CENTERS FOR MEDICARE AND MEDICAID SERVICES

Medicare Evidence Development & Coverage

Advisory Committee

(Meeting Held Via Webex)

July 22, 2020

Centers for Medicare and Medicaid Services

7500 Security Boulevard

Baltimore, Maryland

Panelists

Chairperson

Peter Bach, MD, MAPP

Vice-Chair

Joseph Ross, MD, MHS

MEDCAC Members

Timothy J. Barreiro, DO, MPH, FCCP, FACOI

Anita Fernander, PhD, ABPBC

Michael J. Fisch, MD, MPH, FACP, FAAHPM

Melissa M. Garrido, PhD, BS

Kim Kuebler, DNP, APRN, ANP-BC

Greg Manship, DBe, Mdiv, MA

Joy Melnikow, MD, MPH

Carla Perissinotta, MD, MPH

Marcel Salive, MD, MPH

CMS Liaison

Joseph Chin, MD

Industry Representative

Laura Mauri, MD

Panelists (Continued)

Guest Panel Members

Gerard J. Criner, MD, FACP, FACCP

Peter C. Gay, MD

Neil MacIntyre, MD

Invited Guest Speakers

John M. Coleman III, MD

Michael E. Wilson, MD

MEDCAC Coordinator

Tara Hall

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PANEL PROCEEDINGS

(The meeting was called to order at 8:00 a.m., EDT, Wednesday, July 22, 2020.)

MS. HALL: I want to welcome the committee chairperson, vice chairperson, members and guests to our first virtual MEDCAC meeting. I am Tara Hall, the Medicare Evidence Development and Coverage Advisory Committee coordinator.

The committee is here today to look at the state of evidence on home use of noninvasive positive pressure ventilation in patients with chronic respiratory failure consequent to chronic obstructive pulmonary disease. We are seeking the MEDCAC's recommendations regarding the characteristics that define those patient selections and usage

criteria, concomitant services and equipment parameters necessary to best achieve positive patient health outcomes in beneficiaries with CRF consequent to COPD.

The following announcement addresses conflict of interest issues associated with this meeting and is made part of the record. The conflict of interest statute prohibits

government employees from participating in matters that could affect their or their employer's financial interests. Each member will be asked to disclose any financial conflicts of interests during the introduction. We ask in the interest of fairness that all persons making statements or presentations disclose if you or any member of your immediate family owns stock or has another formal financial interest in any company, including any Internet or e-commerce organization, that develops, manufactures, distributes and/or markets consulting, evidence reviews or analysis or other services related to the use of CPAP, BPAP or mechanical ventilators. This includes direct financial investments,

consulting fees and significant institutional supports. If you require a financial disclosure statement, please email Leah Cromwell so she can send you the form for completion. Her email is Leah, L-E-A-H, dot Cromwell, C-R-O-M-W-E-L-L, 1@cms.hhs.gov.

We ask that all presenters adhere to the time limits. We have numerous presenters to hear from and a tight agenda; therefore, we

cannot allow for extra time. During each presentation I will let the presenters know when they have hit their halfway mark and when they have a minute remaining to help the presenters stay within their allotted time. Presenters will receive a prompt prior to their speaking time to ensure they are ready to present.

During the open public comments, attendees who wish to address the panel will be given that opportunity on a first come basis. Please email Leah Cromwell if you want to address the panel by 9:30 a.m. eastern standard time.

For the record, voting members present for today's meeting are Joseph Ross, Timothy Barreiro, Greg Manship, Anita Fernander, Kim Kuebler, Michael Fisch, Melissa Garrido, Joy Melnikow and Marcel Salive. A quorum is present and no one has been excused because of conflicts of interest.

The entire panel, including nonvoting members, will participate in the voting process. The voting results will be available on our website following the meeting.

We ask that all speakers state their name each time they speak, speak slow and precise so everyone can understand, speak directly into your computer mic, and do not use your speaker phone to help achieve best audio quality. Insure your devices are on mute if not speaking and while speaking, please place the ringers on silent. Remove pets from your area and anything else that will minimize distractions and limit background noises.

This meeting is being held virtually in addition to the transcriptionist. By your attendance you are giving consent to the use

and distribution of your name, likeness and voice during the meeting. You are also giving consent to the use and distribution of any personally identifiable information that you or others may disclose about you during today's meeting. Please do not disclose personal health information.

In the spirit of the Federal Advisory Committee Act and the Government in the Sunshine Act we ask that the advisory committee members take heed that their conversations about the topic in hand take place in the open

forum of the meeting. We are aware that many attendees including the media are anxious to speak with the panel about these proceedings. However, CMS and the committee will refrain from discussing the details of this meeting with the media until its conclusion. Also, the committee is reminded to please refrain from discussing the meeting topics during breaks or lunch.

And now I would like to turn the meeting over to Dr. Joseph Chin, CAG deputy

director.

DR. CHIN: Thank you, Tara, and good morning. Good morning, panelists and participants. I would also like to thank Dr. Peter Bach and Dr. Ross, our chair and vice chair, and the panel members who are really helping us by participating on this MEDCAC.

We have an important topic that we're discussing, the chronic pulmonary disease. It's very prevalent in the population and our decisions on these types of devices date back to 2001. So there's been a number of developments and much evidence that has been published since then, so it's helpful to get

input into what the evidence is showing at this point. We appreciate the input of the MEDCAC to help us fully judge the strength of the evidence to go through a very complex sort of environment with the number of different devices that have come into use since our last decision. So I think we should see fully based on good interaction with patients and your comments, the MEDCAC does not make coverage determinations but your input and your review

of the evidence does inform our decisions and our decision-making, so again, appreciate that.

And our team Tara, John and Michele and our division are here to support the meeting and if you have any questions or difficulties during the day please email them. Since this is our first virtual meeting I think as glitches occur we will try to work through them as quickly as possible, and ask for some patience during those times, but again, thank you and we look forward to the day, so I'll turn it back over to our chair, Dr. Bach. Thank you.

DR. BACH: Good morning, MEDCAC members and speakers. Good morning, CMS staff.

I am the chair today. I think of myself, this primary role as a ringleader, en emcee or something like that. A lot of my role will be to help the meeting move along to cover the steps that we've all agreed are necessary to have an open decision, to proceed with that discussion and produce useful votes and comments for the purposes of CMS's coverage

process. Part of this job for me is being a bit of a pain with regards to speakers and keeping everyone on time. I'll say in advance that I will seek to stop you when your time is up. It's not that you don't have important things to say necessarily, it's not at all that, it's just that we have an agenda and we have other speakers to get to, and things can very quickly fall off the rail. So with that in mind, I will ask everyone if you are able to and if not, let's discuss how to do it, is to please open your chat windows. I've been sending a couple of test chats both to CMS staff and to some of the speakers this morning already and not getting responses, so if you can look in your chat, that will be a useful way for me and probably for CMS people to

communicate with people individually about only logistical things. A reminder to MEDCAC members and panelists and speakers, panelists, that we are supposed to communicate openly in front of the panel and the public, so please no chatting about anything that isn't logistical, that all needs to be out in the open.

With that, I want to thank you again for coming and participating in this process. I think with that I will, we should get -- is it okay, Tara, Joe, if we get started? We are a little bit early. Let's get started with Dr. Katonak's presentation.

MS. HALL: Rachel, are you ready?

DR. KATONAK: Yes. Good morning. My name is Lieutenant Commander Rachel Katonak, and I just want to reiterate, thank you for everyone coming today and the panel members and invited GOEFTS for taking the time and dedication to participate in this important event. Next slide.

The Center for Medicare and Medicaid Services is conducting a Medicare Evidence Development and Coverage Advisory Committee panel to examine the scientific evidence

pertaining to the various types of noninvasive positive pressure ventilation or NIPPV devices in order to help us assess the characteristics as to selection criteria, the usage parameters, the associated services and equipment

parameters that are necessary to best achieve positive patient health outcomes and beneficiaries with chronic respiratory failure that is consequent or related to COPD. Next slide.

Chronic obstructive pulmonary disease or COPD is a productive disease that can cause acute and chronic respiratory failure which interferes with the ability to breathe. Its prevalence is heavy in our Medicare population. Respiratory failure is a condition that may be treated with various methods both pharmacologic and non-pharmacologic. In certain individuals NIPPV may be safely provided in the home and improve the beneficiary's clinical condition.

For the administration of such treatment, it's possible to choose from a selection of equipment that for the purposes of Medicare may be broadly classified into three categories, from mechanical ventilators,

bilevel pressure positive airway pressure devices or BPAP, and continuous positive airway pressure devices or CPAP devices. Next slide.

CMS's national coverage determination

for durable medical equipment reference list indicates that ventilators may be covered for neuromuscular disease, thoracic restrictive disease and chronic respiratory failure consequent to COPD. However, when necessary, each of these diseases may also be treated with other types of respiratory equipment. The choice of the appropriate treatment plan including the determination to use a ventilator versus BPAP versus a CPAP is based upon the specifics of each individual and if it's a serious medical condition. Next slide.

Currently there's substantial variability and, you know, regarding the prescribing patterns, guidelines and policies for these types of devices, yet the inappropriate prescription of such devices can lead to clinical deterioration, poor quality of life and ultimately death. We want to note that from 2009 to 2019 the growth and the number of Medicare beneficiaries receiving

ventilators has risen 1,278 percent, which is of great concern to us. Next slides.

In the afternoon session today the panel will vote and provide additional discussion on the following questions which I'm going to read for the record. We want to know that the types of NIPPV devices being referred to in the voting questions are used in the home for chronic respiratory failure consequent to COPD, and as I already mentioned, they're both home mechanical ventilators, BPAP and CPAP devices. Next slide.

Voting question number one: How confident are you that the evidence is sufficient to determine the patient selection criteria that will improve health outcomes? For example, laboratory values, comorbidities, frequency of exacerbations requiring ER or hospital admissions, hospital discharge timing, pulmonary function tests, et cetera, when used with any category of home NIPPV devices? Next slide.

Voting question number two: How confident are you that the evidence is sufficient to determine the NIPPV equipment

parameters necessary to promote successful

patient-related outcomes? For example, decreased mortality, decreased frequency of exacerbations requiring ER or hospital admission, increased time to hospital readmission for respiratory-related disease, and improved physical function and quality of life. Next slide.

Voting question number three: How confident are you that any improved patient-related outcomes noted above made with any type of NIPPV device in the home can be attributed to the use of the equipment alone as opposed to the concomitant provision of other support services like home respiratory therapists, home medication reconciliation and repeated elective hospital admissions? Next slide.

Voting question number four: How confident are you that the evidence is sufficient to provide the patient usage parameters that are necessary to achieve the successful patient outcomes in question two?

Thank you.

DR. BACH: Thank you very much for

that presentation, and thank you on top of that for ending early.

I already have messed up in my role as chair because I was supposed to ask each of the MEDCAC members, panelists to both introduce themselves and state their conflicts. I'm going to call out names, I'll start with myself.

I'm Peter Bach, I'm chair of the MEDCAC. I'm a physician at Memorial Sloan-Kettering Cancer Center, and I have no conflicts in relation to this meeting.

I call on my vice chair Joe Ross to introduce himself and also describe his conflicts, if any.

DR. ROSS: Good morning, everyone. My name is Joe Ross, I'm a general internist and on the faculty at Yale and also the vice chair of MEDCAC, and I have no conflicts as it relates to this meeting.

DR. BACH: Peter Bach again. I also remind the panelists please to turn on their cameras as part of doing this in the public. Everybody understands if you have to turn your camera off for a second or so, but please turn

them on as part of your participation in this meeting. I'll call next on Dr. Barreiro.

DR. BARREIRO: Good morning everybody, my name is Tim Barreiro, I'm a pulmonary critical care physician in Youngstown, Ohio, and I have no conflicts of interest.

DR. BACH: Next, I have Dr. Fernandez.

DR. FERNANDER: Dr. Fernander. I am on the faculty at the University of Kentucky College of Medicine, I have no conflicts.

DR. BACH: Apologies for that. Dr. Fisch?

DR. FISCH: Good morning, I'm Michael Fisch, I'm a medical oncologist, internist and palliative care physician. I'm a clinical professor at M.D. Anderson Cancer Center and I'm employed by AIMS Specialty Health. I have no conflicts as pertains to this topic.

DR. BACH: Dr. Garrido?

DR. GARRIDO: My name is Melissa Garrido, a health economist and on the faculty at Boston University's School of Public Health and the Partnered Evidence-Based Policy Resource Center at the Boston VA Healthcare Center, and I have no conflicts of interest.

DR. BACH: Thank you. Dr. Kuebler?

DR. KUEBLER: Good morning, I'm Dr. Kim Kuebler. I am the director of the Multiple Chronic Conditions Research Center, I'm a specialty provider in spine and orthopedics, and I have no conflicts of interest.

DR. BACH: Thank you. Dr. Manship? Greg Manship? Okay. I know we saw him earlier today but all right, I will go on. Dr. Melnikow? Oh, no.

MS. HALL: You're on mute.

DR. MELNIKOW: Can you hear me now?

DR. BACH: Yes. Hi, Dr. Melnikow, can you hear me?

DR. MELNIKOW: Yes, sorry about that.

DR. BACH: Something froze. Please go ahead and introduce yourself and state your conflicts.

DR. MELNIKOW: I'm Joy Melnikow at the University of California, Davis. I'm a family physician and I direct the Center for Health Care Policy and Research, and I have no

conflicts of interest.

DR. BACH: Great, thank you. And I

don't know, I think we sort of got frozen there for a second. Is Dr. Manship on?

DR. MANSHIP: Yes. Can you hear me now?

DR. BACH: Yes, hi. Good morning.

DR. MANSHIP: Hello. Greg Manship, I currently serve as the manager of the Human Subject Protection Program for OSF Healthcare that is headquartered in Peoria, Illinois, and I have no conflicts to disclose for this meeting.

DR. BACH: Thank you very much. And Dr. Salive?

DR. SALIVE: I am Marcel Salive, I'm a physician at the National Institute on Aging, NIH, and I have no conflicts.

DR. BACH: Great, thank you very much. I think, Tara, we might as well introduce the other members. I don't know, Tara, if conflicts need to be disclosed for them, I can't recall.

MS. HALL: You said presenters?

DR. BACH: It's just Laura Mauri, industry rep, and the guest panel members.

MS. HALL: Yes, okay, we can start

with them.

DR. MAURI: So good morning, everyone, I'm Laura Mauri, I'm an interventional cardiologist, I'm employed by Medtronic and I'm the industry representative. And as a disclosure, Medtronic does manufacture ventilators although in the United States not for home use; outside of the U.S. they are occasionally used for home use.

DR. BACH: Thank you. Dr. Criner?

DR. CRINER: Yes. I'm the chair, thoracic medicine and surgery at Temple University School of Medicine. I have research grants from Fillantrust (phonetic) regarding noninvasive ventilation, and I have about $1,500 of consulting fees with them in study design over the last five years.

DR. BACH: Great, thank you very much. Dr. MacIntyre?

Dr MacIntyre: This is Neil MacIntyre, I'm

a professor at Duke University in pulmonary and critical care medicine. I do intermittent consulting with VieAir, Pentec and HillRon, all of whom do, are in the noninvasive ventilation field. I primarily advice their engineers, I'm

not involved in their marketing.

DR. BACH: Thank you very much. Dr. Gay?

DR. GAY: Pete Gay, I'm a professor at Mayo Clinic Rochester pulmonary and critical care and sleep medicine, and sadly I have no conflicts at this time.

DR. BACH: We will see what we can do about that. All right, so I think we can proceed now. The first speaker, invited speaker was Dr. Coleman, who can introduce himself, state his conflicts, and then we can proceed with his presentation. Dr. Coleman, I'll hand it over to you for your review.

DR. COLEMAN: Can you hear me?

DR. BACH: Yes.

DR. COLEMAN: Okay. I thought I was going after Dr. Wilson, I just wanted to clarify.

DR. BACH: You know what, you're absolutely right, you are, it's my mistake. I'm having a rough morning. Again, I'm not in my caffeine therapeutic window. I apologize. Thank you for your presentation, Dr. Coleman, we will now go to Dr. Wilson. Again, my

apologies.

DR. WILSON: Good morning. Can you hear me okay?

DR. BACH: Yes, Dr. Wilson.

DR. WILSON: Okay.

DR. BACH: So we will get your slides up here and again, my apologies.

DR. WILSON: Excellent, thank you. It's really a delight to be here. My name is Michael Wilson, I am a pulmonary critical care physician at the Mayo Clinic in Rochester, Minnesota, and also an investigator with the Mayo Clinic evidence-based practice center. And the topic is to discuss noninvasive positive pressure ventilation in the home in patients with COPD. This was part of a large systematic review that our evidence-based

practice center performed in the past two years or so regarding noninvasive positive pressure ventilation in the home for all disease conditions, and today we will speak on patients with COPD. Next slide.

I would like to thank the director and associate director of our evidence-based practice center and all of the colleagues that

we worked with on this systematic review practice, Dr. Hassan Murad and Dr. Zhen Wang. Next slide.

The full report of this systematic review is available through the AHRQ website and of note, a portion of the report regarding patients with COPD was published in JAMA in the past year. Next slide.

I have no relevant disclosures in relationship to this project or this meeting. Next slide.

I would also like to acknowledge the multiple other people who were involved in this project, so colleagues at AHRQ, Dr. Lionel Banez, Dr. Elise Berliner, and colleagues at CMS, Dr. Susan Miller and James Rollins. And

in addition we have several key informants who helped guide this project and several peer reviewers who reviewed the final report and gave significant input, and I would like to thank all of them. Next slide.

Okay. So let's start a little bit with the background, and we discussed this just a little bit, but the condition that we are all here to discuss today is chronic respiratory

failure, usually an inability to maintain normal oxygen or carbon dioxide levels, and this is a condition that goes on for some time and it's not just an acute issue for these patients. As discussed before, there can be many different types of causes of chronic respiratory failure, COPD, thoracic restrictive disorders, neuromuscular diseases, obesity hypoventilation syndrome and additional causes as well, and if chronic respiratory failure is not adequately treated there can be low oxygen levels, there can be high carbon dioxide levels, and there can be potentially significant consequences associated with it,

including possible decreased quality of life, sleepiness, hospital admission, intubation, respiratory arrest, even death, and there's a high health care utilization and cost associated with each of these things. Next slide.

So one treatment for chronic respiratory failure is noninvasive pressure ventilation. In its most basic form it consists of a machine and a hose and a mask or mouthpiece or some other noninvasive interface.

And in the home this is typically at least initially delivered usually at nighttime so nocturnal use, although some patients may use it at night, some patients may use it during the day, and some patients may use it nearly continuously during the daytime and the nighttime.

As discussed before, there's three general types of machines that can deliver noninvasive positive pressure ventilation. The first is a BPAP machine or a Bi-PAP machine; second is a home mechanical ventilator machine; and the third would be a CPAP machine. Next

slide.

So there's different settings. Yeah, so previous slide. Thank you. So under BPAP, there can be different settings or different modes for a BPAP machine. Some examples include BPAP S or BPAP spontaneous, which is where you have a positive pressure when you inspire, you have a positive pressure when you expire, and there's no backup rate. You can have BPAP SP where you have a backup rate added on to that. You can have volume assured pressure support which tries to target a

certain minimum ventilation or a certain tidal volume, and there's other settings for BPAP machines.

Home mechanical ventilator machines, some common modes of ventilation in these types of devices include pressure support, pressure control, volume assist control where you can give a preset tidal volume in addition to others. Next slide.

So there's quite a bit of variability between these different types of machines, BPAP

machine, home mechanical ventilator machine or a CPAP. Some machines are approved to be used through noninvasive or invasive interfaces. An invasive interface in the chronic setting would usually mean a tracheostomy. They can differ in their modes of ventilation, they differ in the respiratory circuits, monitoring capability, safety and alarm systems, internal battery life, form of oversight and servicing, as well as the ability to perform device maneuvers such as long volume recurring. Next slide.

So there's several clinical dilemmas including, there's marked variability in usage,

prescribing patterns, policies and guidelines of these different devices and the questions remain which devices are optimal for which patient population and how do these impact outcomes. Next slide.

The objectives of our systematic review were to evaluate noninvasive positive pressure ventilation in adult patients with chronic respiratory failure in terms of initiation criteria, effectiveness, equipment

parameters, respiratory services and adverse events. Next slide.

The key questions we had for our systematic review are based on those questions, including which characteristic criteria were used when initiating noninvasive positive pressure ventilation, what was the effect of these different devices on patient outcomes, which equipment parameters were used and which home services were provided. Next slide.

So now I'll go to the methods of a systematic review and then analysis that we performed. Next slide.

So first we defined the study eligibility criteria and this is where we used

stakeholder and key informant input. We performed a literature review including nine databases. We evaluated studies for possible inclusion. We assessed the risk of bias of individual studies. We abstracted the data and outcomes of those individual studies. We performed a meta-analysis where we looked at where possible the outcomes of all studies

combined together. We assessed the strength of evidence based on all of this for the four main outcomes, and then we wrote the report which was then peer reviewed and with input from public commentary as well. Next slide.

So here are the inclusion criteria and exclusion criteria that we used. So the population is adults 18 years of age or older. We did not evaluate pediatric patients. Interventions were any studies that used any of these types of machines through a noninvasive mask or mouthpiece interface. We evaluated studies which had a comparative arm, so compared device use to usual care or no device use, or compared one device use to a different type of device use, or one type of mode from one device to another type of mode. Studies

needed to include one of these following outcomes; the four primary outcomes that we looked at were mortality, hospitalization, need for intubation and quality of life, with a wide variety of secondary outcomes including ICU admission, outpatient visits, ER visits, exacerbations, ADLs, dyspnea, sleep quality,

exercise tolerance, and adverse events. Timing, we evaluated studies that enrolled patients where they used the device at least one month in the home setting, and we evaluated patients who used the device in the home or assisted living settings. Study designs, we included randomized controlled trials, we also included nonrandomized comparative studies, prospective and retrospective, as well as looking at relevant systematic reviews and current clinical guidelines. We did not include before and after studies with single arm intervention. We evaluated studies that were published in the medical literature from 1995 up until November 6, 2019. Next slide.

For the four main study outcomes which were mortality, need for intubation, quality of life and hospital admission, we assessed each

one of these outcomes as strength of evidence according to published criteria. So for example, high strength of evidence means that we are confident that the estimate of effect lies close to the true effect and that the body

of evidence has no deficiencies and was judged to be stable. Moderate, the body of evidence has some deficiencies and is likely to be stable. Low strength of evidence means that we have limited confidence that the estimate of effect lies close to the true effect, or estimate of effect that we found in the systematic review lies close to the true effect of what actually exists. And insufficient evidence means we could not make a conclusion about the strength of evidence. Next slide.

So the determinants -- so thank you. So the determinants to come up with the strength of evidence include the study limitations, so each study was individually assessed for risk of bias, the directness of the evidence to the key questions, the consistency of the results, precision, and publication bias. Next slide.

Okay. So now I'll go to the results

of this review that we performed. Next slide. So for all of these categories we looked at about 6,000 abstracts. We looked at a thousand full texts and included 68 studies in our

review on all disease categories. Of those, studies evaluated patients with COPD. In addition to that, we did find 13 current guidelines as of 2019 regarding home noninvasive positive pressure ventilation. Of note, among the 68 studies that we included, the majority were published, the majority of the published studies were performed in Europe with a few in the United States and throughout other parts of the world. Next slide.

So here's the first key question. What characteristics criteria were considered when initiating noninvasive positive pressure ventilation in patients with COPD? To cut to the chase, they were widely variable amongst all of the different studies. Some studies used one criteria to start home NIPPV, some studies used criteria to start home NIPPV. Common criteria but not exclusive criteria were let's start it in patients with COPD who have hypercapnia. The definition of hypercapnia or

the cutoff range to enroll patients in this study was quite variable as well, ranging from

a 45 to greater than 56 millimeters of mercury. Studies often used pH above normal, or normal or above, to enroll patients. Some studies used hypoxia in addition to those other criteria. And some studies, and studies often used low FEV1 as part of the definition to include patients with COPD. Next slide.

Oh, sorry, we'll go back, let's see, oh, disease stability. Okay. So 24 studies enrolled patients with quote-unquote stable COPD which was defined as no recent exacerbation. 11 studies enrolled patients with unstable disease, so after hospitalization for an exacerbation. And a few studies enrolled patients with both stable and unstable COPD, and one study did not. And I'm so sorry, I can't really read the last bottom portion of the slide. Okay, it's the next one.

So in addition to the criteria used to start NIPPV, the processes used to titrate NIPPV were also quite variable. Common criteria included reduction of hypercapnia, reduction in hypoxia including nocturnal

hypoxia, achievement of preset target tidal

volumes, and a reduction in patient symptoms. Some of the studies had quite elaborate processes to titrate NIPPV including being admitted to a hospital, and some studies initiated and titrated an NIPPV at home, and some studies just used preset criteria and did not really use any process to titrate NIPPV at all. Next slide.

So the next key question is what was the effect of these different devices on patient outcomes. So the first comparison is studies that evaluated BPAP device use compared with no device use and I've lifted the four primary outcomes here, so mortality, hospital admissions, need for intubation and quality of life. So with regards to mortality we found that there was lower mortality in patients who used BPAP compared with no device. This was based on 13 studies enrolling 1,400 patients including eight randomized controlled trials and five observational studies. The odds ratio was .66, and 55 fewer deaths per thousand patients in those who used BPAP compared to no device. And our assessment of the extent of

evidence was moderate strength of evidence to support this conclusion.

With regards to the number of hospital admissions we found no difference in patients who used BPAP compared with no device. Again, this is based on five studies with low strength of evidence.

One study reported the number of patients with hospital admissions and this study showed fewer hospital, fewer patients with hospital admissions, and low strength of evidence, in patients who used BPAP compared to no device.

With regards to need for intubation or the number of intubations we found that there were fewer intubations in patients who used BPAP compared to no device. This is based on three studies and about 267 patients, with moderate strength of evidence.

Regarding quality of life, we found no difference in quality of life, and this was based on ten studies and about a thousand patients. Next slide.

If we look at secondary outcomes, so again, this is in Bi-PAP or BPAP compared to no

device, here's all of the secondary outcomes we looked at. So one study showed that the number of emergency department visits was lower in patients who used BPAP. The number of ICU admissions was almost statistically significant lower but not quite the number of patients with ICU admissions -- sorry, there's a lot of beeping on my computer and I'm going to just shut this down. Okay.

So the number of patients with ICU admissions based on one observational study was lower. Regarding COPD exacerbations, four studies majored this. There was no difference between BPAP and no device used. Activities of daily living, no difference. Dyspnea based on six randomized controlled trials, there was a statistically significant reduction in dyspnea and, or sorry, improvement in dyspnea associated with device use. No difference in six-minute walk distance tests, and one randomized controlled trial did show an improvement of 72 meters in the shuttle walk test amongst patients who used BPAP. Next slide.

Now if we look at studies that

enrolled patients using HMV devices compared to no device, there were far fewer studies who reported this, so regarding mortality there was no difference in mortality. This is based on two observational studies. Regarding hospital admissions, there was one study, it was observational and it did show a reduction in hospital admissions amongst patients who used HMV devices compared with no device, and again, this was a low strength of evidence.

If you look at studies that compared HMV device use compared with BPAP use, there was one observational study, and this showed fewer patients with hospital admission. If you look at HMV compared to CPAP use it was the same study, a large observational study, and the number of patients who used, I'm sorry, the number of patients who required hospital admission in the BPAP was lower compared to those who used CPAP. Next slide.

We performed a subgroup analysis in patients with stable COPD versus patients with unstable COPD and we showed benefits, or there

were benefits in both of these groups. In patients with stable COPD there was lower

mortality, higher activities of daily living and reduced dyspnea. In patients with unstable COPD or recent exacerbation there was reduced need for intubation. Next slide.

Based on reviewers' comments --

MS. HALL: No, you have 25 minutes left.

DR. WILSON: Okay, thank you. Based on reviewers' comments we performed a post-hoc analysis to see if different CO2 initiation thresholds had an impact on outcomes and there were no direct comparisons, so no study compared patients with, you know, CO2 of 46 to 49 versus higher or anything like that, so we performed an indirect comparison regarding this, and regarding mortality and hospitalizations we found no statistically significant differences regarding the level of hypercapnia used to initiate home NIPPV. Regarding quality of life there was a very modest improvement or higher reduction in quality of life for patients who had higher CO2

initiation thresholds. So for example, the initiation threshold of 50 to 51 to 52, there was a larger improvement in quality of life

compared to those studies where there was a lower initiation threshold such as 45 to 49. Again, this is very few studies and this was a very, it was just very few studies to support this and again, no direct comparisons to evaluate this data. Okay, next slide.

So looking at other device comparisons what we've done so far is BPAP compared to no device, HMV compared to no device, and then both of those compared to each other. If we look at BPAP compared to CPAP there was one study, number of patients with exacerbation was mildly reduced but not significantly. If we look at BPAP, volume assured pressure support ventilation versus BPAP ST, there was one randomized controlled trial that evaluated all of these different outcomes, and basically did not show any statistically significant difference in outcomes. If you look at HMC pressure controlled ventilation versus HMV

pressure support ventilation, no significant difference in quality of life or six-minute walk. If you look at length of use of patients who were on BPAP on six months versus patients who were on BPAP for less than six months,

there was one randomized controlled trial which showed mild increase in six-minute walk distance that was statistically different, but really no other difference in other outcomes they measured. If you looked at a group of patients that used either HMV or BPAP pressure controlled ventilation high intensity versus low intensity, there was no impact in quality of life. Treatment adherence versus nonadherence, there was one observational study that showed a reduction in all-cause hospital admissions that was statistically significant. There was one randomized controlled trial that looked at BPAP ST started in the home using telemedicine versus BIPAP ST started in the hospital and the outcomes there are listed, with really no statistically significant differences noted. Next slide.

So regarding the kind of main

outcomes, here are the forest plots from the JAMA article on patients with COPD. So if you can advance, so if you look at BPAP versus no device those are the studies as were listed, some are randomized controlled trials and some are observational, and again, there was a

reduction in mortality in this group.

If you look at HMV versus no device there was no statistically significant reduction in mortality and this is just based on those two studies there. And then if you do a pooled analysis, you know, combining all of the studies together, BPAP or HMV versus no device there was a statistically significant reduction in mortality. Next slide.

Looking at hospital admissions again, BPAP versus no device, there was no difference in the number of hospital admissions. HMV versus no device, one study, observational, showed fewer hospital admissions with HMV. If you combine all of those results together, it's not statistically significant, the number of hospital admissions. Next slide.

Number of intubations, BPAP versus no device, there was a statistically significant reduction and these are the studies that were included in that analysis. Next slide.

These are the studies that evaluated quality of life in BPAP versus no device. Regarding HMV, there were no studies that evaluated quality of life that met the

inclusion criteria, and you can see the pooled analysis at the bottom with the light green diamond shape, shows that there might be a slight improvement in quality of life but it is not significant. Next slide.

Okay. So in summary for patients with COPD based on this systematic review, our conclusion was that HMV versus no device is associated with fewer hospital admissions, low strength of evidence. HMV compared to BPAP was associated with fewer hospitalization admissions, low strength of evidence. HMV compared to CPAP was associated with fewer hospital admissions, again very low strength of evidence. BPAP compared to no device is associated with lower mortality with a moderate

strength of evidence; reduced need for intubation, moderate strength of evidence; and fewer number of patients with hospitalizations, low strength of evidence. Next slide, or advance.

And again, there were a number of secondary outcomes which had some improvements and a number of secondary outcomes that had no differences noted. Next slide.

So key question three is which equipment parameters were used in these studies which enrolled patients using home NIPPV for COPD. So the BPAP modes that were used and described in these studies included BPAP S, BPAP ST, BPAP volume assured pressure support, pressure control, and some studies did not specify which mode of BPAP they used. HMV modes used pressure support and pressure control. The prescribed daily usage for the individual studies was quite variable. Studies ranged in suggesting that their patients use the device for greater than five hours, although we have two greater than or equal to

eight hours a day in the BPAP studies, and up to 12 hours a day in the HMV studies. And the actual usage was a range; means nightly for these patients included a mean of four-and-a-half to nine hours amongst the different studies. And again, there was significant variability in these modes, prescribed daily usage and actual usage for the studies. Next slide.

Regarding home services, so there were 38 studies on COPD; only 15 of them talked

about anything related to home services. The home services that they discussed included a telephone hot line staffed by nurses, scheduled phone calls by a respiratory therapist, home visits by respiratory therapists, smoking cessation programs, and one study evaluated a comprehensive home care program with evaluation of physical, occupational and dietary needs in addition to prescribing them the device.

At this time we did not find any evidence or any studies that included criteria which assessed the efficacy of, or the impact of these different home services on the

outcomes of interests. Next slide.

Regarding adverse events, so we categorized adverse events or either serious adverse events or non-serious adverse events. Examples of serious adverse events, so I guess first of all, death, hospitalization need for intubation are serious adverse events but we characterized those as primary outcomes on this study and not as adverse events. So the adverse events were respiratory failure, any life-threatening illness, any disability, any required intervention or congenital anomaly or

birth defect. Non-serious adverse events were skin symptoms, eye symptoms, nose or mouth symptoms, GI symptoms, device or mask intolerance. Next slide.

So only 28 studies, and sorry, this is going back to all studies on all disease conditions, I will speak specifically about COPD in just a second but only about a third, and this is about the same for COPD, reported adverse events. So the majority of studies did not report adverse events and among those

studies that did report adverse events there really was no consistent approach for evaluating and reporting adverse events. But if you look at all studies, for example in these different device use categories, so for example at the top, HMV, the incidence rate of serious adverse events was quite low in all of the categories, including the no device category at the bottom. Then if you go to non-serious adverse events for all patients who used an at-home NIPPV of any type, or of these different types, it's about 35 percent or 31 percent, or 27 percent or 39 percent, so roughly a third of these patients experienced

non-serious adverse events, and then none in the groups of patients which used no device. Next, or you can advance. Advance.

And here are the different types of serious adverse events that were reported. So there were several reports of acute respiratory failure in patients, treatment failures, TIA, stroke, arrhythmia, so these are the serious adverse events that were reported in these studies in patients who received these

different treatment arms. Again, very few serious adverse events. Next slide.

We will go to the middle section, so there was really no difference in adverse events or treatment withdrawals in groups who used the device compared to groups who did not use the device or was amongst different devices in comparisons. In patients with COPD, six studies directly compared adverse events in patients who used home NIPPV versus those who did not use home NIPPV, and there was no difference, statistically significant difference in the total adverse events in those groups. Next slide.

So that is the data for the systematic

review that we did in patients with COPD. Taking a step back, we realize that there are significant limitations to the systematic review and analysis that was performed. One of the primary limitations is really the vast variability and heterogeneity amongst all of the different studies that were included, including the devices used, the modes used, the

duration of use, the prescribed uses that ancillary respiratory services provided, the definitions of the outcomes, the measurement tools to measure the different outcomes, the follow-up length of time, the amount of time the patients used these devices in the home. In addition to that, the conclusions from this are based really on low to moderate strengths or moderate strength of evidence, suggesting that for moderate strength of evidence the conclusions are, we would estimate would likely estimate a true effect in these different categories, but for low strength of evidence there is some, there's room for higher level or higher quality studies. There's limited evidence on studies that directly compare HMV devices versus BPAP devices. There's limited

evidence to evaluate the impact on clinical outcomes of the initiation criteria, the parameters that the home respiratory services provided. Amongst many studies there's a lack of reporting of the device type or the device mode. Part of this might be that a lot of the studies were done in Europe and there may be

less, well, there might be different regulations in comparing different devices in home devices in Europe compared to the United States and other countries around the world.

There's a lack of consistent approach to reporting adverse events with, you know, two-thirds of studies not reporting adverse events. We included studies that were published only in English and excluded studies that were not reported in English. Again, the majority of studies were conducted in Europe and the provision of home respiratory services may be different or is different in several European countries compared to the United States, and some of the reporting of the home respiratory services may not have been explicit but rather implicit, and it's unclear.

And in addition, all the studies that

we included only enrolled patients who used nocturnal COPD in the home. We did not find studies that met our inclusion criteria where there were patients in COPD who for hypercapnia required daytime usage for COPD. In addition,

we were unable to assess for publication bias because the number of studies was low in each individual direct comparison. Next slide.

So there's several areas for future research, I'm sure which many of you on this phone call are well aware of, but there is room to evaluate which devices and which modes are best for which patient population, what is the impact of home respiratory services on outcomes, what are the initiation practices which are optimally associated with improved patient outcomes, and how do all of these things differ or change when considering patients who require daytime NIPPV support. And again, this last one is probably more, there's just fewer patients with COPD who use daytime support but it does exist. Next slide.

So in conclusion, in patients with COPD who use BPAP compared to no device, there was lower mortality, lower intubations, fewer

patients with hospital admissions, improved dyspnea, no change in quality of life. In patients who used home mechanical ventilator devices compared individually with BPAP, CPAP

or no device, there were fewer hospital admissions. These conclusions are based on low to moderate strength of evidence as we could assess them. Current comparative effectiveness evidence is really not available to the impact of many device capabilities on patient outcome. The criteria to initiate and titrate home NIPPV and home respiratory services are quite variable and not really validated in comparative studies included in this study. And there's significant variability in the devices used and the modes used for each of these different devices. Next slide.

So that concludes our presentation, or my presentation. I will turn it back to Dr. Bach. I don't know if we have time for questions now or if we want to save that for a different time in the day. Thank you so much, I really appreciate being here.

DR. BACH: Dr. Wilson, thank you very much for that presentation, and it was

extraordinarily clear. Thank you also for finishing on time, which I'm of course obsessed

about, you're actually early. The process for you and everyone, we are going to hold questions until we have had input from all speakers and then there's a section immediately after lunch where there can be questions to the presenters, which would include Dr. Wilson, who I assume knows he's with us for the entire day or a better part of it.

So I'd like to move on now to Dr. Coleman, it's your second time to start presenting. I apologize again for my mess-up earlier. So if we can pull up Dr. Coleman's slides, great. Dr. Coleman, do we have you?

DR. COLEMAN: I'm here.

DR. BACH: Okay, and I'll ask everyone to please open your chat windows also so that for logistical issues we can be communicating as are needed. So Dr. Coleman, thank you very much for coming, and go ahead with your presentation.

DR. COLEMAN: Great, thank you, Dr. Bach. I am John Coleman, I am a professor of pulmonary critical care and sleep medicine

at Northwestern University, and today I'm going

to talk about noninvasive ventilation in chronic obstructive pulmonary disease. I thank the panel for my time here today. I am a clinician and spend the majority of my time dealing with chronic respiratory failure so it's an issue that's very important to me and very relevant for everyone to hear about this. Next slide.

I have no financial disclosure. Next slide.

So my role today is to take you on a journey of kind of what Dr. Wilson commented on earlier, and we are going to talk about the role of noninvasive ventilation in chronic obstructive pulmonary disease. So we're going to talk about, a little bit about the epidemiology and pathophysiology of what we're trying to achieve with noninvasive ventilation, and then I'm going to take you through the data that Dr. Wilson just went through and tell it in a story. Chronic respiratory treatment has evolved over time and I think that's very important to an understanding of where we are today and where do we go forward in the future.

I'm going to talk about the early stages of noninvasive ventilation and then talk about how the paradigm changed and how we are applying its use in our clinic today. Next slide.

So in a pre-COVID world, COPD was the fourth leading cause of death in the United States and the third most common cause of hospital readmission among the Medicare population. It is a disease that has a high burden both in quality of life and financially and this in turn contributes to a strain on the U.S. health system. Because of this strain and the effect on people's quality of life, this has led to an exploration of therapies beyond traditional pharmacotherapies, pulmonary rehab and oxygen, and this is where the role of noninvasive positive pressure ventilation comes into play. For my talk today so I'm clear, when I say noninvasive ventilation I'm referring to noninvasive positive pressure ventilation, so you'll know what I'm referring to. Next slide.

So what is the hypothesis, or what are we trying to achieve with noninvasive ventilation? (Unintelligible, static) and

improve respiratory mechanics, focusing specifically on hypercapnia, so you'll see this in two elements. We have emphysema starting at the alveoli and we have chronic bronchitis.

Emphysema leads to a hyperinflation of the lungs, the hyperinflation of the lungs from emphysema increases the lower airway resistance. This lower airway resistance puts increased pressure on the diaphragm muscle, increases the work of the diaphragm and it can lead to diaphragm muscle atrophy. So as you can see on the bottom of the slide, on the left side you have a normal lung, you have the regular diaphragm curvature, and then on the right side you can see the hyperinflated lung. The diaphragm is pushed down, the muscle fibers are stretched. It is this combination of diaphragm muscle atrophy and the increased area of resistance that leads to an increased muscle load for our patients with emphysema, and this contributes to that (unintelligible). Next slide.

So what are the goals of noninvasive ventilation? So the target on NIV is to offset this diaphragm dysfunction and actually achieve

a control of breathing with near abolition of diaphragm activity, thus reducing hypercapnia. We know from studies that chronic hypercapnia can induce skeletal muscle dysfunction, it can impact the function of the diaphragm. We also know that chronic hypercapnia can lead to suppress innate immunity, and reduce CO2 levels which may reduce COPD exacerbations.

Today I'm going to talk about chronic hypercapnia. It's well established in the literature that noninvasive ventilation in this study, versus COPD reservation, reduces mortality, reduces COPD exacerbation and reduces hospitalizations and length of stay. What I'm going to do today is talk about chronic COPD. Next slide.

So what does the data show? So I'm going to talk you through the data that Dr. Wilson kind of put together in his meta-analysis, and kind of pull it out and focus on how it has evolved over time.

So the story of COPD started around the turn of the century as Dr. Chin mentioned

earlier, it was in 2001. So the first study I'm going to talk about was done by Ciro

Casanova. The purpose of the study was to look at the role of COPD versus, the role of noninvasive ventilation for severe COPD versus long-term oxygen therapy. This was a randomized controlled trial, they looked at 52 participants, and what they did in this trial, they randomized noninvasive ventilation spontaneous with no backup rate versus home long-term oxygen therapy, and they included all patients with an FEV1 of less than 45 percent. The outcome of the study looked at the rate of COPD exacerbation, hospitalizations, intubations and mortality. They followed the subjects for one year and what they saw in this study was that after one year there was no difference in mortality, intubations, or any difference between interventions.

So this was followed by a study the next year by (unintelligible) and colleagues. This was a study that had 122 patients with chronic hypercapnia, so they had LEV1 greater than 50 percent in the study, and these

patients all had levels of hypoxia where they required supplemental oxygen. It was a multicenter prospective trial that looked at

the role of noninvasive ventilation with a backup rate and supplemental oxygen versus long-term oxygen therapy alone, and the outcome was, what was the change in hypercapnia with CO2 levels and hospitalizations? They followed the patients out for a year and didn't see any change in the hospitalizations, but what they did notice was that the patients who did the therapy longer actually had decreases in their hypercapnia and CO2 levels, and they actually showed improvement in their dyspnea. Next slide.

So this was followed by a large study by Dr. McEvoy, so this was a study where they (unintelligible) ventilation patients with severe COPD for improved lung function, survival and quality of life. It was a large multicenter randomized controlled trial that looked at the role of noninvasive ventilation plus long-term oxygen therapy versus long-term

oxygen therapy alone. All these patients were admitted to the hospital and started on noninvasive ventilation over a period of three to four days. They all had evidence of hypercapnia with a baseline CO2 level of 46

with the average being around 53. They were also administered noninvasive ventilation in a spontaneous mode, so BPAP without a backup reading, and their average pressure was somewhere around 13 to 5, and what they do is they monitored CO2 levels.

What they saw in this study was that people on the long-term therapy actually had increases in their hypercapnia the next morning. While there was an improvement in the patients that -- while there wasn't as high an increase in the patients using noninvasive ventilation, there was still an increase in the CO2 levels. And so again, there was no benefit in this study that showed noninvasive ventilation had any usefulness. They also found in this study that patients started a decline in the quality of life. Next slide.

So this was early around the turn of

the century, a lot of trials, randomized controlled trials, not a lot of success, right? These were well conducted randomized controlled trials that showed no clear benefit, showed no change in CO2 levels, it showed that survival did not change. The (unintelligible) therapy

and the readmission rates were not impacted.

Next slide.

So people with chronic severe COPD, they kept having hospital readmissions. Something, they were out of therapy, so the IPE team guy said well, you know, it works in the acute setting, why is it not working here? So around this time a new paradigm for severe COPD kind of evolved, and the thought process was that if we give patients a larger inspiratory pressure leading to a wider pressure support difference, so if we give a higher IPAP pressure and a low BPAP pressure, it will give them a big pressure support and will increase their tidal volume. If we increase their tidal volume it will improve alveolar ventilation, if you improve alveolar ventilation it will

improve gas exchange, if you improve gas exchange it will improve CO2 levels. And so as the CO2 level starts to go down the diaphragm will relax, the muscles will get their strength back, and so this was where the development of what Dr. Wilson kind of led to as high intensity pressure support kind of started. Next slide.

So building the foundation for high intensity noninvasive ventilation, so again, high intensity targets high inspiratory pressure and they also included backup rates. So some of the earlier studies around the turn of the century did not include a backup rate, it was just spontaneous mode, so the whole idea was to control ventilation. So this was a study done in 2009 by Dr. Windisch and it was a retrospective case study of 73 patients with severe stable COPD. All the patients had an FEV1 around 30 percent predicted. In this study they targeted a normal PaCO2 level and improvement in oxygenation. And so they looked at patients and the average inspiratory pressure that they had was somewhere high

around 28, the average expiratory pressure they had was low, around four or five, so these were really low pressures. In addition they were given backup rates so the whole idea was to control that.

And what they saw in this study was that when they used high intensity pressure support ventilation with a backup rate, you improved PaCO2 levels and you increased or

improved oxygen levels. Next slide.

So this was very different than what we have seen previously, right, so now we're giving high intensity pressure support ventilation which might mean okay, we're on the right track, but there's always the fear that that's a lot of pressure and if we're giving somebody a pressure of 24 or 28 it's like drinking out of a fire hose. So the idea was well, how (unintelligible) which the earlier studies showed? So there were some very small randomized controlled trials done by Dr. Dreher that looked at the role of high intensity versus low intensity pressure support. Again,

these were very small randomized controlled trials, kind of a proof of concept, so there was a trial that was just 17 cases in a randomized controlled trial with chronic hypercapnia and they randomized them to a high intensity pressure support, so a pressure as high as 28 with backup rate, versus low intensity pressure, and what they saw in the study was that the high intensity pressure support actually had improvement in the tidal volume. An improvement in their tidal volume

led to improvement in their hypercapnia. In addition, they saw that patients noted improvement in their dyspnea, their FEV1 and their quality of life. Also, they noted that more patients that were treated with the low intensity actually dropped out of that study. So high intensity compared to low intensity seemed to have some benefit, but there was always (unintelligible) distrust, and so they did another very small randomized controlled trial and they put again high intensity versus low intensity, and they did polysomnography in this study, and what they saw was in this

study, was that there were actually more patients that dropped out that were on the low intensity model, and that there was no change in SWS with the low rate, and again, they noticed that there was an improvement in hypercapnia. Next slide.

So high intensity is gaining momentum, we're seeing a beneficial therapy, and then came the Kohnlein study. And so the Kohnlein study was a randomized controlled trial, a multicenter randomized controlled trial that looked at severe COPD and then looked at high

intensity noninvasive ventilation versus no noninvasive ventilation or long-term oxygen therapy. They looked at 195 patients, 93 were in the control group, 102 were in the intervention group, and they did a one-year followup. And all these patients came in, again, were chronic severe stable COPD, so they had a PCO2 level greater than 52, and they had GOLD Stage 4 COPD with FEV1 levels less than 30 percent. They looked at patients and they got them high intensity pressure support about

22 over four with a backup rate, and the goal was to reduce the PaCO2 levels. All patients were admitted to the hospital but, (unintelligible) you get the targeted therapy. What they saw in the study was there was an improvement in mortality. This was the first multicenter trial that showed improvement in mortality.

So they saw that as a primary endpoint, 31 patients in the control group versus 12 patients in the intervention group actually died after one year, which is huge. So now we're seeing mortality benefits for high intensity, it's the first time we are seeing

improvement in the mortality level. Next slide.

Great, we're cooking with fire now, we're like okay, high intensity is the way to go for COPD treatment. This was followed very shortly by the RESCUE trial, so with the RESCUE trial it was again a multicenter randomized controlled trial and there was 201 patients. All these patients had severe COPD GOLD Stage 3 or 4 and evidence of persistent hypercapnia

greater than 52. The patients came to the hospital with acute exacerbation and they were treated with noninvasive ventilation and the noninvasive ventilation was stopped and it still had elevated PCO2 48 hours after the stop of noninvasive ventilation. They were again restarted, and what they were again started on was high intensity noninvasive ventilation, so high positive pressure with backup rate. And what they saw in this study was just here on the right, so we saw that there was really no mortality difference, there was less decrease in the PCO2 levels both through arterial blood gas and through tracking TcCO2 monitoring, we saw there was actually no change in the

spirometry and that they had no improvement in their quality of life, no improvement in mood, no improvement in dyspnea. Next slide please.

Here we have a Kaplan-Meier graph that shows no change in survival, no change in hospital admission. How is this so different from what we just saw in the Kohnlein study? Patients enrolled in the RESCUE trial were

enrolled as acute COPD patients. They were all given (unintelligible) bundled care, access to respiratory therapists, nurses, close followup. The question for this was why was it so different, and the hypothesis is that the hypercapnia seen in the acute period may not have represented true chronic hypercapnia and may have been transient, and if the patient had more time to reset after the exacerbation perhaps they would have normalized their CO2 levels and that's why we saw that. In addition, it was noted that the patients didn't have hypoxia. Next slide please.

So now I'm confused, right, the data is all over the place. We have one study that says it's great, one study that says there's mortality benefits, and one study that says

nope, wrong. So then came out the HOT-HMV trial, and this was a randomized controlled trial of noninvasive ventilation in hypercapnia post acute exacerbation. So the timing of these studies is very important and plays a role in when we should time therapy. This was a multicenter randomized controlled trial that

looked at 116 patients. 59 of them were given HOT therapy or home oxygen therapy, and 57 of them were given home oxygen therapy plus home mechanical ventilation. The patients all had evidence of hypoxia and hypercapnia, with PaCO2 levels of 53. The mean PaCO2 level was around 59. They all had evidence of severe COPD with FEV1 of 23 percent and they had low BMIs, so there was very little concern that concomitant OSA. The patients were targeted again with high intensity pressure support so they got inspiratory pressure around 22 to 26, low expiratory pressure, and control of breathing with a backup. And what they saw in this study was they looked at a composite endpoint of mortality and admissions; patients with home oxygen therapy and home mechanical ventilation or noninvasive ventilation actually had

improved by 4.3 months compared to those with just home oxygen therapy that died at about 1.6 months, so there was a mortality benefit and hospital admissions benefit.

This was planned post exacerbation so

what was the timing of this study? So the timing of this study was that they looked at patients that had persistent hypercapnia two to four weeks after their acute symptoms, so very different from the RESCUE trial, the RESCUE trial was set at 48 hours. The Kohnlein study looked at just chronic without any timing, but here in the HOT-HMV trial they were looking at post exacerbation and returning back to their levels of chronic hypercapnia. And so we think that this endpoint that saw a benefit resulted from, again, targeting that chronic hypercapnia. Next slide.

The HOT-HMV study was done in Europe, and so if we translate the facts that they saw in the HOT-HMV trial to a U.S. model, let's say, we see that the potential cost of noninvasive ventilation in the chronic hypercapnia patient is saving more than $3,900 per patient in the U.S. We know that the home

noninvasive ventilation saves money, improves quality of life and decreases hospitalizations. Next slide.

Great. We have some really strong

data in the evolution of how treatment has grown. This was all done in Europe. How does this apply to a U.S. model, right?

So the next slide we're going to look at two different U.S. studies. So there are no randomized controlled trials that have been done, they are both retrospective trials, and the first trial was done by Dr. Galli. It was a single center retrospective study that looked at 166 patients, 88 of them were not on noninvasive ventilation, 78 of them were and they were diagnosed with chronic hypercapnia but at much a lower level, with an average PaCO2 level of 45. They were again given high intensity noninvasive ventilation but interestingly these patients were started on noninvasive ventilation in an acute setting and they continued it throughout. And what this study showed was that there was a reduction of hospital admissions and there was improvement in mortality.

Now this is confusing, right, because the last trial showed none of that, and now

this retrospective trial showed it, so okay, why is that a factor here? Next slide.

So here are the Kaplan-Meier curves for the RESCUE trial and the Galli retrospective study, and they both looked at post COPD exacerbation in treatment. So why is there such a difference? Well, I think if you look at it, I think there's a difference in the model. So there's the role of noninvasive ventilation but then what else is included in that model? So in the RESCUE trial all those patients were started with noninvasive ventilation but the also had access to a home respiratory therapist, in-home care, someone checking on them kind of providing followup. The U.S. study did not have that, so it was just noninvasive ventilation. In addition when you look at this U.S. study, when you look at the characteristics the patients tended to have higher BMIs. The question was, was the noninvasive ventilation used in the retrospective study in the United States really true hypercapnia or are we treating untreated

sleep apnea, and that remains unclear. Next

slide please.

The second retrospective study came out of a VA model out in the west, and so it was 397 patients over 2010 to 2014, and it was on patients that had been hospitalized with two or more hospitalizations for acute COPD exacerbation in the last year. Then they looked at patients with severe COPD so they had GOLD Stage of 2 or more, and they had BODE index of greater than 5, and they either had hypoxia with a PaO2 level less than 60 or a PaCO2 level of 52. These patients were started on a bundled therapy program. They were given access to a pharmacist for medical teaching, understanding how their procedures worked, they were given access to a respiratory therapist. They were started on noninvasive ventilation, they were given home oxygen, and they had in-home care coordination where someone is checking on them.

What they saw after four years of watching, that they went from 397 patients with greater than two admissions down to nine. The question was, again, was it the noninvasive

ventilation that they were getting or was it the bundled therapy. Next slide please.

So I think it's very important to take Dr. Wilson's meta-analysis and actually break it down into the way that the treatments have evolved. So in Europe we had these great strong multicenter randomized controlled trials and prospective trials. These patients had benefits with chronic hypercapnia. The severe stable COPD not in the setting of exacerbation had benefits.

The United States only had retrospective studies. We see that there are some improvements in readmissions after acute exacerbation but again, what was the target there? Was the target sleep apnea or was the target actually chronic hypercapnia? And the model that worked in the United States was through the VA and that's a bundled program and they add home care; how much of an impact did that have?

The common hurdle that runs with noninvasive ventilation, and especially in high intensity, pressure and power, so if you want to get to the target of high intensive pressure

support you've got to deliver a lot of pressure, and how do you get patients acclimated to that? How do you get patients acclimated to a mask who are not used to a mask on their face? The European models provide a prolonged acclimation that showed in increased adherence to noninvasive ventilation, and what they showed was that it effectively chronic stable CO2. Next slide.

So to take the data and kind of break it down from low intensity to high intensity, so we see the early low intensity that showed no benefit, so there was no improvement in the development, no improvement in mortality, no improvement in hospitalization. Then we switched the model, we changed the paradigm and went to high intensity, full control of ventilation. What we saw was that if we treat chronic COPD and hypercapnia, there is an improvement in mortality and hospital readmissions, and the timing is very important. Next slide.

So if we look at the evolution of noninvasive ventilation in chronic COPD there is evidence that it was truly beneficial, if we

target chronic hypercapnia it is beneficial, but how do you actually apply it to your patients in the United States? Next slide.

So I want to take --

DR. BACH: Dr. Coleman, you have about three-and-a-half minutes left.

DR. COLEMAN: Perfect. So let me step back here and talk about BPAP, so BPAP is essentially a respiratory device, a respiratory device plugged into a wall and it doesn't have any alarms, it provides different modes of therapy. Compared to a home mechanical ventilator that has an internal battery, allows portability, it is a licensing issue. In the United States in order to qualify a patient for a BPAP machine or a respiratory assist device under COPD guidelines, you have to show evidence of hypercapnia and hypoxia, and when you do that, the best you can do is give someone a BPAP machine without a backup rate. Next slide.

In order to get them a BPAP machine with a backup you have to show a failed

(unintelligible) with therapy with BPAP. You have to repeat all the things happening while

they've been on noninvasive ventilation. Next slide. Skip this slide.

So what is the cost of therapy? In the United States a respiratory device or a BPAP machine costs about $400, a home mechanical ventilator costs about $1,500. Next slide.

Because of this, as Dr. Patel referenced earlier, people want to treat COPD, there's evidence that supports it, but the criteria to get a BPAP or CPAP respiratory device is extremely too stringent, so this has led to an increase in the use of home mechanical ventilators, which is overkill therapy. Next slide.

You can see since 2009 to 2015 the number of home mechanical ventilators has increased exponentially to treat COPD, and this could have been resolved if there were easier more applicable therapies to get through noninvasive ventilation. Next slide.

Why are we doing this? Because the

Affordable Care Act of 2012 actually started to penalize hospitals for hospitalizations so there's an urgency today, how can we prevent

COPD? Next slide.

So where do we go from here? Well, while limited to European trials, there are several randomized controlled trials that show benefit with noninvasive ventilation with a backup rate, to reduce hospitalizations and mortality. The target of noninvasive ventilation should be hypercapnia, not hypoxia. And under the current U.S. guidelines it is extremely difficult to qualify a patient for noninvasive ventilation, especially when the backup rate with all the data have proven beneficial. This has led to an increased home mechanical ventilation at a much higher price point and less stringent criteria. Next slide.

So there needs to be a revision to the respiratory assist device guidelines to simplify the ability to obtain devices that can provide high intensity pressure support with a backup rate. These revised guidelines should

be based on chronic stable hypercapnia and not include hypoxia. If we improve and resolve our respiratory device issues, we can make the criteria more applicable, and we will improve and decrease our home mechanical ventilator

issue. Next slide.

That's all I have for you. Thank you for joining me on this journey.

DR. BACH: Dr. Coleman, thank you so much for that presentation, again for finishing on time. I'm sorry about the little bit of a crunch on that. That was extremely helpful to us. We are as I mentioned holding questions until a period after lunch so I hope you are prepared to stay with us for the day.

To everyone, we are going to take a 15-minute break. Like everything else we're going to stay on time here so I have us coming back at 9:53 for the beginning of the scheduled public comments. The first person who I have is Dr. Robert Owen listed, and we will see you at 9:54.

(Recess.)

DR. BACH: Thank you everyone for

rejoining. We are going to go on to the next part of the meeting having completed our break, which are scheduled public comments. Each speaker will have eight minutes. Like all these other things I will add, I will keep you on time, please. Our first presenter is Robert

Owens from the University of California San Diego. I ask you that you do your disclosures or give a disclosure slide, that's terrific. Thank you very much.

DR. OWENS: Thank you very much for the opportunity to present today. Can you hear me okay?

DR. BACH: Yes, we can, thank you.

DR. OWENS: Okay, thank you. So as mentioned, my name is Bob Owens, I'm calling in from California, and I'm in the division of pulmonary and critical care and sleep medicine and I'm speaking today on behalf of the American Thoracic Society. Next slide please.

So by way of disclosures, ResMed, which is a maker of PAP devices, did give a donation to our UCSD Sleep Center. I've also

received an honorarium and travel reimbursement from ResMed and was site PI on a multisite research study. Next slide please.

The reason I'm presenting to you today on behalf of the American Thoracic Society is it's an organization of 16,000 clinicians; this includes doctors, scientists, nurses, respiratory therapists all designed to, or all

trying to improve respiratory disease and sleep disorders. I was most recently the chair of a clinical practice guideline which is coming out next month, long-term noninvasive ventilation in chronic stable hypercapnic COPD. Dr. Coleman, who just spoke, was a member of the panel as well. Next slide please.

So in preparing for this meeting there were several voting questions that were posed, and I briefly summarized those questions as what were the patient selection criteria that could improve outcome with any NIPPV device; what are the NIPPV equipment parameters necessary to improve patient-reported outcomes; can the improvement in outcome be attributed to the use of NIPPV equipment; and what are the

patient usage parameters that will improve outcomes?

I wanted to approach this problem by presenting two use cases or two patient scenarios, and that's patients who have COPD and obstructive sleep apnea, which is common, not quite as sick patients, and then those patients with chronic stable hypercapnic COPD. Next slide please.

So thinking about our COPD and obstructive sleep apnea, this is often termed the overlap syndrome, it's fairly common. And I think in the absence of hypercapnia, continuous positive airway pressure or CPAP can be used. And when CPAP is used in these patients there are associations with improved mortality, reduced ER and hospital admissions, and better quality of life. While more use is better, I'll show you some data that more hours per night is still the magic number, and I don't have it on the slide but when CPAP is provided it's usually little more than the device, so any improvements here are really

related to CPAP itself, not to other associated care. Next slide please.

So this is the study by Jose Marin about 10 years ago showing that patients with overlap syndrome have high mortality and if you use CPAP the mortality can improve. So the red curve there, patients with COPD and OSA have reduced survival with COPD only. The blue curve is patients who have COPD and OSA who use this. So if we can advance the slide please, and next slide.

Besides mortality, patients who have COPD and use CPAP also have reduced ER visits and admissions, so studies by Konikkara and colleague looked at patients who were in the hospital with COPD. They were rapidly diagnosed with obstructive sleep apnea and were provided with CPAP. On the left panel there you can see the difference between patients who used their CPAP device and those who did not use it, and there was a reduction of about two or three ER and hospital admissions over the next six to 12 months. Next slide please.

Now more CPAP use is associated with

improved survival. This is a study by Stanchina, Mike Stanchina at Brown, where he showed a nice dose-response with the more CPAP that patients with sleep apnea used, there was a better survival outcome. But what I wanted to point out on this slide is that even using CPAP for just two to four hours per night, there was a pretty robust improvement in survival. Next slide.

So those are patients with obstructive sleep apnea and COPD, you can treat them with CPAP and CPAP probably by itself to lead to

improved outcomes without a lot of associated care. This is speaking to patients with COPD and stable hypercapnic failure. This is a smaller group of patients, they have high morbidity and mortality, and we have very few treatments that show improvement such as smoking cessation or oxygen therapy. Part of the problem is that these patients have defects in both oxygenation and ventilation, and we rarely think about ventilation. So the panel on the bottom left is an old trace from David

Flenley showing that oxygen drops during, or oxygen saturation drops during the night. But more rarely measured, like in the panel on the bottom right, is the transcutaneous CO2 which is also rising during the night. Next slide please.

So we took there are problems with both -- well, I see you skipped one slide here, but because there are problems with both oxygenation and ventilation, it will be best to treat both of these things at the same time. So John Coleman just went through the Kohnlein study, but these are sick patients who have severe COPD. It's notable that they exclude

patients who have high BMIs of more than 35 or who have other heart and other lung disease; perhaps those are the patients that a true home mechanical ventilator might help. But in this study with Kohnlein, again, the intervention was a bilevel PAP with a high backup rate trying to reduce CO2. Next slide please.

And again showing how sick this patient is, or the patient group is, 33 percent of controls had died at the end of one year, so

this is a higher mortality than some cancers. There was a substantial impact from noninvasive ventilation. You can see the curves separate and again, you'd rather be in the curve that got noninvasive ventilation. Even though we think of these pressures as perhaps being uncomfortable, they improved without noninvasive intervention. Now this intervention did include scheduled hospitalizations and extensive followup and there was a very high rate of adherence, close to six hours a day. Next slide please.

Again, this is the Murphy trial, I think these slides were unfortunately out of order, but again, it's testing the hypothesis

that these patients don't only have an oxygenation problem but an oxygen and a ventilation problem, and in the Murphy trial here it is providing both was superior to providing oxygen alone. Next slide.

Now one of the criticisms have been that since it required substantial efforts to bring patients into the hospital and to set

them up, Peter Wijkstra published this paper last year showing that you don't necessarily have to bring people into the hospital, there are good outcomes, not inferior, with starting people at home with their NIV machines. Next slide please.

So in terms of the voting questions, what are the patient selection criteria, I think if you have a patient with COPD and obstructive sleep apnea they can be treated with CPAP. If you have a patient with COPD and chronic stable hypercapnia they probably need bilevel PAP with a backup rate. In terms of improvements attributed to NIPPV equipment alone, I think merely yes with CPAP equipment for COPD and OSA; for those with chronic hypercapnia they need ancillary services as

well. In terms of patient usage parameters, four hours per night is not a magic number, more is better, and in some of these studies it takes people a long time to get adherent and you might need a longer period to get them on therapy. Next slide please.

I'd just like to finish with some

additional comments. First as was alluded to by Dr. Coleman, bilevel PAP with a backup rate is really what's been studied for improvement on these patients but often it can be easier to satisfy requirements required to get a home mechanical ventilator. So modifying the requirements to obtain bilevel PAP with a backup rate will impact HMV utilization.

The last thing I would mention is that particularly with a sticker group, COPD and chronic stable hypercapnia, I think patients would also benefit from ancillary services as well.

Thank you very much for the opportunity to present this morning.

DR. BACH: Thank you very much, Dr. Owens, for that presentation. Our next presentation will be Dr. Nunez.

DR. NUNEZ: Hi, yes, good morning. My name is Dr. Carlos Nunez, and I want to thank you first and foremost for the opportunity to speak today, and to the panel for their time and consideration of the comments that we

submitted. As I mentioned, my name is Carlos Nunez, I am a physician, I am currently the chief medical officer at ResMed, who is one of the leading manufacturers of all the equipment we have been talking about today. Very briefly, I am an anesthesiologist and intensivist, critical care physician by education and training, and as mentioned, I work as the chief medical officer at ResMed. As the chief medical officer obviously I am a full-time employee. I am compensated not only with salary but also with equity in the company.

Also just to note, there are a couple of my colleagues on the line from ResMed who are listening in, and if there's a need for them to chime in during th Q&A I may refer to either Larissa D'Andre, our vice president of government affairs and market access, or Amanda Voldeer who's our senior manager of government

affairs. So if you can go to the next slide please, oh, that is my disclosure slide so I just went through that so we don't need to mention that again, so if you'd go to the third

slide.

I want to just quickly mention the culture of innovation at ResMed. I'll start by saying the slides are a little busy because obviously we wanted to get a lot of comments into the public record, but I'll highlight just the real big takeaways here. As I mentioned, ResMed is one of the leading manufacturers of all the technologies we talked about today, from CPAP devices to bilevel devices to home mechanical ventilators.

But I also want to mention something that's really really important that was just mentioned by Dr. Owens actually when he talked about more than four hours is better and ancillary services. You can't talk about these devices in this day and age without talking about the fact that these devices are now much more modern connected and allow the physicians and providers to remotely not just access data about the patient's care on a daily basis but

manage that care, and even to do telemonitoring and use the data as the basis for telemedicine.

Now more than ever, especially in the throes of the COVID-19 pandemic, we have seen an explosion of digital health, telemedicine, telemonitoring and virtual visits, and so we need to think about this as we move forward through these discussions.

We are talking about taking care of patients in the home with very advanced devices that do require ancillary services and we want to make sure that when you think of ancillary services, part of that is the software, the platforms, the connectivity and the digital health capabilities that make these devices more modern and more suited for the health care system we have today. If you can go to the next slide please.

On this slide I will reiterate some of the things you heard from the last two presenters. There is a bit of a discrepancy in the requirements for patients to receive a respiratory assist device versus a home mechanical ventilator. And you see, there is a growing body of evidence, some stronger than

others, that shows that this type of care is

important for patients. But when you restrict access to an appropriate type of care for a lower, potentially lower acuity of patients, you see an overuse or potential overuse of higher spec devices, I believe it was one of the earlier presenters who said it just like this, that you created an artificial situation where patients who can do just fine with a less expensive device, and I think he used the average of about 400 bucks, that are often being prescribed devices that are over spec and more expensive than what they need. These are not one size fits all options, and I think we have to keep in mind that clinicians need the flexibility to look at these very complicated patients with lots of comorbidities and understand which technology will work the best for them, which settings, the features and the capabilities that the devices have, and can we have payment and reimbursement guidelines, policies, requirements to make it easy for patients to get the therapy they deserve. Next slide please.

Again, busy slide but I will hit on

the highlights. You've heard a lot of presentations about the current state of the evidence and as you see, there is a lot of evidence and a growing body of evidence that shows that quality of life and other measures are increased with noninvasive positive pressure ventilation. The HOT-HMV study which I talk about here on this slide was mentioned by several of the previous presenters so I won't go into the details there, but again, we see a growing body of evidence that shows treating patients with chronic hypercapnia in a variety of situations outside the hospital helps improve their quality of life, helps improve their clinical outcomes, and the evidence continues to get stronger. So these studies that have happened in recent, in the recent years that have strengthened the body of evidence that led to an update of the GOLD guidelines for 2020 and an update to ERS guidelines, the European Respiratory Society guidelines at the end of 2019, and we just heard from Dr. Owens the ARS is working on similar guidelines themselves. If you can jump to the next slide please.

The evidence also showed that there is a cost effectiveness to noninvasive positive pressure ventilation. Going back to the HOT-HMV trial, there was a cost effectiveness study that was done looking at both U.K. and U.S. models of care and the data from the HOT-HMV study looking at home mechanical ventilation in addition to oxygen. And what they found is this therapy, looking at the findings from the HOT-HMV study was not only more effective but it was also less costly when you calculate the incredible cost effectiveness ratio or ICER, and what they found was the cost effectiveness ratio was minus over $50,000 per quality adjusted life year that was gained. It doesn't mean everybody going on to a mechanical ventilator all of a sudden sees that $50,000 a year but what it shows is for every quality adjusted life year, a year of quality life adds savings to the health system. And so we now see this therapy is not just more clinically effective but also more cost effective in the long-term. And I've got about a minute left, so if you'd jump to the next slide. I'm still seeing the original slides.

DR. BACH: We're looking at the recommendations to MEDCAC.

DR. NUNEZ: All right, I will jump to it, for some reason something froze.

So the recommendations we have is that MEDCAC should consider the spectrum of technology available, it is not just the bilevel with a backup rate versus home mechanical ventilation. It is those ancillary services, it's the software, the platforms, the connectivity, all of the technology of the modern devices that make it more appropriate for their use as home devices, and make it easier for providers, clinicians, physicians and others to manage that care.

Should consider all of those technological innovations especially in light of the pandemic and some of the clinical changes that we're going to see in health care going forward.

Should prioritize recent evidence and recent clinical guidelines, I mentioned the 2020 GOLD and the 2019 ERS.

And then lastly, the patient usage criteria in coverage recommendations, there's

insufficient clinical evidence and this could interfere with clinical decision-making.

I hear the timer so I will be quiet.

DR. BACH: Thank you very much for your presentation, and we're going to go on to the next speaker. And just so everyone knows, I'm taking the soccer ref approach to this, you get extra time if we have technical problems, but thank you very much for your presentation.

I'm going to go on to Dr. Lisa Wolfe.

DR. WOLFE: My name is Lisa Wolfe. Can you guys hear me?

DR. BACH: Yes, we can.

DR. WOLFE: Okay, great. First of all, I am here today representing CHEST, which is the American College of Chest Physicians. And in addition to all the other thank yous from other folks today, I'd like to give a thank you to Tara, who has done an amazing job herself as being an innovator, as this is the first online version of the MEDCAC meeting, and it's been a great experience. I'd like to go

to the next slide please.

Okay, I'd like to address the four questions before us by taking our patients with

COPD and dividing them into three distinct groups which other speakers have already done, I'd just like to do it more formally and do this in a way in which we can look at these groups together. In terms of patient criteria, we're going to look at those with OSA and COPD. The patients that have normal CO2 and oxygen levels are frequently referred to as the OSA and COPD overlap syndrome. Notably these patients are determined through polysomnography, as compared to patients with COPD who are found to have acute exacerbations requiring hospitalizations with hypercapnia, and their COPD is determined clinically.

If we then compare that to the more common group in the U.S. which is least likely to have been studied, this is an overlap of obesity hypoventilation syndrome with COPD. These patients are distinct because they have BMIs greater than 35 and the COPD is associated

with more hospitalizations and hypercapnia.

Please go to the next slide.

If we look at our next issue which is NIPPV equipment parameters, we can look at our three predefined groups and easily determine

how equipment parameters fall into these locations. In our OSA field with COPD overlap syndrome the most commonly used device is CPAP. The difference between our patients with overlap and a standard OSA patient is that frequently these patients require oxygen in addition to CPAP therapy.

Whereas, our severe COPD patients usually are treated with Bi-PAP with backup rate as has been described by many of our speakers today in order to provide high intensive pressure support which is far superior, as described in Dr. Coleman's talk. It is important, however, to remember that some of these patients require home mechanical ventilation either due to very high need for oxygen bleed that will require an internal blender, or the need for backup batteries or daytime portability.

The last group which is the American group which is less described in the literature which is mostly European are those with obesity hypoventilation and COPD together. These patients frequently require home mechanical ventilation because technologically they

require auto EPAP in order to treat the sleep apnea component together with volume assured pressure support to treat their ventilation component, and the only way to get this therapy is with home mechanical ventilation. And lastly, these patients frequently require high pressures that are outside the range that can be provided by a BPAP device, and because they frequently require pressures greater than 25, we need to get them on a larger machine. Next slide.

So why treat, is the evidence sufficient, this is our third question. So we know that in our patients with OSA COPD overlap syndrome, and this is the data that Dr. Owens has just reviewed with us, that the decrease in mortality is associated with the use of CPAP in

these patients, and it's frequently due to improvement in cardiovascular outcomes, typically pulmonary hypertension.

But if we look at the group with severe COPD and we look at mortality, exacerbations and hospitalizations, and especially if we look at those treated with high intensity pressure support there's

significant benefit to the therapy. And I would refer you all strongly to the very recently published European Respiratory Society task force recommendations on the use of home-based noninvasive ventilation for those with hypercapnic severe COPD. And as they state, the ERS suggests the application of long-term NIV to improve outcomes specifically with the goal of reducing COPD and -- I'm sorry, reducing CO2 -- and it's really important that we focus on the fact that the CO2 is the most important outcome here. It's the mechanistic thing that makes the difference.

Then lastly if we look at our patient who have that American phenotype of obesity

hypoventilation together with COPD, what we see is that in this recent respective analysis of almost 300,000 patients the obesity, which is a BMI greater than 30, is consistent with a significant increase in mortality. And we're going to see in our next slide the importance of NIV in mitigating that mortality. Could I have the next slide please?

So if we look at equipment versus

other support services, which is our next question, it's important to know that that really isn't an issue in our OSA COPD overlap patients who don't have significant hypercapnia. However, in our severe COPD patients we do think these support services are relevant and important. Significantly in the RESCUE trial and the Struik trial that was reviewed by Dr. Coleman extensively, it's important to note that some on NIV failed in that group because we couldn't demonstrate in them significant hypercapnia. But it's important to know that both groups got significant support in the home, getting

support with nursing, respiratory therapy, pharmacy, et cetera, because that is the standard of care. In all of these European studies the use of significant support in the home is a given, its not even mentioned in the papers because it's significantly part of their overall health care policy. If we compare that to the Galli study in the U.S. there's no way to provide that kind of support in the home unless the patient is also getting noninvasive ventilation, and so it's important to see that

in the Galli studies we have success, where in the rest of the studies we didn't, and that helps to drive home that we need wraparound 360 care that allows us to get some flow of noninvasive ventilation together with significant support in the home.

Lastly, in our patient with that more American phenotype with the obese hypoventilation and COPD, it's important to know that we can't delay the initiation of care in this group because even a three-month delay in the issuance of noninvasive ventilation for those who have had hospitalizations due to

hypercapnia, have a measurable and significant mortality that is associated with it and that can be mitigated by the use of noninvasive ventilation. Next slide.

So when is PAP use sufficient? I agree with Dr. Owens, we don't have a specific number, except today in all of our studies four hours is sufficient, and as a take-home message, the more you do the better you do, and the longer that you're using therapy the longer your nightly use is prominent. So if we look at our patients with overlap syndrome,

four hours is necessary in order to see benefit.

If we look at our severe COPD patients in the Kohnlein study that showed that significant mortality benefit, usage time less than three hours was only noted in 18 percent of patients and the mean use was six hours per night. In the Murphy, or the HOT-HMV study, we'll see that as you go from six weeks to 12 months the compliance increases from just over four hours to up to almost

seven-and-a-half or eight hours.

In our obesity patients who have obesity together with severe COPD, you can see that --

DR. BACH: Dr. Wolfe, you're out of time.

DR. WOLFE: Oh, sorry, I thought I was getting a warning.

DR. BACH: No, sorry. You're at nine-and-a-half minutes.

DR. WOLFE: Sorry, I was waiting for my warning. Okay.

DR. BACH: Okay. No, thank you very much. We are going to go on to Dr. Frazier.

DR. FRAZIER: Good morning. Am I coming through? Good morning.

DR. BACH: We hear you.

MS. HALL: We can hear you.

DR. BACH: You muted yourself.

DR. FRAZIER: Good morning, everyone. Can you hear me?

DR. BACH: Yes, we can, Dr. Frazier.

DR. FRAZIER: Thank you very much. Can you advance to the next slide for me?

Thank you. I'm Bill Frazier, I'm the chief medical officer of VieMed. VieMed is a durable medical equipment supplier, we're the third largest supplier of home mechanical ventilation in the United States. Additionally, I'm a pulmonologist, critical care doctor and sleep disorders doctor with more than 30 years experience treating COPD, CRF.

We've talked about some gaps in the data, especially in the U.S. Medicare beneficiary population. To try to help close those gaps, VieMed has started a series of studies. We've completed two of our investigations and we're going to briefly discuss those today. Next slide please.

Study one was presented at CHEST last October, the manuscript has been presented or been submitted for publication. This is a Medicare limited data set study in which we queried the database looking for all patients with COPD CRF between 2012 and 2017. We excluded patients who also had OSA or obesity hypoventilation. That resulted in 410 patients

in that group all on home mechanical ventilation, and approximately 32,000 controls. We used the inverse probability of treatment weighing to help balance those groups and we ended up with a nice balance. Of note, 60 percent of these patients were set up immediately after hospital discharge.

The mortality hazard ratio for patients treated with home mechanical ventilation is .62. The one-year mortality for patients treated with HMV, 35 percent. 47 percent one-year mortality in the control group. You can see on the screen the absolute risk reduction, the relative risk reduction, and the number needed to treat to save a life. For every 8.6 patients with COPD CRF that were placed on mechanical ventilation, you saved a

life. The hospitalization and ER visit were also statistically significant showing a statistically significant reduction in health care utilization associated with HMV use in this group of patients. Next slide.

We repeated the study now incorporating data from 2012 to 2018. This

study has been accepted for presentation at CHEST in October of this year and that manuscript is in preparation. This time we chose to use propensity scoring with a one-to-one nearest neighbor matching technique to balance the two groups. That gave us 517 patients in the noninvasive ventilation group and 517 controls. Mortality hazards ratio for HMV use was .5. The one-year mortality in the treated patients, 28 percent; 46 percent one-year mortality in the control group, the COPD CRF who did not receive home mechanical ventilation.

In both of these studies the mortality showed up very early, within the first week, during that very critical time for patients with COPD exacerbation or hospitalization. The biggest drop occurred in the first week. There

was a slow decremental decline in effect of home mechanical ventilation mortality and at the end of 69 weeks the benefit was gone.

Taking our data together with our vast experience with well over 10,000 patients in

the field, together with the data that we've all been reviewing all morning long, VieMed has four recommendations to answer the four questions the committee is considering. Next slide please.

So as for our care, we know that it's easily defined and easily measured, but we all know hypercapnia seems to be the best predictor and we know it's the most common phenotype studied, but that's different than saying it's the only phenotype that might benefit from HMV. Our data showed only 12 percent of the CRF patients in the Medicare database were coded as having hypercapnia. We looked at everyone coded with ICD-10, only 12 percent. It may make the numbers a little higher than that but the point is we showed a dramatic improvement with concomitant health care utilization in an all-comer model not simply related to people who had chronic hypercapnia failure.

Dr. Wilson went over data showing there was no correlation with the degree of hypercapnia and mortality and hospitalizations. We need to open our minds. Other phenotypes of

CRF may well benefit. We recommend using clinical findings such as GOLD stage D and PFT findings such as GOLD stage 4 obstruction as also indicating patients with disease state that warrants intervention with home mechanical ventilation. Next slide please.

The hours of use data we've talked about, there's no magic number, more is better, we all agree with that, but there's no magic line in the sand that says under this there's no benefit. We should not limit continued use based on hours of use in a small population. Next slide please.

Concomitant services. As you guys know, CMS classifies HMV as requiring frequent and substantial services, and that's exactly right, we completely agree. We think at VieMed this means the DME supplier is responsible for 24/7 365 initial, repeat and emergent access with a provider, with an RT or an RN, and that this interaction can be by phone, by

videoconference, by patient engagement portal, or it could be of course in person. The point

is that patient must be able to get to some expert any time he needs that support. That's the way we're going to get the best outcomes.

And finally, equipment parameters. As discussed, there's no direct RAD versus mechanical ventilation data, it doesn't exist. I've tried that in my studies, I tried to see if there was enough Bi-PAP data inside the Medicare database to make a comparison and there wasn't, simply not enough of RAD use to make an analysis. Why are RADs used more in the settings? I think part of it's because of the differences in specifications that we've been over, and it's also because of the different FDA approvals. Remember, all mechanical ventilation is approved for chronic respiratory failure, for the most part RAD devices don't carry that approval. And of course we've been over the differences in the qualification requirements.

We also worry about this idea of a try and fail strategy with RADs. I can't think of another disease state where CMS mandates that a

patient fail an unapproved therapy before

allowing them to move on to an approved therapy. And really, how are we going to even define a RAD failure? Is that a deterioration, is it a hospitalization, is it even a death? The risks of such a try and fail approach seem too high. Our position is that until head-to-head trials prove that RADs are not inferior to home mechanical ventilators, we recommend home mechanical ventilators be the sole equipment used to treat COPD CRF. Thank you very much.

DR. BACH: Thank you very much, Dr. Frazier, for that interesting presentation. I'd like to move on to Dr. Vohra, and one comment about timekeeping. My apologies for Dr. Wolfe's presentation, I actually lost my ability to unmute my phone for a few minutes there, or my screen, so I wasn't able to give warning of the time expiring, so Dr. Wolfe, my apologies for that. We'll move on to Dr. Vohra. I also ask that you redundantly keep your own time in case this happens to me again.

DR. VOHRA: Thank you, Dr. Bach, for

the opportunity today and to the MEDCAC. Is everyone able to hear me today?

DR. BACH: Yes, we can hear you.

DR. VOHRA: Great. I'm here to represent the American Academy of Sleep Medicine which is the, in the sleep field we set the standards, promote excellence in sleep medicine health care, education and research. It has a combined membership of 11,000 accredited sleep centers, individual members, physicians, scientists and other health care professionals. Next slide please.

I have no financial disclosures at this time. Next slide please.

So for my presentation to the MEDCAC I will focus on the percentage of the CRF due to COPD. We have been discussing most of the morning today about a lot of data that has been generated in randomized controlled trials and prospective trials, and there were several studies over the past years that have been looking at this and the benefits of the NIV, noninvasive ventilation to COPD, CRF, chronic respiratory failure have been seen in quality of life, hospital admissions and the mortality.

And I would move on to the next slide please.

So I'm going back to this paper by Murphy, et al., that has been discussed before. And in this particular study, randomized controlled trial, they had a series of four weeks before they decided to enroll the patients, and they had these patients on high intensity noninvasive ventilation. The IPAP for these patients was set at 24 with an EPAP of four and the backup rate on these was 14. Use in the study was 4.7 hours and their primary endpoint was a time sufficient for test, and as is demonstrated in the graph, there was a significant difference between home oxygen plus the home high intensity noninvasive ventilation versus the home oxygen alone. In the first arm that the ventilation was used, admission time was 4.3 months, and the second arm it was 1.4 months, and there was an improvement parameter. The absolute risk reduction was 17 percent. Next slide please.

This is a slide from the Kohnlein paper that has been discussed before. And again, a randomized controlled trial, 190 patients, and their criteria was 64 GOLD

patients. They did include CO2, the CO2 was more than 51.9, (unintelligible) of 7.5 and these were, again, stable patients, no exacerbation of more than the whole (inaudible, static) and their primary endpoint was death, which they were able to very clearly show that in the intervention where noninvasive ventilation was used there was a, the death rate was 12 percent in the intervention group and 73 percent death rate in the nonintervention group. And in their case the IPAP was 21.6, EPAP 4.8 with a backup rate of (inaudible, static) so again a high intensity noninvasive ventilation setting with a high backup rate. Next slide please.

This is a graph from the Duiverman study where I wanted to look at the yellow stars which showed mostly positive results applied to ventilation and the IPAPs were around eight and the EPAPs were kept somewhere around five or less, and we saw positive results with that (unintelligible). Next slide please.

This is going back to the Kohnlein paper again and on the next slide these are

looking at the Short Form 36 scores that are better with ventilation. (Inaudible, static) questionnaire where the scores scored were better with the intervention (inaudible, static) and were higher, which is also better. Next slide please.

So coming back to do we have the data, yes, we do have data. There are studies available to show that reduction in mortality and hospitalization in patients with hypercapnia. The evidence also has a high level of confidence for (unintelligible) ventilation. And the current coverage for Medicare beneficiaries has requirements discussed in this presentation also throughout the morning. Next slide please.

So the problem is that the current reimbursement policy creates a disconnect between the patient's clinical status and reimbursement because the policy focuses on the devices rather than the clinical situation. Our suggestion would be to change the NCD for

noninvasive ventilation for all forms of CRF to align with the best evidence, and providing better care for Medicare beneficiaries. Next

slide please.

So the pathway would be that we support the multi-society supported expert panel today that has been speaking all morning to provide CMS with the recommendations from clinical experts to provide reasonable and necessary treatments. Data suggests mortality is reduced, hospitalizations, decreased cost of care, and better quality of life. I'd like to thank the MEDCAC panel for the opportunity. Thank you, Dr. Bach.

DR. BACH: Thank you very much, Dr. Vohra, for that presentation. I ask everyone who is not speaking to please mute your microphones. We're going to go on now to our last scheduled presenter, who's Dr. Gregory Holt.

DR. HOLT: Good morning. Can everybody hear me?

DR. BACH: Yes, we can.

DR. HOLT: All right. My name's Dr. Greg Holt, representing Respiratory Quality Services, a DME company based out of Texas. Next slide.

And I do have nothing to declare.

Next slide.

This is the first slide that comes up and Dr. Coleman briefly presented this slide, but this is the reason why we're here. I think everybody understands that there's been a shift in the utilization of the HCPCS Code E0466 to COPD and chronic respiratory failure, away from neuromuscular disease, and this is over a period of six years but this is when things really started to happen. Next slide.

So the first thing that came up was a decrease, a 30 percent reduction in the reimbursement rates for the code in 2016, so this was pretty significant all the way around. But then it was added to the competitive bidding process. Along with the OIG reports there was other things that Medicare was looking at, and it was also added to a potential list of codes that didn't require, or

that would require preauthorization without any further discussion, so it's on a list right now of a noninvasive code for ventilation that they're going to have like other restrictions placed onto it. So recently, everybody knows that ventilators were removed from the

competitive bidding process because of the pandemic, but there's other things going on that weren't reversed, and what were not reversed is some policy by third-party companies of a rent to own ventilator policy which is never going to happen, it's not a good idea but it's coming around from Blue Cross Blue Shield in Louisiana and Mississippi. Next slide.

So when we take a look at what happened, so how did we get here? Well, we are meeting about noninvasive ventilation and COPD, but first there was that OIG report. And then what shifted the utilization of the noninvasive ventilators was this reimbursement of RAD devices requiring frequent substantial servicing. So that was like the ongoing thing

and when they backed out of that, you know, there was some audits that went on originally, and then everything shifted to home mechanical ventilation because the devices were coming up, the way the devices were used and the capabilities were getting better all the time. So when Respironics rolled out the Trilogy, everything started to get better as far as home

mechanical ventilation goes. But when you look at the COPD population and chronic respiratory failure, by definition it fits almost 20 million people right now. So when you look at the qualifying criteria for COPD as far as CMS regulations go it fits everybody, and that's the scary part about it and that's where home mechanical ventilation really started to take off almost on a logarithmic scale. So the code was being used, ventilators were out there and they found that it does work, but we'll also look at some studies from the AHRQ reports of 2017 and 2020. So when, this last line here, nonuniform acceptance criteria, so DME companies were using RAD qualification criteria to go to home mechanical ventilation but not

all DME companies were doing it the same way. So in some places they were using an inpatient overnight op symmetry study to qualify for ventilation, and some places were just going on PST data and some places were using blood gas data. Next slide.

So looking at the AHRQ report, so you know, I'm really glad that we went over a lot of this but some of the selected papers here

just shows that there's not a lot of evidence to say one way or the other. Vasquez's paper in 2017 when I looked back into it, it was covering 1.9 million enrollees and I thought that was everybody, I thought that was everybody as far as like how many people they looked at, but the idea that went with it was they looked at 1.9 million COPD patients and of that 1.9 million, 92.5 percent were not on any positive pressure therapy at all, so we're looking at just relatively a few guys of the entire population that are on positive pressure therapy.

But another point that came up was

there was only a thousand people on home mechanical ventilation out of that study. So running some numbers, if that was roughly two million people enrolled out of 20 million, a thousand people there that were on home mechanical ventilation, it looks like, you know, there was probably 10,000 guys and maybe $120 million based on current rates of reimbursement, depending on you paying a thousand dollars a month.

So you know, one thing that struck me

that we should mention is that a ventilator isn't really $1,500, it's more like between $7- and $14,000 depending on the device and depending on the age of the device, so it is substantially more, plus all the disposable equipment that goes into it, preventative maintenance schedules that have to be maintained, there's a lot of other things that go along with the device.

So when these other studies look at survival odds, readmission rates, quality of life, and it looks like everything is better with positive pressure therapy, I think that

everybody accepts that. Next slide.

The thing about it is, is that from the data there's nothing to exactly lean on. When they talked about strength of evidence there was like a lot of areas of low strength of evidence. And in that 2020 AHRQ report no study examined an initiation criteria of home mechanical ventilation versus Bi-PAP versus CPAP, so it wasn't like we did this to start them on CPAP, we did this to start them on Bi-PAP, it was just using like a CO2 criteria or oxygenation criteria, something like that,

or an overnight sleep study to document some type of like complex sleep apnea to put you on a RAD.

So if you say that the data is there, that we're good to go, the reimbursement is going to fall apart. Home mechanical ventilators will be problematic in other populations like ALS, but right now the first thing here is like you can't wait for the literature to catch up to utilization. If we try that we'd still be discussing that. We

tried to like come out with criteria before a few years ago and it sort of fell flat, but you can look at establishing a panel to look at NIV criteria in this new population, specific criteria. That's why a diagnosis of, you know, like having a combination, problems of obesity and obstructive sleep apnea and COPD, things like that, but when you look at that you can compare it to like other national standards.

You can also look at initially things like RAD tolerance. You look at RAD tolerance when they're stable as severe COPD patients. I couldn't believe that all of those guys were able to jump on, something like 26 over 4

centimeters of water pressure and everything was fine. Most of the time the chief complaint is shortness of breath and they don't want anything on their face. So you know, maybe trying the RAD early on in the diagnosis and looking at a RAD with recurring exacerbations, and also trying to find out if they're on a RAD, if they have it like to where they can bring their CO2 down during the exacerbations, because you have to look at the transition

points of RAD to home mechanical ventilation and you have to decide when to switch and when you need the secondary settings, battery backup power, and that was a good thing about the secondary settings, because it's baseline settings and then it's like an exacerbation of rescue breathing setting, and that's about --

DR. BACH: Dr. Holt, you're out of time.

DR. HOLT: All right, that's fine. So respiratory failure you need home mechanical ventilation, you need to know the transition points and you need to decide how you're going to reimburse that, should you include a respiratory therapist, or just look at a

schedule that includes some type of support. Thank you.

DR. BACH: Dr. Holt, thank you very much. As I mentioned earlier, I had a technical problem on my end that interfered with Dr. Wolfe's presentation and I'd like to, Dr. Wolfe, if you're there and it's possible technically, CMS, if we can go to slide seven

of Dr. Wolfe's presentation, I'd like to give her a few minutes to go through that slide, and number eight. Does that work on a technical level?

DR. WOLFE: That would be wonderful, yes.

DR. BACH: Thank you. I know this has set us to change our schedule. While we are waiting for this slide, a couple of changes. We are ahead of time because of everyone doing a phenomenal job on the presentations staying on time and only a few technical glitches, almost all on my end. So my preference here is unless there are objections, to move part of the agenda up and keep lunch which is scheduled right now at 11:30 eastern at the same time, so we will hear Dr. Wolfe, a couple of slides,

there's someone waiting to give an open public comment, and then we will start the questions to presenters and we will do what we can, then, until we break for lunch. If there are any objections to that plan or logistical problems, please privately chat with me about that so I can fix them. Dr. Wolfe, please go ahead.

Thank you very much.

DR. WOLFE: Thank you. Can you hear me?

DR. BACH: Yes, we can hear you.

DR. WOLFE: Okay, great. So just very quickly, I've broken my summary down into the four key questions in front of us.

First of all, patient selection criteria. Most important is going to be daytime hypercapnia and it is the only marker that seems to be relevant.

Number two, NIPPV equipment parameters. With the COPD phenotype, if you look at them the way I've broken them down, they easily allow us to assign appropriate PAP therapy. And I would emphasize as Dr. Coleman said at the end of his talk, fixing the RAD criteria will allow us to more appropriately

give the right NIPPV to the right patient.

Number three, is it important to have concomitant provision and other support services? The presence of daytime hypercapnia is a hallmark that we need to be more

aggressive with support in the home and in order to do that, to reduce the frequent and substantial servicing on the HMV has been a benefit; if it can be provided other ways, it should be. The evidence isn't sufficient to provide the patient usage parameter, time cutoffs are not specific, but the greater the use the greater the effect. Next slide.

Is that the last one? Oh, there it is. And my final thoughts were summarized before, that we need to modernize how we approach this because we no longer have the old data with low intensity, high intensity should force us to expand how we look at these things, update the RAD criteria, and encourage more research in the U.S. that looks at our patient phenotype, and that's it.

DR. BACH: Well, thank you very much. We are going to move on to public comment. We have one registered speaker for public comment.

We give two minutes for each public comment, and that is Kathleen Lester. Dr. Lester, are you on the line?

MS. LESTER: Hi, it is Kathy Lester

and I wish I were a doctor but I'm only a lawyer, but I appreciate the opportunity for comment today, and I want to give huge kudos to Tara, Leah and Marvelyn for making this virtual meeting so seamless, it is working great from our perspective. I am the executive director of the Council for Quality Respiratory Care and the CQRC is a coalition of the nation's seven leading home oxygen and sleep therapy providers and manufacturing companies, so together they provide in-home patient services and respiratory equipment to more than 1.5 million Medicare patients.

As you can tell, our members don't prescribe these devices but they are filling the prescriptions written by the qualified health care professionals and are the subject of the documentation audits that apply in the coverage criteria, and some of the ideas you all are thinking about today.

We submitted written comments but

wanted to emphasize the importance of making sure that the patients who medically need NIV

in the home can access those devices. Thus we need standards that are recommended, especially around clinical criteria. It should be objective and very clear to document. The more subjective the criteria the more likely there will be documentation problems and auditing issues that could result in patients not being able to get access to the equipment.

So building off today's great presentations, we support the comprehensive look at coverage not just for NIV but for the RAD policy, to allow for the complete discussion that recognizes the broad spectrum of devices and various patient populations who medically require them. We also believe it is important to avoid the tried and failed method, as others have stated, or standards that would result in time-based criteria which are nearly impossible to document and have created serious access problems in other parts of the Medicare program.

Given the importance of understanding the documentation issues as well as the

clinical criteria, the CQRC and our members

would like to be part of this process, to have a seat at the table as we move forward, and we agree with other commenters who suggested a technical expert panel.

So thank you again for considering this very important area and allowing us to provide comments today.

DR. BACH: Thank you very much for those comments, and we are going to move now to the questions to presenters section. We have about an hour scheduled for that. In my experience it can go a little shorter sometimes and longer sometimes. We need the time to have an open discussion. This is all new in terms of the technical challenges so let me say what my at least initial plan here is. I have a participant menu in front of me, I have a panelist menu in front of me. You can raise your hand, you can also chat with me privately to say you have a question, this is for the panelists, or I would actually propose being redundant so that I can try and monitor this and do my best. But I do know there were a couple of questions that were already sent to

me that they want to address to the panelists. As far as the speakers -- I'm sorry -- as far as the presenters, questions need to go to the people who presented them and the answers have to come from them. We can't have any other input from people who aren't registered to speak at the meeting, that's part of our rule.

So anyway, I'm happy to start anywhere. If you would like to raise your hand I'll call on you and if you can address, if you have a person you would like to address with your question, please make that part of the question. I'd also like to remind you when I do call on you or if you would like to just speak if you're having trouble getting called on if there's no one talking, please make sure your camera is on and you identify yourself so we can have a transcription.

DR. MACINTYRE: Dr. Bach, this is Neil MacIntyre. I don't see a hand to raise, I sent you a chat. Is it okay just to ask questions like this?

DR. BACH: I think that's fine, just please identify yourself and identify who you would like to ask the question of if that's

possible.

DR. MACINTYRE: My name is Neil MacIntyre, I'm one of the invited panelists. Again, I'm from Duke University, a critical care pulmonary physician. I'm not sure these are questions or comments, they probably focus more on Dr. Coleman's comments, but I would like to point out, I think the distinction between home mechanical ventilation and Bi-PAP or RAD is really quite ordered. Both supply inspiratory pressure to augment tidal volumes and on those muscles, both supply expiratory pressure to assist triggering, both have backup rates, and indeed the terminology, the Bi-PAP ST is in effect pressure assist control ventilation on a ventilator, and Bi-PAP spontaneous is in effect standalone pressure support.

Moreover, these devices have very similar pressure capabilities. HMV, home mechanical ventilation devices do offer more alarms and volume assist control loads which, I don't think these are really important in the home. But my point is, because of the very blurred distinctions trying to argue

superiority of one device over the other is an exercise in futility.

And this leads me to my second point and I would be interested in Dr. Coleman's comments here. I have found over the years that clinicians really opted for HMV, that is home mechanical ventilation, not for superior performance capabilities, not for ease of prescribing, but because of the extremely important link of home mechanical ventilation to the availability of clinical and technical support, and I think this is a critical point here. I think we should be arguing, or not arguing, but addressing this critical component of the home mechanical ventilation provision, and get away from the device performances and rather focus on the clinical and technical support. In theory the, not theory, reality, these devices are lifesaving and are life support devices, and tolerance, adherence and making sure patients are doing what they need to be doing to me is the critical decision driver here, not the actual technical specs of

the device.

So Dr. Coleman, thoughts on that?

DR. BACH: Dr. Coleman, you are on mute. And before you answer, Dr. Coleman, I have a Ross, Garrido, Barreiro and Fisch queued up for questions right now.

DR. COLEMAN: So would you like me to answer now, or wait?

DR. BACH: Yes please, go ahead.

DR. COLEMAN: This is John Coleman. Thank you very much for your comments. I agree with you that I think, I agree with you a hundred percent in the sense that the servicing of in-home respiratory care support is essential for the activity of noninvasive ventilation. I do think, you know, being in the hospital on a daily basis and seeing patients that are trying to get set up with this, I think that while the benefit of home mechanical ventilation gives the respiratory care and advocates home ventilation, we acknowledge that basis, I think the fact of the matter is that this is being driven by a lot of primary care physicians, being driven by a lot

of hospitals, being driven by a lot of internal medicine decisions. We need to understand the differences and when they try to say oh, I want

to order a Bi-PAP machine, they are getting in some ways kind of encouraged to do home mechanical ventilation, it's easier to meet that criteria.

So again, while I think it's a twofold problem of getting the benefit of in-home respiratory care support and the frequent services of the home mechanical ventilator, I also think you need, the criteria is less stringent, and if you'd go through all of these things with a Bi-PAP sheet, I think it would be more readily prescribed.

DR. BACH: Thank you very much. I'd like to go to Dr. Ross next for his questions.

DR. ROSS: Thanks, Peter, this is Joe Ross, and I'd like to thank Dr. MacIntyre for asking that question because as a general internist I was having trouble differentiating Bi-PAP to HMV and was trying to figure out what exactly was the difference between the two,

although I've never prescribed them.

The question I really had was for Dr. Wilson. I was a bit surprised that some review he presented combined evidence from randomized controlled trials and observational

studies to arrive at your effect estimates, and given my concerns about observational studies and confounding, particularly when you're considering more national health plans and my concerns about socioeconomic status and being able to obtain these devices, I just wonder if you could comment a bit on the effect from randomized controlled trials alone.

DR. WILSON: Hi, this is Michael Wilson, can you hear me okay?

DR. ROSS: Yes.

DR. WILSON: You can hear me, okay. So, agreed that when summarizing the data we looked at randomized controlled trials and we looked at observational studies. So when we did see a JAMA paper we did a subgroup analysis where we looked at the impact based on study design. So for example, what were the effects on outcomes when we just looked at randomized

controlled trials, what were the effects on outcomes when we looked at just observational studies? And primarily the effect when we looked just at randomized controlled trials, the effect size went away and was not significantly significant. There were trends

in improvement when we looked at randomized controlled trials but a majority of the effect is coming from observational studies.

So we combined the effect size for both types of study interventions for this paper based on what, the results were consistent, they were in the same direction, and I think if more randomized controlled trials would be done, the effect size will agree with that in the observational studies. But agreed, there is a difference there and we're trying to evaluate the data, we're just trying to look at all the studies which are currently available.

DR. BACH: Does that answer your question?

DR. ROSS: Yes.

DR. BACH: Let's go on to Dr. Garrido.

DR. GARRIDO: This is Melissa Garrido. My question is for Dr. Wilson. First, thank you for your very clear and comprehensive presentation. You mentioned one post hoc trial with completely different hypercapnia levels. I was wondering if any of the other studies included in your review were powered to assess

any other treatment effects, or in other words, differences in outcomes for patients with different baselines.

DR. WILSON: So thank you so much, this is Mike Wilson again. What specific characteristics were you looking at, or do you have any in mind?

DR. GARRIDO: I don't have any specific ones in mind, I was just curious if any others came up in your review.

DR. WILSON: Yeah, so the only ones that really came up were the ones that I mentioned in my presentation. So there was, when we looked at comparisons of different devices for different disease categories, different modes, so some studies looked at

stable versus unstable, so patients with a recent exacerbation versus no recent exacerbation. I don't recall that we found that the studies that enrolled patients with different FEV1s or something like failed to compare or even enroll, you know, patients with severe COPD versus less severe COPD. And again, we didn't find studies that looked at the different levels of hypercapnia, this was

just looking at, you know, if we have 10 studies and they all have different levels of CO2 and we sort of indirectly analyze that, is there a signal there somewhere which would have no direct comparisons.

DR. GARRIDO: Thank you.

DR. BACH: All right, on to Dr. Barreiro.

DR. BARREIRO: Thank you, Chair. I have two questions and I hope I can do it that way. Number one is -- both questions are for the complete panel. The first question is why was Europe so much better, meaning why are there so many studies done there, and most of

the studies done by pulmonologists like they are here, or are they mainly ordered by intensivists or family practitioners, and that's why they are often so different?

My second question goes along with Dr. MacIntyre's. The technology that was mentioned repeatedly and the use of respiratory therapists in an inpatient or outpatient setting in order to help with compliance and adjustment seemed to be mentioned in each one of the presentations. I wanted to know if they

looked at was there a timeframe in which the respiratory therapist was available, was there a number of visits that were important in order to increase compliance? Was there training that also went from the respiratory therapist? In other words, were they all certified or not certified? Because my frustration as a pulmonologist is I rarely can get someone to go out to help these patients when they're in trouble or have questions. So I would like to know the percent of changes that were made with each visit if possibly known.

And the other part is the connection,

we keep talking about technology, the connection with my office. So we use DMR, but the connection between what the DME companies are doing and getting me the information to make changes doesn't seem to be very unique and/or unified, and is there this task force that keeps being mentioned by all the panel members, is there a way, who would you ask on this task force? Thank you.

DR. BACH: Whichever -- go ahead, Dr. Nunez.

DR. NUNEZ: Just to follow up on two

of the questions from Dr. Barreiro, and the first one about Europe. So most of the studies that I am familiar with, and I've worked directly with some of the subject matter experts in Europe on some of these studies, are conducted by either intensivists or pulmonary specialists. It seems to be a very specialty driven approach in Europe to this research and so these principal investigators and the majority of these PIs are not just doing this every single day in their clinical practice but

researching this quite extensively for many many years. So some of the names you saw mentioned like Dr. Dreyer from Germany, you know, he's a pulmonologist and thinks about this all the time.

I would say in terms of the question regarding the connection of information between your EMR or your office, the HME and the patient, based on some of the comments I made earlier, the new generation of devices, the ones that are connected to the Cloud that allow you to see that information directly, we are slowly ushering in a new age where both the DME, HME, providers and patients themselves

will have access to the data, and what we have found is the more access to data from the therapy, the better the adherence. You know, medication adherence in the U.S. is 50 to 55 percent at best, which is about the same for CPAP or home mechanical ventilation. But when you add in the connective device or when you add in patient engagement and the ability to connect with them even remotely, the adherence to therapy rises significantly. And so I think

we need to work on those connections. It is the entire community here whether, it's not just the vendor, the patients and the providers, we need to work on making sure the data is available so that as we move into an era of remote care, remote monitoring, virtualized care, how we can take advantage of the technology that already exists.

DR. BARREIRO: Is there a HIPAA restriction to this as well?

DR. NUNEZ: Obviously there are because there's a potential of personal health information being transmitted but again, modern platforms, modern devices have that all built in, security is designed in from the ground,

and so we want to make sure that we don't lose that critical connection so that any provider, any clinician does have the appropriate access to that type of information in a private and secure manner.

DR. BACH: Thank you very much, Dr. Nunez. Dr. Lisa Wolfe has an answer about the technical panel which was the previous

question, if you'd like to jump in, Dr. Wolfe.

DR. WOLFE: Okay, thank you. Can you hear me?

DR. BACH: We can.

DR. WOLFE: This is Lisa Wolfe. As the representative of CHEST I'd like to give a little bit of background on the technical panel. The original, original technical panel that established the RAD criteria dates back to 1998. That was convened by AARC which is now part of CHEST, in which many members who are here today actually helped to contribute information that allowed us to establish the criteria by which different diagnostic criterion are used to say bilevel is appropriate, bilevel with backup is appropriate, et cetera. Since 1998 those

criteria have not been updated. The discussion of things such as high intensity pressure support and the importance of hypercapnia that we now know can cause research was not available at that time. And so although technically not part of our four questions today, we find that there is significant

interlacing between our ability to understand how HMV is used and our ability to fix the RAD criteria allowing us to better and more appropriately use high level PAP in the home.

And so what we are asking is that for Medicare as an organization as we address the issues of HMV, as we address the issues of chronic respiratory failure and COPD, that we also take a 10,000-foot view, step back and say we'd like to fix the system globally. That includes a new technical panel and an updating of the out of date RAD criterion.

DR. BACH: Great, thank you very much, Dr. Wolfe. Dr. Fisch, did you have a question?

DR. FISCH: Yes.

DR. BACH: So I have Dr. Gay, Dr. Frazier, Dr. Criner and Dr. Kuebler who are queued up, so please take down your hands if

they are still up.

DR. FISCH: Thank you, Dr. Bach. So I have a question I would like to address to Doctors Wilson and Wolfe, and it has to do with the fact that we are focusing our questions

here on Medicare beneficiaries, but we've heard a lot about how things are different in Europe compared to the United States. One, the different distributions of phenotypes being treated, and different models related to the wraparound services that go with what is actually the intervention of one of these devices plus the settings being used plus the other services like respiratory therapy or pharmacy consultations, et cetera.

So the question is, one question is how comfortable should we be in generalizing the data from Europe given that there are no randomized control trials in the United States? And then the other question I have is, it's a bit of a naive one I guess, I'm a medical oncologist, and it seems there are, you know, there is maybe 230,000 lung cancer patients per year in the United States, yet we routinely see randomized trials in the United States

enrolling 500 patients overall, and there's just no trials in this whole field of 200 patients or more. I'm just incredulous as to how that could be for such a prevalent and

serious condition like COPD.

DR. WILSON: So this is Dr. Mike Wilson. Thank you so much for your comment. So with regards to generalization, I agree with you on that, life in Europe is different than life in the United States, both in terms of the devices but like you said, in terms of the services and the whole infrastructure that is set up to deliver this. And so I think for today, if I understand correctly, CMS is able to talk about or provide coverage for the devices but I don't know if CMS is able to provide coverage or who in the United States would provide coverage for the associated respiratory services. And so I think trying to say well, does device use alone with or without respiratory services provide a benefit, and then the second question is in the United States, will the addition of those respiratory services provide benefit and if so how can we achieve that in the United States, but there

are questions with regards to generalization. That being said, the observational studies in

the United States do go along, some of them, with the conclusions that are made based on the European studies. And so I do think that even in our population in the United States, there are benefits from device use alone.

And to your second question, why are there so few randomized controlled trials, A, in the United States, and B, that have enrolled fewer numbers of patients. I think one in power, so the ones that have been conducted have been adequately powered usually to see this but not to detect all outcomes, and so I agree with what's been said previously. We need more randomized controls in the United States, this would help significantly.

DR. BACH: Thank you very much, and we're going to move on to Dr. Gay please.

DR. GAY: First I want to address the MEDCAC group and thank them for the opportunity to speak with this fantastic array of people here. Ultimately the historical comments really deserve perspective. I was one of the fossils that was part of the 1998 guideline

committee that has moved so little over these

decades, but it's difficult to understand that insofar as we knew hypercapnia was the key, but we are all short-term focused in a three-month study that showed that CO2 can be changed, but now we're focusing on much more important things.

But in the process of all of this, CMS had to address delivery of equipment and reimbursement issues that completely distorted the criteria from a patient-focused problem to a device-focused problem. There was a huge difference in reimbursement for not only a home mechanical ventilator, which was not part of the RAD criteria, and early on the backup rate was twice the cost of producing something with a spontaneous rate. So these artificial barriers grew out of all this and rather than addressing the specific patient phenotypes we got locked into the devices.

The devil's in the details, and I've spent a lot of time reading the pendencies of these randomized controlled trials, and they in fact attempt to address these different phenotypes. They talk about whether they did

sleep studies, they talk about the BMI, and ultimately recognizing that it's so hard to do these. The Kohnlein trial took six years to do. All of those require such an immense consideration of how to get these done that now the best evidence narrows this to the point where it's very difficult to get perspective on the clinical issue.

So I'm going to move to my question for Dr. Wilson. I know him as a superb researcher, I also know him as a great clinician. And recognizing all this intense evidence pointing to this small subgroup of patients, we've been trying for five years now to get CMS to give us this expert panel, and I'm going to ask Dr. Wilson if we were to empower you and turn you into a policy wonk now instead of the great researcher that you are, with your interest in obviously taking care of patients with hypercapnic respiratory failure, how would you direct this expert panel that we all are asking for to create criteria that would ultimately take this evidence, would deliver a product to the Medicare beneficiary?

DR. WILSON: Okay. So thank you,

Dr. Gay, for your question. Can you -- you would say how would I direct the expert panel to do what?

DR. GAY: To create the focus on chronic respiratory failure as not just so specific to these questions coming out of hypercapnic COPD, but recognizing that the phenotypes in these specific studies are more broad than what you can actually talk about in just a single study. So now, how would you bring all of these phenotypes together and take advantage of the more specific evidence that you addressed in your meta-analysis. Put it all together.

DR. WILSON: So I think putting it all together, I think there is, regardless of the device type, we have more evidence for Bi-PAP compared to HMV machines. But if you look at noninvasive positive pressure ventilation as a whole, I think independent of the respiratory services offered, I do think this is significant evidence to support its use in the home. But I think that still specifically, you know, which exactly, who do we put on these devices, so out of all the patients with COPD,

who deserves to be on, who needs, or who would benefit from a noninvasive positive pressure ventilation?

I think that the criteria for that is quite gray, so what level of hypercapnia do we do? Some studies use a level greater than 45 and they enroll and they show a benefit. So used a CO2 level greater than 56, they enrolled and they can show a benefit. And so I think, but I think generally speaking there is support for people with stable COPD, unstable COPD, and some degree of hypercapnia to use these devices in the home. And so then the question begins if you look at that, then how do you make that happen for individual patients, and that's kind of translating the data to a policy.

DR. BACH: Thank you very much for that thoughtful answer. A couple of things logistically. I would ask that people turn off their cameras so we can preserve bandwidth if you are not speaking. We are, we have a couple more minutes before the lunch hour, which is 11:30 eastern. The next person to ask a

question is actually one of the speakers,
Dr. Frazier.

DR. FRAZIER: My question's for Dr. Wilson. Dr. Wilson, you're getting all the action this morning. Thanks for your presentation and thanks for the wonderful paper you wrote up. I've got to nitpick with you, I want you to answer for me.

There are two studies comparing home mechanical ventilation to no device that you chose for the review, one is the Heinemann paper and the other's the Paone paper. I reviewed those in great detail and in fact the Paone paper didn't use home mechanical ventilation, it used a Respironics Synchrony, which is a RAD device. What's important about that is that's the study that showed a higher mortality in the treated group, not statistically but numerically, 13 deaths versus 10 deaths, and with putting that with the Heinemann paper you reached a conclusion that there was no evidence that HMV reduced mortality. But if you remove the Paone paper, which was actually done with a RAD device,

there is a statistically significant reduction in mortality, though obviously it's only the one study, the Heinemann study. I think that

makes a difference.

DR. WILSON: So thank you for your comment, I really appreciate that. For that specific thing, I guess I will have to go back and look and review it myself. From what I understood, that this was classified as an HMV device, but I will be happy to go back and look at our files to look that up, and if for example that's what you have noted, then the conclusion may be different.

Again notwithstanding, I think that even if you combine all the studies, noninvasive positive pressure ventilation versus none, it does support the mortality benefits, so I think there are signals on several levels, where this device used or NIPPV is associated with better mortality, or less mortality for patients with COPD.

DR. FRAZIER: Certainly, no question. I just want to make sure because it does say in

the paper conclusion that HMV did not show a mortality benefit when in fact in reclassifying the device, it does. That's my point. You're right, put together it all shows a benefit, but it specifically in this meta-analysis, HMV does

if we reclassify it. Thank you.

DR. WILSON: Yeah, thank you.

DR. BACH: Thank you very much for your question, Dr. Frazier. Dr. Criner.

DR. CRINER: Yes, Jerry Criner from Temple University in Philadelphia. This is directed to, again, Dr. Wilson, and I want to assimilate a lot of disparate information and make it understandable. So some of the limitations that you mentioned both in your paper and your presentation kind of looks at the ability to take the aggregate body of data and really come up with specifics, although there's a directional improvement with therapy, but who to treat, how to treat, when to treat, and really the specifics of the why we're treating patients. Do you feel that the current information is adequate to show that now, or is there not a need for additional

studies, but for a larger multicenter randomized controlled trial where really the technique, the specifics of patient characteristics and the outcomes are better defined in the United States population, not because the United States is different than the

rest of the world but because our patient population in terms of comorbidities, obesity, concomitant medications are different?

DR. WILSON: Just sort of -- thank you so much for your comment. Yeah, so I would agree with you. So I think the status of affairs from the best that could be summarized, I think show a directional impact of these devices on outcomes. That being said, the variability, the heterogeneity in all of these studies and sometimes disparate conclusions between one study versus another, we need some better level evidence here. And so even if you look at the European studies, there's still several questions to be answered when applying this to a United States Medicare population. So I completely agree with you that further

studies such as the one you suggested would be very beneficial.

DR. BACH: Thank you very much. Thank you, Dr. Criner, for your question. We'll take a question from Dr. Kuebler.

DR. KUEBLER: Can you hear me?

DR. BACH: Yes, we can.

DR. KUEBLER: Some of the questions

that I had have already been answered, but it's glaring to me the inconsistencies in the data and the use, Dr. Wilson identified 13 different guidelines, and some of the other studies relied exclusively on the GOLD criteria and the St. George Quality Of Life Questionnaire. But my, I'm shocked at the amount of increase in ordering. I'm wondering who's ordering these devices and what is, you know, if it's pulmonologists, you know, that's one thing; if it's primary care providers or nurse practitioners that's another thing, you know. But from the information or guidelines we rely on, it looks like the last guideline that we had was 1998, and Dr. Owens mentioned that a new guideline was being developed.

Are these addressing all providers? I mean, who is ordering these devices in the United States?

DR. OWENS: This is Bob Owens from UCSD. I'm not sure that I can answer all of your questions. I do think our guidelines are designed for all people that take care of patients with COPD. I think that a consistent theme through all of these questions really has

to deal with the fragmentary nature of our care for patients. You know, they're coming in with an acute exacerbation, they're being taken care of in an ICU. They go to the floor, they're under the care of our hospitalists. They're discharged, they're under the care of a DME. So in my mind one of the differences between Europe and America is the integration of care and how we practice in different settings. I think that explains differences in outcomes, it explains why we don't have large studies, you know, it's just very hard to do these kinds of things.

So again, our guidelines are for all

providers. I think perhaps some of the DME companies can speak to this. My sense, and Dr. Coleman, Dr. Wolfe and others, the panel can probably give their opinion, but my sense is often these devices are ordered upon discharge from the hospital and trying to help patients, and it's easier to go the HMV route than to get a patient to a qualified provider very quickly and do Bi-PAP or bilevel PAP with a backup rate.

DR. BACH: Thank you very much,

Dr. Owens. Dr. Melnikow?

DR. MELNIKOW: Can you hear me now?

DR. BACH: Yes, we can. Put your hand down when you have a chance.

DR. MELNIKOW: Okay. So I have some kind of basic questions that maybe everyone else on the panel understands, but as a family physician these are not devices that I interact with very often. And I'm still, there's been a lots of discussion about HMV versus Bi-PAP and I'm not really sure what the difference is, and other than differences in what's covered and what's not, why one would order one device

versus the other, and the justification for doing separate analyses of these different devices as well. So maybe Dr. Wilson can speak to that or maybe Dr. Coleman could educate me further about this.

DR. WILSON: Dr. Coleman, this is Dr. Wilson, so feel free to chime in. Right now there are different criteria in order to qualify someone for use for one of these devices. So if you want to qualify somebody with COPD for a Bi-PAP S then there are certain criteria that you need to fulfill. If you want

to qualify somebody for a Bi-PAP ST device or a device with a backup rate there are different criteria that you need to use to qualify them. If you want to qualify somebody for a home mechanic ventilator or a life support or lifesaving device then there are separate criteria. And so some perceive that the criteria to get a home mechanical ventilator device is easier to qualify an individual patient sometimes for this such device compared to a Bi-PAP S or ST or something like that, so

that could be one of the reasons why a lot of people are using this, using home mechanical ventilator devices. But that being said, the reimbursement and costs and everything is much more expensive with the HMV devices compared with the Bi-PAP devices.

Dr. Coleman, I don't know if you have any other thoughts on that.

DR. COLEMAN: Sure, so thank you very much. Great question, and I would like to, I prefer to keep things simple so if you look at the two big categories. Bi-PAP, when we talk about all these different modes of ventilation we're talking about pressure support, we're

talking about how do we get ventilatory support, right, and I agree with Dr. MacIntyre that all the terminology gets jumbled up.

So when we talk about giving bilevel or Bi-PAP support, those devices are what are called respiratory assist devices, so those are, if you think of treating one of your patients at home with sleep apnea, those fall into the categories of respiratory assist device machines. They provide different modes

of ventilation, they can provide CPAP, Bi-PAP, Bi-PAP with a backup rate, and they have to be plugged into a wall. They have to, they don't have any alarms, they are not like the seeing devices per se because if the power goes out there will be no support beyond that.

Home mechanical ventilators kind of grew as chronic respiratory failure moved out of the ICU and into home usage. It's very common in patients with neuromuscular diseases like ALS or muscular dystrophy. They are a life support machine so they have internal batteries, they have portability. A home mechanical ventilator can be used in different ways. It can be used noninvasively with a mask

or a nasal cannula, or it could be used invasively with a tracheostomy.

When we talk about different modes of ventilation, the Bi-PAP or Bi-PAP with a backup rate, they can be used on both machines so that's where it gets confusing. In the United States under the current respiratory guidelines if a patient comes into the hospital with acute

COPD exacerbation, and Dr. Owens kind of alluded to this, that patients come into the hospital with acute COPD but this is the third or fourth time they are coming in, and now hospitals are working to prevent hospital admissions. So the thought is they come in, they had acute chronic hypercapnia, we gave them Bi-PAP and they get better, so if they had that Bi-PAP to go home maybe they won't come back as often. And I think that that is where this is being driven for why there's being so much use of noninvasive ventilation.

So criteria currently in the United States, giving somebody a Bi-PAP machine or a respiratory assist device is much more, is very challenging, so instead you can just do a blood gas and call someone hypercapnic and get them a

home mechanical ventilator. They are using the same type of respiratory ventilation support, it's just that the device is, again, it's just like a Tesla versus like a Honda, they both get to the same point if you have the same drivers, but you don't need to actually have the Tesla.

DR. MACINTYRE: Peter, this is Neil

MacIntyre. Can I make a comment here? Peter?

DR. BACH: Dr. MacIntyre, you are free to make a comment and then we're going to stop after this question for lunch.

DR. MACINTYRE: I will be very brief. I just want to reiterate that the technical differences between a Bi-PAP or a RAD and a home mechanical ventilator are really quite subtle and blurred. And in fact in many parts of the world what we call a Bi-PAP machine is often used in an ICU as a full-fledged ventilator because the technical features are somewhat similar.

I will agree with the other speakers that the choice of using a Bi-PAP or using a home mechanical ventilator actually rests on things other than the technical differences. The ease of qualification has been emphasized

by several, and I would also want to reiterate that one of the major drivers, I think, of ordering a home mechanical ventilator as opposed to a Bi-PAP system is that you get the very very important frequent servicing by

technical experts.

DR. BACH: Thank you very much.

Dr. Wolfe, I was going to take a break here.

Is this in relation to this question?

DR. WOLFE: Yes, 30 seconds.

DR. BACH: Absolutely, if it's in

relation to this question, everyone should have

a chance to speak and then I'm going to take a

break.

DR. WOLFE: So Dr. Melnikow, just a

couple of things that are very hard differences

between the two devices. A RAD device maxes

its pressure at 25, if you need more than 25 of

pressure you've got to go to a bigger device.

Since ventilation which is used during the

daytime is only available on a home mechanical

ventilator, it's not available on a RAD, if you

need a set interface with the mouth for daytime

you've got to go to the other device. Also in

our patients that need portability, the

internal battery on the home mechanical

ventilator allows them to have that

portability, and if they are so in need of care

that if their electricity were to suddenly go

out like we see in our tornado and hurricane corridors, the need for that internal battery is essential, so I just wanted to summarize that in short form.

DR. FRAZIER: Peter, this is Bill Frazier. I want to make one quick comment on this very same question. Another difference is regulatory. Remember, HMV, home mechanical ventilators are indicated by the FDA to treat chronic respiratory failure, for the most part RAD devices aren't.

DR. BACH: Thank you very much. If that is the totality of the answers to Dr. Melnikow's question we are going to break for lunch.

Just so you know, I currently have two questions for the panelists, Dr. Fernander and Dr. Salive, which we will do immediately after lunch. If you also want to ask a question and I didn't get to you, please send me a chat. We are going to stop for one hour, it is currently

11:40 eastern or 11:39. We're going to reconvene at 12:40 on the dot. Please, as I

said, if there are any issues please feel free to email me. Everyone enjoy your lunch and we will talk soon.

(Luncheon recess.)

DR. BACH: Good afternoon, everyone. I'd like to get started with the afternoon session. We had a handful of holdover questions to the presenters from the morning, I'd like to start right off with those. First from Dr. Fernander, are you back from lunch yet.

MS. HALL: Peter, before you do that, can I do the rollcall to make sure all the panel members are on the line please?

DR. BACH: Oh yes, thank you, Tara. Please, Tara, go ahead, we will do the rollcall for the MEDCAC panel.

MS. HALL: Okay, thank you. Of course Dr. Bach is on the line. Dr. Ross, are you there?

DR. ROSS: Yes, I'm on the line.

MS. HALL: Dr. Garrido?

DR. GARRIDO: Yes, I'm here.

MS. HALL: Dr. Kuebler?

DR. KUEBLER: Yes.

MS. HALL: Dr. Manship? Dr. Manship? Dr. Barreiro? Dr. Fernander? You might want to wait a couple minutes to make sure everybody gets back on.

DR. BACH: We are down a couple of people it sounds like, so we will give this a few minutes here.

MS. HALL: Okay.

(Recess.)

DR. BACH: Tara, whom are we waiting for still?

MS. HALL: I thought Dr. Manship, I was going to wait until 12:45 and then ask him again. Dr. Manship, are you on the line?

DR. BACH: I don't see him in the attendee list either.

MS. HALL: Okay, I'll send an email. Dr. Barreiro?

DR. BACH: Also not here.

MS. HALL: Dr. Fernander?

DR. BACH: Dr. Fernander is on.

MS. HALL: I know Dr. Fisch is on. Dr. Melnikow? And I saw Dr. Salive. Dr. Gay,

I see you. Dr. MacIntyre.

DR. MACINTYRE: I'm here.

MS. HALL: And then Dr. Criner? Okay. So I will email those to see what's happening and you can go on with your questioning. Thank you.

DR. BACH: Tara, can I proceed.

MS. HALL: Oh, yes, I'm sorry. I thought you heard me, I said you can go on with the questions and I'll email them.

DR. BACH: All right. I now have Doctors Fernander, Salive and Garrido waiting to ask questions. Can we start with Dr. Fernander please?

DR. FERNANDER: Good afternoon, everyone. I just have a question. Given the patient population and what we know about health disparities and health inequities related to respiratory illness, I am curious as to whether any of the presenters can discuss any studies or any data that might exist regarding health inequities related to the use or prescription recommendations regarding the use of any of the devices based on the etiology of the disease or otherwise. We know that

there may be various differences in etiology among marginalized populations for a variety of reasons whether it's race, ethnicity, socioeconomic status and so forth, as well as comorbidities that are related to those same issues. So I'm just curious if there's any data that discusses disparities as well as inequities in treatment recommendations and how they may influence outcomes that we are interested in this afternoon.

DR. WOLFE: If anyone else doesn't have an answer, I have one.

DR. BACH: Please, Dr. Wolfe?

DR. WOLFE: One of the things that I spoke to in my slides is the big interplay that we see in obesity on top of COPD. It's a huge confounder in our population that have more complications with access to care. It's something that very unique in terms of what we see in the American population that's not in the European population, probably in large degree to the overlap in the risk of developing obesity and diabetes with it in this group. And so I think that we need to think broadly about assuring that as we make changes to

access in COPD that we recognize that these patients may also have obesity hypoventilation and that needs to remain having equal access to care.

DR. BACH: Thank you. Would anyone also want to address this question?

DR. OWENS: This is Dr. Owens from UCSD. You know, I think we are not (inaudible, static) but when we formulated our upcoming guidelines we also were concerned that providing home mechanical ventilators as an expensive therapy needing specialized input that there was the potential to worsen health disparities. I would emphasize what Lisa said. I think that providing high quality care and providing the right care for patients, kind of one of the themes we've been talking about, providing care around the patients as opposed to around the device, I think will be very important for the panel to consider. Thank you.

DR. BACH: Thank you very much. I'm going to move on to Dr. Salive, who has a

question.

DR. SALIVE: Thank you, Marcel Salive

from NIH. So it's kind of a followup to the last comments. I think, you know, we heard some interesting comments about the comorbid conditions such as obesity, obstructive sleep apnea. I had a question more broad about other potential comorbidities. It seems like congestive heart failure was excluded from the review for some reason, and then some of the comorbidities of obesity can be things like diabetes, goes along quite commonly with that, so it may be really multi-morbidity rather than just pairs of conditions that would link to potential outcome of these studies.

So my question is for, I have two questions, one I think is for Dr. Wilson and the other is broader for anybody. But in the systematic review, were you able to look at the comorbid conditions in the meta-analysis, because sometimes that is possible since you had so many small studies, and did you see any, you know, effects from the comorbid conditions linked to the outcomes? Or could that, as I

think was suggested by Dr. Wolfe in her comments, would certain comorbidities be relevant for the device selection in this case?

And then my overarching question is since I think this is a big gap, it's commonly seen in guidelines as was mentioned a moment ago, that guidelines need better evidence on groups of people that have the common comorbid conditions, how can we get better evidence with this question here? Thank you.

DR. WILSON: Can you hear me okay? This is Mike Wilson. Thank you for your question. So in our systematic review we analyzed patients with COPD and we also analyzed patients with obesity hypoventilation. Now in looking at the COPD, patients with COPD, I would say a majority of the included studies excluded patients with concomitant sleep apnea or suspicion of sleep apnea, I would say maybe two-thirds of them, I don't have the exact number. So it's much, but no, we did not a priori pre-specify should we analyze outcomes based on did they include any patients with

sleep apnea or with mild sleep apnea or severe sleep apnea or obesity or these types of things, so we don't have that data available. So that's probably the answer to your question.

DR. FRAZIER: This is Bill Frazier;

may I answer that question? In the study that I talked about, our Medicare database retrospective looking at limited data, we pulled the 36,000 patients diagnosed with COPD CRF and in the subgroup, the 410 that were placed on HMV, remember in the limited data set I only get five percent of the data, that's all Medicare offers, and so that 410 is the five percent I got. In that group I can tell you that 86 percent were Caucasian, eight percent were African-American. In that group 14 percent had a stroke, 32 percent had congestive heart failure, four percent were panplegic, eight percent had a recent myocardial infarction, four percent had chronic liver disease. Their Carlson comorbidity numbers were three and four. So your point is exactly right, these people have a lot of very serious comorbidities that are in the HMV group

and they're also in the control group as well.

DR. SALIVE: So is your publication in press now or is it, you said it --

DR. FRAZIER: Yes, sir, this first one is revised and the revision has been submitted. The second, the manuscript is under

preparation, it will be presented in a slide show presentation to CHEST in October.

DR. WOLFE: This is Dr. Wolfe. Can I just say one thing real quick? I'm sorry to interrupt. Specifically to address the issue of heart failure, we know that heart failure patients can present with Cheyne-Stokes respirations which is a different valatory issue. The hallmark of Cheyne-Stokes respirations is actually a low to normal CO2 level so the pathophysiology is very different. We know from the trial that that actually increases mortality, so the reason that heart failure is not discussed with the comorbidities in this set is that if we had a heart failure with low CO2 they wouldn't qualify for the device and it wouldn't be prescribed given the

increase in mortality with the device, so heart failure is off the table.

DR. BACH: Thank you very much.

DR. OWENS: This is Bob Owens. If I could also just add and put what was just said in slightly different form, from the studies we saw in the Kohnlein study, you know, a third of patients were dead in one year, so this is a

really sick population that you add comorbidities just to go back to what some of the speakers have been saying. It would be great to have more data but, you know, if it takes many years, these patients don't live that long. You know, it's very hard to get a large study in these people.

DR. SALIVE: So I would say it needs to be measured, that's kind of my point, not that we needed -- you know, it's just not measured a lot of times. I think the claims data makes it pretty well, if you don't look and say what comorbid conditions people have, you know, what, you just have to make assumptions.

DR. BACH: Thank you very much. We

will go on to Dr. Garrido with a question.

DR. GARRIDO: Thanks, this is Melissa Garrido. This question is for any of the speakers and it's actually closely related to Dr. Salive's question. So we heard today about some of the observational studies that are seeking to understand whether it's just a matter of noninvasive ventilation or associated with improved outcomes in an overall sample of

patients with COPD. And some of them, like Dr. Frazier's studies, are using propensity score matching or waiting to match the treated and comparison patients based on patient care metrics.

So one of the, the benefit of some of the observational designs is to the ability to help identify patient subpopulations for whom an intervention is most likely to be effective, so to better target the intervention. And from what I have gathered today, I haven't heard anything about studies having the explicit goal of doing that. I just wanted to double-check if any of the observational studies that any of

you have mentioned or are otherwise aware of how an explicit goal of identifying the population of patients with COPD who would be most likely to benefit from any of the types of noninvasive ventilation we've discussed?

DR. GAY: This is Peter Gay. If you look at the retrospective study that Coughlin did, that was a clear directive of taking sort of a mixed bag of hypercapnic COPD patients, they had all the comorbidities, but the directive was clearly keep them out of the

hospital, we will pay you immense amounts of money not to have them come back. So the aggressive effort in that way to use HMV whether it needed to be or not, it got this device and with all their comorbidities it immensely reduced the readmission rate. Thanks.

DR. GARRIDO: So to clarify, in those analyses, yes, they had a very open inclusion criteria, but the analyses didn't try to identify which subgroup of the included patients were most likely to benefit, correct?

DR. BACH: Dr. Gay, you're muted, so

we're not hearing your answer.

DR. GAY: I'm sorry. They clearly concentrated on the acutely ill hypercapnic COPD by their very nature but you're right, it was not well tabulated, there were a lot of assumptions in there that there were generally many comorbidities in a southern, southwestern population.

DR. FRAZIER: This is William Frazier again. I've also started another study that I have tried to carve out of the Medicare database looking at hypercapnia as a predictor

to response, to see if now with including the completed 2019 data I'll have enough ICD data for hypercapnia that we will be able to make some comment if that shows up as an independent predictor of outcome with HMV therapy.

DR. CRINER: Dr. Bach, this is Jerry Criner from Temple. I'd like to address Dr. Garrido's question.

DR. BACH: Go ahead, please.

DR. CRINER: I'm thankful that Joe was the senior author and the purpose of that was

trying to define subsets of people that were acutely ill that could benefit from noninvasive ventilation and towards design of an NIH submission for treatment. So what was defined from that study is that patients that were acutely ill and hypercapnic from discharge who were overweight with prior history of respiratory failure within at least two weeks of that admission were the ones more likely to benefit, so that was an observational study that was designed for that purpose.

DR. GARRIDO: Thank you.

DR. BACH: Thank you. And I will remind everyone to turn on your cameras when

you're speaking just so we can, you know, to improve the interactivity. I'm not seeing any other questions. Is there anyone who wants to ask another question? Otherwise I'll be happy to move on to the open panel discussion.

DR. ROSS: Peter, I have one more question, this is Joe Ross, if I could ask.

DR. BACH: Sure.

DR. ROSS: Sorry, let me turn on the video, sorry about that. Dr. MacIntyre made a

passing comment about the difference in the devices that are used in Europe and the United States, and either the similarity or dissimilarity between the RADs and the HMVs. I was just wondering if our commenters could just say a bit more about that given that so much of the research that has been discussed came from Europe.

DR. MACINTYRE: This is Neil MacIntyre, I can make an introductory comment here. I've been trying to reiterate, I think it's the settings that are used, how the device is used rather than the device per se, because again, the technical features on RADs and home ventilators are very similar. I think the big

difference is how those settings are applied to an individual patient and what kind of support is available to assure compliance adherence and effective therapy. Thank you.

DR. COLEMAN: This is John Coleman, I'm going to respond to that as well. So I think just to kind of put it in very broad based terms, when we think of respiratory

support or ventilation we have acute and chronic, right? So when we have acute respiratory failure those are our patients that end up in the medical intensive care units, some have influenza, they come up COVID, they get intubated or they end up with a tracheostomy and they get inpatient ventilation.

Then we talk about chronic respiratory failure and we talk about noninvasive ventilation, and noninvasive ventilation can be done in many ways, it can be done through various devices, and those devices include home mechanical ventilators and they include respiratory assist devices. Within respiratory assist devices there's multiple modes of ventilation, so Bi-PAP with a backup rate,

Bi-PAP without a backup rate. You can do the same thing with a home mechanical ventilator. They're both forms of noninvasive ventilation.

And so I think that is where, you know, like Dr. MacIntyre said, there's a lot of alphabet soup that goes, that makes this issue very complicated, right? You hear things like

NIV, NIC, HIV, RAD, BPAP, there's a whole bunch of different anagrams. I think the important things are that when you talk about noninvasive ventilation for chronic respiratory failure you are talking about respiratory muscle support, and that can be done through a variety of different devices. It just so happened that in the European model sometimes they used pressure support devices, sometimes they used home mechanical ventilators. The same thing happened in the United States.

Currently to treat chronic respiratory failure in the United States under Medicare guidelines, you give them a respiratory assist device, so a machine like Dr. Wolfe alluded to, that needs to be plugged into the wall, does not offer portability and is not really a machine that has alarms. You have to meet

criteria and that criteria is very stringent to meet, and so that's why we have gone down in America the increase of home mechanical ventilators. Both devices are similar, it comes down to the modes of ventilation. That

is the point that I wanted to make in my presentation here.

MR. GAY: This is Peter. I think, John, you did a very nice job with your presentation. I think it should be understood that the difference between Europe and the U.S. is that the Europeans do not have the distinction between a backup rate and a spontaneous rate. They expect as a standard of care, for example, obesity hypoventilation, the vast majority of patients are started in the hospital with a backup rate and many of them never even get a polysomnogram. The French study that looked at the use of a high level backup rate in fact pointed out the fact that without that high backup rate it really didn't work very well. So it's the standard of care there, they're not worrying about the backup rate. It made it very simple for them to have a majority of these devices be a BPAP with a

backup rate rather than a mechanic ventilator.

It's just the opposite here in this country since the backup rate is immensely difficult to get, dating back to 1998 studies I

apologize for, but ultimately that created this artificial barrier. Thanks.

DR. FRAZIER: This is Bill Frazier, I want to comment as well. I have a little different perspective. I think the difference in performance characteristics makes a difference between ventilators and RAD. I think the increased IPAP and I think the increased peak flow really does make a difference here. The outcomes data from the U.S. that we generate is all the patients need, and I could see some RAD-generated data in the U.S. Medicare populations that would tell me that those were equivalent outcomes. I'm not sure they're going to be.

DR. VOHRA: This is Dr. Vohra, I have a comment, Dr. Bach.

DR. BACH: Yes, please.

DR. VOHRA: Thanks. Another condition that can lead to a positive differential can be stent or bypass, and I think that's a very

important intervention, but we don't look at the cost of care, especially if that is as

common as it is, and the demographic change, so I think that is something that has to be considered.

And taking off of Dr. Gay's point about having, alarming patients having the ST mode and the S mode, and having to accommodate for that, it's helping with the issue a lot, and practitioners won't have to exacerbate the same intervention, which is Bi-PAP all the time. Direct comparison studies, yeah, they are hard to do but it would be nice to have a study like that, but those studies are hard to do. That's my only comment. Thank you.

DR. BACH: Thank you very much. Would anyone else like to --

DR. BARREIRO: This is Tim Barreiro, I had a question and I just want to make sure that I didn't miss anything. We spent a great deal of time with the experts discussing the cause of the hypercapnia. In the big packet which we reviewed prior to the meeting, however, there was a lot of comments and diatribe that talked about the role of FEV1,

which I'm not necessarily a huge fan of because

I think you could have a very high FEV1 and still be hypercapnic, and some of these studies go as low as severe COPD with FEV1s that were less than 30, and some that are mainly moderate. So I just want to make sure if the panel could be clear to me, are we saying that hypercapnia, which I agree is most likely the driving factor, then we should eliminate the FEV1 role? Any comments to that?

DR. GAY: Clearly severe COPD is important here. This goes back to really the Jones study back in 1995 which was the hallmark study that allowed noninvasive use for COPD and hypercapnia. If you look at the only study that really carried Medicare into this arena it was that study, and I think the subtlety there was if you looked at their oxygen run-in, those are the patients that in fact developed more hypercapnia on supplemental oxygen. If you looked at his studies when he did the polysomnogram criteria, his average AHI was 10 per hour. These patients in fact had mixed disease, they had mild overlap syndrome, and I think that gives you the perspective in the

degree of just, is it FEV1 or is it something else. They have to have that nocturnal hypoventilation component that I think drives this hypercapnia.

DR. BARREIRO: Yeah, we may be saying the --

DR. GAY: You're muted, Tim.

DR. BARREIRO: Thank you, sorry about that.

DR. BACH: Dr. Barreiro, let me, let's hold for one second, hang onto your thought. I just want to tell the CMS people, it appears we have naturally segued to the next phase of the agenda so just to be clear, I think we are done with asking questions of the presenters and we are now having an open discussion between the panel. I've gotten a couple of messages as well that people want to ask each other on the panel questions, that is what we are scheduled to do right now. Again, it's scheduled for an hour but we will be, we're going to go with the flow here to some extent. It is not uncommon for presenters to have things they want to point out during this discussion. I'll ask that you not interrupt but just message me, and

I will try and work it in even though we are now within the panel discussion, so that we can proceed from there. So Dr. Barreiro, I'm sorry for interrupting you, you were about to respond to Peter Gay on an issue, so go ahead.

DR. BARREIRO: No problem whatsoever, Chair. I think we may be saying the same thing and I want to be sure that Dr. Gay and I were saying the same thing. I was struggling with the concept of the heterogeneity of COPD and that you could have, we would all agree that the likelihood is here that advanced lung disease causes more hypercapnia but we still see people with mild disease that might be hypercapnic and as he mentioned, the overlap phenomenon or some other practice would go to this.

As I'm thinking about our charge moving forward, I just wanted to get some clarity that maybe the FEV1 may not be included in a criteria that we should be using, and I wanted to make sure I was thinking along the same lines, or maybe I was wrong.

DR. WOLFE: This is Lisa. Can I just say one thing real quick? One of the sources

of confusion is the use of the standard GOLD criteria to decide what's severe and what isn't. That would still require FEV1 measurements. However, for the purposes of home-based ventilation, severity is based on hypercapnia and it really doesn't matter what the spirometry shows. The vast majority of inpatients during an exhibited exacerbation of COPD are diagnosed with COPD, they are treated for COPD, they do not get spirometry because it's typically not available in a medical ICU. And as such I would agree, FEV1 should not be part of the criteria.

DR. BACH: And so let me point out again, first of all we can, people can turn their cameras off it it's easier for bandwidth issues, but if you're speaking try and turn your camera on unless it freezes your computer.

This is, just to be clear, this is a conversation between the panel. I am asking CMS as a courtesy to leave this open to the presenters. Please respect that courtesy. To the extent that if you feel there's some

critical factual clarification that is needed
please do let me know, message me, but please

let the panel have their discussion. I hope
that's okay with everyone.
DR. VOHRA: So I have a comment on Dr.
Barreiro's question and Dr. Wolfe's comment.
DR. BACH: If this is a factual
clarification, that's great, but otherwise we
need to move on to our part of the discussion.
DR. VOHRA: Okay, just for the panel,
one of the things about the CO2 versus the
FEV1. In the HOT-HMV study they did use CO2,
that's one of the parameters that was
monitored, and actually showed a significant
decrease in the transient CO2 at 12 months.
DR. FRAZIER: This is Bill Frazier,
again being a contrarian. I'm an either/or guy
on this issue. Certainly hypercapnia is
sufficient for NIV but I'm not sure it's
necessary. All these people that have been
studied have hypercapnia, so the question
answers itself, of course it's beneficial. It
begs the more important question, is there a
bigger group of patients who might benefit and

how do we identify them, and I think FEV1 is one of those tools. I think a clinical characteristic such as a GOLD D, a frequent

exacerbated recurrence is another way to measure that. I don't want us to shut our minds that there may be other patient groups, because we've only studied one patient group. And again, in my data set only 12 percent were said to be hypercapnic, okay, maybe it was 50, maybe it was 60, but it certainly wasn't all of them, and in that all comers group there's real mortality and health care utilization benefit with HMV. Let's keep an open mind.

DR. BACH: Thank you. So I think some of the panelists had questions or discussions they wanted to have with the other panelists and this is the time for that. Without putting any pressure on you, Dr. Holt, I think you were one of them.

DR. HOLT: Yes. I just wanted to bring everybody back to why we're here at the meeting. We're still trying to figure out what Medicare is asking all of us, is there

something else that needs to be done, is there some kind of adjustment, revision to the qualification criteria, and I know Dr. MacIntyre would say, you know, it's not the device but, you know, it's more of like the

right device for the right patient. So it doesn't have to be a progression of CPAP to Bi-PAP to Bi-PAP ST or Bi-PAP S to home mechanical ventilation, it's getting the right device. But there still has to be an answer on how do you get the right device to the patient, because right now Medicare is saying it's not working and something extreme is going to happen to the entire NIPPV code unless we say that this is what we should do. Thank you very much.

DR. BACH: Thank you. Panelists, please. So one of the things that can be useful for the panel I think at this point is pretty soon I'm going to ask you to vote on the questions that everyone has. So sometimes it's useful to take a look at those questions at this point and ask yourself if you feel there are questions of clarification, something

worthy of discussion that would start off a discussion amongst all of us. If you want to start a discussion, you can feel free, we are waiting, which is fine. I don't want anyone to think the line has gone dead. We will take a few moments here and I'm going to check in with

everyone in two or three minutes.

DR. GAY: Well, out of human compassion, Dr. Bach, I'll just mention that ultimately I think we're here about hypercapnia in severe COPD, so in the patient selection criteria you can open with that base. But we've had a lot of discussion about the fact that there are subtle comorbidities, there are subtle mixes of population, whether the BMI went to 35, whether they had specific PSC to rule out all of the sleep disorder, some of them allowed an HI up to 15, so I think a good discussion should talk about that selection criteria. We know it's hypercapnia and severe COPD we're talking about but in those studies there is more of a variation to answer question number one and that discussion needs to take

place. Thanks.

DR. BACH: Thank you very much, Dr. Gay. Other panelists? For what it's worth, I'm not, I don't participate in the actual discussion as I mentioned, I'm just the emcee if you will. Other panelists who'd like to chip in?

DR. MACINTYRE: So this is Neil

MacIntyre. I'd like to sort of clarify point number two or question number two when you talk about NIPPV parameters, where I feel somewhat strongly that the settings, the high settings, the necessary settings, there is a good evidence base for settings, but as I've repeated several times over the course of the day, I'm not convinced there is enough evidence to pick a particular type of device. If the device can supply the necessary pressures, backup rates, et cetera, et cetera, I'm not sure what it really matters what the name of the device is.

DR. MELNIKOW: So, Joy Melnikow. It seems like there's maybe some qualifying language around which I don't, being new to

this process, I'm not even sure that's possible, but by what is meant by equipment parameters, right? Because that's kind of a vague term and it could be that it means which device or it could be that it means the device setting. And reflecting on this it strikes me that although the evidence is clearly quite imperfect, it's certainly advanced since 1998 when the last determinations were made, and it

does seem like there's the need to revise what is covered or how it's covered compared to 1998.

DR. BACH: Thank you, Dr. Melnikow. So as we go through the voting, just a small preview, we will have the opportunity, or you will have the opportunity not only to vote but then I will poll you and you will also be able to clarify the reason for your vote or if you want to articulate it, and we will also have discussion depending on how the votes work out, we may have more discussion allowing you to clarify these things. And to remind everyone who's attending this meeting today, these votes

are to guide CMS and so this input is not binding in any way on the agency, and so I generally think about this voting as a quantitative way of assembling information and then a lot of discussion and presentations from today, and the discussion around the voting, will give them more qualitative information about what's known, what's lacking, what a vote means. I don't know if that helps you.

Dr. Fisch, you had a question?

DR. FISCH: Yes. I guess I wanted to

just reflect out loud that, you know, in the course of our presentations this morning, the Kohnlein study really had a lot of weight, you know, in Dr. Wilson's paper when we looked at the forest plots that we were shown, it was both the largest study in that meta-analysis, it had a little over 10 percent weight in the meta-analysis, and it had the most significant magnitude of treatment effect with the odds ratio of .27, so it was really an outlier. And that was of course a European study that excluded patients with a BMI greater than 35, and excluded patients with heart failure or

other significant lung or cardiac disease, and had relatively high thresholds in terms of the PCO2 being at, you know, around, greater than 52, and the GOLD 4 criteria. So I'm just sort of raising that as a point that I noticed in trying to figure out how that affects my level of confidence that this will generalize to the Medicare population in the United States, in sort of how I put all that together.

DR. GARRIDO: This is Melissa Garrido. I just want to kind of echo Dr. Fisch's statement. Beyond the generalizability I think

a lot of the study designs that were included in his reviews and the individual studies themselves, they weren't designed to really inform a lot of these questions, so we might know that there were improved outcomes within a specific sample that had X, Y and Z patient characteristics, but we do not know from those studies which of those characteristics are most important in predicting better performance with any of the devices.

DR. BARREIRO: This is Tim Barreiro,

Mr. Chair, if I may speak. So I would like a little bit of a more robust conversation on question number three, how confident are we that the evidence is sufficient to provide patient usage parameters? There's been multiple discussion that for CPAP, CMS required four hours based on studies X, Y, Z, and then we've seen some of the studies that were presented today that six hours, and then the longer you allow people to try it, the more compliant it may be, and I think that's important.

The other point goes back to Melissa, if I may use her first name, is that we are

also in the business of helping patients live better lives, so while mortality is the holy grail, improvements in patients' symptomatic scores may be reasonable enough for us to try multiple devices along the way in order to help them live a better quality of life. Two things that we know, at least I think from what was presented today and my readings, is that hypercapnic patients with the use of this have a reduction in mortality and are reduced in

hospitalization, which we know in the COPD patients in and of itself, there's a reduction in mortality and staying out of the hospital, so there's some robust information provided that I feel confident in that.

I'm not sure I know how to handle whether or not, I personally would say, and I'm sorry for my long diatribe, is that I've had multiple patients have their equipment removed and I think this was eloquently stated in some of the handouts where people wrote the same thing. If you wear it for three hours and 59 minutes we take it away, but if you wear it for four hours and one minute, we keep it, and I'm not sure that's the ideal way to do that,

although again like every policy, we have to have some kind of cutoff. So I'd like some additional discussion if I could from other experts. Thank you.

DR. GAY: If you want to know the magic of the four hours, it really came from dichotomized observational data of Krebbs in 1994, where he was looking at the use of really

just a CPAP device, and ultimately it was just that the patients that wore it more than four hours had a better response than those who wore it less than four hours. And right around that time when there was a flurry of studies, people were just fishing for a cutoff point, and four hours got embedded into the literature.

But what's apparent is, I think looking at Struik with less than 50 percent of the patients using it more than five hours a night, Murphy's was better, more is better is the mantra and take home point.

DR. BACH: Thank you, Dr. Gay.

DR. MAURI: This is Laura Mauri, sorry, if I may?

DR. BACH: Please.

DR. MAURI: I just wanted to make one

comment looking back replying to one of Dr. Fisch's questions earlier about the impact of heart failure, and I wanted to pick up on that as a cardiologist as well, understanding the presence of heart failure in the study means something quite different than for example excluding patients with the study

criteria with heart failure from a prospective randomized trial like the Kohnlein study, is a bit different from the report of heart failure and comorbidities, not to say that that's not an important descriptor of the patient population that was studied under Medicare and is currently being treated. But I think it is appropriate to still view the results from Kohnlein as being important for defining the impact of the therapy on this specific population that has hypercapnia and excluding those patients who might not benefit having a different mechanism for respiratory failure, as Dr. Wolfe was commenting earlier. So I just wanted to comment that that discrepancy between what exists in Medicare and what exists in the Kohnlein paper, I don't see that as a deficiency of the conclusion, but the fact that

it was not studied.

DR. BACH: Thank you very much.

DR. CRINER: Dr. Bach, this is Jerry Criner, I would like to --

DR. BACH: Dr. Criner, just before

you, I think Dr. Garrido was going to ask a question, maybe I'm wrong.

DR. GARRIDO: Yes, Peter, this is Dr. Garrido. I just wanted to ask kind of a clarifying question to Tim. As one of the non-clinicians on this group, I guess I could use a little bit of clarification from any of you really on how often patients present with chronic respiratory failure but do not have some level of hypercapnia. From what I understood that was present in almost all of the patients, but I want to make sure that I'm understanding the clinical parameters better.

DR. BARREIRO: I think the question was directed to me, thank you for the question, Melissa. I will approach this question in multiple different facets. I think first and foremost, what we in the pulmonary literature would support, and other experts on the panel as well, is regardless of your FEV1, everyone

has an exacerbation, but whether we define that exacerbation as being hypercapnic probably could be somewhat argumentative. We do know that it's more likely the worse your symptoms,

the more likely you will be hospitalized because of it, but still regardless of that, all patients some way or the other in this mixed heterogeneous disease may end up in the hospital. Clearly the literature supports the more often that you have an exacerbation or are in the hospital, the more likely you'll come back to the hospital, and that carries a significant mortality with it. So for me, this is where patients usually get intervened with trying to start these noninvasive ventilators or whatever we want to call these, at this point that might be subject to argument, but as an adjunct in order to help keep them out of the hospital and improve survival, so I think, hopefully I answered that question in that regard.

So I'm not necessarily sure that hypercapnia, it may continue to be argued may not be the only criteria, I think that was what one of the presenters mentioned, that it's

always a fascinating aspect of it, but that all patients with COPD doesn't absolve you from

having an exacerbation, whether that's defined by hypercapnia or not. But we do know reducing the concept of hospitalization does reduce mortality, and so this does appear that these devices do do that, and if it does that, that's I think relatively important from my perspective.

DR. BACH: Thank you. Dr. Ross, do you have a question?

DR. ROSS: Yeah, I had a question, thank you. So this is Joe Ross and I really had a question for Dr. Gay, who seems to know the literature really well, and I'm sure Dr. Coleman covered this, but one of the things that I'm sort of struggling with is not just how good the Kohnlein study looks, but how bad the Struik study looks, it's a bigger study and it's clearly negative. You had kind of made a comment around adherence and is that the general assumption in the pulmonology community, that the reason that trial failed was that people were nonadherent?

DR. GAY: Actually if you want it

quick and dirty, one of the nicest reviews was

Nick Hill's editorial of the Murphy paper where he goes at the Struik dissection that you're asking me for. The big two that were in that was, number one, were these truly the chronic hypercapnic, and to help Melissa too, these patients come in with hypoxia or hypercapnia or both, and the hypoxic are not what we're talking about. So the ones that came in with acute hypercapnia, a couple of days later with antibiotics you take care of their hypoxemia, their hypercapnia is gone. The argument was, you didn't really establish the hypercapnia level when you grabbed them when they came into the throes of the hospital very very ill.

Number two was the actual usage criteria was lousy in Struik. They had 43 out of their 101 patients that broke five hours. In most interventional trials where you can't even get half the people to do what you want them to do are highly suspect, so I hope that answers your question.

DR. ROSS: That's helpful, that is helpful, thank you.

DR. FRAZIER: This is Frazier. I'm

old like Peter so I've read some of this literature when it came out as well, you know, you get bored when you get to my age. Here's something else to think about. Kohnlein, they were stable, not in the hospital, right, you found them and then you put them on therapy. Struik, they were in the hospital but you washed them out for two to four weeks before you went back and put them in the study. What we now know is there's a tremendous mortality the first two or three weeks after a COPD exacerbation requiring NIV; that's Lindenauer's work from December of 2017. Then that mortality starts to plateau at about 30 days. So what you've done is not enroll people with a high risk of mortality because they died during that two- to four-week period where you washed them out, and therefore you get a less at risk for death patient, a lower pretest probability as we would say, and it's harder to show mortality benefit because you've lost the chance to save their life earlier. That same kind of thing shows up in my Medicare database, very early reduction in mortality that first 30 days.

DR. BACH: Actually, so I'm not participating in the discussion, I just want to ask a clarification, Dr. Frazier. Are you saying that the covered period should only be until that plateau then?

DR. FRAZIER: No, it doesn't go away for 69 weeks, but the biggest decrease occurs in the first four to five weeks, but you have a mortality benefit in my study until week 69, when the lines cross.

DR. BACH: Okay, thank you. And so back to the panelists, I think Dr. Barreiro, and I will emphasize again, this is a discussion in the panel. The speakers, because I have found it useful in the past, if speakers have factual clarifications, and I think everybody knows the difference between facts and conjectures based on facts, if I can draw the line between those two things, I would like to, if you'll indulge me, but I would like to go back to the panel discussion, and so Dr. Barreiro has his hand up.

DR. BARREIRO: Thank you, Mr. Chair. I wondered, and maybe I'm doing this wrong after that comment. I wondered if the fourth

question that wasn't answered, or maybe should be added, is my frustration with trying to get people the device. And I know there was a very nice discussion and I'm glad we had it about disparities. In the studies published longitudinally we see that 30 to 40 percent of over a million admissions to the hospital every year for COPD exacerbation or chronic respiratory failure happen to have, happen to occur in minorities. And again, we didn't seem to have any information of whether or not there is diversity and/or discrepancies in the gender/race role and ethnicity within this, and I think we'll continue to struggle with that.

But I guess my question is since there might be people that are from the DME companies, I can't seem to get them to comply with much of anything, and/or supporting the patients that need it, and I wondered if others were sharing the same aspects. We can talk about the criteria but it doesn't seem to be getting delivered to the patients effectively, and/or being removed inappropriately.

DR. BACH: Does anyone have a response to that?

DR. MAURI: I would, this is Laura Mauri again and on that topic, because I think it does tie into the comments of Dr. Ross as well, I think these things are all linked. We worry that the more adherence there is, the more successful the treatment will be, and so as we look across the different studies we see that in the studies or in the patients from an observational standpoint, those that got more treatment did better, so we think more treatment is better. But what we don't have is something that would prescribe a certain amount of treatment as being more effective, because we don't really have a randomization that would show that. And we also know from what has been presented earlier today that the trials that show more services provided, they're the ones that have had more success in terms of showing the effectiveness of the NIPPV. So I think on the topic of whether it makes sense to require a minimum amount of therapy or the administration of therapy that a patient would

be compliant with in order to receive high intensity noninvasive ventilation, the problem with prescribing a threshold is that that

adherence pattern depends on the services a patient receives, and we know that those are markers for better outcomes, but they're also things that are strongly influenced by socioeconomic status and access to care, and the services that we can provide for those patient populations.

So I think, I would be concerned that if we depend on an arbitrary threshold of amount of usage and don't provide a mechanism to ensure access, that that will potentially increase the potential inequities in terms of the delivery of adequate care, and it's difficult to measure and I think that one of the corrections that, you know, we would like to see going forward, is more data on whether those variations exist. But from what we're hearing from the clinicians presenting today, at least on the level of access to similar modes of ventilation, but using for example the

Bi-PAP with backup rate, modes of ventilation, that there are differences that are not directly related to patient needs, and ultimately we want to bring this conversation back to getting the right therapies to the

right patient.

DR. BACH: Thank you very much. Dr. Criner, do you have a question?

DR. CRINER: No, I wanted to follow up with Dr. Fisch's statement about the Kohnlein study and how generalizable it was, and address a little bit the last speaker as well as Dr. Barreiro. I mean, one of the issues are is the quality of the data that exists right now that we're trying to extrapolate to form for a U.S. policy, or how to improve the U.S. policy that currently exists for placement, there's a problem with the studies that exist that we're basing this on, the three largest most recent randomized controlled trials, none of them are pragmatic trials that tried to mirror clinical practice. Some of them had special features that made it not very acceptable to patients and hard to broaden the conclusions to the

general population at large.

The Kohnlein paper which, you know, is judged to have the greatest treatment effect on a forest plot, that had 36 centers that recruited 200 patients over seven years. So these patients, these centers overall recruited

in some cases less than one patient per year. And in the Murphy study, the most recent, the HOT-HMV study, that rejected 95 percent of the patients that were screened. So we're really talking about subsets of populations that were enrolled who basically were making conclusions for broadened therapy.

When we look at PCO2 elevation, that's not a monolithic marker to identify all patients who may benefit from the therapy. Hypercapnia can result because you have high dead space, or it can result because you're hypoventilating, or it can be a combination of both. So there's not a good physiological endpoint that you can identify your patient population with reliably.

And I think the third point about the

adherence and compliance, it's just not because patients can't get the therapy or patients don't want to use the therapy or don't know what the therapy provides. In some cases with COPD compared to other diseases that do cause hypoventilation such as obesity or restrictive neuromuscular disease, these patients have dynamic changes in lung function that can

contribute to hypercapnia and intolerance of using an applied pressure. So I think it's a little bit more complicated than saying we choose a PCO2 high or low to identify patients reliably that may benefit or not benefit from the therapy. Thanks.

DR. BACH: Thank you very much, Dr. Criner.

Tara, I think you have a procedural announcement.

MS. HALL: Yes. For the presenters, I'm going to switch you out of the panel member group into the attendee member group where you can just listen now to the rest of the meeting so that the panel members could have their discussion. So we thank you for your

participation thus far, and please continue to listen in.

DR. BACH: Thank you very much, Tara, and thank you again to the presenters for all of the input and insight. I have I think Dr. Manship.

DR. MANSHIP: Thank you very very much. I wanted to begin by thanking everybody. I am a non-clinician, philosopher and

theologian by training, and it's been fascinating to listen to all this and to think and to put all of this together. And Dr. Mauri and Dr. Criner and a couple of others just over the course of the day have mentioned compliance and adherence and those are resonating with me, and so my question is probably more on phenomenonological or lived experience, philosophical question, and I'm curious to know from the experts, the clinicians, how do patients experience the use of this equipment, how do they experience their own illness, and how does that inform your response to them, your treatment for them, and then how does that

inform how we should be thinking about this with regards to answering questions about patient populations? So it may be somewhat of a nebulous question, it's not quantitative, it's certainly more qualitative, but to me that provides context, so I'd like to hear from members, from clinicians, how do patients experience COPD, how do they experience hypercapnia, how do they experience, you know, obstructive apnea and the overlaying obesity comorbidities, and then how should this inform

how we're thinking about our questions for today? Thank you very much.

DR. BARREIRO: A question to the chair for clarity. Is this open for all of us to discuss?

DR. BACH: Yes, it is, amongst the panel it is open for all of us to discuss, absolutely.

DR. BARREIRO: Great. I'd like to try to answer that question from my own personal experience, and that is that I usually would say I break it up into groups. 50 percent of people that get first started on it love it and

if they do love it immediately, you usually don't have to worry about them, they're going to remain extremely compliant, usually stay out of the hospital, not all the time, but it's significantly reduced. Of the 50 percent that's left, 25 percent of those patients continue to wear it because I tell them the benefits in the long term, keeping them out of the hospital, reducing the chance of heart failure, irregularity, things of that nature. And then 25 percent just don't want, no matter what we try, interfaces that we use, just don't

seem to get used to it, get on it, or can be adjusted to get it to work well for them.

I would say that a fair amount of patients, and this would be a perspective of where my office is, I'm a disparities scholar and so I work in a free clinic in part of the hospital system for Inogen, and so my big complaint is something that you've probably heard me state over and over again, is trying to get the companies to provide my patients the equipment has been frustrating. They would

love to have it, loved it when they got it but it was removed or, you know, again, it's a tough patient population with difficult and mobility issues, those things occur and we usually end up having to do multiple restudies to get them back on the equipment, which seems also to be a waste to Medicare if we're talking about cost-effective processes that occur in this discussion, so that's my experience with it.

DR. BACH: Thank you very very much. Any other comments or followup to Dr. Manship's question?

DR. KUEBLER: I have a comment. In

terms of compliance and adherence, you know, in listening to and reviewing all of the studies, listening to the presenters today, providers are not given standardized information, there's not a lot of data readily available to us right now to determine which device to put a patient on. And without that if we're, you know, practicing in the dark, kind of trying to figure out what it is that we should put a patient on, what device to put a patient on,

that interferes with adherence and compliance and if we're not clear, we're not going to be able to educate the patient in order to stay compliant and to utilize it appropriately.

DR. MANSHIP: I understand that, and thank you for that.

DR. BACH: Dr. Kuebler, did you have another comment you wanted to make or was that it? I have you queued here.

DR. KUEBLER: Well, I think it's important to recognize that if we look at comorbidities that three out of four Medicare beneficiaries had two or more chronic conditions at any given time. And if we look at standardized BMI across the country for

adults, women and men 18 and older, the average BMI for women is 29.6 and for men it's 29.2, so we're bordering on obesity as an average in the United States, and those markers have to be considered when we look at our qualitative new studies.

DR. BACH: Thank you.

DR. GAY: I'd like to make a comment

about compliance, since I see this kind of going towards the number four, usage parameters, and it very much parallels the OSA CPAP population as we see very similar to the chronic respiratory failure, that it's really how you come out of the blocks that determines your compliance overall. It's hugely important to get them involved very quickly, empower the patent with paying attention to what's going on. We say how can we get them going if we don't know what kind of box to put them on. Well, it is a bit of a salesmanship prospect, but how well you do almost in the first week, certainly in the OSA literature is strongly supported, so that patients who have a good initial experience with a lot of service attention, physician, whoever is the caregiver

that teaches them right from the get-go that this is important, really determines that outcome more than it does the actual device that you're working on. Thanks.

DR. BACH: Thank you, Dr. Gay. Dr. Salive, do you have a question or comment?

DR. SALIVE: Thanks, Marcel Salive.

So I had a couple comments. I think it's higher than what was stated about the comorbidities for COPD really in the Medicare population, not that that number was low, but it is actually more like four conditions, I think, people have if they have COPD on average, there's a few with only that. So Medicare is a highly comorbid population and this particular group, I think, you know, they're near the end of life, as people stated earlier.

I think that, I wanted to reflect on the comments about, that were just made about using this in the home. I think that we were asked about device versus the surrounding services and I think they're inextricably linked, I don't see how we can really disentangle that and in fact we wouldn't want

to really in my opinion. I think the, you know, it's the whole package that was studied in these studies and that's what works to improve the health, so I don't think we can split that out, but that's my opinion.

And so I think the home care piece of it needs to be really pretty aggressive. I know that, you know, Medicare has seen a large growth of home care, but this particular part has a lot better evidence than most home care. And you know, the device is not, you know, it's not like your FitBit or anything like that, right, so it's a complicated thing that takes some learning I think by the patients in that home setting, and I don't think folks learn it somewhere else while they're being discharged and dealing with all the hospital situations.

One of the gaps I noticed that I think is puzzling to me, I guess it's not a crucial point to me, but the comment was made about adverse events not being studied in these trials at all, like 75 percent of the trials had no adverse events even, they weren't even looking for them. And you know, I guess it's not, you know, we're not that worried at this

point about the devices having safety problems, but it still seems like, you know, a missed opportunity, because I think that the patients do want to know things like that and you really

run the risk of being in a situation where the patient might, you know, read something, you know, the classic case, read something in the front page of the New York Times about some adverse event and suddenly feel like their thing is very dangerous. Well, you know, if you're not studying that systematically we don't really know the answers, and maybe we just missed the piece from what the FDA has found, you know, since these devices have been on the market. I don't know, I'm not that concerned, but I would wonder, you know, because these devices are always prone to, you know, generational change as they get two new chips, new prices, and you know, things can happen. But those are my comments.

DR. BACH: Thank you, Marcel. Tara has put in a chat box which we can message each other now, because only we on the panel can see those messages. I do not see, maybe I've missed, Dr. Criner, your hand is up?

DR. CRINER: Yeah, I just wanted to make a comment about the discussion with

Dr. Kuebler and the last discussion also. One of the things to consider is like was mentioned, these people are frail, people with COPD, 90 percent of them have at least two comorbid conditions, and about 75 percent have four, and they're older. And some of them, as was mentioned by Dr. Barreiro, they're impoverished. And trying to get patients to do additional tests, that need to come back and forth when they've just been discharged from the hospital and they're still fragile and ill, those are important barriers to get therapy.

One of the questions that was asked, how do you know what's going to work in an individual patient to promote adherence? Assign the support mechanisms and have someone who's genuinely interested in evaluating the therapy and titrating them. It's also really trying to make the patient understand and having a long-term relationship with them. And when you have a patient that it works and then you put other barriers in front of them, then you have to do this or that. Another thing, to

be able to qualify for the therapy that they

proved was efficacious for them, those are needless barriers I think in terms of regulations, those can be addressed and make it easier for the patient to get effective therapy or continue effective therapy they've been compliant with and has shown physiologic or some other parameter of clinical benefit.

DR. BACH: Thank you. Dr. Fisch?

DR. FISCH: Yes, I was just kind of reflecting about that interesting question about the lived experience for the patients. I don't have enough experience with these particular patients in my oncology practice, but I was just thinking about first, the fact that in Dr. Wilson's meta-analysis, the forest plot of the quality of life was pervasively negative, and even the strongest positive study that we mentioned, the Kohnlein study, was negative for, or mostly negative in quality of life. And I found myself like an oncologist, kind of wishing I knew what proportion of people who use these devices get a major response, you know, like we heard, like they get on it, they like it, they're clearly

benefitting. There's no doubt in my mind that selecting certain patients with a certain phenotype and parameters give major benefits. So, you know, we want to be able to figure out how to bring that major benefit to the right people.

There's a bunch of patients, I can imagine, that are minor responders that have to be kind of coaxed to stay on it and hoping that they get some mortality benefits, and then there are some that are non-responders that don't tolerate it, and I wish I had a sense of the proportion, right, for any given way of selecting the cohort and defining the composite intervention. You know, is it a 15 percent, you know, major response rate, or is it 25 percent or 45 percent, you know. That would really, I think it would really help clinicians and patients if we had some idea about that.

But again, my major observation is that at least quality of life wise, there doesn't seem to be any study that showed a signal in that realm.

DR. BACH: Thank you very much.

DR. GAY: I can perhaps give you a

perspective on that. As you pointed out, these are people who are very sick, they have the burdens of comorbidities, and here you are adding another thing that they have to do. It doesn't work once a week, it doesn't work twice a week, you've got to use it every night, so you are adding another burden to their life. Now if you ask about what proportion of these, I might give this perspective. I think at least as a clinician and looking at the studies, and Dr. Coleman might chime in at this, when you see a seven- to nine-millimeter change in CO2, that can be really life changing to a patient, a patient that can ventilate that dramatically different is really going to have a better sense of well-being. So the studies that showed that higher change, and if that's the 50 percentile that changed seven to nine millimeters, that is in fact a ballpark idea, if half of them do that, that's the kind of respond rate that's going to be dramatic. Maybe that gives you some perspective.

DR. BARREIRO: If I could add on to Dr. Gay's comments, we also should be careful about clinically significant criteria versus

statistically significant, and those can be different depending on how you look at the data, right, even with St. George's Respiratory Questionnaire. So as an oncologist you probably understand that just as well, right, with people that get treatment. And everybody's quality of life may look at different aspects. I mean, we do know with treatment alone, and the amount of depression in patients with COPD and chronic respiratory failure adds to the variable as well. So I do agree with the parameters that we're looking objectively that are so important are the physiologic ones but there's other aspects of it too that may not be statistically significant but clinically significant, and I don't remember him mentioning that in his slide.

MS. MAURI: If I may, I would add, you know, I think just to follow on to your comments that patient experience is so important as we think about, you know, what are the next steps here, including that patient

experience I think would be really critical, because it's difficult to represent that

uniformly in a quality of life questionnaire. When you look at the really excellent meta-analysis that Dr. Wilson presented earlier, you know, it's quite clear that there were consistent improvements in JCL, which is the most specific thing that one could look at, and although it's not labeled as quality of life, the feeling of shortness of breath certainly would impact the quality of somebody's life.

But I think that that, it's so complex in terms of what an individual might select in terms of avoiding hospitalization. You know, we have patients who live in remote locations who may actually find it quite difficult to be able to return to the hospital environment and, you know, particularly in this current setting with the pandemic, that brings even heightened awareness to that. So I agree that at this point to look at the meta-analysis results and not see an overall impression of a positive impact, but then I think you also have to

recognize that the heterogeneity of the data and the low standard of evidence that Dr. Wilson observed is a marker of the

uncertainty of that estimation. And on the other hand, there's, you know, moderate certainty around the estimation about the important effects on mortality, hospitalization, dyspnea, that I think are meaningful to a patient's lived experience.

DR. BACH: Thank you very much, Dr. Mauri. I am not seeing any further comments but I want to check in with everyone, if you'd like to make a comment or ask a question of fellow panelists. Okay. Barring that, next I propose we take a break now. It is 2:02, we'll take a 15-minute break and at 2:17 we'll come back for the next step on the agenda which is the formal remarks and voting questions. Thank you very much, everyone, for sticking with this. I know it's difficult on line but I'm finding the discussion to be productive and engaged, and I very much appreciate everyone's effort on that.

(Recess.)

DR. BACH: Hi, I'd like to start reassembling for the next stage of the MEDCAC meeting, please. Tara, should we do a rollcall of voting committee members? Tara, are you on?

MS. HALL: Hello.

DR. BACH: Hi, okay, great.

MS. HALL: Yes, I'm here.

DR. BACH: Should we do a rollcall of the voting MEDCAC members so we can go on to the voting section?

MS. HALL: Okay, that's fine. Dr. Ross, are you on?

DR. ROSS: Yes, I am.

MS. HALL: Dr. Garrido.

DR. GARRIDO: Hi, I'm here.

MS. HALL: Dr. Kuebler?

DR. KUEBLER: Yes, I'm here.

MS. HALL: Dr. Manship?

DR. MANSHIP: Yes, I'm here.

MS. HALL: Dr. Barreiro?

DR. BARREIRO: Yes, I'm here.

MS. HALL: Dr. Fernander?

DR. FERNANDER: Yes.

MS. HALL: Dr. Melnikow?

Dr. Melnikow?

DR. MELNIKOW: I'm here.

MS. HALL: Dr. Salive?

DR. SALIVE: Here.

MS. HALL: And Dr. Fisch?

DR. FISCH: Yes, I'm here.

MS. HALL: Okay, everyone is present.

DR. BACH: I'm sorry, I asked for -- there's, the subgroup of people who just did the rollcall are the people whose votes are counted by CMS for the scoring on the questions. There is a number of members of the committee whose votes do not count who have also been participating and we can do a rollcall of them as well if you'd like.

It's Dr. Mauri, Dr. Mauri, are you here?

DR. MAURI: Yes, I'm here.

DR. BACH: Great. Dr. Criner?

DR. CRINER: Yes.

DR. BACH: Dr. Gay?

DR. GAY: Present.

DR. BACH: And Dr. MacIntyre?

DR. MACINTYRE: Yes, present.

DR. BACH: Great. Joe, do you want to say something about the voting or do you want me to make a couple remarks about it, or which do you prefer?

DR. ROSS: Peter, this is Joe Ross; you mean Joe Chin, right?

DR. BACH: I mean Joe Chin, yes, although Joe Ross, if you'd like to say some formal comments about the voting first, that's fine.

DR. ROSS: No, that's fine.

DR. CHIN: Thanks, Peter. I don't have any specific comments about the voting.

I think one question that I heard earlier about adding a new question or modifying, I think that will be difficult in this format. I think if there are really, if there is information that you would like to supplement in the discussion part of the answer or your voting, that might be an area that you can mention comment on any particular point so that we would have that on record. I think we

will go ahead with the votes that we have.

DR. BACH: Okay, thank you, Joe. And to emphasize as I said earlier, I hope I said, I tried to say, CMS takes into account all that's transpired today, not just the votes. And so certainly comments, including many we've already heard, but comments around these questions and your, you know, wholesome description of the answer is warranted, it is

something that they will take into account, but as Joe has already suggested, we can't change the questions per se at this point.

In that case, I think I will try and start the voting. If you do not know how to vote at this point, I know we tried a dry run, there was no shame in that because of the technology, please privately message Tara and she will privately message you back how to log on if you are one of the people whose votes counts.

We're going to vote. When we have all the votes collected, I'm going to be notified that we can proceed, at which point I'm going

to poll each of the MEDCAC members regarding their votes, and then we will have, when you do that, you will state your vote out loud and your name, although I'll just call on you, and if you have anything you want to say about your vote, that's a good time to do that. So why don't we try the first question here. I will pause, just ask Tara if anyone is still waiting to get logon information, in which case I should wait.

MS. HALL: I don't have anyone asking

me questions right now, so hopefully everyone knows how to do it.

DR. BACH: Thank you. Okay. The first question is: How confident are you that the evidence is sufficient to determine the patient selection criteria that will improve health outcomes, for example laboratory values, comorbidities, frequency of exacerbations requiring ER or hospital admission, hospital discharge timing, pulmonary function tests and the like, when used with any category of home NIPPV device? And we'll get to the discussion maybe depending on how the votes come in. So

please vote now.

MS. HALL: We're waiting for one more vote. If you're unable to vote or you haven't voted -- okay, everyone has voted.

DR. BACH: Okay. Tara, are you going to display the results at this point?

MS. HALL: Yes, everyone has voted.

DR. BACH: Okay, the mean value is 2.89, greater than the intermediate confidence cutoff, I will come back to what that means in a second. I'm going to now poll the panelists, ask your vote, and this is a time to clarify or

explain, that is not required, but that's the opportunity. I'm going to start in the order of the list in front of me. Dr. Barreiro?

DR. BARREIRO: Thank you, Mr. Chair. I voted a four, but would have went with a 3.5 but we weren't allowed that. My clarification is I feel there's adequate evidence that, if a decrease in mortality and a decrease in hospitalization is enough for me to support the continued utilization of any form of noninvasive ventilation based on those

parameters.

DR. BACH: Thank you very much, Dr. Barreiro. Could we just, we're all used to doing this in person, just so people, it's not obvious on line, there's four individuals whose votes, if you will, don't count, the industry representative, Dr. Mauri, and the guest panel members. I should be recording their own personal votes, I am going to poll you and ask for your input on them, they're not counted in the tabulation, but what you say and your comments are things that help CMS, so just to know, I will get to you here as I go down the roll.

DR. BARREIRO: Mr. Chair, may I extend my comment, and I apologize, I wrote it on the side. I would also like to add that because there was clear data that there was no serious or non-serious adverse events, I think that those two parameters with the lack of serious adverse events is enough for me to feel more confident there is adequate data.

DR. BACH: Thank you very much, Dr. Barreiro. Dr. Fernander?

DR. FERNANDER: Four.

DR. BACH: Okay. Dr. Fisch?

DR. FISCH: Sorry. My answer is a three, and I'll say that I sort of started at a four based on my prereading, but going over the discussion with some of the presenters and the panelists' comments, and understanding how difficult it is to generalize this information, brought it down from a four to a three for me.

DR. BACH: Thank you very much, Dr. Fisch. Dr. Garrido?

DR. GARRIDO: Thank you. I voted a two. I think we know that it is efficacious in hypercapnic patients but I don't believe that we have enough data on real world

effectiveness, especially compared across different patient populations. All the observational studies that have been created, or conducted rather, have been small and they're not powered to examine heterogeneous treatment effects.

DR. BACH: Thank you, Dr. Garrido. Dr. Kuebler?

DR. KUEBLER: I voted a one. I'm not comfortable with the data set that supports the exacerbation criteria, FEV1 criteria, it just seems like there's no standardization or specific measures, the data is all over the place for me.

DR. BACH: Thank you. Dr. Manship?

DR. MANSHIP: I voted three, and the primary reason for that three was as it's been expressed by others, that heterogeneity, the difficulty in taking what data we currently have to make larger generalizations, so a three for me.

DR. BACH: Thank you. Dr. Melnikow?

DR. MELNIKOW: I voted three, which to me, intermediate confidence is pretty good for the kind and quality of evidence that we have.

This is really a question about patient selection and it seems to me the evidence for selecting hypercapnic patients for these interventions is moderately good. There may be other patients that also benefit or other criteria that could be used, and that was my reason for a three and not going higher.

DR. BACH: Thank you very much.

Dr. Salive?

DR. SALIVE: I voted a three for similar reasons to what Dr. Melnikow just stated. I believe there is some criteria available for patient selection but it could be better, but the ones that exist are, you know, have a pretty decent evidence base.

DR. BACH: Great, thank you. I now move on to the other panel members. Dr. Mauri?

DR. ROSS: Peter, this is Joe Ross. I wasn't sure if I was part of the --

DR. BACH: Oh, I'm sorry, Dr. Ross, you're right.

DR. ROSS: I voted a three and like Dr. Melnikow and Dr. Salive, I felt like there was strong evidence for selecting patients on the basis of either a severe COPD or persistent

hypercapnia, but felt like there were limited trials, and observational evidence didn't support selection criteria based on any other patient characteristics, including timing of hospital discharge or other related criteria

like that, obesity and other comorbidities.

DR. BACH: Thank you. All right, now, I'm sorry, Dr. Mauri, your vote?

DR. MAURI: I voted a four. I agree that the data presented is a strong evidence base for some specific areas where there's a clear benefit. I also really think that the input from the experts who presented is quite valuable and gives another level of security that the physician community can identify based on the data available, patients with true benefit with reduction in mortality and dyspnea.

DR. BACH: Thank you. Dr. Criner? I will come back to Dr. Criner. Dr. Gay?

DR. GAY: I gave the evidence level a four. I think as a person who has been doing this now for about 30 years, I have no difficulty in saying I can select patients that will benefit from this. And I think the fact

that all of the parameters aren't clear, weighing a vote to say that the evidence is poor is why I stay away from a one, two or a three, but to say that a hypercapnic COPD

patient that I can recognize to that degree is not going to have a good outcome, I'd have to say that's a four or five, but I'll say a four.

DR. BACH: Thank you very much. Dr. Criner, are you with us?

DR. CRINER: Yes, I am. I gave it a three, I believe that the evidence suggests that patients with COPD and hypercapnia may benefit, but the specific details to permit me to characterize that patient population to definitely improve their outcome as broad therapy need to be better defined.

DR. BACH: Thank you very much. Dr. MacIntyre?

DR. MACINTYRE: So I gave it a four, primarily because I think the evidence for hypercapnia and important outcomes, the evidence is just pretty good. Other criteria for selecting treatment I think are less compelling, and some of the other outcomes are less compelling, but CO2 and things like

mortality promote me to a four. Thank you.

DR. BACH: Thank you very much. Now

the discussion, because we cleared as you can see the two-and-a-half cutoff, we are being asked, I'm going to ask you to provide selection criteria for the specific categories of equipment. This question is to the panelists first.

DR. ROSS: Peter, this is Joe Ross. Do you just want us to chime in with what we thought the selection criteria were good, or do you want to go in order?

DR. BACH: It makes sense to just chime in. If you have an organizational framework for it, let's start there.

DR. ROSS: So for me it was severe COPD based on GOLD criteria or persistent hypercapnia, those are the selection criteria.

DR. BARREIRO: A point of order. Isn't this the same thing you're asking in question number two, or am I looking at that wrong?

DR. ROSS: This is Joe Ross. I thought question number two was about how the devices, I don't have the wording in front of

me, but the actual --

DR. BARREIRO: Oh, so it says the equipment parameters, not necessarily the parameters to get the equipment.

DR. ROSS: Yeah, not the patient selection parameters.

DR. BARREIRO: Okay, thank you.

DR. BACH: I think CMS wants us to discuss CPAP, HMV, bilevel positive airway pressure, and if we can further articulate selection criteria at this time based on today's discussion.

DR. BARREIRO: Yeah, this is Tim Barreiro, I made notes. I would say unfortunately for me, I didn't think there was any clear criteria. However, it would more likely remove some. One, I didn't feel there was any significant evidence that any degree of hypercapnia was ideal, given the fact that I would say that any hypercapnia may be reasonable enough for me, since the mortality benefit was seen with it, to be more appropriate than to have a cutoff of 55 or 58 or 60.

I also was in favor of eliminating

FEV1 as that FEV1 rarely changes over time and in turn seems to put you into a category where only the severest of patients will benefit from this device, when we know that the heterogeneity of FEV1 and COPD is quite vast.

I will however add that I would like to have at least a criteria where one additional comorbidity was present since we know that would be easy to meet criteria, and we know that they have at least four based on the comments today, that that should be a reasonable thing to add into the criteria or keep into the criteria, so that we know there's additional benefit to those patients. Thank you.

DR. BACH: Great, thank you. Further discussion with regard to the selection criteria for specific categories of equipment?

DR. MELNIKOW: Joe, I have a clarification question really, going back a little bit to this discussion point versus question two. Are we talking about selection criteria of patients for NIPPV devices, which we heard this morning seems like other than the distinction between CPAP and the others, there

isn't necessarily a lot of difference in how they might be used, or are we talking about selecting patients to be eligible for this intervention at all?

DR. BACH: My interpretation of this is it's both, but it's more the former. And I think the comment you just made, feel free to elaborate, is useful information for CMS, that the delineation between the devices is not fully spec'ed out, if you will, I think to summarize what you just said, more so than the general question of eligibility. But I, both CMS can give us feedback but also other panelists, feel free to weigh in.

DR. MELNIKOW: Yeah. I mean, this is a learning experience for me about these devices, but my understanding from the discussion this morning is that while, you know, CPAP is the preferred device for obstructive sleep apnea, in terms of chronic respiratory failure really the distinctions between Bi-PAP and home mechanical ventilation are fairly limited, and other that the backup battery, there's not a lot of reason to make a distinction between them. That was my

understanding, but maybe others who know more will correct me.

DR. GAY: This is Peter, I'm sort of reading this a different way. If you voted, for example, that you believe that the selection criteria tell you that it will have that outcome, it's not a comparator of whether one is better than the other, the question is if I think, like I voted a number four selection criteria, can I do that with an HMV, can I do that with a Bi-PAP, yes, yes. Could I do that with a CPAP, clearly no. So the idea is, I don't think the question's asking whether it's clear you should use a Bi-PAP versus an HMV, that is question two, where it's asking the parameters of the equipment. This question asks if your selection criteria is this, can you get that outcome with an HMV, can you get it with a Bi-PAP, and that is where I would say yes, yes, CPAP no. Is that the way I should interpret that?

DR. BACH: I think that input is very helpful. Are there other comments on this?

DR. FISCH: Yeah, this is Mike Fisch. I guess, you know, I sort of recognize that the

best master clinicians are going to be able to select patients and get good outcomes, but I'm just a little bit concerned about the idea of really broad inclusion criteria that enhance access, but also, you know, is probably going beyond where the data are. I guess I'm more comfortable choosing access criteria that mostly resemble where the best data were and not getting too broad. You know, we heard one comment, we don't want to wait for the literature to catch up with utilization, but you know, I think using the literature parameters as a guide is a good idea, so you know, stable hypercapnic respiratory failure with parameters that resemble the best evidence is what I would favor.

DR. BACH: Okay. Barring any more comments on that part of the question, I would like to move on to question two, please. The question is: How confident -- John, I don't know why there's a one showing there. Has somebody already voted when you cleared out the

votes? We seem to be having -- here we go. All right. Can we proceed with voting on number two?

I'll read the question: How confident are you that the evidence is sufficient to determine the NIPPV equipment parameters necessary to promote successful patient-related outcomes, for example decreased mortality, decreased frequency of exacerbations requiring ER or hospital admission, increased time to hospital readmission for respiratory-related disease, and improved physical function and quality of life? Please vote now.

MS. HALL: Everyone has voted.

DR. BACH: Okay, I'd like to poll, starting with Dr. Ross.

DR. ROSS: This is Joe Ross. I voted a one because I didn't really get a sense of differences by equipment parameters, either by low intensity or high intensity, or by different equipment types even.

DR. BACH: Thank you. Dr. Barreiro?

DR. BARREIRO: Again, thank you,

Chair. I voted three but was again in turmoil. I thought there was insufficient data that the parameters are adequate for the use of the equipment alone. However, I struggled with the mere fact that it seems that it did not matter

except for CPAP alone based on the discussion today. But it seems that the patients with chronic respiratory failure secondary to COPD and hypercapnia should receive some type of device other than CPAP alone based on the information that we have. In addition, the criteria of adding increased responsibility to the accepting DME company and providing increased support for education home care, I thought was adequate. I did not feel that there was enough information for the definitive evidence on very few small trials that the high flow changes present, that was presented today, was adequate to suggest that it should be the standard of care, but suggested adjusting the machine in frequent followups seems to be more important. Thank you, Mr. Chair.

DR. BACH: Thank you. Dr. Fernander?

DR. FERNANDER: Three.

DR. BACH: Dr. Fisch?

DR. FISCH: Two for me. I would have started pre-meeting at a one, but I think some of the expert commentary has nudged me to a two.

DR. BACH: Dr. Garrido.

DR. GARRIDO: I voted a three. I'm viewing the word parameters very loosely similar to Dr. Barreiro. I think we don't have much evidence about the effectiveness of CPAP but we do have better evidence on different outcomes with the other types of equipment. But beyond that I don't think there's any, there's insufficient evidence of other equipment parameters.

DR. BACH: Thank you. Dr. Kuebler?

DR. KUEBLER: I voted a three. In the technology assessment report the tables showed that patients that were using something versus no equipment at all did reduce hospitalization and exacerbation data.

DR. BACH: Thank you. Dr. Manship?

DR. MANSHIP: I voted a three. I have

no substantive comments to add.

DR. BACH: Dr. Melnikow?

DR. MELNIKOW: I voted a three also, thinking that the evidence from those studies that were reviewed has equipment parameters in it, and clearly when those equipment parameters are used there are, you know, on balance, improved outcomes.

DR. BACH: Thank you. Dr. Salive?

DR. SALIVE: Yeah, I voted a three basically for the same reason. I think the top line conclusion of the technology assessment was, you know, said enough evidence to give me a three on this question, that's about it. I think there was still that mix of observational trials, so it didn't go any higher.

DR. ROSS: Peter, this is Joe Ross. I'm sorry to interrupt, can I just make a clarification on my comment?

DR. BACH: Of course.

DR. ROSS: I just want to make it clear that my, the reason I rated it as a one is I didn't think there was evidence that differentiated either high intensity or low

intensity, or home mechanical ventilation versus Bi-PAP, not that the machines themselves, the NIPPV wasn't effective.

DR. BACH: Okay, thank you. We're going to go on to the nonvoting panelists. Dr. Mauri?

DR. MAURI: Yes, thank you. I voted a four. I think when we look across the different options for treatment, I thought

Dr. Coleman's presentation showing the evolution of care and how that impacted the findings over time was an important one, and each of the studies presented did have fairly clear parameters associated with the outcomes looking at effectiveness. I guess I would also add how important I think it will be to incorporate physician decision-making, expert decision-making in selecting the modes of care, I think Dr. Wolfe outlined that very clearly in her presentation, and so I would actually be supportive of continuing to work with experts and patients in the future to develop some of these pathways.

DR. BACH: Dr. Criner?

DR. CRINER: Yes, I say it's a two, and I think it's a reflection of the small nature of all the studies that doesn't allow the heterogeneity of setting changes across the patient groups which have different degrees of air trapping and physiology under them, so I think it's the quality of the data that makes my confidence a two.

DR. BACH: Thank you. Dr. Gay?

DR. GAY: I think it's a four. I

agree very much with Dr. Mauri that HOT, high intensity changed the outcome of COPD patients' mortality, and it was strikingly supported again by the Murphy data. I think to look at this and try to dissect the individualities of should it be a delta ten, should it be a delta 12, should it be a range of 12 to 14 is not the question. It's specifically whether or not a high intensity really was well supported by the best studies, that's why I gave it a four, and that's when I think Dr. Coleman really took over the top when he pointed out how things changed.

DR. BACH: Thank you. Dr. MacIntyre?

DR. MACINTYRE: So this was a multipart question to me. I would give, the summary I guess would be a three. I think four, I have high confidence that things like high level support does improve outcome in hypercapnic COPD, but I have lower confidence about the difference between Bi-PAP and home mechanical ventilation, and I have a higher level of confidence that CPAP is inferior to both those other two devices. So I took into account multiple different things and am going

to, what did I say, a three or a four, I can't remember, I'm sorry, so I think three looking at all things put together.

DR. BACH: Thank you very much. There are two discussion questions. Is there any other point anyone wants to make? Okay. There are two discussion questions. First, are there any outcome measures that should be considered other than those noted above, and the next relates to the equipment parameters for specific categories of equipment. A couple of

things.

One is, I'm going to ask Joe Ross to temporarily take this over because my computer is doing some things very odd and I'm going to try and log back in. But I'll ask that you discuss the outcome measures that should be considered other than those noted, and I'm anticipating with regard to parameters a similar discussion to the earlier one, I want to have it, but understand that if the answers are akin to those we can, to the ones on the prior discussion, that's very helpful as well. I'm going to log off here for a second. Joe, have you got it covered?

DR. ROSS: Yes, no problem, I can steer that conversation. So let's start with that first point, are there any outcome measures that should be considered other than those that have been noted above, which were mortality, frequency of exacerbations requiring emergency room or hospital admission use, time to hospital readmission for respiratory-related disease, physical function or quality of life? And I guess like last time, we can just ask

people to chime in.

DR. KUEBLER: This is Kim Kuebler. There's nothing here about symptoms, dyspnea, exercise intolerance, things that would be specific to an exacerbation.

DR. ROSS: Thank you, Dr. Kuebler. Anybody else?

DR. SALIVE: This is Marcel Salive. I think adverse events should be considered as an outcome measure always.

DR. ROSS: I agree, Dr. Salive. Is there specific adverse events or serious adverse events that you would be most interested in seeing?

DR. SALIVE: Not -- yeah, I would be

interested in serious events. I didn't see much and I'm not that worried, but I think it has to be always included.

DR. ROSS: Okay. Any other comments? I will note that at one point during our conversation somebody noted depression and other psychiatric or related disease as a potential outcome.

UNIDENTIFIED SPEAKER: I think the symptom scores and the depression was as you mentioned, I included those in the quality of life at the time the question was asked, some aspects to that, but I'm glad the panel agreed to think outside the box just to make sure that they were included, and I agree upon them.

DR. GARRIDO: This is Melissa Garrido. I agree with anxiety and dyspnea being important outcomes.

DR. ROSS: Thank you, Dr. Garrido. Who else was speaking at the same time?

DR. FISCH: This is Mike Fisch. Caregiver, sort of a caregiver satisfaction might be something to consider as well.

DR. ROSS: Thank you, Dr. Fisch. Okay.

DR. BARREIRO: Joe, we talked about health care resources so that may be obviously, I think we're including that -- I'm sorry, this is Tim Barreiro -- utility or health care utilization, how many, that may be included under hospital/ER visits but there's also other aspects of that, and obviously that may be

something to consider.

DR. GAY: One of the things that is not often spoken about is whether they returned to work or a level of productivity. We used to quip, did they file a tax return the next year, just showing the improvement in their ability to function, or whether they were placed in a nursing home, so that kind of outcome.

DR. BACH: Peter Bach, I'm back. Further discussions on the question of additional outcomes to consider? Okay. Barring further discussion on that point, I would like to move to the second discussion question, which is triggered by having the intermediate confidence greater than or equal to two-and-a-half. Please provide the equipment parameters for the specific category of equipment. And as I said, I am not trying

to lead the discussion but I'm going to start with a baseline response, which is that the data regarding parameters is presented in various manuscripts and reviews and evidence reviewed that we have discussed today, and I'm

wondering if that is a fair summary of the panel's response. Please correct me as you wish.

DR. MACINTYRE: So this is Neil MacIntyre. We didn't really discuss this and there aren't much data supporting or addressing it. But one feature of these home devices that I think could make an impact is mobility, the ability of the patient to actually walk with it or move around the house with it. The idea of increased mobility improving outcomes is important in other studies, it's never really been looked at in this, or with these devices, but I would just like to have that comment on the record. Thank you.

DR. BACH: Thank you.

DR. KUEBLER: This is Kim Kuebler. There was a lot of discussion that this patient population is not really a candidate for randomized controlled trials. I think it would

be important to look at these different devices from a comparative effectiveness research perspective, and maybe CMS could partner with the Patient-Centered Outcomes Research

Institute to develop some studies in this area.

DR. GAY: I agree with that. I think the difficulty is in the clinical arena, the reason they use an HMV has generally been moved towards the more severe patients without dichotomizing the patient population into the severe, which favors in a lot of cases an HMV versus a bilevel device. For the less severe you're biasing your outcome the minute you go with the selection criteria.

With respect to the actual question here, I think again, maybe I'm interpreting this a little differently than others, we talked about number two, the question of the equipment parameters, how do you set the thing, it's pretty clear to me from the data that setting high intensity is pretty overwhelming in terms of the outcomes, it's changed the way we practice. In terms of what devices can do this, the question is not whether it's better or worse, we're not doing a comparative thing

in the discussion in my mind, we're just saying can an HMV do this, can a BiPAP do this, yes,

yes. Can a CPAP do this, no. That's the way I'm interpreting that. Thanks.

DR. BARREIRO: Yeah, I interpret it as you did, Peter, this is Tim Barreiro, the same exact way as with the equipment. I would like to add to the equipment a way to interface with the physician in order to make changes, and put some responsibility on the DME. I know that may be nearly impossible, but nonetheless in an ideal world I would still request it. The equipment itself I would say is adequate regardless of the type except for CPAP, in the setting of hypercapnic COPD and chronic respiratory failure, CPAP likely could not be ordered.

DR. BACH: Thank you. Other comments?

Okay, barring other comments I'd like to move on to question three please. The question reads: How confident are you that any improved patient-related outcomes noted above made with any type of NIPPV device in the home can be attributed to the use of the equipment alone, as opposed to the concomitant provision

of other support services like home respiratory

2 therapists, home medication reconciliation, and
3 repeated elective hospital admissions? Please
4 vote now.
5 MS. HALL: We're still waiting on one
6 person to vote. Everyone has voted.
7 DR. BACH: Okay, I would like to poll
8 the panel. Dr. Ross?
9 DR. ROSS: Yeah, this is Dr. Ross, Joe
10 Ross. I voted a three, intermediate
11 confidence, not that I felt like the trials
12 really disentangled these, it was very
13 difficult to know about how home respiratory
14 therapists play a role, but I just don't have
15 confidence that home medication reconciliation
16 or repeated elective admissions would have the
17 impact that was observed in the trials
18 otherwise.
19 DR. BACH: Dr. Barreiro?
20 DR. BARREIRO: Thank you, Mr. Chair.
21 My vote was a two. I mainly voted for a two
22 because I thought that the question
23 specifically asked the device alone, where I
24 found that there was more evidence to suggest
25 that the equipment necessarily played a factor,

NIV use did not, but without the concomitant addition including some of the studies that were presented earlier in our packet, that some patients got respiratory and pulmonary rehabilitation, some people got home medication adjustment, those things seemed to be adjunct and additional parameters that seemed also, I couldn't eliminate from the data, thus I gave it a two.

DR. BACH: Thank you. Dr. Fernander?

DR. FERNANDER: I gave it a four. I do agree that there was not much data provided or discussion to tease out the adjunctive therapies. However, I just kind of kept falling back on that four-hour minimal exposure and timing. To me that indicated that there was some efficacy with these devices alone, but clearly I'm not sure that we have done the studies necessary to really tease out the adjunctive therapies, so that's just kind of the reason for my score.

DR. BACH: Thank you. Dr. Fisch?

DR. FISCH: I also voted two, and the recurring theme for me is just this was based on integrating the sense of evidence, which is

kind of a one, and my sense of the medical reasoning and expert consensus which was more of a three, so I integrated it to a two.

DR. BACH: Thank you very much. Dr. Garrido?

DR. GARRIDO: I gave it a one, swayed by the fact that a lot of the studies have been done in Europe where respiratory therapy is part of the intervention and the fact that we can't see that.

DR. BACH: Thank you. Dr. Kuebler?

DR. KUEBLER: I gave it a two and for the same reasons that have already been voiced, the fact that we only have two retrospective studies here in the United States and that the majority of the studies came from Europe with comprehensive home care support.

DR. BACH: Thank you. Dr. Manship?

DR. MANSHIP: I also voted a two. The only thing that I would add to the comments that have been made so far is that we had a couple of presenters throughout the day who did make comments about the importance of wraparound services and that resonated with me. So that being said, it was hard for me to have

any greater confidence that the device alone would have those outcomes, so I voted a two.

DR. BACH: Thank you very much. Dr. Melnikow please?

DR. MELNIKOW: I gave it a two as well mostly for reasons that have already been stated, and then in terms of the evidence, I don't think that we really have the evidence to separate out the device by itself, and then also combined with my clinical experience in other areas of trying to get home support services along with equipment rotations and the difficulty of coordinating that, where without the support the equipment is not as effective.

DR. BACH: Thank you very much. Dr. Salive?

DR. SALIVE: I also gave a two, I think for similar reasons to what has been stated. I think, you know, the device has a great effect but you can't do it alone with the device, and we do need maintenance, training and reassurance in the home, I think many things like that.

DR. BACH: Thank you. We will now move to the nonvoting members of the panel.

Dr. Mauri?

DR. MAURI: Thank you. I gave it a four. I actually agree with the comments that Dr. Salive just made, which are that the device has an effect but it helps to have the additional home support to make it more effective. The reason I gave it a four is that I read this question as really, is there an independent effect of providing NIPPV over oxygen therapy alone or less intensive therapy, and I think the randomized trials in Europe clearly show that, where in both cases there are provisions of home services, so I gave it a four.

DR. BACH: Thank you very much.

Dr. Criner?

DR. CRINER: Yes, I gave it a three. I do that based on our personal experience and our family reports from our institution, and the patients in both arms received as much intensive care, in fact the ones that were admitted more were the ones that did not

receive that NIPPV, and the rest of them got the same outpatient care, so I think this is a three.

DR. BACH: Thank you very much.

Dr. Gay?

DR. GAY: I give it a four for the reasons being that, first of all, nobody drop ships these devices to the front door. And you also read into the methodology of every single study, nobody even imagined not going through in detail with the device, how it works, what to do with it. It's implicit to me the way they designed the trials that you would not even expect the device alone to do what it needs to do unless you provide the education, the support, the kind of things that make you come out of the hospital or chronically want to use this, so I think it's implicit in the methodology that you have to have the support services.

DR. MACINTYRE: So --

DR. BACH: Was somebody --

DR. MACINTYRE: I was jumping the gun,

this is Neil MacIntyre, I was going to be called next. But Peter, if I may, did you really mean, it sounded like you were supporting the, or you were not supporting the idea of the device all by itself, which would

put a low number. You gave it a very high number, that you thought the device could be used alone. Did you vote that correctly?

While you're thinking about it I'm going to give it a one, because, and I'm going to -- (inaudible, crosstalk).

DR. GAY: I did read that backwards, so it's just the opposite of the spectrum, I agree with you.

DR. MACINTYRE: Thank you for clarifying that. Okay, because I was going to use your comments to defend my position of a one. And just to solidify, my position is just personal experience. We've heard multiple talks over the course of the day, these patients are frail, they're depressed, they're anxious, and getting them the support they need to work with these rather complicated devices that require cooperation every night of their

life, I don't see how you can do it without, I love the term wraparound service, so I gave it a one.

DR. BACH: Thank you, Dr. MacIntyre. Since this is unusual, but Dr. Gay, your votes, as I pointed out before, do not count towards

the tabulation, but you have spoken a vote. If you'd like to add to your comments that you would have voted some other way, you read the question differently, you're free to do so and CMS will be able to use that information, but there's no requirement for you to do so whatsoever.

DR. GAY: No, I'm very thankful for Neil. We essentially said the same thing, only I reversed the interpretation of the question. I clearly agree that it should be on the one side, that without the services this does not work alone.

DR. KUEBLER: Peter, can I support my clarification about the question?

DR. BACH: Okay.

DR. KUEBLER: It's a question of

clarification. How I interpreted the question was does the device work in and of itself, and then does the device work best when you have adjunct therapy. I did not read the question as does the device work if you have an expert showing you how to use it. Those other therapies or support services are additional therapies, not directed on how to use the

device. Am I misinterpreting it?

DR. BACH: I don't think -- I think that's a perfectly reasonable interpretation and the reason we have this discussion after the votes is to add just that kind of clarity so that CMS can consider the input, you know, beyond just the numerical vote. And I certainly understood what you just said, I think CMS will as well from the transcript and from being part of this discussion.

And I'm perfectly happy to pause now and if there are any other panelists who would like to clarify the reason for their vote, I can't let counting votes get revoted per se, that's the process, there's this line to the input from others, but you can certainly

clarify if you feel it's important, how you interpreted the question.

DR. BARREIRO: This is Tim Barreiro. I don't want to change my vote. However, I would also say that idealistically when we look at people that enroll in a clinical trial, it also may not be the general population which we also look at. So if we just look at the previous discussion, which I thought was very

enriching, it's also known that the people that enroll may be highly motivated individuals as well, and all the other things that may come with that such as supported and nonsupport. But generalizable however, I do have issues with the mere fact that we should be cautious about the machine alone and without that, going back to why I voted the way I did, was merely the fact that most people may not have the ideal support that is done in a clinical trial.

DR. BACH: Thank you very much, Dr. Barreiro. Any other comments from the members, the voting members at this point?

Okay, we are going to go on because discussion is not triggered in this case, we did not cross the greater than or equal to 2.5 mean vote threshold, so we're going to go on to question four now please, John.

Question four reads: How confident are you that the evidence is sufficient to provide the patient usage parameters that are necessary to achieve the successful patient outcomes listed in question two? I don't know who has these in front of them so I will just

read to you what those patient outcomes were, I'll remind you that this is related to the discussion we just had about what other outcomes should be considered but are not in that question. The question two outcomes are decreased mortality, decreased frequency of exacerbations requiring ER or hospital admission, increased time to hospital readmission for respiratory-related disease, and improved physical function and quality of life. And so the question is with those outcomes again, how confident are you that the evidence is sufficient to provide the patient

usage parameters that are necessary to achieve those outcomes? Please vote.

MS. HALL: All members have voted.

DR. BACH: Okay, I'm going to poll the committee, starting with Dr. Ross.

DR. ROSS: Yeah, I voted a three, intermediate confidence because many people spoke throughout their presentation about the need for patients to use four, five or six hours, or four or five at least, hours of use.

DR. BACH: Thank you. Dr. Barreiro?

DR. BARREIRO: I too voted a three,

intermediate confidence. I was not exactly extremely excited about the role of using criteria such as an hour time of use based on the information in the packet and what was presented, despite the fact that we know the longer that you use it, the more beneficial it may be. However, I didn't think it was robust enough. I should note, however, patients should not have to necessarily fight for the equipment. Based on the data presented today less than half, 15 of 38 studies showed, which

is less than half, showed that they got adequate support from the equipment and/or home care, and I think that is sufficient enough to give me intermediate confidence.

DR. BACH: Thanks you. Dr. Fernander?

DR. FERNANDER: Three.

DR. BACH: Dr. Fisch?

DR. FISCH: Three.

DR. BACH: Dr. Garrido?

DR. GARRIDO: I voted a one. I think there's minimal evidence to suggest that some number of hours is effective for reducing all-cause hospital admissions, at least in the trial evidence. I think we really need more

real world evidence to understand ideal parameters and I wouldn't recommend that any decisions about whether someone should or shouldn't be using these devices be based on the existing evidence of usage parameters.

DR. BACH: Thank you. Dr. Kuebler?

DR. KUEBLER: I gave it a one. I am a little discouraged that a lot of the criteria is based on the 1998 guidance that's almost 32 years old, and I'm hoping that the new

guidelines that are being produced through Dr. Owens' presentation that he alluded to will make a difference in some of these outcomes.

DR. BACH: Thank you. Dr. Manship?

DR. MANSHIP: I voted three, the reason being that there was this consistent reiteration of, again, four hours, even though it was immediately disqualified as the Golden Rule. With that being said, for me there's sufficient evidence that we do have at least the beginning of establishing a firm parameter. More data is definitely necessary but for now, I am comfortable with a three.

DR. BACH: Thank you very much. Dr. Melnikow?

DR. MELNIKOW: I voted a three.

DR. BACH: Dr. Salive?

DR. SALIVE: I voted a two. I think it's actually pretty hard to develop good evidence for patient usage parameters and we did not have that. These were mostly efficacy studies and then some observational studies that were not really measuring that too well,

so that's why I gave it a two.

DR. BACH: Thank you very much. I'm going to now move to the nonvoting panelists. Dr. Mauri?

DR. MAURI: I voted a one. I agree with the comments that we might observe an increased effect with longer duration of treatment, but I think that that's an observation that has to do with how well patients tolerate the treatment. And as you heard from the clinician presenters, it's not always easy immediately to tolerate, especially the more effective higher pressures, but they may be quite effective in reducing mortality, and I'm afraid that if we restrict to those who are able to achieve those parameters in a certain timeframe, then we may be actually

putting limits on the access for some of the sickest patients who may have the most trouble actually adapting to the effective therapy, and also be putting the burden on patients who may not have the support that they need to be able to achieve those successful durations of treatment.

DR. BACH: Thank you very much.

Dr. Criner?

DR. CRINER: I gave this a two, although I believe that you have to use it to get benefit in hours of use, and therefore it should go along with benefits. There's no reason to believe that patients need to use it for the same time each day, they might episodically use it based on their symptoms overall. In most of the studies, the data was reported by hours logged of use; that means the machine might be running but you don't know whether the patient is appropriately applying it or not, so I think the data is poor to show exact parameters of usage correlating with outcome.

DR. BACH: Thank you very much.

Dr. Gay?

DR. GAY: For more or less the same argument that Dr. Criner offers, I give it a three. I do think more is better with Kohnlein being close to six and Murphy being close to five, and Struik clearly being the least. But

I follow Dr. Mauri, in fact advocate the comment that it should be noted to CMS that there are patients that gain benefit from relatively lesser use, and to have these arbitrary 30-year-old criteria saying if you don't meet the 4.0001 hours we're going to take it away can't be supported. Thanks.

DR. BACH: Thank you very much.

Dr. MacIntyre?

DR. MACINTYRE: Yeah, I'm going to go with a three here. Again, I've got sort of two conflicting views here. It's going to seem trivial and trite, but I do think you have to have some documentation that the patient is using it. I've heard many a war story about devices being delivered to patients' homes that never even get plugged in, so I think there needs to be some criteria that the patient is actually using it. Having said that, I would agree with most of the panel members that I

have no idea what the threshold should be, and it's going to be arbitrary, and I would keep it low; I would rather treat as many patients with low levels of effectiveness than not treat

people that way.

DR. BACH: Thank you very much. We did not meet the threshold once again to go on to the discussion regarding patient usage criteria so we're going to move on to the next section of the agenda having completed the voting session, which is final open panel discussion, that I will lead.

As it is sometimes the case that after the course of this day and the voting and the discussion we've just had, there's a feeling, some panelists might have a feeling that there's more to discuss, there's other issues to raise. This is a discussion for CMS. I've already heard a few things mentioned that might really be things that the Agency, you feel the Agency should hear based on this review and the votes and the rest of it. So now is really the time for that.

There's just a few of us, please feel free to just speak up, and of course you can

also private chat with me and I will call on you if that's more comfortable for you, but

anyone who cares to open this discussion should feel free to do so. It's also okay if people feel that most of the things that should be discussed have already been discussed in this forum, if that's -- and again, everyone probably thought the day would be a long day, but now here's someone who may want to talk, so Dr. Gay?

DR. GAY: Yeah, I think that belittles why we spent all this time here if we walk away from this. First of all, I've been delighted to participate in this, I think it's a fascinating way that great minds exchange ideas that brings us forward in Medicare. And I think as tragic, as human as it's been, it's brought us out to understand that we're out here to make things better for our patients and when we are pushed to the limit, we do better, and the people that do better are those who work with the data and really are the experts in the field that share their experience, their ability to analyze data.

The reason I assume, at least I'm

going to say, just editorializing why we're

here to talk about hypercapnic COPD is that it was a life changing event, certainly in Europe, to see the high intensity effect. It's sad to say that this was in 2014 that the Europeans published data that was in their mind for years by the time this went forward, and we're not talking about the things that we feel strongly about in this country, for example the obesity hypoventilation, which may be another topic for us, I'll throw that out to the MEDCAC people who I'm sure have nothing to do right now.

But ultimately that really, I think came forward because there is some pretty strong data that now the real outcomes like the hospitalizations, like the mortality are being talked about. When we started this back in the stone age when I was still building the ark, ultimately this was all about gas exchange, we just, boy, if the CO2 got better that was a touchdown, we started talking a little bit about quality of life. But the way that it first was introduced by Medicare was the fact that the CO2 went down in the Meacham-Jones trial. Incidentally, that was the only one.

My trial was negative, C.C. Lind's trial was negative, Nick Hill's trial was negative. So one trial that said woo, there's something to this, triggered 20 years worth of use.

So I think the reason we're here for this hypercapnic COPD is that this data is I believe real, and how we now parse this out to what subset of patients should be, how long we use it, we've still got a long way to go.

Please, let's not stop here. Again, we've been talking about it, pleading with CMS for a while about getting more experts together to take this to the next step. The next NCD should not just be about hypercapnic COPD, we've got to talk about what this technology is doing for a host of patients.

Where is the HMV? The HMV is out there for a reason, it was built for a reason, the market bought it for a reason, it has its use. We need to define that, not just say it's expensive and it was used in such a superfluous manner that it's a bad thing, we really need to take it to the next step.

And again, I thank everybody for the time they gave here and sharing their thoughts

with me. Thank you.

DR. BACH: Thank you, Dr. Gay. Anyone else?

DR. MANSHIP: Yes, Dr. Bach, this is Greg Manship, and again, I've been reflecting on the entire day and with Dr, Gay just spoke and what others have said, I have a question again for the clinicians and subject matter experts, and the question, here's some context and the context is this. That is that in the research portfolio that I'm seeing at OSF, we're seeing more and more clinicians who are using machine learning, so natural language programming, building algorithms, you know, pulling huge data sets, creating these algorithms in an attempt to integrate this into medical devices, and not just for theoretical predictive modeling, but to enhance the interconnectivity between device, provider and patient.

And my question is, you know, based on the conversation we've had here today, where this may or may not go in the future. Does anyone have any thoughts or comments about how using machine learning in a situation like this

would improve the, not only the effectiveness of this equipment for patients, but would improve our ability to make decisions about which patients would benefit more and how patients would actually be able to interact in real time with those, with that equipment, with providers? And perhaps in some cases there's going to be a user interface that would actually predict based on real time data how that machine would adapt to a particular patient's needs. So it's probably more philosophical, but I'm curious to know if anyone has thought about those things and how that informs where we go from here. Thank you.

DR. BACH: Thank you very much.

DR. MAURI: I can speak to that a bit just broadly in that, you know, you heard from one of the medical device companies earlier today, ResMed, but I think this is not unique as is true for many other companies who are involved with medical devices, that the level of care and telemedicine are currently possible and are currently, and machine learning to be

able to utilize data across different types of sources of data, whether it's from the devices,

from the patients or from their medical records, is a common thing that I think we're all trying to work together with providers and patients to achieve. So I do think that that's the future and that we're already working on that, and COVID, if anything, has highlighted that we can do that and that it can be quite useful and particularly being able to manage patients, connect patients, physicians, their other caregivers in ways that are remote.

DR. BARREIRO: This is Tim Barreiro. This may be a little bit different than what you're asking, but the concept of machine learning I think can be really complex, especially some of the information that's out there about how it breaks down data. When we look at, and I'm going to just glance over, when we look at the obstructive sleep apnea equipment and how it can auto titrate and regulate, and the information we get back from those machines to help us adjust patients, I think is a form of machine learning to some

degree and it really does help us adjust those machines to a greater compliance and more comfort, which gives in the end likely better

outcomes. So I think we've started doing, started the possibility of doing that in the basic sense of some machine learning.

DR. GARRIDO: This is Melissa Garrido. I'd just make a plug for going beyond machine learning which has its uses, but to use administrative data on who's used these devices, what are their outcomes, what are their baseline characteristics, pool data from multiple different sources so we can get a better understanding of who's mostly going to benefit under which circumstances, which extra or supportive circumstances in addition to the ventilators. And so that's more of an entrance framework than the predictive modeling that machine learning is usually using, but more data is usually a good sign.

DR. MELNIKOW: This is Joy Melnikow. I think just trying to integrate what's being reviewed and what's being said and thinking

about going forward and what are the research needs, it seems to me that definitely in the last 22 years there has been, the field has moved forward in terms of the evidence, and Medicare really needs to respond to that, hence

the technical report and hence this meeting, and hopefully there will be some positive changes in terms of what patients can get access to improve their outcomes. But there's also definitely a need for more research, more U.S. based research, more research that really examines that interface between using, you know, the home ventilation device and what support services can optimize its use to improve outcomes.

And then the other thing that really we didn't talk about today but I think maybe is an issue that is at least worth getting expert consideration of is the possibility that the use of these devices in the home may contribute to transmission of COVID-19 in certain circumstances, and whether or not there needs to be any whatever, warning label or such depending on what happens with this pandemic,

but it certainly seems to be continuing.

DR. SALIVE: This is Marcel Salive, I have a couple comments. I think, you know, this has been an interesting experience for me to see some of the things. I think it's a cautionary tale that this coverage was put in

place, you know, so long ago and let stand for this long, hearing that the evidence was so sketchy back in the late '90s. And so, you know, guidelines do need to be revisited periodically and this, you know, it's very hard to translate a guideline if it's a coverage in my experience. I wonder if this coverage has inhibited trials taking place in the U.S., because it seems like the evidence we saw, you know, may suggest that, but I'm glad we had a lot of trial evidence and I'm glad that Europe has conducted these trials because it is helpful and I think it will advance coverage. It seems like fairly normal that the reconsideration is based on increased use of this technology that catches the attention of the policy-makers, so I think it's good that at

least we are reconsidering things, and I thought it was very good that this technology assessment was able to align observational evidence with trial evidence and still draw some conclusions which were, I thought supported kind of equally by both sets of evidence, so that was very interesting for me.

DR. CRINER: This is Jerry Criner. I

just wanted to comment on what was just said about the lack of U.S. based data, and it has been a mixed bag. I think some of it is probably related that it might be more available in the U.S. compared to other countries, but it's not available to all Medicare beneficiaries, it's somewhat uneven in its availability. The problem with these studies is this patient population is set, and the studies that would be well done multicenter prospective shared controlled studies would need to be large and well conducted, and those are going to be populations that are going to be probably a thousand to 1,200 patients to be able to be enrolled across multiple sites to be able to get the endpoints that are needed, the

things that we're struggling with today.

And just like with lung volume reduction surgery and with long-term oxygen treatment trial, these are the kind of studies that only Medicare would be able to support with scientific guidance from agencies like the AHRQ or the NIH, to be able like we did with BOT (phonetic) and what we did with the NET trial was to be able to come up with what

patients benefit from those patients that might not get any benefit or could be harmed. So I think it's time to really think about how to design the studies that would address these important questions.

DR. BACH: Thank you very much. The floor remains open.

DR. GAY: If I might, I might pick up on what Professor Melnikow spoke of in the COVID era with respect to what's going to happen when they come home. There's a lot of concern about these things, in fact it's almost a dirty word, they're called aerosol generating procedures, and AGP is a frightening thing to

say in the hospital environment, it generates a lot of droplet when mask leak takes place and these things blow around the room, so that is being considered.

But the other thing again, about the COVID tragedy is with, now depending on telemedicine, whatnot, and we shouldn't overlook this, and it's not in any of those studies, is the effect it's had on patient empowerment, the patients have to play more of a role, they have to be able to work with their

own mask and engage with their clinicians through telemedicine. I think somehow or other if we incorporate these things into future studies where it's not just the respiratory therapist, it's the respiratory therapist empowering the patient to participate in these chronic therapies that go on for the rest of their lives will make an impact on this. Thanks again, everybody.

DR. BACH: Thank you. Okay, we're back. I'm going to draw this portion of the meeting to a close with a few closing remarks. I'll start and then Joe Chin will also make a

few remarks.

I want to thank everyone, including the presenters, for their unflagging dedication to this day-long meeting. I know even in person how long a day it is, I really appreciate the engagement. I know CMS does as well. I appreciate how much the information in the pre-meeting and information presented and discussed today was integrated by all of you in your thinking. I could see it in the votes and the comments and the discussions, and I think it will be of great utility as everyone is

obviously aware, not only from this discussion but from more general contexts, how critical it is for CMS to have this kind of input. These types of decisions often do get embedded for rather a long period of time, so the best decisions that can be made with the current information is always desirable and has long-term effects.

So I just wanted to thank everyone, also for putting up with the technology. I actually thought it went pretty well, we didn't

have a lot of glitches, and that's about it. Thank you very much for serving on the MEDCAC today. Joe, I will pass it to you, Joe Chin.

DR. CHIN: Thank you, Peter, and also, I wanted to thank the panel, the presenters and the experts today for the discussion and the comments which have been really helpful to our understanding of these complex patients and devices. We greatly benefit from the input of experts such as MEDCAC and the presenters, and our team will really be considering the evidence and the presentations over the next few weeks. We are interested in your special society recommendations and guidelines that

were mentioned so we'll look for those publications, I think they are also important to inform our consideration.

I think we have a common goal and we're really trying to provide the best evidence-based treatment and devices to the Medicare populations. So, and also based on that, are committed to having the most appropriate policies in place for potentially lifesaving treatments and devices for those

patients.

So thank you to everyone that participated today. I would like to acknowledge the efforts of Dr. Susan Miller, our medical expert, and Dr. Rachel Katonak, who have really put a lot of effort into preparation for the meeting today. And of course Tara Hall, our coordinator, for a great running of the meeting, and she has been behind the scenes for what I think has been a very successful first virtual MEDCAC for us. And our chair Dr. Bach, and vice chair Dr. Ross. So, thank you again, and we look forward to really continuing our discussions in this area and look forward to future interactions.

DR. BACH: Thank you, Joe. With that, I will call this meeting to a close, and thank you all for your participation.

(Whereupon, the meeting adjourned at 3:43 p.m. EDT.)

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