligibility groups we have alluded to but haven't really specified include the largest group, which was building occupants and passersby, people in the area of the collapse on 9/11. The next largest group is rescue, recovery and clean-up workers, not just in Manhattan but in Staten Island and on the barges any time between September 11th and

June 30th, 2002. Then another big group is the residents south of Canal Street on 9/11. Originally, the Registry intended to restrict the population to the group below Canal Street, thinking that was the highest exposed group, but things never being quite the way you intend them, 1,000 persons actually enrolled who lived north of Canal Street, as they shared residence zip codes that straddled Canal Street. So this has some importance in terms of being able to look beyond the arbitrary boundaries we set up for the Registry. Finally, the Registry includes groups of children and school teachers who worked below Canal Street. We think the children, of course, being among the more vulnerable populations, are an important part of Registry.

In terms of coverage, we estimated totals here, in which there is again a certain amount of art. We estimated there were about 360,000 passersby and building occupants, and the Registry enrolled 43,000, or 12 percent. We estimated about 91,000 rescue and recovery clean-up workers, of whom we recruited about 30,000. And then regarding residents, we estimated 57,000, with about 14,600 in the Registry, or about 25 percent. And finally, for school children we estimated 15,000, with 2,600 in the Registry. You can see the populations we have currently in the Registry represent different proportions of the exposed population. But it is a diverse Registry, and it is unique in that sense. It includes people from many different parts of the exposed population. Is it representative? I think that's a question that always remained with the Registry and will be something we'll have to address in future studies. In terms of the concern, we have seen the press has been very active in asking questions. Is there evidence of mortality caused by the World Trade Center exposure?

Here is an article recently in the Village Voice recounting an individual case that then triggered questions that became scientific questions, as well as personal and political questions to the politicians. How do we deal with this kind of issue? One research question that the Registry is attempting to address - is there an excess of overall or cause

specific mortality among our registrants in the Registry? If so, are those exposures that John has described actually risk factors for those excesses, if we do see an excess? If it is World Trade Center related, is there a dose response or response relationship between those exposures and outcomes? If we can identify other risk factors that might contribute to that, maybe there are biases that make that relationship not as truly causal. Lots of things have happened since 2001. There are other factors like smoking that maybe we can do something about. That's the other important aspect of the Registry: Are there some prevention steps that we can take now to prevent future deaths?

Next: What are the mortality research questions? Our goal is to set up a mechanism that is scientifically valid and politically viable to track mortality over the next 15, 20 years - at least through that period when we expect or begin to see potentially longer-term health effects. Exposures of concern: I will quickly pass by this. We talked about it fairly extensively. Witnessing events, we think, is a major exposure we are concerned about. It certainly has already showed up most with depression and anxiety and may be a potential risk factor for suicide. We heard reports from Pat Bahnken and other labor advisors that, certainly, cases of suicide are being reported among first responders and others that may be related to the events. Proposed methods: we are proposing a prospective cohort mortality study. Exposure assessment for these studies will be based on our baseline survey, as well as the follow-up survey which we are now in the middle of conducting. We have received now over 32,000 responses to our follow-up survey. We are aiming for an 80 percent response rate among our participants. We are planning to match World Trade Center Health Registry data with the New York City Vital Records. Actually, the first match is happening this week.

We are also planning to match the national death index with our registrants, since 40 percent of our registrants live outside of New York City in all 50 states, Europe, and

other parts of the world. So we are facing a major challenge to track all those people wherever they may move over the next 20 years.

Also, we have addressed how to match against other state vital records and sources,. and Social Security Administration is another potential source. Once we have a mortality tracking system in place, the Registry will continue to do that over the next 20 years - we plan to calculate directly standardized mortality rates and compare those rates over time. We'll then look for excess or deficit mortality rates adjusting for age, gender and ethnicity or race. We'll look for potentially statistically significant increases in those rates and develop survival curves. One of the ways to look at force of mortality, as well as the newer methods, is Cox proportional hazards regression, extending traditional analysis of mortality and looking at multivariable adjustment for that force of mortality. Relying on some of our expert consultants: Bill Halperin has been very helpful, and Leslie Stayner, very helpful in the initial stages of crafting our methods for this analysis.

How frequently will we be able to analyze this? Well, we have been told it is probably not worth doing it more frequently than about every two years. We may at various points need to do it more frequently. I expect every two years we'll be able to do this kind of matching and confirmation of the match. We'll then use the person-years at-risk Life Table Analysis System NIOSH has developed and Mary Schubauer-Berigan will speak at length shortly about that system. We'll then get to compare. That's one of the questions we are going to be asking you and others, how do we really, what populations do we use to best compare the experience of the Registry? For example, in the ‘residents’ portion of the Registry, we can compare the observed rates to the the New York City population. Should we use a subset of the New York City population? For example, we know most of the residents are still residents of lower Manhattan. Should we look at more subsets of comparison populations? For workers who were rescue and recovery workers or commuting in from other states, for example, New Jersey and Connecticut, we can't

really use the New York City population. So what population should we use for those comparisons? Regional population? Or should we use the United States population since most of the data available is at the more national level?

We will actually get the most complete death certificate data from the Vital Statistics match. Unfortunately, the National Death Index provides only a subset of the information available on individual death certificates, so our analyses would be limited to a certain extent unless we get the death certificates from each state where the registrant died. We will then be able to fill in some of the additional data. It's not currently available in a computerized summarized form. We'll get an output that will give cause of death. We'll have the observed and expected, and ratio and result of statistical measures of that rate in a table, mostly developed in the Life Table Analysis System.

We will also use geo-spatial analysis technique, particularly for the residents, looking at the possible effects of living or being near a particular part of lower Manhattan. We'll be able to use mapping then to see if there are observed geo-spatial effects. Then we will do follow-up studies of the most important outcomes. We will do case-control studies looking at specific causes of death to see if there are detectable risk factors.

Issues at the breakout session following this I'd like you to address are listed in your handouts, and I won't go through them in detail, but we look forward to your answers, hopefully giving us some guidance as we approach this next phase. Each of you has experiences that may help us in this process. We have invited you here to give us some of your best wisdom as to things to avoid and mention what we should definitely do in this process of developing what we hope will be a state of the art mortality and cancer assessment. We really recognize this as a challenge. This is one of the more difficult things in terms of also explaining to the public what the methods are. What are the outcomes and how do we explain those methods and outcomes in a way that the public

and press, particularly, will be able to understand and hopefully work with us as we work through this period for the next 15 to 20 years?

As Mayor Bloomberg has said, "What is unclear and can't yet be possibly known are those illnesses that may appear in the future. But that's not going to stop us from caring for those who are sick today and building the capacity to identify and respond to those illnesses that may reveal themselves tomorrow. We are not about to abandon the men and women who helped lift our city back onto its feet during our time of greatest need. They will deserve first-class care without exception, and we will work to ensure that they get it." We have to make sure people are being taken care of properly. That's the challenge the Health Department has to face - giving the best care. Thank you very much.

DR. THORPE: We'll have our next speaker.

DR. SCHUBAUER-BERIGAN: First, I wanted to thank Jim and the rest of the people at the New York City Department of Health for inviting me to speak with you today. My name is Mary Schubauer-Berigan. I am a research epidemiologist at NIOSH in Cincinnati. I am here representing a large group of people developing the new NIOSH Life Table Analysis System which we call will LTAS.NET. I hope as we go along I will be able to think about all the things that Jim mentioned that I wanted to comment on regarding the utility of the system for the study that you're doing. As background, we developed a Life Table analysis program to answer the very basic question that Jim asked. In any given cohort or study group, is there evidence that the mortality rate or cancer incidence rate observed in that group is greater than what one would expect compared to the general population, or in comparing people who received higher exposures with those who received lower exposures?

To answer that question really requires pretty specialized software which I will talk about now. So in these analyses you do what's called stratification. Initially, the basic unit of analysis is not the person but it's the person-time that they contribute to the study. So in these analyses, person-time and observed events, either incidence of cancer or deaths, are apportioned into strata or groups. These strata are defined by a number of characteristics that I'll define in a little bit. Then, one calculates the standardized event rates; for example, standardized mortality rates or ratios are calculated among the strata to produce a standardized ratio comparing the group of interest to the population or another group within the cohort. And the standardization variables that we use include data that are available at the population level. That set of variables is fairly minimal with respect to age, sex, race and ethnicity and calendar period. NIOSH has been in the business of developing software to do these analysis since the 1970s.

We found there was no commercially available product that would serve the needs of occupational cohort studies. This is just a list of fairly recent studies that have used the NIOSH Life Table Analysis System for the personal computer, a DOS based program we are trying to move away from as we develop this program. It's a pretty wide range of exposures. Often the outcome of interest is cancer. That's not always the case, however - there are many, many other examples of studies that have used the Life Table system. Well, how does the program work? Just stepping through the process, I had hoped I'd be able to give you a computer demonstration of it. Unfortunately, my computer won't speak to the projectors. If you'd like to see a demo at a break or lunch, I will show anyone who is interested exactly how it works.

One question that was mentioned was, when do we begin follow- up for the people in the Registry? In a typical occupational study, a worker enters the cohort when she begins being followed up or comes under observation. Usually, that's the date they begin employment. In our studies, the worker is then followed through time using many of the

same research Jim mentioned. That index, Social Security, databases through time until his or her death or the end of the study. The Life Table software stratifies, that means assigns into groupings, all the follow-up time for each worker based on the categories I mentioned. Then each observed death is assigned to the stratum in which it occurred. So each stratum has a number of person-years and a number of deaths. Then you calculate the expected number of deaths from that stratum by multiplying the person-years by the comparison rate for that stratum, which you derive from the general population.

The analysis consists of standardized mortality ratios which compare observed to expected in the general population, or a standardized rate ratio based on internal comparisons of workers highly exposed with those who are not. There's another method that can be used with the Life Table system. This is called proportional mortality analysis. This is a study group consisting of death certain collections. Since that's not really relevant for today, I won't spend that much time on it. I have included that in your notes if you want to read about it. What are some of the new features of the Life Table program? We were relying on a pretty old DOS program. Those of you who used DOS programs in the modern world have found they are not user friendly and tend to suffer from computer-related issues. So we are trying to move to a more flexible and reliable platform.

We also have implemented a number of features that we think are advances for Life Table software. In addition to the typical standardized variables or stratifying variables, each user is allowed to use any number of user time or time dependent covariates that can also be stratified on. You can also include global dates that you think might have affected everyone in the cohort. For example, in the radiation world, if you know that a new method was instituted in the 1970s that results in improved dosimetry you can enter that date and apply a new cut point at that date and time. If there's something occurring in the future that you think would have an effect on everyone in the study you can define

a global date. Another feature that may be important for your study is the fact that there's been a lot of attention in the epidemiologic literature about something called the healthy worker survivor effect. This generally results in the observation that a worker who worked very long periods of time tends to be healthier than those working shorter periods of time.

We have included a variable called active and inactive status. That allows you to stratify on whether the worker was actively employed at the time or was not. We also have included the capability to analyze more than one exposure simultaneously. And I think for your analysis this would be very important. If you'd like to conduct a more complex analysis not possible in the LTAS program, the program allows you to export the stratified data for further analysis. I certainly won't bore you with statistics at the meeting today, but I wanted to include the details for those who are interested. You could look at those at your leisure. I do want to mention the standardized mortality ratio, SMR, is an indirectly standardized, not directly standardized ratio. I also have an example of the standardized rate ratio - a statistical calculation of two set of rates, one for highly exposed, one for less exposed people in the study. An uncertainty is inserted via intervals based on Poisson distribution of the event.

So with the detailed computer features of the program, it is a platform that works well in Microsoft. Those of you have who are MAC users may be out of luck. We haven't tested it with MACs. I would be interested in hearing feedback if it works or how well it works. We have allowed for the flexible import and export of data and reports using different types of computer files. And we have extensively tested the system for use on a variety of different PC platforms. One we haven't yet incorporated is Windows Vista. So I anticipate we'll get to that as soon as we get Vista and can actually test it. The version that we have created is much more flexible and interactive, and I think user friendly and provides lots more options than previous versions had. We have incorporated a lot of self

documentation and on-line help systems. There's a very detailed users manual that describes all of the statistical and other calculations in great detail.

And very importantly, this product is freely available to the public health community. We have been keeping track of the number of users of the PC version of the Life Table. Right now we have over 500 registered users, more than half come from countries outside the US. Right now the software is in the final stages of development, and I have got a list of various things that we have completed here that, again, you can read at your leisure later. We have a few things left to do. We are in the process of writing this into a manuscript describing the new features. We are getting ready and close to rolling out the program to NIOSH and external partners. This will be happening later this spring and early summer. Then we'll communicate with the entire LTAS user community group through e-mail and website and probably in the NIOSH e-news. It will be available for download from the website linkages you see here.

As with any software program, we expect we'll have to maintain the system. So we plan to continue that as well as to add new features, many of which have been selected by our users. So those of you who use life-time systems, we greatly appreciate your comments on it. Again, as I said, I hoped to have an on-line live demo, but my computer wouldn't hookup to the projector. So instead I will step you through the wizards for importing your data, just to show you what the feel of the program is and what you can do with it. The very first thing you do is to import your data. You describe your study. Select the reference rates you'd like to use for the study. At the moment, we have just the US death rates. You see that each rate is preceded by a number. In this case it's 92. That refers to the number of categories that you can use for your outcome data. So all the ICD codes have been grouped into just 92 categories for analysis. You also define when your study begins and when your study ends, and here is where you specify if there's a global date you'd like to use.

The system is very flexible with importing of files. There are three different files that need to be imported. The person-time contains demographic information in your study. The outcome file is about deaths and cancer incidence. The history file is important where you include information from the job exposure matrix or whatever exposure information you have been able to develop. You can tell the program very flexibly when you want to begin time at-risk. Generally, you want to consider their first exposure date or when the person began follow-up if their exposure didn't begin on that date. You can also choose to end the accumulation of risk either as date last observed, if you know you have lost them to follow-up, or at the end of the study if they are presumed to be alive.

You can choose - it's very flexible, the way you code the data, if you're using mortality data you can choose to use the ICD in effect at the time of death. You can have a global ICD code that applies to all deaths or individually indicate in your outcome file which ICD revision should apply. And your history file allows you here to specify all of your time dependent variables - any type of factor, like smoking history - that do not have to be related to the main exposure of interest. But, basically, this list is what determines what is in that file. I will hopefully show you an example of that. For each of these variables, you can choose to look at the level of exposure. So in this example, we are looking at GAMMA radiation in a cohort of nuclear workers. We wanted to look at the level, we had a fairly precise level of exposure. If you don't have that, you might want to look at duration of exposure time since first exposure or time since last exposure. Or you can look at “status” to look at active or inactive periods of employment.

And here is the beginning of the stratification wizard, so you would pick this from the pull down menu, you can barely read it. In stratified data, when you select that, this screen comes up and asks you which of the things you'd like to stratify on. You wouldn't be able to deselect gender, race, age and calendar period. Those are default stratifiers.

But you can choose to stratify on any of the variables you have selected in that input step. Then you develop categories. In this instance, we were looking at gamma exposure. We knew the units, that's in the box. I don't have a pointer, it says, “threshold values represented”, that's the unit of exposure. Underneath the category label you can specify what the categories represent, and then cut points that will be applied to the stratified X data. This is time since first exposure. Frequently, you want to look at this because cancers have a latency period. Along with looking at times since first exposure, you can also use what we call “exposure lagging” - exposure in which you consider that the most recent exposures a person received aren't contributing very much information to the risk that they are experiencing right now because we know cancer has a fairly long latency - most cancers do anyway.

One of the outdated features of this slide is it doesn't show the lagging adjustment. There's an extra step in the wizard that allows you to specify the lag period for each of your exposures. Then we are ready to analyze the data once you stratified it. You can choose to look at the distribution of person-years as a first step. Then standardized mortality ratio and observed and expected deaths for each stratum. Then choose to look at internally adjusted standardized rate ratio comparing workers with higher exposures to those with lower exposures. This is where you select, once you have picked which stratifiers you're interested in analyzing, you can then choose the levels that you're interested in reporting on. You can choose to look at only males or only females, or only certain age groups or calendar periods. You can choose from all 92 causes of death. If you want to look at every single one, which I don't recommend because the report takes quite a while to produce, you can check this button that says “causes”. Or you can go in individually and select individual outcomes that are of interest.

We have a large number of groups for cancers, obviously, as well as for other diseases like nonmalignant respiratory diseases which I am sure would be of great interest to this

group. Then you can customize the report. Here I wanted to look at the standardized rate ratio comparing workers with high gamma exposures to those with low exposures, and I wanted to look at age on the other axis so I could see if there were differences in the relationship for workers within different age groups. That's where you would specify this. I have some examples, again my flash drive couldn't be read on this computer so I am having all kinds of difficulties with computer linkages. I have examples of the reports I can show you. I would encourage any of you who are interested to contact me to get a copy of the software. At the moment we are in Beta testing, we're expecting to produce our release in the next couple of months. I'd be happy to address any questions people have about the software or as you think about what the needs of the Registry data are. Questions will arise.

DR. THORPE: I think we are going to move to our next presenter. We have saved time. Kitty Gelberg.

MS. GELBERG: I'd like to introduce Nakeshia Knight-Coyle, also working on the study. So any questions that you have can be addressed to either of us about this study. I think it's important to point out that this is a cooperative agreement with NIOSH, and we are really in our infancy with this study. We tried to hit the ground running and moving as quickly as possible, but this really got off the ground in December 2006. The point of this is actually it's not a study. It's a program, a surveillance system. The idea is to collect information of fatalities that have occurred among responder workers and volunteers at the World Trade Center. We are trying to take a systematic approach to collecting information on the fatalities. This is hypothesis generating. Hopefully this study will be running about two to three years. The information will generate where we should go with the case-control studies and other types of research that are being conducted.

Also, the plan is that if we are finding any clusters or problems we can get that to the medical community for issues and protocol changes. So our case definition is anyone who volunteered, worked or responded at the World Trade Center, at the pile, as defined by the World Trade Center Health Registry, on the barges or at the Staten Island landfill, putting in at least one shift - that's probably up to interpretation how that can be defined - anytime from September 11 to June 30, 2002, and they died, not during the exposure or the actual problems at the World Trade Center, but basically starting September 12 and following forward. I am calling this community-based surveillance because we are trying to collect information from a variety of sources. We are collecting information from anybody or anything that will tell you about a death which occurred. This represents unique challenges as far as surveillance goes.

We are working with all the WTC health programs that are out there, and I appreciate all the cooperation and being invited to speak today. I think Dr. Cone pointed out on one of the sheets in your packet the issue of legal and ethical issues associated with sharing the data between our programs. This is really huge, and we are trying to work on this. And we are getting great cooperation, but it's definitely time-consuming to do this. So we are working with these programs. We are also working with unions and other groups, with the firefighters, EMS, police, construction community, medical examiners, funeral directors, government agencies, 9/11 support organizations, attorneys, and volunteer organizations. I don't have the media up here or politicians - all of them we are reaching out to and that's what Nakeshia is basically doing - trying to get into these groups as much as we possibly can, and get information to share with their people. And when we contact their members who might have had a death of a family member they are willing to cooperate with us also. So what we are collecting once we identify a death is a death certificate on each person with all causes of death; autopsy records, if they have been conducted, including toxicological records; medical records for the condition they died from, along with underlying causes back to 1999; World Trade Center exposure history;

and occupational exposure history. Not only what they were doing at World Trade Center, but what were their other jobs, other potential exposures.

What we are doing with this information is not statistical. These are really case summaries. It's following another program that we have in the New York State Department of Health which is our FACE program. This is the "Fatality Assessment and Control Evaluation Program", where we describe each occupational fatality. We go out and investigate circumstances around each death. These summaries for the WTC-exposed fatalities will be shorter but the idea is that each death will have a summary with demographics, age, sex, date of death, employment information both at World Trade Center and normal employment information. The World Trade Center exposure would include when they were there, what they were doing while they were there, if they were caught in the cloud and if we can get information on what respiratory protection may have been worn. We will also collect the cause of death, including underlying causes and any significant findings from an autopsy.

Also, any past medical history prior to 9/11 and subsequent to 9/11. Smoking, alcohol history. And also one of the questions is do the people participate in the other World Trade Center programs? Some of the deaths that have been identified were not included in any of these other programs. We are looking at ourselves as sort of universal data collection with the idea that we collect the information on the deaths and share it with all the other programs out there to help populate the fields with the different programs. So everybody wants results. These results don't really say very much at the moment, but I know everybody wants them. Numbers are changing daily. I think I wrote these slides on Tuesday or Wednesday. We are up to 50 cases at the New York State Health Department.

A few months ago, Dr. Cone shared that the WTC Health Registry has counted 116 deaths among rescue and recovery workers, that's probably higher. Two other groups identified 39 deaths and 62 deaths. Just a matter of time until we can figure out ways to collect this information. So the information on the 47 deaths is very preliminary, we don't have death certificates. The cause of death is what we have been told, not necessarily what's on the death certificate. We do have 11 traumatic injuries, seven of which are suicides. We have 35 illnesses, 18 of them are cancers of various types: Nine respiratory, five cardiovascular disease and a number of unknown, where we have just been given the name, this person died on this date, and we haven't gotten any further information up until now. The data that we have is very biased right now because of the sources who are giving it to us. So it's very heavily weighted towards one group that gave me their data, and, therefore, I am not going into the occupation of these people, because it's reflective of who is sharing the data with us. The one thing I left out - we are only collecting deaths in the United States as we haven't figured out a mechanism for collecting outside of the United States, but they are occurring everywhere throughout the country right now.

We are stuck with sort of a logistical nightmare of having to go through an IRB to collect the death certificates from each locale, which is one of the reasons we don't have them at the moment, and we are still working on this. If you have any questions definitely feel free to contact me. We have information. If you have information, you can send it on this website, WTCfatality@health.state.ny.us. You can call us also.

DR. CALLE: Eugenia Calle, American Cancer Society. Jim, I wanted to ask, I am not sure if I understand entirely but in your presentation it seemed like the group that you'd be following for all-cause mortality and cancer incidence were those folks living south of Canal Street, close to 15,000 who had registered in the Registry. I wonder, for that group of 57,000 residents, for the two outcomes of death and cancer incidence, why not include

all of those folks? Because you certainly can do linkages by address. You won't have all the other information you have collected but you will have a much larger residential population that potentially has been exposed.

DR CONE: Good suggestion. Something we wish we had was the complete population. Definitely, if we have that ability to use the entire population of Lower Manhattan as of 9/11/01 through 6/30/02 that would be ideal.

DR. CALLE: You cannot do it for respiratory events, but you can do it for cancer incidents.

DR. THORPE: One interesting note to point out about the New York City population - if you have done research here, you know it's a highly mobile population. We have a lot of migration in, a lot of migration out. Lots of migration around the city. So a person's address at diagnosis and a person's address at death does not necessarily equate to their exposure or address on 9/11. That's a challenge. One of the first things one would do is what we call an ecologic study where we look at cancer rates by a region without really having a link that those individuals were exposed. So that's an ecologic geographic assessment.

DR BRACKBILL: My question is, actually, I was struck by talking about the Life Table Analysis System program that the start of follow-up was the start of employment. I guess when you talk about the cohorts for the Registry you start follow up on September 11, except I am thinking that most of these people working had exposures in their occupation prior to September 11 and all those exposures contribute to any outcomes you look at. I don't have an answer to that question. I am sort of curious how you can handle that.

DR. SCHUBAUER-BERIGAN: You really need to begin following up on the date the person came into the observation, in the study. I would strongly advocate having follow-up date be the date of entrance into the Registry. The reason for that is that people who were ineligible for the Registry won't have made it in, won't be observed. So that can lead to a bias in your standardized mortality also if you don't account for that. However, that said, you can certainly account for exposures received previously by people in your cohort. There's no barrier whatsoever to do that in the Life Table software. If someone comes in with exposure that you want to account for you can certainly do that. But the date that you actually start counting their person-years should be the date that they came under observation. And for worker studies, it's generally the date they began employment in the industry of interest.

DR. BRACKBILL: I loved your presentation on the Life Table analysis. Does it only look at mortality comparisons or also can it be adapted? Since you're loading in all these ICD codes, if you loaded in incidence and prevalence studies for diseases we could get a lot more use out of this.

DR. SCHUBAUER-BERIGAN: You need to have accurate data on your defined population. That's fairly well established for mortality statistics, not only at the US level but we have rate files containing that data at the state level and county level. It may be possible. The program is extremely flexible with respect to the rates that are used for comparison. One can derive their own rates for diseases of interest, outcomes or populations of interest. But you need to have a well defined denominator for that population. So if you want a city rate for New York, it is equivalent to county rates combined. You can use different permutations for county rates. We can make rates that put that information together. The only non-mortality outcome data we have rates for are the Surveillance Epidemiology and End Results (SEER) cancer data. The rate statistics

are well defined within the SEER population, we know we can produce a rate. That's the quality of data to develop.

DR. THORPE: This gets back to the question, we have clear data on mortality, 100 percent reporting, we know that. The cause of death is available. Some causes of death are very, very specific and well captured on the death certificate. Others have more variability and misclassification. We have relatively clear data on cancer. When you get into other diseases, it's more difficult from the medical surveillance in terms of getting complete data locally or nationally.

DR. WALLENSTEIN: Sylvan Wallenstein, from Mt. Sinai. The 91,500 number is twice as big as numbers that have been used traditionally in most of the publications that have come out for the number of responders, actually around 50,000, so a little less than twice the amount. Can you explain how that 91,500 number came about and why we are off almost a factor of two from everyone else's estimates - which we all know they are estimates? But why, it's a huge factor?

DR. THORPE: I also want to raise one point. The methodology that was used to develop that estimate, and I think we all need to take a critical look at the various estimates, and understand the limitations ourselves. But the methodology is posted on the website and pretty detailed. (See http://www.nyc.gov/html/doh/downloads/pdf/wtc/wtc-article-20070207.pdf) It's a large document. We have gone to some of the various programs and sat down and said, this is our estimate. We'd love to compare our methods with your methods and try to figure out where we are. We have a challenge. I think ours is well documented, and you can poke holes in it. Part of the reason why it's large is there was a lot of work done to research who was exposed. Lots of work done on the numbers of people who volunteered down at the site. And these were organizations and also cadres of individuals. So from our best understanding from the meetings we have had, the

estimates that are large such as ours take into account a very large volunteer population that isn't always accounted for in the estimates that are smaller. One approach might be to compare the various methods for estimating the denominators. Robert, did you want to add anything?

DR BRACKBILL: What I want to add: what is posted on the website is a report that was documented and processed and a procedure that the contractor used in coming up with an estimate. In the lower published estimates I think that you are talking about, there were numbers offered early in the process without a whole lot of substantiation. I actually have not seen anything that has actually shown how that number of 40-50,000 was derived. I want to point out to some extent that the 91,000 estimates we have might be actually lower than the number actually present because we have been told by people, for instance in the Police Department, that instead of being 5,000 police there were 30,000 police. This number can be even larger than that 91,000.

DR. THORPE: It is complicated, and we welcome a critical dialogue.

DR. STELLMAN: Jeanne Stellman, Columbia. One big difference is the definition of a worker. The responder study requires it to be a responder worker on the site for a particular number of hours. My understanding from the website is that it is workers or workers who were present in the building during the attack. And that would be a substantial number of thousands of difference. I'd be happy to share with you the information that I have regarding our numbers.

DR. THORPE: These are the important differences I think you need to understand. There's not one right versus wrong, it's a matter of what we are looking at and what's the definition.

DR. HALPERIN: Bill Halperin, New Jersey Medical School. This comes back to Jim's presentation, with John's presentation. But Jim, when you introduced the cohort, it was 70-plus thousand, highly exposed. Part of the discussion was there were a lot more highly exposed. But the question we're trying to get an answer for maybe doesn't require everybody being in the cohort, just requires enough to get an answer. But if it's 70,000 highly exposed compared to an unlimited number of very low exposed we kind of eliminate the dose response that we were talking about in the first response. So where do the moderate and low exposed come from versus the non-exposed? They don't appear to be in the cohort, and they are in the general population but we really wouldn't know because we are not going to ask each of them.

DR. CONE: I think the Registry was intended to include highly exposed. But then we realized we actually captured much more diversity than intended. So I think there's some luck in that. We have more of a gradient of exposure than our intended population really would suggest. We do have people who were present who went West after the attack and were never actually exposed to the dust clouds. They didn't come back, luckily for them, and for the Registry. They were basically a non-exposed group even though they were included in the Registry. There were thousands of others who were on the street, escaped and did not come back to the workplace because it was closed and the area was cordoned off for weeks after the event. To better address the issue of comparison with a truly unexposed population, the respiratory study that Steve and Carrie are going to be doing is planning to include unexposed people who volunteer to participate via the community health survey. That is potentially another population we will get in that case-control study that's been planned to try to expand our exposure gradient. However, your point is well taken. We still need to be cognizant of the fact that the Registry is tending toward the higher exposure.

DR. THORPE: We'll go to breakout sessions. Leslie Stayner here. Bill Halperin on the third floor. And Steven Stellman, room 315, also on the third floor. (BREAKOUT SESSION)

(RETURN FROM BREAKOUT SESSIONS) DR. THORPE: We have a presentation from Mount Sinai, Henry Sacks, Joan Reibman and David Prezant, FDNY.

DR. SACKS: First, thank you for inviting us. I am delighted to be here. Maybe just a clarification, we are listed on the program as mortality studies, but I think I am speaking for us and the people who are going to be following us that we don't think of ourselves that way, and actually a lot of what we're doing is trying to prevent or at least delay mortality in the people we are seeing. So what I brought is a brief description of our program, who we are seeing, what we are doing. I will try to whip through that as quickly as I can.

Our program is actually a consortium that includes a data and coordination center, which is where I work, and five clinical sites that see the patients in the New York and New Jersey metropolitan area. They are listed here. A little bit of history. The program, as most people probably know, was funded by NIOSH. The original goal was to develop a clinical program providing free screening examinations to World Trade Center responders in this area and all across the country. Federal funding for treatment was added late last year. Before, the program had been doing treatment with a variety of other sources of funding. Just a little bit about who we have been seeing or what we have been doing in the consortium that I am here representing. As of last month we had seen a little over 19,000 responders who have received an initial examination, over 7,000 received a first follow-up, and we are just beginning the second follow-up exams. They are scheduled at approximately 18 month intervals. There was some discussion earlier about eligibility. The definition of who is eligible for our program is narrower than some of the

other programs, particularly what Kitty Gelberg spoke about. To be eligible for our program, someone must have worked rescue, recovery, clean-up or related services at this site for at least four hours in the early stages or 24 hours later. Narrow criteria, but a lot of overlap with some of the other groups. Who are the people that we are seeing in our consortium? As it says, it's fairly large and heterogeneous. Firefighters, not members of FDNY. We'll hear from Dr. Prezant about their population. So traditional first responders plus a lot of other people who came to try to help. This is from a paper by Robin Hebert and Jackie Moline and others published about the first half of the population. Not too surprisingly, mostly they are male, median age 42, mostly union members. Close to half of them had been there on 9/11, and the majority within the first three days. Those were people who were there early on. Mostly construction or law enforcement. A lot of other occupations.

What do we do? There are standardized medical and exposure interview questions, physical examination, mental health assessment, chest x-ray, pulmonary function tests, some blood tests. The program was originally designed focusing on the individual patients and trying to find out what health problems they had and how we could help them with those. And as it's evolved we have become more interested in trying to look for patterns and learn from this and try to find ways so that what we are doing can help both lead to things that we might be able to do to help the health of this population, and also things for future possible disasters. So some of the questions asked don't lend themselves to looking for patterns, they have been evolving as we go, over time. Some of the things that we are particularly interested in looking at right now are sarcoidosis, pulmonary fibrosis, and cancers. We are collecting information on deaths and mental health. The tracking process, trying to find cases and look for patterns, is extremely complex and involves a bunch of steps people are probably familiar with. First, we have to identify cases in the records that we have - try to go back to those records, the records that we have, get more information, try to get additional medical records and try to evaluate

because most of what we get is from self-reports, so we have to try to evaluate and assign levels of certainty. Where do we get the information that's coming to us? Most of it is from the monitoring questionnaire that we collected on these 19,000 or more subjects. We look through those to look for diseases of interest.

We also have a large phone bank where people call in and tell us about things that have happened to them, we try to record. We learn from the health care providers of our patients. We learn sometimes from the newspapers or television about someone who has an illness that they believe may be related to the World Trade Center. We learn new diagnoses that patients are being seen for. Eventually we are hoping to have all of this done in real time. We are in the process of developing it. So once we find a possible case, we look through the charts, then we try to get more information about the treatment, we try to get external medical records. There's a team here that works on these aspects and spends a lot of time calling the patients, sending out the requests for medical records, et cetera. So we try to obtain the records. Then we get as much detail as we can. Obviously, the ultimate is to have tissue diagnosis. We have lots of people who have given us very detailed information from their own information without the medical records, but some of them are very clear and very convincing. And then we have the largest group of things we are working on, trying to get information back determining whether they are indeed a case of something that we are interested in.

What are the different criteria for each disease? We have information in our questionnaires about exposure at the site. How long people were there. What they did. Whether or not particular equipment was issued, whether they used it. What other exposures they might have. So there's been a lot of discussion this morning and in the focus group we had on how do you put all these things together. There are concerns of the responders. In the pulmonary function test we have been doing, we see at least many of the people were near the top in the spectrum of health and fitness. On the other hand,

are the people who come in, are they the sickest? Or are they the healthiest? Are they the people who are feeling fine? Or are people who don't come in the ones that can't get away from work, so we don't know. We struggle with some of those things. Some of the other additional methodological challenges - most is self-reported. So, we try to work with issues about how we can share data with other groups, and we are working on some of these with Kitty Gelberg. I am delighted to be here, we welcome the chance to collaborate with anybody else who is here, and I would be happy to be the point person for our group in working with some of these other groups.

DR. PREZANT: It was a great beginning presentation by the Mount Sinai people in that I don't have to go over all of the methodological concerns. Our study is very similar, and we use similar instruments, and have similar methodological concerns. We have one thing that we have that's an advantage. We have pre-9/11 data, and we have a clear understanding of what the denominator is in our cohorts and what their exposure was. So if we look at our entire cohort, we had, in the year of 9/11, 11,500 firefighters - I am rounding off. We have about 2,900 EMS workers. The one section of our cohorts we don't have a clear understanding of what the end denominator is include the somewhere between 1,000 and 2,000 retirees from before 9/11 that volunteered to come in. From that group we are only able to know the group that comes to us. So there isn't a total capture of that group. To date, we have classified everybody on the basis of exposure, and we have used the FDNY arrival time exposure index, very similar to the exposure index that was discussed earlier this morning. We have 14,350 people as of the last date of March who participated in at least one visit of the medical monitoring program. And we have over 9,000 who had participated in the second visit, and over 1,000 people who have participated in a third visit. Where are we in terms of disease incidence rates? I am going to use two examples of an incidence study . One is sarcoidosis, and the other one will be a quick discussion of cancer. We have been following sarcoidosis since 1985 because there have been well known, though controversial, epidemiological links

between sarcoidosis and exposure to smoke, wood burning stoves, fires, et cetera. We figured this was a reasonable disease to look at. The way we ascertain our cases for sarcoidosis is very similar to what was described before in the Registry. We have a monitoring program that has gone back to at least 1985, though it was updated in 1996 and again in 2001. We have disability cases. We have pension cases with sarcoidosis. We have not been looking at retirees. So we have not looked at post-health 20 years later or 10 years later. We know very carefully all of our pre-9/11 incident data going back to 1985. We have published that in 1999 in CHEST. Essentially, we averaged in the New York City Fire Department 11,500 firefighters, we averaged about 2 case per year with a range from 0 to five cases per year, for an annual incidence rate per 100,000 of 13 per 100,000. Actually, incidence rates for sarcoidosis was mentioned before this morning - incidence data is very difficult to obtain. Incidence rates for sarcoidosis throughout the United States and the world are not clear cut.

Most studies of sarcoidosis, which there are a plethora of, are prevalence studies, not incidence studies, not new disease studies - they are total disease from tuberculosis control data. But if you sought very carefully and worked hard, you can find incidence data on sarcoidosis from the U.S. Navy and several other organizations. Based on the ethnic racial makeup of the Fire Deaprtment you would expect an incidence rate of somewhere between one and 7 per 100,000, and ours was, as I said, 13 per 100,000. After 9/11, in the first year after 9/11, we had 13 cases for an incidence rate of 86 per 100,000, using exactly the same ascertainment techniques that we used before. By the way, sarcoidosis, every case (pre and post-9/11 was confirmed pathologically by biopsy and not counted otherwise. Due to the fear of missed lymphoma, none of our cases refused biopsy. The only thing that was different is because 9/11 was such a big issue, we did more chest x-rays that year than we did annually in the prior years. And that does introduce an ascertainment bias since that is the way you basically diagnose most of sarcoidosis. Yet when we adjusted for that we still had a many fold, statistically

significant increase in sarcoidosis independent of whether it was found by symptoms or whether it was found by monitoring. In the next four years our incidence rate has dropped to four per year for an incidence rate 22 per 100,000, which is still statistically significant. In addition, what you learn from a true incidence study is also about the disease itself.

There are many different ways the disease can present. There's severe disease, minimal disease, et cetera, and the disease pattern for sarcoidosis has changed markedly. Where before 9/11, most of our cases, nearly all of them, were essentially asymptomatic, after 9/11, almost all of our cases, 65 percent, have symptoms of respiratory disease and much greater incidence of constricted airway disease and hyperreactivity in this group. About 30 percent are hyperreactive, that's markedly different than our previous years and markedly different than the literature. So for our incidence study, the first part of the talk, sarcoidosis, we think we have done a really a good job adjusting for things, comparing for things all based on a prior track record. This is coming out in CHEST May 2007. It is available on-line as of last week.

The importance of this incidence, and any incidence study from any group, is it tells the other groups this is what we are finding. We need to get up to speed and find out whether this is distinct for this cohort or whether it's shared by multiple cohorts. We have heard and have personal communications from the other cohorts that they have been finding a similar pattern. Next comes to cancer. I had some slides to show that, but we have done the same thing with cancer, but with cancer we don't have a track record of doing this every year. So we actually have to go back and get our data up to speed. We collect the data, the same as described before, and the same as I described for sarcoidosis. But for cancer we weren't checking the medical records for every case. But for cancer, all we did was either write down for most of our cases that you say you have cancer if we don't have a biopsy. For some of our groups we do have biopsy results, but for some of our groups

we don't. So we have to go back and confirm all these cases. So we have a similar issue as what the other cohorts are having. Once we finish this confirmation process, we'll have pre-9/11 data, and it won't be retrospective because we collected the cases prospectively.

The confirmation will be historical. Some of these patients may have died. Some of these patients may not be interested in talking to us, though we haven't had that as an issue. What's the point of the story? Well, in the absence of slides, we have found that for the vast majority of cancers five years before 9/11, five years post-9/11, we have not seen any change in the incidence rate. However, there are some cancers that might have increased slightly. Yet what are we to make of these findings? Talking hypothetically, let us say for example, that we have eight or 10 lymphoma cases in the five years after 9/11, but only had two cases in the five years before 9/11. Well, that's a dramatic rise. Yet it's only eight cases, yet it's only six cases different from the five years before. We're doing much more ascertainment than we did the five years before. And, here is the kicker, let us say that there are possibly 60 cases that have been listed as cancer in the five years before that we don't yet have medical records with confirming diagnoses. What if all 60 were lymphoma? Obviously that would be impossible. But what if six were? Then the incidence rate would be identical. So for a variety of diseases, we are uncertain.

And we need to make certain we actually have numbers for every disease. We have some questions about three specific types of cancer. And we need to follow-up. It is critical when you are dealing with small numbers that you don’t miss cases. But that challenge makes data interpretation far more difficult and worrisome. I will summarize with this: if you're having, like we had with the World Trade Center cough, approximately 3,000 people with World Trade Center cough, if we are missing 10 of these cases, or even 100, it doesn't matter. If we were missing 10 of these cases before 9/11, it doesn't matter. We only had about 10 to 40 cases of really significant asthma per year in the Fire Department before 9/11. Who cares if it's 50, or even 100, when that is compared to 3,000 post-

WTC? But when you have small numbers of cancer cases, then every case that is lost becomes critical to your conclusions. Unlike a disease with a high incidence rate, when you're dealing with small rates, the absence of nearly 100 percent follow-up can change your conclusions dramatically. I am not trying to say that this is a reason why we should not do this, we all must do it. We are have considerable resources to do it, as does Mount Sinai and everyone else.

But there may be many provisos to our conclusions about cancer. Provisos that were not needed or applicable to our conclusions about either WTC-PTSD (post-traumatic stress disorder) or World Trade Center cough. And I thank you for your time.

DR. THORPE: Joan, do you want to come up and add your comments? One question quickly, Dave. I assume you have identifiers on your 43 cases, your hypothetical 43 cases. So you can submit those to the State Cancer Registry given that most of your firefighters (because you have such a unique cohort) are New York State residents and you can try to use the strength of the New York State Cancer Registry for confirmation, correct? We'll be spending the afternoon on that. But that is a very, very important tool for all of us.

DR. PREZANT: Yes, not just for the unconfirmed, but for the whole cohort.

DR. THORPE: The whole cohort, absolutely. Joan?

DR. REIBMAN: I didn't realize I was suppose to be talking today. I never understand why my name was next to mortality, you can't be dead to come into our program. Let me tell you a little about our program and tell you all the problems that we are facing, many which are magnified compared to all the problems you have been hearing earlier. I am a pulmonologist, not an epidemiologist. Bellevue actually has two programs, one World

Trade Center screening and monitoring, and another program that really began out of a study we had done with the New York State Department of Health looking to see whether there were adverse respiratory effects in residents of lower Manhattan. Those studies were performed and completed in 2002 and recently published. A third one is coming out. Because of these studies we ended up working with a number of community groups and some of them asked us whether we could see some of the residents who they felt were ill. Our first response was, no, we didn't have the resources to do it. We began seeing people in our asthma program, and, in 2005, we were working with a number of groups from Beyond Ground Zero.

In 2005, we were funded by the American Red Cross to begin a treatment program for residents and responders. And in the summer of 2006, we were funded by the New York City Mayor's Office to expand our program. So we have sort of had to move very quickly in terms of developing a program. It's a very different program than the ones you have been hearing about from the firefighters and from the World Trade Center monitoring and screening programs. Our program is not a screening program. So in order to come into our program, you have to have some symptom. So that is already a major difficulty if you're starting to look at prevalence of any symptom of disease whatsoever. Our population is also very different because of the groups we have been working with. We have residents, we have office workers, and we have a group of responders, most of whom were clean-up workers. So it's a different group than, again, you're seeing in the Registry because many of these people would not have entered the Registry. And some of them are in the World Trade Center screening program. We have a treatment group modeled to some extent like some of the other programs: interdisciplinary. Individuals have a medical evaluation, a mental health evaluation, and now we can add mental health treatment, as well.

And also we have Social Services associated with the program. To date, in the year and a half we have now 1,200 individuals who are currently under treatment in our program. About 450 of these individuals are clean-up workers, the rest are residents and office workers. We are getting calls at the rate of about 100 a week to enter the program, with questions. Not everyone wants to enter the program. We are about 70 percent non-English speaking. So we have active translations into Mandarin, Cantonese, Spanish, Polish, Russian. We have an on-line ability at Bellevue to be able to do this. We are about 50/50 female/male. A lot different than many of the other programs. But we are an adult program, not pediatric program. So our median age is about low forties. I came without data, this is by memory, but I think it's pretty correct. What have we been seeing? Because you have to have a symptom, everybody coming to us has an illness of some sort or another. Most of the time, we don't understand what it is. Shortness of breath, dizziness- we treat it as if it's asthma. We have been seeing some cases of sarcoidosis, some interstitial lung disease. And the big question is, are we seeing cancers? It's very difficult for us to answer that right now. We certainly are looking for it. We have identified some.

Again, we don't know whether this is related, and since we are so concerned, we are working with the Department of Health and other groups to look into these cases in more detail. The only thing, I guess I would say, we are a difficult group to look at, to do real epidemiological studies with, because you have to have symptoms. But, clearly, we are trying to devise studies to do in our population. The only thing I would say, one of the important things about having these three groups, World Trade Center, Mount Sinai, FDNY and our program, it's important to communicate with each other. If one group identifies something, we can quickly look for it in the other populations. So we have three distinct populations to be looking for diseases in, and we can then survey and either confirm or not confirm, at least keep an eye out for many of the other diseases people are

recording. So if Dave sees something, we'd like to know about it. Or other groups. It's important for us to know. Thank you.

DR. THORPE: The Health Department is responsible for the health of New York City residents. Also, if there's ever a time you think a concern is great enough, you should inform the Health Department of your findings. Give us a call, we can work with you to look further into the cases that you're concerned about. Our standard approach is to respond to:such cases detected through heightened awareness on the part of the clinicians. From here we are moving rooms up to the third floor board room.
(RECESS)

DR. CHANG: The next study population within the World Trade Center Health Registry that we're looking at is those diagnosed with cancer. Within the Registry there are four subgroups - rescue/recovery and cleanup workers; residents; school students and staff; and building occupants, pedestrians and people in transit whom we have been calling the Occ/Trans group. We are going to compare the rates of cancer in these groups with comparison populations. That's one of the problems we are having, determining which is the proper population for each group. So far, we have calculated expected rates based on the New York City population historically in New York City, with the idea of also comparing each subgroup separately with different populations. We will talk about this a little later. Cases were self-reported through the baseline study that was done in 2003 and 2004, and the first follow-up study that's being conducted right now, as well as from e-mails, phone calls, and letters. People have contacted us from within the Registry, as well as family who have contacted us about health conditions they have. These self-reported cases we plan to verify by matches to the New York State Cancer Registry and other state cancer registries, which we will hear about soon. The data from state cancer registries generally indicates date of diagnosis, site of cancer, and cancer incidence rate

that would be expected. We are looking at probably doing a WTC Health Registry match on a biannual basis.

One issue that will come up is that it takes about a year or two from date of diagnosis until cases are in the database at the state cancer registries because of their verification process, et cetera. Also, by matching the data from our WTC Health Registry cohort with the state cancer registries, we can identify other cases who have not self-reported through us but are listed in the state cancer registries. In the WTCHR, 60 percent are New York City residents; another 15 or 20 percent are New York State residents outside New York City; The rest include residents of out-of-state areas, New Jersey, Pennsylvania, and Connecticut, who are commuting into the city, as well as a lot of other states. There is a lot of mobility within the city. A lot of people since 9/11 have moved to anywhere in the world, really. In cases reported to us, if they are diagnosed in states without registries or abroad, we would have to get medical record reviews. And the protocol for how to verify these cases we still have to decide. Exposure data based on the baseline survey and data coming in now is pretty good data, cross-sectional data. Obviously, we are looking at the presence in the dust clouds; worker time and date of first exposure; location of work, either on the pile, the barge, or Staten Island; duration of work; tasks by time period; and mask use by time period. We are looking by time period for residents. And for school students and staff, whether they were evacuated from their school or home and when they returned.

Also, we are looking at condition of the residence. Were the windows open? What kind of cleaning methods were used, if any? Of special concern are potential carcinogens such as - asbestos, benzene, silica - and from the combustion and from dust and debris from the buildings collapsing. So, in analyzing our data, first, we need to determine our exclusion criteria. Obviously, cancer diagnosed before 9/11 will be excluded, but we will also consider building in some latency period for cancers, particularly for solid tumors, as

mentioned by Dr. Schubauer-Berrigan previously. This is still to be determined, as well as with hematological malignancies. What date should we pick that could be the first plausible case biologically? Calculating directly standardized rates of cancers by site of cancer, and looking for any differences between that and expected rates calculated from comparison groups, we still have to determine and look at statistical significance. We will develop Kaplan-Meier survival curves and conduct Cox proportional hazards regression analyses.

We'll be using the Life Table Analysis we heard about this morning through NIOSH. There are possible future studies Jim had talked about. First, geo-spatial studies where we can overlay some of the data with meteorological patterns, wind pattern dispersion, where the residents were - their location and time - to look at a special relationship between the incidence of cancer and where people actually were. Also, nested case control studies, focusing on work activities or other previous work or risk factors - information we don't have in our surveys now. This information could be different in different cases and controls. Controls could be selected from the WTCHR and matched by age, sex and race. We could actually go back and interview our subjects for the type of information that we need that we don't have currently. And this will obviously need approval as a separate study. Some of the many questions that we have started with include what to use as a comparison population. Which population is appropriate: New York City? New York State? Obviously, the residents are all New York City residents. Some of the rescue, recovery and clean-up workers come from all over the country. We're going to compare the different subgroups to different comparison populations. New York City for residents, you would be looking at the subset of New York City residents, Manhattan, or even a subset by zip code, looking at lower Manhattan.

The Occ/Trans group includes a lot of people who were also New York City residents, but also a lot of commuters into downtown were there that morning from the tri-state area. Like I said, workers came from all over the country.

Regarding the year for comparison, first you want to look at the year before, the incidence rates before 2001. So you could just decide to do the year 2000. But if anything changes in the future, such as a virus vaccine, that would change the baseline. We will look at the rates over the next 20 years. Especially, given New York City is such a mobile population, and as people age, they tend to move out of the city. Age is a very important factor in cancer rates. Date of entry into study - we talked about this in terms of mortality data - as well. We need to decide whether their date of interview or date of first exposure should be the time we start follow-up. Date of interview (entry into the registry) looks like a unanimous recommendation from this workshop so far. We also need to think about the 160 registrants who were registered by proxy - between September 12, and they actually died by other causes. Do we include them, and if so, what would their date of entry be? In terms of cases - date of diagnosis - what's the earliest and acceptable date for inclusion of cases?

What should be the lag time for latency period for solid tumors and leukemia? In terms of matching, what are we going to call a definite match versus a probable match? Some of that might be addressed by the cancer registry protocols. And how often should these matches be conducted? With the State Cancer Registry, we're thinking about every two years because that's about the time lag we'd be able to work with in analyzing the data. But with other state registries, should we do it quite as often or more or less often? Cases diagnosed outside the United States are a challenge. Given that there's a couple years turnaround time for data to be included in the Cancer Registry, should we go ahead and do medical record reviews if we don't have verification from the Cancer Registry? If we do do medical reviews, what are we looking for? Are pathology reports sufficient? Or

in rare cases or difficult to diagnose would we want independent review of slides? Then, data analysis: we were looking at the Life Table Analysis System from NIOSH. If anyone has suggestions about different software tools, we would welcome this.

The question about the power of the cohorts we might have if we are going to be analyzing the subgroups in the Registry separately. Do we have enough power to actually detect a level of risk in five or 10 years? 20 years? Biases, of course, affect the WTCHR, particularly volunteer or self-identification bias. People who come into the Registry who were not on recruitment lists. About 60 percent of the Registry is people self-identified through public messages, ads, throughout the city recruiting people. There's about 40 percent of people drawn from lists that we have from either employers or buildings and residents, et cetera. One way we can actually estimate the bias is by comparing outcomes of people in the Registry to those actually actively recruited, but not registered, such as clean-up workers, for which we did have names, but probably just names. I don't know how much contact we might have from the different agencies that employed them. As well as residents in lower Manhattan.

And the healthy participant's effects. For example, the building occupants were mostly people working downtown, obviously people healthy enough to hold down a job and at work. How much occupational exposure did the rescue, clean-up and recovery workers already have? They might be more unhealthy in some ways. If we find decreased incidences of cancer, and it appears that exposure to the World Trade Center is protective against cancer, how do we communicate these kinds of findings to the media?

DR. CONE: We have about two minutes to open up discussion.

VOICE: The doctor talked about lymphoma. Given how many possible cancers there are, and how many diseases, it might be useful, though no one has mentioned this, to develop

specific hypotheses regarding cancers we might expect given the types of exposures present. Given multiple comparisons you're going to be making, there is at least 100 possible causes of death. There's probably dozens of different cancers. At least three or four different subgroups within your cohort as you start to include the workers and children. So you're going to have at least 200 different comparisons. It's inevitable you're going to find positive findings. You might want to think about having some plausible aims to start with so if you find something you can actually believe it. Otherwise, whatever you find is probably going to be just statistical artifact.

VOICE: Does anyone know what the historical rates are in New City versus New York State? Decide whether either of those make a difference if you could find that out. The other thing is, cancer is generally a disease of latency. So obviously, if a case had been diagnosed September 12 you would not be likely to want to attribute it to the exposure. So, have you thought about a start date other than September 11 for your data accrual of cases?

DR. CHANG: Yes, but which date in particular is what we haven't determined yet. We were discussing six months or longer for leukemias. For solid tumors, much longer. But we would like your input, also. How would you determine that?

DR. CALLE: I would like to get ourselves grounded in the numbers because in all these questions about power to investigate, you have got a population of a certain size. You can actually decide when you can possibly have power to look at Non-Hodgkin's lymphoma, for example. You mentioned possibly using the year 2000 for New York City. I would guess, having never looked at the data for New York City, there aren't enough cancer cases in New York City in a single year to consider just using a single year as a comparison. So a lot of things that you're proposing cannot really be considered without

knowing the numbers. So, as I said, I would encourage you sooner rather than later to make this less of a hypothetical.

DR. CHANG: If we were comparing pediatric cases of a certain type of cancer, those numbers will likely be insufficient.

DR. CALLE: I would think lung cancer is your most compelling initial hypothesis.

VOICE: What's the latency?

DR. THORPE: To bring some concrete hypothesis to the discussion, we're going to talk about something that is clearly associated with respiratory disease. So, presumably lung cancer would be a hypothesis with long latency. You can look at a scenario with the power to look at lung cancer in 10, 15 or 20 years. That's a real scenario.

DR. CHANG: For the Registry as a whole. If we were going to break that down, my question would be rescue and recovery workers verses residents, because we wanted different comparison groups. Then to break that down especially by site of cancer.

DR. SCHUBAUER-BERIGAN: You're likely doing these 200 comparisons or so. For each individual comparison, what are the chances we actually find anything? I'd suggest you don't decide on an initial date of cancer. One of the features the NIOSH program has is a latency feature. You can establish the lag and not only does that discount the exposure received right before death, but also takes the first years and initial follow-up period and groups them into unexposed classes. This adds another level of hypothesis generating performance. I agree with Dr. Calle's suggestion.

DR. CALLE: You may soon realize that the study of pediatric cancers, well, when you actually look at some numbers, you might find a lot of these questions are moot. In fact, you can focus on what you look at in this cohort.

DR. CONE: Crude as they may be, the original Registry protocol gave some study size and power calculations for some of these hypothesis, e.g., lung cancers related to silica. We're going to have to do a lot more of that. I appreciate the suggestion and look forward to your assistance.

DR. BRACKBILL: This morning in the session, Bill Halperin had talked about some of the same issues we talked about modeling exposure to other issues to see if we can actually get some differences between our high exposure and low exposure groups in the Registry. Try to see, that's another problem of power, trying to detect a difference in incidence, different exposure levels as they are in the Registry itself.

DR. CONE: Thanks again, Dr. Chang, for your presentation. Next, we will hear from Dr. Wallenstein from Mt. Sinai who will discuss some of the statistical and methodological issues regarding tracking of disease reports using screening visits and phone contacts over time. (This presentation was not transcribed due to technical difficulties).

DR. CONE: Originally, we had a discussion session scheduled for this final hour, but in honor of the time - Dr. Howard and others need to leave to the airports - we will have a discussion on coordination between monitoring programs and treatment programs and WTCHR. John Howard, from NIOSH.

DR. HOWARD: What I thought I'd do is maybe put myself in the position of the funder. From the federal perspective, we find two large groups of work here. One, which I call analytical work, which is the World Trade Center Health Registry, which is statutory and

funded since 2002 and refunded in 2006, lasting until 2009. Then, a non-statutory program, which there's both federal money and New York State money in - fatality investigations. Then a number of care programs. The historical program is at the Mount Sinai consortium, which started out as the screening program in 2002. And then more fed into a medical monitoring program and part of a treatment program. FDNY picked up the medical monitoring phase in 2003, then added treatment in 2006. Then there's two sort of police worker programs, one through the New York City Police Department through their project, and actually funded through their Foundation, not the Department, which was funded in 2006, statutorily. And the Police Officers Providing Peer Assistance, or POPPA, also funded in 2006.

I think the thing I would emphasize, since I have been doing this, is the need to coordinate. I think this meeting today is a great start in that. I have an idea for how we can expand that. But the thing I wanted to emphasize in terms of the care programs, especially the monitoring and treatment programs, is that we started out monitoring individuals and treating individuals. And there's an evolution going on, part of what we are doing here, the evolution is from that individual focus to a more epidemiological focus. We're now looking at them as groups and trying to figure them out or answer certain questions. So now that we are in 2007 looking at 2008, there's a couple of questions that you could ask for the analytical studies. I think we have been asking these questions all along. I think the serious policy question that's being asked by policymakers from an analytical viewpoint is, what is World Trade Center associated and what isn't? That really is an important policy question. It's an important scientific question to answer. Unfortunately, the legislative and policy time frame is a tad shorter than scientific time frames by decades, unfortunately. So I think that's a real issue. We're looking at how do we address that major analytical thing we have been talking about, and I think we have right now, in Washington, a number of different proposals on the table that are fully fleshed out. HR43-47, sort of an expansion of existing programs, but in that bill there's

important language about research, and HR16-38 - I'm sorry 16-38 is the program extension bill - HR17-47 is the other bill, but within those two bills the idea is we need to start looking at these qualities within the department. We are talking about how do you get out that issue of causation. That's something we have been struggling with all day given the type of structure we have. What's the advantage of a longitudinal study, case control design, with whatever physical health effects or mental health effects, with mortality being a part of that? And cancer being one of those physical health effects we can look at. What is the role of the already existing cohorts in doing that? The cases are there, how do we work with them to assemble them in some kind of study? That's really a serious issue. It's one that as we know, these kind of studies are very resource-intensive, take a long time. And the serious question that David Prezant brought up this morning, that I think is important for us from an ethical and policy standpoint is, who benefits from a long term longitudinal study? Are these responders, are they the people who are going to benefit or the population hence forward? I think Mary Schubauer-Berigan is long involved with studies of Hiroshima victims. These people did not benefit directly, others have benefited. We have to understand that because there's an ethical dimension to policy, and I think David Prezant this morning phrased that for us, I think it's a serious one. As he said, and I apologize also for saying the same thing, the analysis and reanalysis of exposure assessment is a serious scientific issue. But I am not sure within this current climate that we have to do that. Lorna Thorpe added after that we are fine-tuning what we have. That's a different approach, obviously, than doing something. We have got to figure out where we are in that.

But looking within that area of longitudinal studies of health effects, one of the big policy implications is, if we only had enough policy resources to look at certain areas, what would we look at? What would you all have to confine yourself to? Clearly, respiratory disease would be on that list. Clearly, mental behavior and health effect issues would be on that list. We have to look and focus, as someone said in our break-out group this

morning. Focus is extremely important. We have to decide what we can do in a short term. We can do it and get the information out there. So I think a respiratory disease characterization study is an important aspect to those big study ideas. Clearly, fatality investigation is something that we initiated ourselves as a surveillance program as Kitty Gelberg mentioned. And I think we have to continue that.

About the issue that was brought up by Dr. Halperin this morning, when would you, as a policymaker, when will we be able to tell you when the excess mortality will be seen? That's very important to have some time frame. You can't answer it, you have to be honest about answering it. I think that's extremely important. Then the next big area is this care money that we have out for FDNY and Mt. Sinai. The question there is how many people need it? How long do they need it for? What do they need exactly? What are we seeing and why are we seeing it? Those are really complicated questions. At the same time, when you're seeing people and taking care of people, you can't really do and answer those kinds of questions. You need some kind of clinical findings follow-up kind of studies. So that's another big scientific area that we are looking at in the department - to say we need to put some money in that. We can't have a bunch of coalitions running around seeing these people and doing the science at the same time. It's remarkable this money put out in 2002 for individual care monitoring and now treatment has produced the science it has. I think we need to continue it, not stop it, but give it money for people doing the separate sort of free time kind of work that needs to be done there. That kind of time frame I think is a little shorter than some of these longitudinal time frames.

So I think we have a lot of work to do, we have a very short time frame. These bills are pending, as well as the President's FY-'08, proposed budget. The House appropriations bill for HHS is coming for a mark up in the next couple weeks. This is a very important time. So we are going to know what our pathway is. And I think that's extremely important because we can't really plan very well. We have been doing stuff sort of ad

hoc as we go. I think we need to get beyond this fiscal years budget, FY-'08, so we can decide what we need to do. I think one of the things that we need to do is do exactly what we are doing today. I applaud the Health Department for doing it. We need to come together regularly, have workshops around issues like the ones we are having. I'd like to see an annual science seminar. If we're able to have that kind of long pathway, if policymakers give it to us, and brings us all together, I think that's the best way.

The idea of coordinating our communications and our education so we can establish those kind of important things in terms of educating people about what we are doing and what we are likely to find and not likely to find. I think those things we talked about in my breakout session are very important. There has to be a basis for legislation and policymaking, but it doesn't have to be an absolute gold standard. There are a lot of shaky signs that produce a lot of policymaking. We have to provide some basis for policymakers. But a lot of presumption can also occur in policymaking, and we have to give them some basis for presuming certain things. So I would say we have a lot of challenges ahead of us and I think we need to really do some realistic focusing when we talk about what we can do scientifically.

DR. CONE: Thank you, Dr. Howard. Discussion?

DR. THORPE: Can I raise two questions about collaboration to see what works best across programs? If one program is doing the clinical study, and we know that the individual is in other programs and already being clinically worked up, I think with informed consent we can probably have some sort of communication across programs, if the patient gives informed consent, rather than putting patients through multiple tests. Are there issues there that need to be worked out or discussed? Because I think it sounds like there are some overlapping clinical workup studies; you are talking about respiratory studies that are ongoing at Bellevue, working with the Health Department and Mount

Sinai. Are there ways to collaborate in terms of the patients themselves who are in those programs?

DR. HOWARD: This is the time we should start forming a working group of the parties and maybe having a neutral party. Dr. Halperin or somebody else could come volunteer for us to be able to coordinate and mediate. I think it's important to do that. David?

DR. PREZANT: I think you have to balance resource utilization and patient's freedoms and individuality. I think from an individual perspective, patients should have the right to do whatever they want to, especially if they are paying on their own, perhaps even with tax dollars, to go to any one of these programs multiple times, cross programs. There will be individuals that do that. They are the extension of doctor shoppers. I don't mean that in a negative way. But looking at the total cohort as I think we do as policymakers, there's the concept of cohort burn out and cohort confusion. And that, to me, looking at my entire cohort and thinking order in terms of policy is of far greater concern. That is specifically, "I didn't go for monitoring because I saw something in the paper, and I went somewhere else for a breathing test. I thought that was part of the project." "I didn't go to your program to follow-up on what I am doing because I am sick and tired of getting 15 post cards in the mail every year asking for this thing and that thing, and that thing. So I tuned it all out." I think these are large concerns, both expressed individually and at the cohort level. I think these are very important questions, but I don't think the answers are trivial.

DR. THORPE: That may be one reason why the collaboration is important - so somebody doesn't go get tested twice and do similar tests.

DR. PREZANT: There are other programs out there, for instance, a body scan program. That body scan program is actually a voluntary concept where different unions have gone

to different radiology groups and negotiated discount rates. It's unclear how any of those abnormalities are followed up. The results certainly are not currently part of a centralized database. And then there is the confusion where you then say to the person, “You know you haven't come to your monitoring or follow-up program.” They say, “I went for that body scan. I thought that was the same thing.”

VOICE: There is unbelievable confusion between what is screening and what is treatment, so it does actually behoove us to have some names and describe what's what, put somebody in a treatment program and keep them in that treatment program. But in terms of studies, I think what you're asking is, down the line, particularly, as people develop studies, who is doing what study? Clearly, that needs to be communicated.

DR. THORPE: That's what the question raises, I think when studies are developed and participants may be participants also in existing monitoring programs that may or may not overlap in terms of testing methodology or treatment. It would be useful to have a mechanis to efficiently make it known to individuals in the various monitoring programs, what studies exist and maybe they will then consent to participate in such ancillary studies as well.

DR. HOWARD: You are talking about, let's say, a website, a World Trade Center studies website, listing the studies that were going on that various individuals were doing. Let's say they were funded by the government and then the eligibility criteria, state the purpose, the design, what people are supposed to do. That sort of thing.

DR. PREZANT: I think that's part of the way there.

DR. THORPE: Yes. That could be maybe some place to describe all the studies. That would be a good collaboration.

DR. HOWARD: You can go to NIH's clinical studies website where you can look for whatever medical condition and do a search for studies that you might be eligible to participate in.

DR. THORPE: From what we see from the Health Department's perspective, researchers are applying to us to recruit participants for studies based on the Registry or for mortality data. We see lots of different study designs. Some are convenience sample studies as you described, some more rigorous and with different populations. So you get a variety. I am hearing two things. One is, if a study is designed, let's say a clinical respiratory study that FDNY, Mt. Sinai, or Bellevue are not running, but you have clinical information on those individuals, and the researchers approach you and they have informed consent from the participants, is your information available to the researcher and does that minimize the burden on the participants? Or will those participants go through another battery of the same or similar tests?

DR. PREZANT: Just like with your Registry, though, it depends on what level of information they need.

DR. THORPE: So if a participant in your registry comes to you and says, I'd like to release my information to the following person, you release that information.

DR. PREZANT: Right, but you also utilize a percentage of your funding to achieve that. Where what we do, I am not saying we wouldn't release it, we are very happy to release information, but it has to be information that is releasable, easy for us. We don't have a separate funding source to find information or do searches. If something is electronic, fine. If it's not electronic it's very, very hard.

DR. THORPE: What you were bringing up is different - putting out information so people can find it.

DR. CALLE: A global comment. It seems to me that so much of what's going on here is just yet another example, but real important example, how difficult it is to do research in this country because of the health care system. Nothing is linkable. The people who are in two or three studies think, aren't you guys talking? Don't you guys talk to each other? Given the energy and the funding and the whole thing around 9/11, it seems like it would be of some benefit to everyone to package the disease of studying the impact going forward of 9/11-exposed individuals. Precisely because of the fact we don't have medical records, we don't have integrated health care where we can capture everybody's stuff. We don't have disease registries other than those for cancer. It seems like it would be a compelling argument. Care about the 9/11 individuals in a way that might resonate in the way this is done in general.

DR. GILLIO: Can I speak to that for a second? I am involved now with New Orleans - through Secretary Levitt down there. I was asked to come down to observe at a health fair because there was no medical system at all left in New Orleans. We have volunteers much like NYPD. Volunteers from out-of-town came in and saw 5,000 patients one weekend at a site located at the zoo. It looked like a refugee camp in the United States of America. We are now building an electronic medical system tied to an identified database. Data from any practitioner, any EMR system can be imported into a research database that can be accessed by any researcher with appropriate credentials to query that said database, ask the research questions of the same data on different patients, but from different angles, different perspectives. So we have learned lessons from this adventure. It's starting to get some funding in New Orleans to do it, but it is still on a volunteer basis. But I would encourage the gentleman with connections back to funding sources and policy to put together New Orleans with the folks here. They are not being strapped.

Secretary Levitt said, break the rules, we're changing Medicare, Medicaid, the funding, make it work. People are hurting. So they are breaking the rules down there. I can see the Registry creating an identified database with relatively similar electronic medical records for all the citizens and create the XML export tools for Mount Sinai, Bellevue, whatever systems they have, let them design what fields they want in searching the data. Also, from a global standpoint, we are not addressing the health issues, we won't have answers for five to 50 years. The kids in middle school, high school, young adults, even senior citizens, they need to be empowered with what to be looking for, what to ask their doctors, and be more on top of their own screening. I think there's a great opportunity here, we are all in the Ivory Tower talking wonderful concepts, but the average citizen out there is skeptical.

DR. KELLY: I'd love to see, from a policy standpoint, funding to improve health literacy of the average citizen. Spending money in the aftermath, especially for those south of Canal Street who are still worried and paranoid about what's going on. I think the programs have been in place since '01 and '02. Mount Sinai and the Fire Department have been working collaboratively pretty much from the beginning. The design of the evaluation was done together. Then building on what we have begun and fleshing it out with additional information. That collaboration has been both with management and unions and has continued on with the Registry and with the other participants as both those programs have expanded. There are regular meetings that go on and information is shared in which we look to redesign the visit 2, now the third visit, both the physical and mental health aspects. When you talk about the World Trade Center conditions, it's based on information gathered in the programs in the first few years of the program. I think what we're struggling with is maintaining those programs without a clear funding source and also looking to say what additional programs to establish regarding the World Trade Center disaster of 2001. There's clearly a lot of pressure in every direction just to make many conditions World Trade Center related. Amazing we don't know the answer.

DR. CONE: We have a few minutes to wrap up. I appreciate the candid comments we have heard. Particularly, the breakout sessions have resulted in a pretty diverse set of opinions. One proposal is to have ongoing relationships with you, first of all, as consultants and advisors to this process. We need an advisory committee that could convene on an annual basis. Or through the WTCHR's Scientific Advisory Committee that could be expanded to include those of you who are interested.

DR. THORPE: John Howard could maybe help set up future scientific meetings.

DR. CONE: We'd certainly like to invite you to continue to work with us. We have existing relationships we can expand upon, mostly ongoing informal relationships. We are starting a process and need to get your help. You're the best people we know. We appreciate all the help so far. We'd like to be able to reach out to you and we have your address and phone number and e-mail.

DR. THORPE: We don't want this to be one way in any sense, to only look at what the Registry needs to do, but to frame it in ways that other forums would be informed also. Thanks again for all your contributions and attendance at this important meeting.

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