# Slide 1: OEF/OIF/OND Airborne Hazards and Respiratory Health: An Update

Good afternoon, everyone and thanks for joining this webinar. My name is Mike Falvo and I’m a research physiologist at the New Jersey War Related Illness and Injury Study Center. Today, I’m hoping to provide everyone an update on airborne hazards and respiratory health in service members deployed to Iraq and Afghanistan.

# Slide 2: Disclaimer

Before I start, let me say that the views I’ll share with you today are my own and do not necessarily reflect the Department of Veterans Affairs.

# Slide 3: Acknowledgements

Also, before I get started, I’ll need to thank a lot of great people who helped get this webinar together, especially my colleagues here at the WRIISC (pronounced “risk”) and those at the VA New Jersey Health Care System.

# Slide 4: Learning Objectives

Alright, so well my goals today are several-fold and here are the learning objectives I’d like to review. First, I’ll provide some examples of airborne hazards in Iraq and Afghanistan and discuss their potential health effects. Second, I’ll review the epidemiology of respiratory health and clinical studies in Iraq and Afghanistan service members. After that, I’ll share with you our experience here at the New Jersey (NJ) WRIISC from both a clinical and a research perspective. I’ll then discuss some current recommendations regarding the clinical approach and workup for a symptomatic Veteran. Lastly, I’ll provide a brief overview of the ongoing efforts at the VA, and then provide some clinical resources.

# Slide 5: Learning Objectives

Okay, so what are airborne hazards and why are we concerned?

# Slide 6: Photos

So whether we are in Afghanistan or here in New Jersey like I am today, airborne hazards and pollutants are always present. From a health perspective, what is critically important is the duration and magnitude of exposures to these airborne pollutants.So moving clockwise on the screen here if you can see these images, these pictures illustrate possible sources of airborne hazards. This includes the burning of waste and open air burn pits, sandstorms that are characteristic of the region, airborne dust such as that generated from tanks, and air pollution in places like Kabul, Afghanistan in the lower left part of your screen. Ambient concentrations of airborne hazards constantly vary and are based on a number of factors including neurological conditions and in the case of burn pits, the composition of the materials being burned. For many, many decades researchers have and continue to thoroughly study the effects of air pollution such as ozone and particulate matter on human health. With most of that work studying long-term chronic exposure, studies have generally found that chronic exposure to airborne hazards such as those found in urban areas of the United States are associated with the development of respiratory and cardiovascular diseases. With this in mind, military personnel, their families, and their providers are justifiably concerned about the potential health effects related to airborne hazards exposure during deployment.

# Slide 7: Burning Waste in Open-Air “Burn Pits”

Arguably, the burning of waste in open air burn pits has garnered the greatest attention and therefore, the greatest concern. Depending on a variety of factors, emissions from burn pits may contribute to health problems in exposed individuals. Although the use of burn pits has declined since the start of the wars and better efforts have been made to avoid burning hazardous materials such as plastics, approximately 273 burn pits of varying sizes were still in operation as of August 2010. The burn pit at Joint Base Balad has received the greatest attention as it was nearly 10 acres in size and burned an estimated several hundred tons of trash daily during *some* periods of the war. Items burned in these burn pits included plastics, metals, rubbers, paints, solvents, and numerous other wastes between 2003 and 2009. Currently, this burn pit is now closed.

# Slide 8: Burn Pit Emissions

So the range of possible pollutants emitted from burn pits have been identified including combustion byproducts, volatile organic compounds, and particulate matter. It is possible that emissions from burn pits combined with environmental pollutants cause acute, long-term and even late health effects. However our stance today with our current level of evidence is strongest for acute health effects.

# Slide 9: IOM Report 2011

In light of concern surrounding burn pits, the VA asked the Institute of Medicine to examine the available evidence on long-term health consequences of exposure to burn pits in Iraq and Afghanistan. Although there is limited evidence to review, the report found that for service in Iraq or Afghanistan, the broader consideration of air pollution and exposure only to burn pit emissions might be associated with long-term health effects particularly in highly exposed populations or susceptible populations mainly because of high ambient concentrations of particulate matter. So let’s talk now about particulate matter and why exposure to particulate matter could be potentially harmful.

# Slide 10: High PM in Southwest Asia

Southwest Asia is known to have some of the highest particulate levels in the world. In fact, concentrations to particulate matter collected during the first Gulf War in 1991 were shown to be two to five times higher than acceptable levels in the United States. Similarly, recent air sampling data in the Department of Defense in Iraq and Afghanistan has also observed particulate matter to consistently exceed military and occupational exposure guidelines. So how exactly do they do this?

# Slide 11: DoD PM Surveillance Program

Well, in an ambitious air sampling program, the U.S. Army Public Health Command performed sampling at 15 different sites in the theater of military operations over a one-year period, and as stated in the previous slide, particulate matter again routinely exceeded military and occupational guidelines at each of these sites. Investigators of this study identified three main air pollutant sources responsible for these levels. These included geological dust, smoke from burn pits, and pollution related to industrial processing that’s common in the region. Of particular note in this report is that the finer fractions of particulate matter exceeded exposure guidelines at each of the 15 sites. Generally speaking, the size of airborne particles is directly linked to their potential for causing adverse health effects. For example, locally here in the United States, the Environmental Protection Agency is concerned about particles that are 10 microns or less in aerodynamic diameter. So they’re concerned about these finer particulate fractions because these are the ones that are small enough to possibly enter the lungs. So how small are these particles?

# Slide 12: Figure

Well, let me give you a quick frame of reference here. So you if you look at this illustration on the top of the slide, I want to point out one thing quickly. So first, the lower limit of human vision is about 50 microns, so that’s about the size of this pin right here. Smaller than that, we really can’t accurately distinguish. For example, a strand of hair on the far right end of this graph is about 100 microns in diameter. Then if we take something, say, bacteria, which is about 1 micron in diameter or 1 millionth of a meter you can see how small these particles get. Moving back to this *particulate matter*, we know that inhalable coarse particles, for those that are of aerodynamic diameter of about 2.5 to 10 microns are generally found near roadways, dusty areas, and even near some industries. These coarse particles are represented in this graph in the bottom right in green here and you can see that generally these only reach the trachea and the main bronchi. The finer particles, however, those that have an aerodynamic diameter of about 2.5 or less microns can deposit a little bit deeper. These are represented in red here. So that’s how this illustration works. So high concentrations of particulate matter in the 2.5 range that were found to exceed military and occupational guidelines in the previous slide are concerning for several reasons. So first, particulate matter of 2.5 contains metals, hydrocarbons, and secondary particles from chemical reactions and these particles can spread over hundreds of kilometers. Studies have found that increases in daily exposure to particulate matter of 2.5 are associated with increased cardiovascular and respiratory hospital admissions as well as deaths. In fact, in 2010, the American Heart Association identified a causal between long-term 2.5 micron exposure and cardiovascular morbidity and mortality.

# Slide 13: Respiratory Health figure

So let’s put it together now. In considering respiratory health of deployed service members, hopefully you can now see that there is significant biological plausibility related to exposure to airborne hazards. However, at the same time we need to also acknowledge additional factors that can affect respiratory health and these factors on how the interact with exposure to airborne hazards. So working again, clockwise on this graph here, these include factors such as exposures to stress and violence. Previously, these have been shown to potentiate pollution health effects in other studies. There’s also military living conditions such as close sleeping quarters that are unavoidable and could lead to respiratory infections. Often overlooked is the active physical nature of military service itself which could exacerbate exposure effects. Unfortunately, we must also consider the high rates of smoking reported in service members as well, and lastly, potentially susceptible populations such as those with preexisting conditions could experience an aggravation of the symptoms.

# Slide 14: Why PM ‘Matters’ For Military

So why does this matter for the military? Well, particulate matter *does* matter to the military. Let’s highlight a couple of these key factors that can contribute to respiratory health effects. First and foremost, military service is a very active job. Controlled studies have shown that particulate matter is more likely to be deposited into the lungs during exercise. For example, particles deposition in the lungs is 4.5 times greater during exercise as compared to rest. This relates to an increase in ventilation during exercise but also that shift during exercise when you move from kind of breathing through the nose to breathing through the mouth. If fact, even carrying a heavy load results in an increase in ventilation. Heavy load carriage is again, part of the job in active duty military. For example, a Marine’s current assault load ranges anywhere 97 to 135 pounds. Combine these two- exercise and load carriage- and particle deposition in the lungs likely could be enhanced.

# Slide 15: PTSD and Respiratory Health

Recently, there has been a renewed interest in studying the relationship between respiratory disease and symptoms with mental health. For example, a recent study showed a moderate association between World Trade Center cough syndrome and probable PTSD in first responders to the World Trade Center attacks. Although there are respiratory symptoms related to PTSD no relationship was seen between PTSD and objective pulmonary function such as that obtained by spirometry. However, in a recent cross-sectional study on adjusted analysis, it was indicated that individuals with trauma exposure that includes those of general trauma as well as those with PTSD had significantly poorer pulmonary function and greater airway obstruction than those without trauma. So if we look on the screen right here, we could see a general, qualitative decline in scores here if you go from “No Trauma” to those with PTSD and the scores on the bottom right of the screen are representative of airflow obstruction. However, after controlling for other confounding variables, significantly poorer lung function was observed only in those with trauma exposure but not PTSD. But like the World Trade Center Study, PTSD was strongly associated with respiratory symptoms. Now, whether these findings are due to a small sample of individuals with PTSD and/or maybe some other limitations of the cross-sectional study that aren’t really clear, regardless, the role of mental health’s relationship with respiratory health can’t be overlooked.

# Slide 16: Tobacco Use in the Military

An unfortunate confounding factor in evaluating respiratory symptoms in employed military personnel are simply the high rates of tobacco use. Compared to the civilian population, smoking is more common in military personnel. For comparison, approximately 23 percent, give or take of the general U.S. population smokes. Now, compare that to about 32 percent of military personnel. These data that I’m showing you were taken in 2005 so these numbers may be off a little bit. But this problem may even worsen when people actually get deployed. You see that greater than 50 percent of active duty in Iraq smoked. Just to point out that heavy smoking in this slide is greater than one pack a day, so these rates are still quite high.

# Slide 17: Respiratory Health figure

So to summarize, there are indeed numerous factors that may affect respiratory health in deployed service members. However, future studies are needed to clarify how these factors interact with airborne hazard exposure.

# Slide 18: Possible Pathways & Health Effects

Let me give you a couple of examples of what we hypothesized of what could be potential pathways and health effects. So for instance, airborne hazards or airborne particles could enter the lung. Once they enter the lung, they could activate the pulmonary reflex arc then alter the balance of the autonomic nervous system. Concurrently, particles could also initiate or activate pulmonary oxidative and stress and inflammation. These factors could result in a number of acute, perhaps subclinical physiological changes. Those include change in heart rate rhythm, an increase in pro-inflammatory mediators, and even a decrease in lung function parameters. So depending on the duration and the magnitude of these exposures to airborne particulates, and whether these particulates can migrate into the blood, those that can embed very deeply, these could result in short-term health effects such as reduced exercise tolerance, abnormalities in pulmonary function testing, and respiratory symptoms more generally. Lastly, long-term exposure may contribute to serious cardiovascular events as well as upper and lower respiratory disease. So from a research perspective, we are very, very much in the beginning stages of understanding whether respiratory health effects persist beyond the acute stage.

# Slide 19: Learning Objectives

So let’s talk now about some of the relevant information that *is* available- some of the published data that we have out there.

# Slide 20: VA/DoD Research Efforts

So both the Department of Defense and the Department of Veterans Affairs are currently and have been performing a series of research studies to better understand the effects of airborne hazards on respiratory health. Two large, epidemiological studies currently underway include these listed here: the “National Health Study for a New Generation of U.S. Veterans” as well as the “Millennium Cohort Study.” Data collected from these studies cover a wide range of health issues but they also include respiratory health and the effects of exposure to airborne hazards. Investigator-initiated and cooperative studies are also supported by the Department of Veterans Affairs’ Office of Research and Development. Actually, in fact, here at the WRIISC, we’re really fortunate to recently receive a VA award to do just that. So we’re beginning that project in a few months. We’re really excited about that. In the upcoming slides, let me show you some of the more pertinent published studies that are currently available and what’s out there now.

# Slide 21: Self-Reported Respiratory Symptoms

So here’s a bit of a timeline. I wanted to start with a series of epidemiological studies that have really heightened our awareness of respiratory symptoms in deployed service members. So one of the initial publications that came out, Sanders et al. 2005, showed that over 15,000 military personnel surveyed from 2003 to 2004, about 70 percent self-reporting as having a respiratory illness during deployment. In addition, the incidence of respiratory illnesses doubled from pre-combat to combat phases. If we move down this timeline a little bit to the Roop et al. study in 2007, they surveyed over 1,100 troops deployed to OEF/OIF and similarly, they found an increase in respiratory symptoms during deployment. This study is kind of unique in that they also showed that the increase was the same in both asthmatic and non-asthmatic military personnel. Unfortunately, only about five percent of the sample reported a previous diagnosis of asthma. If we then move to Soltis et al. 2009, they also found an increase in the rate of respiratory illnesses but if we compare that to the Sanders study, it has actually gone down a little bit but it’s still high at that 40 percent. Authors contributed this decline to a variety of factors. Those include improved living conditions, better increased seasonal vaccination rates, and the like. However, their results also show a 34 percent decline in job performance that’s related to respiratory infection. That’s important because a decline in job performance could considerably affect the operations of the military. Additional survey data from Smith et al. in 2009 which comes from that Millennium Cohort Study I just mentioned- what they found is that deployed personnel had a higher rate of newly reported respiratory symptoms than non-deployed personnel and these rates were approximately 14 percent as compared to 10 percent, respectively. They also found rates of respiratory symptoms to be greater in those with combat exposure as well as those with land-based deployment such as in the Army. Despite these symptoms, authors observed similar rates of airway obstruction diseases and these rates are very low at only about one percent, but from this study it’s not clear, it’s not possible to determine whether rates were due to increases in the baseline prevalence or maybe increases in baseline reporting whether there is any selection bias. With that said, this is kind of our first glance on this timeline here, kind of acknowledging that these respiratory symptoms are quite profound.

# Slide 22: New-Onset Asthma

Shortly after these survey responses were published, Dr. Szema and colleagues of the Northport VA Hospital conducted a retrospective review of asthma diagnoses in Veterans who were deployed to Iraq and Afghanistan from the period of around 2004 to 2007. Out of over 6,000 Veterans, they reported 290 new-onset cases of asthma. Further, deployed to Iraq was associated with a high risk of asthma as compared to those serving States side. That risk is about 6.6 percent in those that were deployed to Iraq versus 4.3 percent of those that were serving States side. So what’s important to note here is that this review was conducted using ICD-9 codes with limited pulmonary function testing data. Whether these findings are generalizable to the larger Veteran population is currently unclear. However, new onset asthma in adulthood is concerning as it has been shown to result in a faster decline in lung function and a poor prognosis overall. Authors of this study suggested that perhaps burn pit exposure may be one of the factors accounting for these higher rates of new onsets of asthma. To address this question of whether exposure to burn pits leads to new onsets of asthma or disease, investigators from the Millennium Cohort team surveyed over 20,000 Army and Air Force personnel. These personnel were deployed between 2003 and 2008 and they did this to determine the prevalence of newly reported respiratory outcomes such as chronic bronchitis, emphysema, asthma, and/or recurring cough or shortness of breath.

# Slide 23: Proximity to Burn Pit

Authors used location of burn pits within 2, 3, or 5 miles as a proxy for burn pit exposure at three different camps with a documented burn pit as well as a control camp that did not have a burn pit. You can see the three camps that had a burn pit here on the screen and the one without a documented burn pit. So authors found no increased risk of respiratory symptoms or conditions for personnel stationed within 3 or 5 miles of a burn pit but they did observe an increase for respiratory symptoms in a sub-population of only Air Force personnel that were located within 2 miles of the burn pit at Joint Base Balad. However, this risk was marginally significant and there is no evidence in human or deployment life.

# Slide 24: Is Deployment an Exposure?

Well, maybe it’s deployment. So whether to determine if it’s deployment itself was associated with respiratory health of deployed personnel, Dr. Abraham and colleagues conducted what is called a “nested case-controlled study” and using medical and counter data, they identified over 50,000 personnel that were free of any respiratory system or symptom diagnoses in the six months preceding their deployment. Afterwards, they identified 533 cases of post-deployment where the primary diagnosis of at least one obstructive pulmonary disease and you can see what ICD-9 codes are here; what that breakdown looked like. For each of these cases they identified, they also picked four controls. These controls were selected at random. As consistent with the report as to pre-deployment, they found an increase in respiratory symptoms and encounters, post-deployment, but interestingly, the observed no association with deployment duration or the number of deployments. So authors suggest that these data are in support of those previously presented by Smith and colleagues whereby post-deployment respiratory illness is likely determined by specific environmental exposures rather than deployment in general.

# Slide 25: Summary of Findings

So to summarize some of these epidemiological findings, in short, respiratory infections are very commonly reported during deployment. Specific environmental exposures rather than deployment itself may be factors in post-deployment respiratory illness. What we need to acknowledge is that there are limitations with these data as most of them relied on surveys, self-report questionnaires, and ICD-9 codes.

# Slide 26: Clinical Case Series

But in addition to these epidemiological studies, we’ve also had a couple of clinical case series that have been published and I think these are deserving of attention. So let me go over these somewhat briefly here.

# Slide 27: Acute Eosinophilic Pneumonia

So in the first, we’re going to talk about 18 cases of acute eosinophilic pneumonia related to military deployed in or around Iraq between 2003 and 2004. These 18 cases came from a total deployed population of about 183,000. Now, acute eosinophilic pneumonia or AEP is a rare lung disease of unknown epidemiology and is characterized by predominant eosinophilia on bronchial alveolar lavage. Investigators of this study that came out in JAMA in 2004 were not able to identify a common source of exposure, temporal or geographic clustering of recognized cause, or link these cases to vaccination. But consistent amongst these cases was new onset of smoking during deployment which was reported in about 78 percent of these cases. This is important because this is a recognized risk factor for AEP.

# Slide 28: AEP - Update

So moving forward a little bit, continued collection of data from the primary evacuation center in Germany that have been updated and reports about 44 diagnosed cases of AEP between 2003 and 2010. Unlike the previous paper, these cases were confirmed with bronchial alveolar lavage eosinophilia. In these cases, 93 percent of them were smokers and 65 percent required mechanical ventilation. So this is very serious. These data have been currently presented in abstracted form but have not yet been published so we’re definitely waiting for that publication.

# Slide 29: Constrictive Bronchiolitis

So moving now to a 2011 paper from the New England Journal of medicine, King and colleagues describe military cases of constrictive bronchiolitis. This, of course, is a rare, irreversible lung disease. It’s characterized by fixed airways and narrowing of the small airway branches. Constrictive bronchiolitis is associated with occupational or inhalational exposures and usually presents with shortness of breath and cough that accompanies some abnormalities in pulmonary function testing and/or maybe some scans such as CT scans. This paper has received considerable media attention and is perhaps the most controversial in our growing understanding of the effects of airborne hazards and respiratory health. So in brief, about 80 soldiers from Fort Campbell presented to Vanderbilt Medical Center with symptoms that are consistent with exercise intolerance. Of those, 49 underwent biopsy. Of these 49 individuals that underwent biopsy, 38 received a diagnosis of constrictive bronchiolitis. What we’re going to point out here as well is that 28 of these individuals endorsed exposure to sulfur virus. The rest of the 10 did not. Perhaps the most controversial aspect of this paper was the decision to pursue an open lung biopsy in individuals with limited objective findings.

# Slide 30: Clinical Characteristics

So in this slide, we’ll see a comparison between the 38 cases of diagnosed soldiers and control subjects, and these control subjects were obtained from a previously published paper, so a historical set of control subjects. What I want to point out is that it’s important to note that these variables were obtained on these cases at a single time point. Therefore, it is difficult to know whether the soldier had experienced significant reductions in pulmonary functions over time. Regardless, if we just broadly look at this sample, approximately 16 percent of the sample of cases had evidence of airway obstruction or restriction based on spirometry. About half of the cases had reduced lung diffusing capacity with an average predicted value of about 73 percent. Results on cardiopulmonary-exercise testing indeed showed some differences and these are consistent with their symptoms and these are reported during exercise intolerance you see increases and decreases here as compared to the historical control subjects. But looking through this paper, only 32 percent of the sample had a type of bronchoprovocation test called a Methacholine Challenge and authors did not mention any additional testing such as bronchodilator spirometry, and/or laryngoscopy. Otherwise, as you can see from the percent predicted values here for the pulmonary function testing (PFT) of spirometry, these values are mostly within normal limits. So in a 2012 editorial, pulmonologists from the Department of Veterans Affairs and Department of Defense do not advocate for lung biopsy in the absence of abnormal findings on PFT or CT scans but they recommend more comprehensive testing such as those we discussed- Methacholine challenge, spirometry, and laryngoscopy but we’ll touch on that a little later on.

# Slide 31: Summary of Findings

So to summarize these clinical series, we need to first recognize that each report and cases of AEP (acute eosinophilic pneumonia) and constrictive bronchiolitis are very concerning. However, these cases do come with some limitations that we need to be aware of. For the published AEP report, there were concerns over case definitions and the lack of regional and geographic clustering. So we’re currently awaiting publication of more updated results- the results of those 44 cases I mentioned and hopefully these will enhance our understanding of the problem. For the constrictive bronchiolitis report, there remains concerns on how representative these cases may be and the lack of additional testing. But most importantly, this report has raised what should be the appropriate post-deployment clinical work up. So we’ll discuss these recommended diagnostic out rhythms for the symptomatic Veteran with unexplained dyspnea a little later on in this presentation.

# Slide 32: Learning Objectives

So to switch gears somewhat and to share with you some of our experience here at the NJ War Related Illness and Injury Study Center or WRIISC (pronounced “risk”) for short, but in order to do that you kind of need to know what the WRIISC is, and for those of you who aren’t aware, our listeners on the line, let me do a little bit of an explanation on that.

# Slide 33: WRIISC figure

So we know, those that are probably on the line right now of health care providers that deployed Veterans have unique health care needs and concerns so to address these needs, I like to think of the WRIISC has a three-pronged approach. So foremost, we perform comprehensive clinical evaluations and environmental exposure assessments for Veterans with chronic, medically unexplained symptoms. Second, we provide post-deployment health education like this webinar today. We provide this to Veterans and their families, health care providers, as well as the general public. With our research program, the WRIISC studies a variety of topics brought under the umbrella of post-deployment health, including my own program of research on airborne hazards research and cardiorespiratory health. So for me, as a researcher an exercise physiologist, I have a greater opportunity to participate in each of these three areas here at the WRIISC. So in short, yeah, I enjoy coming to work so I always have a good time here.

# Slide 34: WRIISC figure

But now, I’m going to now talk to you about some data that we’ve obtained from our Clinical Evaluations. Let’s just talk about the clinical side for a second.

# Slide 35: NJ WRIISC Clinical Data

We’ve previously published some data that demonstrated that Veteran evaluated at the WRIISC are concerned about their military exposures and frequently, these exposures are associated with their somatic symptoms. In fact, my colleague, Dr. McAndrew has recently shown that nearly nine out of 10 Iraq and Afghanistan Veterans evaluated at our center endorsed exposure to both general and specific air pollution and are concerned about these exposures. Specific air pollution in this case refers to airborne hazards such as burn pits, whereas general air pollution is defined as things that such as sandstorms.

# Slide 36: Clinical Suspicion

So in addition to these Veterans’ concerns, several years ago, our clinical team did a great job in recognizing an increase in respiratory symptom reporting in Iraq and Afghanistan Veterans. However, these symptoms were not always accompanied by abnormal findings and test results. In fact, spirometry, when ordered, often would be within normal limits. Despite this, clinical suspicion still remains very high. This is also around the same time those reports were coming out about elevator respiratory symptoms which we touched on earlier. So the leadership at the WRIISC questioned whether more sensitive testing could shed light on these respiratory symptoms. Therefore, they made the proactive decision to conduct full pulmonary function tests or PFTs on all Veterans clinically evaluated at the NJ WRIISC regardless of their presenting symptoms.

# Slide 37: Pulmonary Function Testing

So we’ve got great collaboration within our hospital at the Pulmonary Function Testing Laboratory and they do a great job of performing these PFTs for us which include evaluation of lung volumes, spirometry before and after a bronchodilator, as well as lung diffusing capacity. So again, we have limited time today, so I wanted to show you some data from this program. I’m going to share with you some spirometry data before and after bronchodilator.

# Slide 38: Reversibility Testing

So the purpose of a bronchodilator or reversibility testing is to detect reversible airway obstruction. This is important for the diagnosis of asthma, identifying the acutely reversible component of COPD, as well as evaluating disease severity and treatment efficacy. Let me point out that reversibility testing is not routinely ordered when lung function parameters are within normal limits. Because of this, some researchers have suggested that this could result in a missed opportunity for detecting the early stages of bronchial asthma. The most important component of this test is the magnitude of the bronchodilator response, or simply, how much improvement if any, in spirometry was seen following the bronchodilator as compared to baseline. So we have the baseline test, we administer bronchodilator, and repeat the spirometry. So the larger the response, the greater the risk of accelerated lung function loss over time as well as the development of fixed airflow function.

# Slide 39: Spirometry Flow-Volume Curve

So hopefully just a quick review here on some of the parameters I’ll be discussing so that everyone’s on the same page. So here’s a Flow-Volume loop obtained from spirometry and demonstrates both the maximal inspiration and maximal expiration phase. So remember, this is important for us. Spirometry is a performance test and it is effort-dependent. Some of the common things in the report is how much air is forcibly expired in the first second of expiration and that’s noted as FEV1 as well as the total amount of air expired noted as FVC or Function Vital Capacity. In addition, we’ll also consider the individual’s peak expiratory flow and what is called their mid-expiratory flow.

# Slide 40: Positive BD Response

With reversibility testing, we also are interested in the changes in spirometry, of course, post-bronchodilator. According to the American Thoracic and European Respiratory Societies, and increase of 12 percent and 200mL in either FEV1 or FVC is considered a positive bronchodilator response. In other words, there’s reversibility. So what we wanted to know here at the WRIISC is whether this positive bronchodilator response is seen in Iraq and Afghanistan Veterans even if they have baseline spirometry within NORMAL limits. So I’ll just show you how we did this.

# Slide 41: Data

So do this, we reviewed our WRIISC database and identified 52 Iraq and Afghanistan Veterans that were clinically evaluated at our center and also those of course that had complete datasets. PFTs were only implemented here on a regular basis in late 2011, so 52 Veterans really only represents a fraction of the Veterans we’ve seen here at the WRIISC. Of these 52 Veterans, 4 had unacceptable spirometry – poor effort for a variety of reasons, and of those remaining - 32 had baseline spirometry within normal limits which was about 67 percent of our sample. We then looked at these individuals to determine frequency of a positive bronchodilator response and we found 6 of them.

# Slide 42: Data table

In this table, these are our results from the BASELINE or pre-bronchodilator spirometry. What we did is we came up with 3 different groups: 1) those with ABNORMAL spirometry, 2) the 6 individuals with NORMAL spirometry and a positive bronchodilator response, and lastly 3) those with NORMAL spirometry and no bronchodilator response. Average values and their standard deviations are provided in black, and the numbers in red font illustrate the percent predicted value based on published reference equations. So, as expected, for FEV1, FEV1/FVC ratio, as well as mid-expiratory flow – those with normal spirometry had significantly better performance as compared to those with ABNORMAL spirometry. Not entirely surprising. And for FEV1 and mid-expiratory flow – those with normal spirometry and a positive bronchodilator response still had significantly reduced values compared to those with NORMAL spirometry and no bronchodilator response. So looking just at the percent predicted value in red font, qualitatively – you can see that as we move from abnormal to normal spirometry, we’re generally seeing an improvement here and this is pretty pronounced on some of these. Keep in mind though, that these are clinical data and this was not designed as a research project so I of course had to do a little more digging.

# Slide 43: Respiratory Symptoms

With approval from our IRB, we also abstracted information from these Veterans’ clinical intake questionnaire packets and we also looked into their CPRS record to determine whether the frequency of respiratory symptoms varied amongst these groups. Those with ABNORMAL spirometry are represented in blue bars here; those with NORMAL spirometry and a positive bronchodilator response are here in red; and those with NORMAL spirometry and no bronchodilator response are in green. So if we collapse all the lower respiratory symptoms here defined as presence of ANY lower respiratory symptom, we see that the large majority of them, 60 percent for each group endorsed symptoms. But if we break these out a little bit and then analyze those such as dyspnea, wheeze, and chronic cough, we see that those with ABNORMAL spirometry as well as those six individuals with a positive bronchodilator response but no spirometry are also showing high rates of respiratory symptoms.

# Slide 44: Summary of Findings

So to summarize, 67 percent, a large majority of Iraq and Afghanistan Veterans evaluated at NJ WRIISC had baseline spirometry within normal limits. However, approximately one in five of these or 19 percent demonstrate a positive bronchodilator response with an average increase of approximately 15 percent of their baseline values, clearly exceeding the 12 percent criteria.

# Slide 45: Limitations

Now with anything, there are limitations. So first, reversibility may not be evident by spirometry alone and perhaps if we did volume-related or non-effort dependent tests – such as impulse oscillometry – we would have maybe been able to see some different results. Other researchers have suggested that spirometry may need to be performed over several days to minimize variability whereas our data are obtained only from a single time-point. And lastly, the results of Veterans evaluated at the NJ WRIISC may not be generalizable to larger samples, so we need to continue to collect these data and of course, increase our sample size.

# Slide 46: WRIISC graphic

At the WRIISC, we like to think that our clinical experience fosters research projects and vice versa- that our research enhances our clinical evaluations. So now I’d like to move to a research project from my lab that was developed out of our clinical experience.

# Slide 47: Exercise Challenge

Veterans reporting respiratory symptoms also frequently described that exercise had become more challenging and that their run times were decreasing over time. So we decided to collect some pilot data whereby we recruited Iraq and Afghanistan Veterans and had them perform spirometry both before exercise and after exercise. Exercise in this case was about 6 to 8 minutes of a treadmill-based exercise, of 80 to 90 percent of your maximum heart rate. This type of test is called an exercise challenge and a type of bronchoprovocation test that’s used to determine airflow limitation. So using criteria from the American Thoracic Society, again - when we see a decrease in spirometry post-exercise by at least 10 percent from pre-exercise baseline levels, this is termed an exercise-induced bronchospasm. We see this a lot in individuals with asthma.

# Slide 48: Research Sample

So we recruited 20 Veterans that were deployed to Iraq and Afghanistan for at least 30 consecutive days, regardless of whether they had respiratory symptoms. In this preliminary analysis, we dichotomized our groups based on greater than or less than 6 months of deployment to Iraq or Afghanistan. Although limited, we used deployment length as a proxy for exposure. If we look at the slide here, we can see that indeed for the group deployed less than 6 months, on average, it was about 4 months and for the group deployed for greater than 6 months, on average it was about 11 months regardless of their deployment length. So this did result in fewer individuals in the group deployed for less than 6 months. But otherwise, groups were pretty similar in age. We did have one smoker in this group and one that endorsed a mild pre-deployment respiratory history.

# Slide 49: Exercise-Induced Bronchospasm (EIB)

So, we did the test and we analyzed the percent change in spirometry from pre- to post-exercise, we found that four out of 13 individuals or 31 percent who were deployed greater than 6 months exhibited exercise-induced bronchospasm. However we did not see this at all in the group deployed less than 6 months. For comparison, we looked into the literature for the rates of exercise-induced bronchospasm in other populations. So we started with military recruits and a previous paper suggested a rate of about 7 percent the observed but the civilian population had considerable variability and were as low as 4 percent but as high as 20 percent. Rates in elite athletes are interesting – particularly in endurance athletes participating in cold environments. They’re known to have elevated rates of exercise due to bronchospasm and have been reported to range from 11 to 50 percent. Several studies have shown that Olympic athletes competing in the winter games have a much higher prevalence than those competing in the summer games. For example, winter games athletes have rates that are from 18 to 26 percent whereas data from the summer games athletes reports a prevalence of 11 percent. In one study, nearly 50 percent of the cross-country skiers met criteria for exercise-induced bronchospasm. Therefore, while considering these evaluations for Veteran, we really need to take into account the role of high-intensity exercise.

# Slide 50: Post-Exercise Spirometry

So this graph here is just going to show you the percent post-exercise fall index and we’re just using one variable here, FEV1, and remember that the criteria was about 10 percent and these are for data so this is the average over the entire group deployed for less greater than 6 months and for the group deployed for less than six months.

# Slide 51: Preliminary Research Findings

To summarize, 31 percent of Iraq and Afghanistan Veterans who were deployed greater than 6 months and self-reported exposure to airborne hazards met criteria for exercise-induced bronchospasm. We are continuing, now currently- actually we had a subject this morning, to expand this dataset, as well as examining a variety of other parameters obtained during exercise testing and these include things such as gas exchange variables, ventilatory efficiency, and even VO2 kinetics. So we’re doing a lot of fun things right now and we’re looking to get our results out as soon as possible. So we strongly believe that exercise testing is really a critical component of the comprehensive evaluation of a Veteran that has unexplained respiratory symptoms and/or airborne hazards exposure.

# Slide 52: Learning Objectives

Okay, so now we’ve learned a little about what others have been doing, what we here at the NJ WRIISC have been doing. Let’s talk about some recommendations regarding the clinical approach and work-up for a symptomatic Veteran.

# Slide 53: Causes of Chronic Dyspnea

I want to first start with a reminder of the importance of a step-by-step approach in dealing with dyspnea or shortness of breath. So this graph we’ve drawn is from data of 100 consecutive patients who presented to a pulmonary specialty clinic. These patients underwent a comprehensive clinical evaluation for chronic dyspnea. The purpose of this study is that the authors were attempting to determine whether chronic dyspnea could be explained by clinical impression alone or more accurately when combined with objective test findings. They defined a physician’s clinical impression as a combination of history and physical as well as findings on chest x-ray.

Not surprisingly, they found that when results from comprehensive objective testing were combined with clinical impression – the origin of chronic dyspnea was correctly diagnosed 100 percent of the time as opposed to 66 percent of the time when they just used their clinical impression alone.

But importantly, this slide also conveys another message and that’s that chronic dyspnea can be explained by a variety of conditions – with approximately 25 percent of these being even non-respiratory in origin.

# Slide 54: Factors for Diagnostic Referral

So what do you do as a clinician if you have a Veteran that may have respiratory symptoms and or dyspnea on exertion? Well, a pulmonary health working group composed of civilian and military experts in a variety of disciplines was convened in 2010 at National Jewish Health in Denver Colorado in response to concerns about the respiratory health of deployed military. Although limited data was available for review at the time of the meeting, these experts developed a variety of recommendations including factors that may prompt a diagnostic referral. These include persistent unexplained cough, shortness of breath, spirometry values drastically below normal limits, and even if they were within normal limits, if we had pre- and post-deployment spirometry and we saw a drop of 15 percent, they would also suggest that that’s a factor for diagnosing referral, if the Veteran or individual presented with new onset of symptoms which were at 10 percent decline from previous tests, and even some of the common reports we’ve heard about an excessive decline in physical readiness for their run times.

# Slide 55: Post-deployment Diagnostic Approach

But also from this same working group they recommended approach to diagnostic testing. This approach begins with a complete occupational and environmental history as well as a physical along which they included standard, pulmonary function tests (PFTs). These two right here are currently the same approach that we’re using at the WRIISC. We have our environmental exposure assessments and full PFTs. Again, remember the goal of PFTs being to determine the presence of fixed or reversible airflow obstruction. This group also recommends high-resolution CT scan with both inspiratory and expiratory views, but the authors of this paper did acknowledge that the sensitivity of high-resolution CT for early disease detection is currently unclear. Therefore, they recommend other tests such as a methacholine challenge which we talked about before as well as cardiopulmonary exercise testing- some of the things we’re doing in my lab right now. These two test really help in the differential diagnosis particularly in you remember that first slide we talked about, even 25 percent of cases of chronic dyspnea are explained by non-respiratory factors.

So lastly, the surgical lung biopsy they suggest may be considered on a case-by-case basis but only after thoughtful consideration of the risks and benefits and only after a very thoughtful review of the results of other comprehensive testing. This is a very important decision and one that should only be made by a qualified pulmonary specialist.

# Slide 56: Post-deployment Diagnostic Algorithm

About two weeks ago, Dr. Morris, a pulmonologist from Brooke Army Medical Center, published a similar diagnostic algorithm for evaluating post-deployment dyspnea based on our most current thinking of this problem and with greater detail regarding pulmonary tests.

Authors acknowledge that the patient with symptoms on exertion yet normal spirometry are really one of the biggest challenges we face. Although there is no standardized approach or one-size-fits-all approach for all patients, this algorithm follows that when test results are normal for a given step, one may proceed to the subsequent steps. So as you can see here, that would suggest that after normal spirometry one may proceed to bronchodilator testing which we’ve done here at the WRIISC and then to bronchoprovocation testing which we’ve also done here at the WRIISC as well and so on. You kind of just progress through these subsequent set of steps if the preceding step’s results are normal. Importantly, Dr. Morris and colleagues have highlighted that clinicians need to consider alternative diagnoses such as vocal cord dysfunction and exercise-induced bronchoconstriction in their evaluations. And of course, as indicated by the physician, additional testing should be performed as necessary.

# Slide 57: Stepped Care

So let’s put it together. To provide the best care for deployed Veterans with airborne hazards concerns, we need to remember that it’s a stepped care approach. It begins with and understanding of health care utilization reports and pre/post deployment surveys and then progresses to primary care. At this point, the provider should have a general knowledge of deployment-related health concerns and be able to identify some basic resources. Identifying resources and a greater knowledge of exposure concerns and treatment resources may be enhanced with local post-deployment health expertise via the facility’s environmental health coordinator.

And of course, know that us here at the WRIISC can serve as a resource for providers in the appropriate clinical care of these Veterans and we can do this through several options.

# Slide 58: Clinical Evaluations

Let’s talk about those. So these options are kind of threefold here. So we can perform comprehensive multidisciplinary evaluations. These really focus on symptoms and improving function. At the NJ WRIISC, this is handles as a three-day evaluation. We can also perform environmental exposure assessments. These are included as part of the comprehensive evaluation but these can be a standalone service as well or our occupational health physicians can also conduct these on the phone. We also have what’s called eConsults where we perform a medical record review with individualized recommendations for the next steps. Lastly, we can also have providers email general questions to the WRIISC and ask the WRIISC experts for more detailed answers. I know personally, I’ve had several requests from providers inquiring about the latest research updates. So this is a really great way for us to communicate with providers and clinicians.

# Slide 59: WRIISC Service Area Map

And although I’m speaking to you today from the NJ WRIICS, note that we also have centers in Washington, DC and Palo Alto, California. This map illustrates here our service areas based on VISN locations and I highly encourage you to visit our Web site (<http://www.warrelatedillness.va.gov>).

# Slide 60: Learning Objectives

So finally, just a quick, brief wrap-up. I wanted to give a very general overview of some important efforts on part of the VA.

# Slide 61: Initial Efforts

So based in part of the VA’s review of the previously mentioned Institute of Medicine (IOM) report – the following planned actions have been recently announced to address concerns regarding exposure to airborne hazards during deployment. So these include Standardized Post-Deployment Evaluation Protocols, clinical informatics systems, designing appropriate studies for the future, and conducting and following a long-term cohort study. In addition, the WRIISC was really excited to join the first joint VA/DoD Airborne Hazards Symposium was held last August and we contributed to a pending monograph is currently in preparation.

# Slide 62: Open Burn Pit Registry

What a lot of you have probably heard is the Open Burn Pit Registry Law and on January 10th, Public Law 112-260 was signed and required the VA to take the following actions. Those were to: establish and maintain an open burn pit registry, develop a registry that is robust enough to ascertain and monitor the health effects of exposure, as well as develop a public information campaign to really get the information out there about this registering, and, when we can, periodically notify eligible individuals of significant developments related to research and possible treatments. Here at the WRIISC, we are excited to have the opportunity to participate, in part, to the development of this registry along with our colleagues. Needless to say, this is a very significant undertaking to have completed in a 1-year timeline.

For more information on this, see this Website here on that goes over the VA’s action plan on burn pits and airborne hazards.

# Slide 63: How Can I Stay Updated?

And as this is constantly evolving and these efforts continue to evolve, I would encourage you to use the public health Web site (<http://www.publichealth.va.gov>) for all the latest updates regarding airborne hazards. From this Web site, you could see at the bottom, you can also navigate to the WRIISC website as well.

# Slide 64: References

So I’m also going to show you some references real quick. Lastly, I think on the line, if there are any policy questions, Dr. Paul Ciminera who is director of the Post-9/11 Era Environmental Health Program hopefully will be able to answer some questions as well.