

COPD: Diagnosis, Treatment and H1N1 Influenza Prevention.

David Mannino, MD

Byron Tomashaw, MD

CAPT David Callahan, MD

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Coordinator: Welcome and thank you for standing by. At this time all participants are on a listen-only mode until the question and answer session of today's conference. At that time you may press star 1 if you'd like to ask a question. Today's conference is being recorded, if you have any objections you may disconnect at this time.

I would now like to turn the call over to you first speaker, Miss Alycia Downs. Ma'am, you may begin.

Alycia Downs: Thank you. Hello and welcome to today's COCA conference call. COPD: Diagnosis, Treatment and H1N1 Influenza Prevention. We are very excited to have three subject matter experts present on this call.

We have with us today Dr. David Mannino from the University of Kentucky, College of Public Health and Dr. Byron Tomashaw from Columbia University, College of Medicine. And we have CDC's own Dr. David Callahan. He's the Captain in the United States Public Health Service.

We are using a PowerPoint presentation for this call. You should be able to access that from our Website. If you have not already downloaded the

presentation please go to emergency.cdc.gov/coca, again that Web address is [emergency.cdc.G-O-V/C-O-C-A](https://emergency.cdc.gov/coca).

Click on conference call Information Summaries and Slide Sets. The PowerPoint can be found under the call-in number and passcode. If you have any issues locating the PowerPoint please send an email to coca@cdc.gov again that's coca@cdc.gov and we'll help you locate the PowerPoint.

After this activity the participants will be able to update providers on the current epidemiology of chronic obstructive pulmonary disease, to report the current diagnostic and treatment strategies in COPD and to provide current guidance for vaccinations to reduce risk of complications from influenza pneumonia.

In compliance with continuing education requirements all presenters must disclose any financial or other relationships with the manufacturers of commercial products, suppliers of commercial services or commercial supporters as well as any use of unlabeled products or products under investigational use.

CDC our planners and our presenters disclose they have no financial interests or other relationships with manufacturers of commercial products, suppliers of commercial services or commercial supporters with the exception of Tomashaw and he wishes to disclose receiving honorarium for speaking for Boehringer Ingelheim, Pfizer, GlaxoSmithKline and AstraZeneca.

And Dr. Mannino and he wishes to disclose receive an honoraria and research support from GlaxoSmithKline and Pfizer and an honoraria for being on the advisor board and serving as a speaker for AstraZeneca and Day as well as receiving research support from Novartis.

Presentations will not include any discussion of the unlabeled use of a product or product under investigational use. There's no commercial support. I'll now turn the call over to Captain Callahan.

David Callahan: Thank you Alycia. Although chronic lung diseases of which asthma and COPD are the most prevalent our perennial clinical and public health challenge. The ongoing 2009 H1N1 influenza pandemic has added a real sense of urgency.

Surveillance data and epidemiologic investigations show that persons with COPD are at increased risk of complications from influenza including 2009 H1N1.

Reducing that risk involves preventative measures such as influenza and pneumococcal vaccination but also includes optimizing ongoing clinical management for persons with COPD.

On a previous COCA call on November 10 we discussed 2009 H1N1 influenza and asthma. I'd like to refer the audience to those slides available in the conference call Web archives at emergency.cdc.gov.

In that presentation we focused primarily on influenza in the setting of persons with asthma. In today's call we will focus primarily on COPD as an ongoing public health and clinical problem but have also briefly included the recommendations for influenza prevention in this population.

To discuss the current concepts and the diagnosis and treatment of COPD we welcome two of the nation's top experts in COPD, Dr. David Mannino from

the University of Kentucky and Dr. Byron Tomashaw from the Columbia University.

Dr. Mannino, thank you for presenting and please begin.

David Mannino: Yes and thank you Dr. Callahan. We should now be on the slide that says Chronic Obstructive Pulmonary Disease: Diagnosis and Treatment. This is where we will start and please advance to the next slide which - and this is a slide that shows the traditional overlap that we have used in describing obstructive lung diseases for years.

Where an overlap of chronic bronchitis and emphysema and asthma - and if you click on this slide and you'll see now a green area appears. And this was traditionally what was described as COPD and back through the 80s and into the early 90s.

We always thought that COPD were people who had evidence of obstruction but also had to have a clinical diagnosis of chronic bronchitis or evidence of emphysema.

If you click on this slide again - in the mid 1990s a (C) change occurred in the defining of obstructive lung disease where it was not believed that people who had evidence of obstructed airways so what is called irreversible air flow obstruction.

In fact had COPD whether or not they had a clinical diagnosis or presence of symptomatology. And if you click this again there's now a larger green rectangle that recognizes yet another sort of question of debate here and this is, you know, the presence of reversibility. Of course, you know, some people

who had evidence of airflow obstruction, if you give them a bronchodilator they no longer have airflow obstruction.

And there has been debate as to whether this represents a form of COPD or whether this was asthma or it was something else. And this is an area that is currently being studied.

But certainly epidemiologically people who fit into this large green box whether they have airflow obstruction either before or after a bronchodilator in general tend to do worse if you follow them longitudinally which I will be talking about in the future slides.

If you go onto the next slide now which now it reads COPD Phenotypes (NEW) and click this again. This slide recognizes now that we've really come a long way in the past 20 years that we have gone from a more so of a simplistic definition of COPD to recognizing that this disease which sort of comprises again this green box in the center.

But it certainly represents many different diseases with different manifestations. And the example here is that there are clinical types, people that have symptomatology we now recognize the importance of comorbid diseases in COPD - comorbid factors such as depression and anxiety.

The issues related to loss of weight, people that have frequent exacerbations whether diseases gets worse over a short period of time. They tend to do worse than people who don't have such exacerbations. And this is now something that we're paying more attention to.

In addition although COPD is clearly in the United States related to cigarette smoking there is evidence that people who have never smoked can develop COPD particularly if they have underlying asthma for example.

And in other parts of the world particularly in the developing world we see a large number of COPD cases are found in people who have never smoked but they are in fact exposed to smoke, it happens to be biomass smoke either from cooking or heating.

In addition on the right side of the slide we now recognize the various physiologic markers of COPD including people that have problems with exercise tolerance, people who have evidence of what we call low diffusing capacity. This is the ability of the lungs to get oxygen from the air into the body.

And some people even with normal flow of air into and out of the body have problems getting oxygen into their bodies. In addition we know that, you know, for example people with poor exercise tolerance tend not to do very well.

And in Dr. Tomashaw's piece later on you'll be hearing about the importance of pulmonary rehabilitation. And then finally that last circle talks about some of the radiologic manifestations, that it's still important to look at the evidence of emphysema and airways disease in our COPD patients.

And if you go onto the next slide this slide highlights the self reported prevalence of a marker for COPD which was self reported emphysema or chronic bronchitis. And this is data that starts in 1980 and goes through 2000.

And I think of note here is that COPD traditionally was a disease of men but really are closely mirroring smoking in the population and in recent years has become clinically a disease that is as common in women. And there's some evidence that it's actually perhaps more common in women than men nowadays.

And if we go onto the next slide this looks at another measure of burden of disease in the population and these are deaths from COPD, absolute number of deaths. These are data that we reported in our 2002 MMWR report.

And the year 2000 was a watershed year for COPD in that this was the first year that the absolute number of women who died from COPD surpassed the number of men who died from COPD.

And this number - and this difference, the absolute number of women, has actually continued to increase so now each year in the United States more women die from COPD than men.

And it's also important to notice that this is looking at COPD as the underlying cause of death. And COPD is listed as the underlying cause of death only about 40% of the time that is listed anywhere on the death certificate.

And as I'll show you in some future slides that COPD tends to be relatively undercounted so it is thought that the burden of disease particularly of mortality from COPD is probably higher than what it's getting credit for.

Next slide please. This slide, you know, looks at the association between COPD, asthma and emphysema. And what you see in the center are three

overlapping circles, the pink one being asthma, the blue one being chronic bronchitis and the red one being emphysema.

And of course these do not occur in isolation and in general about 30% of people who have asthma report that they also have either COPD or evidence of chronic bronchitis or emphysema and vice versa, about 30% of people with COPD report that they have asthma.

And in general I think that this group of people that have evidence of both COPD and asthma in general tend to do much worse. They tend to have more symptomatology.

I think they tend to have more utilization and is the group that I am actually quite interested in because one of the problems that we get into clinically is that these patients tend to be excluded from the clinical studies of both asthma and COPD. So although I think they're a very important group of patients these are the people that we know least about in clinical studies.

Now there's another circle and this is sort of the hashed circle off to the right there, these are the people at least in evidence in NHANES III that evidence of airflow obstruction so they meet a clinical diagnosis COPD but have never been diagnosed with either asthma or COPD. And these are people that we refer to as people with undetected disease or undiagnosed disease.

Now the next slide is titled COPD Progression and Death. And in here is a picture of a book. This is a book that I proudly keep in my bookshelf, *The Natural History of Chronic Bronchitis and Emphysema* was written in the mid-1970s based on data that was generated in the early 1960s looking at a cohort of British workers and followed a bunch of British men for a period of eight years.

And this really is the foundation for what was our historical understanding of how COPD developed and progressed.

And if we go onto the next slide, you know, what we have here is a slide that depicts the natural history of chronic airflow obstruction and COPD. This was actually based on data that was adopted from Fletcher and Peto by one of the US's most famous respiratory epidemiologists, Ben Burrows, who started out in Chicago and went on to Tucson where he developed the Tucson Longitudinal Studies.

And a lot of his - a lot of what we know about lung disease is very much based on the work that Dr. Burrows did. But if you click this slide again and you'll see a green line appear. And this represents how some people are thought to lose lung function over time.

Click the slide again you'll see a red line and you click it yet again and you'll see a blue line. And what is important about this slide is that when a patient comes to see us clinically and typically, you know, that Dr. Tomashaw and I see are in their 50s, they have an FEV1 which is the forced expiratory volume in one second which is a marker of COPD that is low so somewhere between a liter and a liter and a half.

And one of the questions is is that we know that they have disease but we don't know how they got there. And what Dr. Burrows is trying to point out in this slide is that there are probably several different pathways that people can develop COPD.

And the one pathway here is the green line. And these are people who never reach their maximal lung function in early adulthood and this either because

of early life exposures or perhaps, you know, illnesses that are very long gauge or other factors.

But basically the thought here is that these people are at increased risk for lung problems from very early adulthood on into later adulthood. And this is one pathway of developing COPD.

The red line represents people who reach near normal lung function early in life but then have multiple events that lead to the accelerated loss of lung function. And these are exacerbations or perhaps other factors.

And then the blue line represents people who have had a - have reached near normal lung function and then at some point in adult life have a very rapid loss of lung function. And the point is that all these people are called COPD but in fact may have, you know, different pathways to developing the disease and perhaps potentially different interventions.

And if we go onto the next slide this actually was a review article in the New England Journal that appeared last year, I guess a year and a half ago now, that was looking at, you know, how this actually plays out in real life.

And here the sample that was discussed are adults survivals of bronchopulmonary dysplasia. And of course bronchopulmonary dysplasia for those of you that are not involved in pediatrics is a complication of premature birth. And the thought here is that infants who survive premature birth - and 50 years ago all these babies died.

In more recent years these babies are surviving into childhood and into adulthood. But one of the complications of their survival is impaired lung function. And if you look at the red line here with the blue line being normal

these children as they grow into adulthood don't reach normal lung function. And it is thought that as they go into later adulthood that there are going to be increasing risks for developing diseases such a COPD.

Our next slide now looks at how we characterize lung function impairment. And this is a sort of a rather simplistic view of how we characterize lung function using a - one of the more standard ways of doing this. And these are the Gold criteria; Gold is Global initiative on obstructive lung disease.

And although this is a classification scheme that is not without its imperfections, that it seems to work reasonably well in most adult patients. And the way this works that if you look at - that there are two major classifications down at the bottom that if a person's FEV1 which is the forced expiratory volume in one second, to their FVC which is the forced vital capacity - and these are measurements that are made using spirometry.

If this was less than 70% we see that this person is in general obstructed and we put them on the obstructed side of this. If the person has this ratio that is more than 70% we say that that person is not obstructed. And then we calculate their FEV1 as a percent of their predicted value.

Now this is determined based on a person's age, height and race, ethnicity and gender. So we know for example that, you know, a person - a 60-year old male who is Caucasian whose height is six feet tall should have an FEV1 that is a certain level.

We then compare their actual FEV1 to that level and get a percentage. And based on that percentage you can classify a person if they are in fact obstructed into any one of these Gold stages. If they're above 80% we call Gold 1 and if they're less than 30% we call them Gold 4.

Now if you look at the other side of this equation these are people that have a normal FEV1/FVC ratio and people can either be normal or if they have symptomatology, you know, we'd traditionally - we formerly was classifying them as Gold 0, which put them in an at risk group.

And some of the more recent Gold stratification schemes - this classification is no longer there but is still thought to be, you know, predictive of poor outcomes.

And then in addition there is a restricted group that is people who have normal FEV1/FVC ratio but have low lung function, either low FEV1 or low FVC. And these people tend to have bad outcomes.

And if you go onto the next slide this reports those bad outcomes. And one of the most important outcomes is death. And as you can see in this slide - and this is a cohort of middle age adults in the US between the ages of 45 and 64 at baseline. And as you can see people who have evidence of severe COPD, Stage 3 or 4, die very quickly than the other groups.

Now although people with any degree of lung function impairment or even people who have symptoms die more quickly than people who are in none of these categories.

Now if you go onto the next slide, you know, this answers the very important question well what do these people die from? And as I alluded to earlier most people who have - even have evidence of severe COPD, that Gold Stage 3 or 4, the majority of them do not die from COPD, that actually you have a large number dying from cardiovascular disease, a very large number dying of lung cancer and people dying of other causes of disease.

And this cohort is around 30% of people who had evidence of severe COPD at baseline who had their death attributed to COPD. And if you look at people in the moderate COPD category it's around 5%. You have far more many people dying of lung cancer and cardiovascular disease. And this is something that we're now paying more attention to, I mean, how COPD relates to the presence of other diseases.

If you go onto the next slide, you know, this slide examines the disease burden in the United States and if you click it twice and you'll see - and this actually stratifies the population by smoking status. And as one would expect if you look at the red rectangles COPD is more common - you look at severe COPD more common in smokers than former smokers and never smokers.

But if you click it again you see moderate COPD and again mild COPD and then the final click is for the restricted group. And what this highlights here is that COPD is both a disease of smoking and of aging. And you do see some evidence of COPD even in the United States in people who have never smoked but it tends to be less severe than what you see in current or former smokers.

If you go onto the next slide this slide looks at the impact of COPD on mortality. And although this is a busy slide I'll walk you through one piece of it. For example if you look at males who have severe COPD so Stage - Gold Stage 3 or 4, you know, what this is predicting is based on NHANES follow up data is how long the person who is at age 65 would be expected to live.

So basically a current smoker age 65 male could be expected to live another eight to nine years if they were currently smoking. If that person were a

former smoker you would expect them to live another 10 years and if they were never a smoker you would expect to live about another 15-16 years.

And this highlights both the importance of smoking and the presence of lung function impairment on survival. And in general people with poor lung function die faster than people with better lung function and current smokers die before current smokers - current smokers die faster than former smokers who also then die faster than people who have never smoked.

So again this sort of highlights the interaction of both smoking and lung function impairment on life expectancy. And this is sort of another viewpoint of that. And this shows that, you know, people who have never smoked who have COPD although their mortality is somewhat, you know, worse than people who have never smoked who don't have COPD that their survival is still very much better than people who are former or current smokers with evidence of COPD.

And as I alluded to earlier in the United States around 20% of people who have evidence of moderate or more severe COPD have never smoked. If you go onto the next slide, you know, this highlights the importance of asthma in this group, you know, whether a person is a current, former or never smoker if you've had a history of asthma historically you're more likely to have COPD.

So in each case, you know, the orange bar which are people who report asthma who have evidence of COPD is much taller than the blue bar. And this is, you know, the strongest effect is seen in never smokers although you see effect both in current and former smokers.

And I think this is something important clinically in that I think many of my COPD patients and I'm sure Dr. Tomashaw has the same experience. They

come and say well you know, I've had asthma for the past, you know, 25 years and the fact they have COPD now although it's been called asthma.

Next slide. You know, this highlights another sort of important factor in why people who have never smoked have COPD and this relates to occupational exposures. And this was a very nice study that came out of the San Francisco group that basically shows that - the relationship between smoking and dust exposure and people who report that they have COPD or emphysema.

And what this shows is that, you know, irrespective of smoking status, you know, for example the green bar, you know, looks at reported COPD in people who have never smoked who've had no exposures to vapors, dust, gas or fumes in the workplace.

And the yellow bar, you know, looks at people with exposure and it finds basically a doubling of the risk of people reported that they have COPD. And you see a similar effect in smokers that, you know, smokers without exposure around 10%-12% of those report evidence of COPD whereas if they reported exposure that then doubles them to the 20%-25% range.

So again highlighting the importance of exposures other than cigarette smoking in the development of COPD.

And with this I will now hand it over to my esteemed colleague, Dr. Tomashaw, to talk about disease treatment issues.

Byron Tomashaw: Thank you very much David. It's a pleasure joining you today and I thank you for inviting me.

I just wanted to re-stress what David had just said. For far too long COPD has been a disease surrounded by misperceptions; the perception has been that it's a disease of the elderly, but as David mentioned we're seeing more and more of it in middle age people.

The perception has been that it's been a disease of men but we're clearly seeing more and more of it in women and in David said since 2000 more women have been diagnosed with it and died with and been hospitalized with this disease.

The perception has been that it is a self-induced disease but around 20% of people with COPD in this country never smoked and many, many people around the world depending upon what they're exposed to.

And even with smokers only a relatively small percentage develop significant COPD suggesting that other factors whether genetic or environmental play a role.

And finally the perception has been that this has been a poorly treatable or untreatable disease and that's what I'm going to talking about and that too is truly -clearly untrue. COPD is almost always preventable and it is almost always treatable.

So as you can see in this first line here which talks about how the disease may progress and your FEV1 may decrease and your symptoms may increase and the management, you can see in that first blue line, the importance of smoking cessation.

If you go to the next slide this is again that Fletcher curve that David talked about before. And what I would stress there is that the green line is the aging

process that we all go through, the red line going down is what happens in people who have smoked or potentially exposed to other things and is susceptible to those exposures.

But what is most intriguing to me is the - are the other two lines, the orange line and the light blue line suggesting that whenever you stop smoking, whenever you stop the exposure that the rate of deterioration in lung function can actually decrease potentially very close to the rate of normal aging.

That's one of the reasons why we have always considered smoking cessation a disease modifying therapy because the rate of deterioration can indeed be slowed.

Now if you look at the next slide recognize again that smoking is not the only cause of this disease and that genetic and environmental factors play a role. Smoking is clearly the most important factor in this country. And the perception has been out there that most smokers don't want to quit and that is too - also not true.

There's a lot of data out there suggesting the majority of smokers want to quite and many try many times. So as you can see here there's data suggesting that 70%-80% of smokers want to quit, that 30%-50% of smokers try quitting year. That it's not unusual for - in a lifetime to have six to nine quit attempts but that only a small percentage of smokers who quit unaided stay abstinent for more than 6-12 months.

Having said that and recognizing that I have a somewhat unusual patient population and I work in a tertiary care facility and people seek me out to some extent because my expertise in these areas. Although almost everyone in my practice smoked almost no one in my practice smokes now suggesting that

if you're aggressive enough with your approach that you can make a difference.

And there are options as you can see in the next slide. Recognizing that smoking cessation can be very difficult there's a lot of evidence suggesting that you can combine counseling, behavioral therapy interventions with some of the FDA approved pharmacologic interventions that you can clearly improve success rates.

It is certainly true that just using counseling for less than three minutes or better yet for more than three minutes can significantly improve quit rates but if you add to those that counseling some of the pharmacologic therapy your chances of success are far greater.

And if you go to the next slide you can see that there a number of FDA approved agents to help people quit smoking. And the data is very clear that we as healthcare providers underutilize what is available.

It's aggravating because, you know, if you look nationwide approximately 80% of people on antihypertensive drugs - are on two or more antihypertensive drugs we tend not to be as aggressive with our therapy with smoking cessation although you could argue that there is nothing more important that we can do than getting people to stop smoking.

So as you can see here there are a number of nicotine products that are FDA approved. There's also Bupropion which as you know is an antidepressant which has been approved for years in the use of smoking cessation. And then the newest of the drugs is Varenicline which has now been approved I guess for two to three years.

It's worth noting that both Bupropion and Varenicline receive black box warnings at the exact same time from the FDA within the last - I'm going to say four to five months stressing that there have been some psychiatric issues raised, some suicide ideations, some suicide attempts raised with the use of these medications.

But I would also suggest to you that it was the fairest black box warning that I've seen in 30-35 years of doing this in the sense that the black box warning basically says while there may be risks with these drugs, as there are with any drugs, that smoking cessation is perhaps the most important thing that anyone can do, and that these drugs have been shown to be effective in smoking cessation and therefore like with any other medications you weigh the risks and the benefits.

It's worth noting that certainly in people who smoked or smoked heavily that using one nicotine agent alone is unlikely to get you anywhere that there's a lot of data suggesting that if you combine nicotine agents that you'll be more successful. You can combine Bupropion with nicotine agents with increased success.

There is no rationale and including agents with Varenicline which is both an agonist and antagonist so there's no rationale really of including them with Varenicline. And there's no existing data combining Bupropion and Varenicline although there is some safety data suggesting you can use it.

I would only stress that smoking cessation is probably the greatest risk factor that we have. It's certainly the most common cause of preventable death and illness in this country, probably some 40% of those relate to smoking. And if you're aggressive with your approach between counseling and available medicines you can make a difference.

If you look at the next slide which brings us back to the subject matter tonight which is COPD you can see where you need to start thinking about looking for COPD.

So you look for exposures particularly tobacco smoke or some of the occupation things that David had mentioned or some pollution effects particularly around the world with exposure to biomass fuels and then you combine that with symptoms, exercise impairment, shortness of breath, cough, sputum production.

And the combination of those things, the exposure and the symptoms, should lead you to consider spirometry which is a relatively simple breathing test that can be done relatively easily. And if it's abnormal it doesn't necessarily mean you have COPD because you need to do bronchodilators to try to differentiate asthma from COPD but spirometry is certainly the way to make a diagnosis of COPD. So exposures, symptoms, should lead to spirometry.

If you look at the next slide you can see that spirometry is clearly underutilized in primary care. It's worth stressing that patient history and physical finding are not enough to accurately diagnose COPD but only 1/3 of patients with COPD have undergone spirometry as part of their diagnosis.

And as you can see spirometry use decreases with increasing age even though as David showed you the risk of COPD probably does increase as you get a little bit older. So we underutilize spirometry and that's part of the reason why - probably half of the COPD patients in this country have gone undiagnosed.

That's undiagnosed, not asymptomatic. Many of these people are symptomatic but have not yet been diagnosed. And one of the problems

dealing with COPD and indeed a number of lung diseases is that people can self-treat by cutting back on their activity level.

And one of the problems we get into in lung disease is that if you're a busy primary care physician and you only have a couple minutes to spend with your patient and multiple medical problems if you ask only one or two questions about their breathing and ask the wrong questions you're likely to get the wrong response.

So if you ask Joe how is his breathing more often than not Joe is going to say it's not bad doc because you've cut back on your activity level. The right questions are how's your breathing compared to how it was six months ago? Can you do what you did six months ago? Can you do what you want to do? If you ask those questions you're more likely to get a very different response.

If you look at the next slide we now then go back to one of the things Dave touched upon which is Gold therapy - the Gold guidelines. If you - you can see here the division between moderate, severe and very severe are based basically upon the FEV1.

That is - the FEV1 is simple to do it's done with spirometry, it's not perfect but it certainly can be used. If you click again you'll see the therapeutic options.

And as you can see with those patients with more mild disease you start with reduction in risk factors particularly influenza vaccination, potentially pneumococcal vaccination, avoidance of smoking and other exposures and the addition of as-needed bronchodilators.

As you move along to more severe disease in moderate you see that the next step of therapy is to add regular treatment with one or more long-acting bronchodilators and then adding pulmonary rehabilitation.

And then as you get more severe particularly in those patients with FEV1s less than 50% and exacerbations that's where you tend to add the inhaled glucocorticoids. And I would stress that that is a significant difference from the asthma guidelines, in asthma if you go beyond short acting as needed bronchodilators the next step in therapy is generally anti-inflammatory drugs particularly inhaled corticosteroids.

In COPD the next - the step with moderates is to use the long-acting bronchodilators oftentimes more than one and then adding the inhaled corticosteroids with more severe disease and with exacerbations.

If you then look at the next slide you can see that we've got a wide range of bronchodilators looking - going from short-acting beta-agonists to short-acting anticholinergics to the long-acting agents. And as you can see on this slide many of them are very effective in helping FEV1 and lung volumes and dynamic hyperinflation and shortness of breath and exercise tolerance.

But we have really little definitive data as of yet suggesting that these drugs can modify the course of the disease by FEV1. Now I would argue that that's because we've been lumping all COPD together and that if we did it in a more careful fashion you would see benefit but that is still something that we are struggling to find.

But it's important to note that the side effects here are really quite minimal. So you have a whole bunch of people who are really quite symptomatic who we

can help and yet it's clear that we are under diagnosed, sometimes misdiagnosed and even when appropriately diagnosed often under-treat.

The next slide actually is data from what we call the Optimal Study, really a small study published in the Annals of Internal Medicine in 2007. But it's important from my standpoint because in point of fact as we deal with this disease especially dealing with the more severe disease, with the exacerbators, this has been a disease that needs to be treated with multiple treatments.

It's not a disease that can be treated effectively with one therapy alone. And certainly the huge bulk of my patients with severe and very severe disease and frequent exacerbations are on combinations of long-acting beta-agonists, the long-acting anticholinergic and an inhaled corticosteroid.

And many of my patients are on triple therapy if you will, exercise regularly and rarely actually end up in the emergency room, rarely end up in the hospital. And while limited most of them would suggest that they have a reasonable quality of life. This is a treatable disease.

If we look at the next slid which looks -- it's the vicious circle of COPD -- what ends up happening as you can see that increasing breathlessness leads to decreased exercise capacity, leading to physical deconditioning, leading to increased ventilation requirements and this immobility cycle, which clearly leads to worsening of function especially if many of these people are - and many of them are - are inappropriately treated with long treatments with systemic steroids.

If you look at the right side you can see what pulmonary rehab does. It decreases breathlessness, increases exercise capacity, increases reconditions

and decreases ventilation requirements. And a point of fact I do exercise all my patients with moderate COPD or more.

Ideally in pulmonary rehab programs if you're in a place where pulmonary rehab is not available then setting them up an exercise program is a critically important step.

If we then go back to that initial slide that I showed you and then double - then click again it brings us to that red column. The red column are the people with very severe disease. Now many of these therefore would already be on triple therapy if you will as well as getting rehab.

But here is where additional therapies need to be considered. And if you click one more time you can see that oxygen for 50 years has been shown to be a drug which can be very effective in COPD and in point of fact several large studies done in the 50s showed that oxygen therapy can improve quality of life, pulmonary hemo-dynamics and length of life.

And for many years oxygen therapy was the only therapy that we had defined as defining improving length of life as well. These days with some of the newer portable light-weight oxygen equipment you can actually really improve your patient's ability to leave the home and have the quality of life.

If you look at the next slide you see the most recent of the therapies that we have that improve survival in this disease and that's lung volume reduction surgery. This is a perfusion scan which shows that in the top areas of these patients that there is very little perfusion.

And for many years now in patients with more of the emphysema form of the disease where our medicines tend to be a little less effective we've looked at

surgical options. The National Emphysema Treatment Trial was started in the mid-1990s. And the results are sort of outlined in the next slide.

So there are 1200 patients studied, if you click again you see that there was a high risk group. These are patients with diffuse disease and decreased expiring capacity and very low FEV1 where there was no benefit and indeed increased mortality.

But if you click again you see that here are upper lobe patients, patients predominantly upper lobe emphysema who indeed had significant improvements in quality of life and exercise capacity with this surgery. And indeed in those patients with upper lobe predominant disease and low exercise capacity really quite dramatic improvements in survival using the surgical approach.

And following the National Emphysema Treatment Trial Medicare did improve this for use in centers of excellence; these are generally lung transplant centers around the country.

So this is a modality that can help but I would also come back to stress what David said earlier - Dr. Mannino said earlier - that this is not one disease, COPD, that there are many (dis invariance) of this disease. And as you can see here lung volume reduction surgery is not for everyone, it's for people with an upper lobe predominant component.

The last couple of minutes I just want to say a couple words about exacerbations which are - David had touched upon and really are a critical issue. These are those episodes with increased cough and shortness of breath which clearly can lead you to a much more rapid downhill course.

Many of us believe that exacerbators - frequent exacerbators should almost review it as a separate disease. You can see that 77% - almost 80% of patients with COPD would tend to have at least one exacerbation.

And as you can see in the next slide which looks at the outcome of COPD exacerbations you can see we don't do well here, outpatient failure rates up to 30%, relapse rates in the emergency room where they have to go back of up to 30%, hospital mortality of 2.5%-10% and ICU mortality of 20%-25%.

So obviously it would be best to try to prevent these because we don't do well with them. But if you look at the next slide you can see that even those people who survived the exacerbations that they take a very long time if ever to get back to their baseline.

So the bottom line, the white line of those with no further exacerbations after a single one the top line multiple exacerbations and you can see that they don't come close. And many of these people do recurrently exacerbate and that's frustrating because we do have some therapeutic options.

As you can see in the next slide which looks at preventative measures there is a lot of evidence suggesting that both the long-acting bronchodilators whether beta-agonists or anticholinergics and inhaled corticosteroids can decrease exacerbations.

There's evidence that the phosphodiesterase inhibitors like the (roflumilast) and the newer PDE4s can decrease exacerbations. Influenza vaccine and pneumococcal vaccine in this population are unbelievably important particularly influenza vaccine is the poster child for preventing exacerbations in the COPD population.

OM-85 is a vaccine available in Europe that has been - show to have some effect. Macrolides as you know are drugs like clarithromycin are antibiotics but also have an anti-inflammatory effect that can make a difference. Lung volume reduction surgery has been shown in those people where it can be effective, can decrease exacerbations.

And case management, what that means is you teach your patients how to deal with exacerbations, providing them with a course of steroids and antibiotics and bronchodilators at home when they check in with you. And if you're aggressive with that it can make a difference.

And if you look at these things and put them into an active role it really can make a difference. I want to stress again there is no clear role for systemic steroids in this disease beyond 10-14 days during exacerbation.

If you look at the next several slides which deal with influenza in the COPD population you have an aging immune system, many of them are on some type of steroids, they have multiple comorbid illnesses as David mentioned. They have impaired airway defenses and reduced lung reserve.

And the evidence is very clear that everyone with COPD should be vaccinated against seasonal flu. In addition everyone with COPD should get pneumococcal vaccination. The data with pneumococcus is much less clear than it is with - thank you - is much less clear than it is with influenza vaccine but I still do use it and I think most of us do.

And there's a lot of evidence suggesting that everyone with COPD should get vaccinated for H1N1 using the injectable form. Now as you know H1N1 is greatest at risk for pregnant women, for children, for healthcare providers who are exposed and for people who take care of children - particularly children

under six months of age who cannot get vaccinated. Those are the highest risk groups.

As you get a little older particularly over 65 the risks seem to be somewhat less. Most of us believe that anyone between 6 months and 23, 24 years should get H1N1 and anyone between 24 and 64 or 65 with any sort of lung disease or medical problem should get H1N1 if they're not allergic to eggs and can safely get the vaccine.

Most of us believe that in your older COPD patients because of the risk of influenza that they should get this as well although I would suggest that the data there is a little bit less clear but most of us do believe that.

Next slide please. So I certainly do agree with this that persons with COPD or asthma should not get the live attenuated nasal spray flue vaccines. And that there is evidence suggesting that the inactivated H1N1 influenza vaccine can be administered at the same visit as any other vaccine and I think that those are important.

I do think that it's important to use this. You know, I know that some areas of the country were hit very hard with H1N1 in the spring including New York area which is where I am. And it's been somewhat less of an issue here in the fall, but we're still not over the hump yet and obviously a lot of places around the country it has remained a major issue.

If you look at my - the last slide I have basically it's that while you should prefer to prevent exacerbations you should certainly try to treat it if it occurs. And the treatment as you see outlined here bronchodilators, systemic steroids, again a short course, generally 10-14 days.

Whether you taper that dose over those 10 days or just put someone on 40 milligrams of prednisone for the 10-14 days really is up to you. There's very little data suggesting one way or the other.

The role of antibiotics is still a little controversial here but most of us believe that if there's puerile in sputum, increased cough, increased sputum production that they should get a course of antibiotics, the data isn't great but it does suggest that it works.

Oxygen therapy if their oxygen count starts dropping below 90%. I would also stress with you that just because someone needs oxygen during an exacerbation doesn't necessarily mean they need it long term and they should be checked again once they get better from the exacerbation to see if they need it longer term.

Non-invasive positive pressure ventilation has been shown to be very effective in hospitalized patients in preventing exacerbation. So if you have someone who's very ill and you can sometimes avoid intubating by using non-invasive positive pressure techniques and it's underutilized and ultimately if you have to intubate although maybe with time we'll see some other modalities that can avoid that as well.

This is the foundation that - the COPD Foundation is a foundation that both David and I work with. Certainly NHLBI has been actively involved with COPD. They have a major campaign. This is their email, www.learnaboutcopd.org. I would suggest going to that for more information.

And finally as David said several times COPD is preventable and treatable and hopefully if we live long enough it'll be curable. And if you click one more time you see Dr. Maninno's license plate which I love.

Thank you guys.

Alycia Downs: Great, thank you so much for that presentation. Operator is it okay if we do the question and answer session now?

Coordinator: Sure. If you would like to ask a question at this time please press star 1, please make sure you unmute your phone and record your name when prompted so I may introduce your question. If you'd like to remove your question from the queue you can press star 2.

Our first question comes from Dr. (Norman Castel), your line is open.

(Norman Castel): Yes. First of all comment, clicking the slide had no effect. I have Office 2007 and it says it's running in compatibility mode so you might look into that. Everything showed, all the colors showed it once.

My question is about the flu vaccine. I mean Bucks County Pennsylvania. We're giving vaccine tomorrow afternoon and evening to the public and our health director has still limited it to people in the priority group. And elderly people who have asthma or COPD are being refused the vaccine.

I think the CDC needs to get on that and say that now that there's plenty of supply of vaccine we can stop using that priority list. That's it.

David Callahan: I can take that question; this is Dr. David Callahan from CDC. We address this on a state call with the state epidemiologist about a week and a half ago providing the state public health officer leeway to decide whether they want to expand the risk groups.

The other thing I'll point out too - and the CDC right now is still recommending the high risk populations over those - over the general populations are those over 65. However the ACIP guidelines are just that, they are guidelines. And we do defer to the local clinicians and the local public health authorities to make the decision on vaccine distribution and administration.

Byron Tomashaw: Yeah I think that it is a critically important question. I don't know anyone who has a definitive answer. I do think that as the supplies have become more available that it's probably wise to widen what we're doing with it. I think all of us who do this however believe that the pregnant women and the younger people do still have some degree of importance here because so many of the deaths have been in those populations.

(Norman Castel): Yes well I think that group has been vaccinated - most of them by this point. We're at the point where were giving the second dose to the children under 10+ members of the general public who are in the priority group. Hopefully the obstetricians received the vaccine for their patients.

Coordinator: Our next question comes from (Joel Greenspan), your line is open.

(Joel Greenspan): Thank you. I have two quick questions. First of all I enjoyed the presentation very much. I really want to think about this whole problem from a public health perspective. So I guess my first question is how well do we know whether this large cohort of people with COPD - how do they fare during the current wave of H1N1? That's kind of one quick question.

And second of all is this - are COPD exacerbations known to be seasonal and how well is that studied? I can imagine that it must be seasonal in terms of co-infection with influenza in the winter but I'm curious to know whether heat,

pollution, high humidity in non-winter months also causes exacerbation and how well that's recognized?

David Mannino: This is Dave Mannino. I can answer sort of like the second question. And we know for example that if you look at, you know, weekly mortality curves for seasonal influenza and COPD they overlap almost exactly, that many - I think often that our COPD patients are almost like, you know, sentinel - the canaries in a coal mine in that they're very susceptible to seasonal influenza.

Of course the H1N1 it has been an entirely different, you know, beast. And I think the epidemiology of H1N1 detection and mortality is that the case fatality rate has been very different, you know, targeting a different group.

Also, you know, Dr. Tomashaw and I can tell you anytime a COPD patient gets a respiratory infection, and exacerbation that puts them in the hospital and that's about event and it's, you know, much more likely to result in death.

Byron Tomashaw: Again I have not - in the New York area at least we have not seen a lot of H1N1 this fall. In the spring during the major hit that we took we didn't see a lot of problems in the COPD population at least not dramatic but I'm aware of.

Are either of you to aware of any specific data with H1N1 in the older COPD population?

David Callahan: In some of our - this is David Callahan from CDC. In some of our epi investigations we've seen a higher proportion of persons with COPD end up hospitalized and in the ICU. However because the population of persons with COPD is skewed towards the elderly even though we do see it in all adult ages the elderly have more innate immunity so we are not seeing the rates among persons with COPD that we're seeing say among the population with asthma.

David Mannino: I think that make sense to me to David.

Coordinator: Our next question comes from Dr. (Migae), your line is open.

(Migae): Unless I missed it I didn't see any discussion of antivirals. Would you please discuss those? Thank you.

Byron Tomashaw: David, you want to comment on this?

David Callahan: Yeah, I'd be happy to. We know with persons developing influenza no matter who they are antivirals particularly started within the first 48 hours reduce the risk of hospitalization. That becomes marked when we look at high risk populations whether they be persons with chronic lung disease or pregnant women or children.

And we encourage those who are at high risk to seek treatment early when they develop influenza symptoms. And Tamiflu is the recommended antiviral for persons with chronic lung disease whether it be asthma or COPD simply because we've seen some bronchospasm episodes with Relenza, the inhaled antiviral.

Byron Tomashaw: My experience has been exactly that. I would also suggest that Tamiflu it may be even more effective as a preventative than it is as a treatment, so that if you have somebody who's in the household of someone who has a documented H1N1 then taking a week's worth of Tamiflu, just one a day, as opposed to the usual therapeutic doses of two a day for five days, can actually be pretty effective in avoiding or developing any sort of significant flu-like symptoms.

So it does if you treat it - so within 48 hours of symptoms you start Tamiflu twice a day you can decrease the severity but if you use it a little more aggressively as a preventative in someone known exposed that can help.

The other question that many of my patients have brought up to me is if you had H1N1 in the past - in the spring do you need to get H1N1 vaccination now? And most of the infectious disease specialists that I have talked to feel that if you've had documented H1N1 that there is no reason to do that.

On the other hand a lot of people who were exposed to H1N1 but not documented where it is a little uncertain most of us are giving them the H1N1 if they fall into the risk groups although if they've been exposed and have it insert a somewhat less.

Coordinator: And I show no questions at this time.

Alycia Downs: I want to thank our presenters for providing our listeners with this information and I'd also like to thank our participants for joining us today. The recording of this call and the transcript will be posted to the COCA Website and emergency.cdc.gov/coca, again that is emergency.cdc.gov/coca within the next week.

You have one year to obtain continuing education for this call. All continuing education credits and contact hours for COCA conference calls are issued online through the CDC Training and Continuing Education online system, www2a.cdc.gov/tceonline.

Thank you again for participating and have a wonderful day. And always remember that if you have any additional questions or comments for COCA

conference call you can always email coca@cdc.gov, again that is coca@cdc.gov.

Thank you.

David Mannino: Thank you.

David Callahan: Thank you, vey good.

David Mannino: That was great.

Byron Tomashaw: Thanks guys. Thank you very much for inviting me.

David Callahan: Yeah, I appreciate your putting up with our CDC clearance process and it was great presentation, I actually - I enjoyed listening on my end.

Byron Tomashaw: That was great. Thank you. Take care, we'll be talking to you soon.

((Crosstalk))

David Mannino: Yes absolutely and I'll see you Wednesday David.

((Crosstalk))

Alycia Downs: Thanks again.

Byron Tomashaw: Bye.

David Mannino: Okay bye.

David Callahan: Okay bye, bye.

END