Oxygen & Oxygen Equipment
Open Meeting
January 28, 2020

DR. FRED MAMUYA

Welcome everyone, and welcome to Dallas. I am going to start out with a few housekeeping remarks. Um the first is please mute your phones. The second is uh bathrooms on the way out, if you are heading towards the elevator you will see a hallway, make a left, that's where they are. The third is uh we have four Medical Directors, we have Dr. Bob Hoover, who is missing but will be here with us in a few seconds, Dr. Ballyamanda, Dr. Brennan and Dr. Gurk. They are the four Medical Directors for the four jurisdictions. Uh we have a long day ahead of us today, uh this first session is on topical oxygen. Uh we held a CAC in uh San Francisco and some faces in the room are familiar. Uh and so we are here today to receive comments about the proposed policy we have posted. Uh by appearing you are giving us permission to uh put everything you say on our website. We are recording this session, so the Medical Directors won't be taking notes, not because they are bored but because we are recording everything.

Um the comments you give today um are wonderful, but please put them in writing and send them to us because we can only respond to the written comments. And we urge you to make them as evidence-based as you can, with a rationale for why you are giving the comments, uh along with any suggestions you might have. Uh if you have literature that we missed that you would like to attach along with your comments, please send it full text along with your comments. Um we have about 20 speakers for this first session, uh and we've divided up the time equally. Uh you will get

um a one-minute warning, a yellow, and then at exactly the time we will just cut off the mike and do a hard stop. And the reason for that is to be kind to the people behind you, because if you go over your time slot you are really taking time away from another speaker, and that's not fair. Um and I believe that is all I wanted to say. Um and Rachel, are we ready? Are we ready? Wonderful. We will get started; I will turn it over.

JODY WHITTEN

Thank you, Dr. Mamuya. Good morning everyone, my name is Jody Whitten and I'm going to be the moderator for this portion of the meeting. Um as Dr. Mamuya mentioned, we do have um roughly 21, well we did have 21 people, we now have 20 people um for uh oral presentations today. Some of them are on the phone, and some of them are here in the room. Um we do have one hour and 45 minutes, so with that being said we are going to be limiting all presentations to five minutes. Um and as we mentioned, we will give you a one-minute notice and then um a red stop sign once your time is up. So, folks who are on the phone um please pay attention to the number. When everybody registered for comments, we sent out an email and gave you a number. So, we are going to be going in that um order basically. Um also if you are not able to complete your presentation, we do encourage you to submit all your comments in writing so that we have that in case you don't go through the whole entire presentation. Um those comments are due by February 10th. So, with that being said, we are going to go ahead and go to our first presenter today, who is Dr. James De Meo. And I apologize if I mispronounce anybody's name.

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JAMES DE MEO, DPM, FACFAS, CWS, SJMC

Good morning. Um, I can't believe I'm the leadoff hitter, I wish my Little League coach could see me now. Um thank you for this opportunity to speak to you today um regarding, regarding oxygen therapy. As was mentioned, my name is James De Meo. I'm a Certified Wound Specialist, a diplomat of the American Academy of Wound Healing and an active member in good standing of the Undersea and Hyperbaric Medical Society. I am here - I am also the Co-Medical Director of a Wound Care Center that utilizes hyperbaric oxygen on a daily basis uh via two monoplace chambers. You might be wondering why I am bringing up hyperbaric oxygen, well I applaud CMS for recognizing the therapeutic benefits of hyperbaric oxygen for treating nonhealing and difficult wounds. Using hyperbaric oxygen, we see good results, but this morning I would like to talk about the patients that are unable to utilize hyperbaric.

We all know the absolute contraindications, um the patients with untreated pneumothorax, bleomycin, cisplatin, disulfiram, taking Doxorubicin and Sulfamylon. Also, the relative contraindications to hyperbaric is the asthma, claustrophobia, patients with uh chronic obstructive pulmonary disease, eustachian tube dysfunction, high fever, pacemaker, epidural pump, pregnancy, seizures and upper respiratory infections. As you can see, there is quite a lot of disqualifiers that prevent patients from entering into the hyperbaric chamber, thereby limiting the hyperbaric option as a treatment option. But in addition to this there is other contraindications.

There is uh transportation issues, time commitment issues, anxiety, obesity, um structural issues like lower back pain that prevents the patients from laying in the chamber for a long period of time. In addition to that, they have social issues. These are the patients that would normally qualify for hyperbaric oxygen, but for whatever reason can't go through with the hyperbaric oxygen treatment. These patients have difficult wounds that are unresponsive to conventional wound care therapies and are at great risk for an infection, for long hospitalization and unfortunately amputation.

Sorry they changed the order. So, I'm here today to be the voice of these patients. I applaud CMS for their wisdom in agreeing with their therapeutic and efficacious benefits of hyperbaric oxygen when it comes to treating wounds, but what about these patients? You have members that can't undergo hyperbaric oxygen therapy but would still benefit from um having oxygen therapy. This is where topical oxygen comes in. This subset of patients would benefit greatly from topical oxygen. These are the patients that I use topical oxygen on in my wound care practice to help heal their difficult wounds. I've been using topical oxygen for several years with great results. In 2017, New York State uh Medicaid decided to review topical oxygen as a paid benefit for their members. They brought in the services of Oregon Health and Sciences University, a well-respected, independent third party that did an in-depth analysis on topical oxygen as it relates to non-healing wounds. Based on their findings, and after great debate, it was decided that topical

oxygen is efficacious and therapeutic in treating difficult to heal wounds and should be a continued covered benefit for their members.

This is what the apparatus looks like. There is an oxygen concentrator with a uh proprietary boot that's connected via a tube. You can see that the boot covers both anterior, posterior, mediolateral and dorsal and plantar, so even if the patient has a circumferential wound it's treated. In addition, if the patient has a bilateral wound, just by adding a simple Y connector they can treat the um wounds on both uh extremities. They do this in the comfort of their own home, at their own convenience.

So, in summation, as a soldier on the front lines, I'm here to tell you, we need topical oxygen in our armamentarium to treat a large growing subset of patients that for whatever reason, medical or not, can't undergo hyperbaric oxygen. I can't say it enough, treating difficult wounds and preventing infection, hospitalization and amputation is a battle, and your members need uh topical oxygen in order to win that war. I am sure my esteemed colleagues you are going to hear from today will echo the sentences that I have said this morning. I thank you very much for your time and consideration, and if I do have any extra time, I would like to uh yield it to Dr. Angie Purvis. Thank you.

JODY WHITTEN

All right, you were just about ready to get your one-minute warning, so it was pretty, pretty good timing there. Our next speaker is Dr. Thomas Serena, and he is on the phone. And um make sure if you are calling in today that you un-mute your own line. We will be un-muting your line from our end, so just make sure you un-mute it from your end. So, Dr. uh Serena, are you there? We will give, again, everybody who is on the phone three chances to speak up. So, one more time, Dr. Serena, are you there? And one more time, make sure that you un-mute your own phone if you are on mute. Dr. Serena, are you available? All right, we are going to go ahead and move onto number 3. Um and if we do have time at the end of the call today, if uh we can circle back around and try to catch anybody that we may have missed. But the next person we have up is Bethany Hill.

BETHANY HILL, MD/MPH

Thank you, my name is Bethany Hill. I am a partner at the law firm of Morrison Foerster in the FDA and Health Care Compliance Department. I am in New York. Topical oxygen is safe and effective for FDA cleared indications. In 2006, FDA issued a proposed rule to reclassify topical oxygen devices into Class II. FDA eventually accomplished that reclassification in 2011. In that process FDA reviewed 20 years of clinical information. FDA determined that sufficient evidence was provided to demonstrate that general and special controls would ensure safe and effective use of topical oxygen, and ultimately reclassified topical oxygen as a Class II device, down-classing it from its original classification in Class III. FDA specifically concluded that human clinical studies

are not required for each new topical oxygen clearance because the safety and effectiveness is well established in existing clinical literature. Furthermore, from a legal perspective, FDA is not permitted to reclassify a currently marketed device unless there is adequate evidence of safety and effectiveness of the device submitted in the reconsideration process. Therefore, FDA determined that topical oxygen is safe and effective for its indications.

Topical oxygen is safer than negative pressure wound therapy and systemic hyperbaric wound treatment. As you can see from the data in this chart, I have thoroughly reviewed the public MAUDE databases, which is the FDA safety reporting databases, and identified that hyperbaric oxygen has a number of deaths and injuries. Negative wound pressure therapy actually has so many injuries and malfunctions reported that the public databases cap out at 500, and topical oxygen has none reported in the public safety databases.

I would argue that the Medical Directors should model this LCD reconsideration after the CMS NCD reconsideration process. The uh NCD for HBO 20.29 had previously excluded topical oxygen, stating no Medicare reimbursement may be made for topical oxygen. Then in April, 2017, CMS included, issued a decision to um not give actual coverage for topical oxygen, saying it was not appropriate, but identifying specifically that ongoing research could provide additional evidence for coverage and determined that they should remove the prohibition on reimbursement and open the door for the local coverage determinations to provide coverage. This action taken on

the NCD should be modeled in the LCD process and a thorough consideration of the NCD history and revision taken into account.

Topical oxygen is fundamentally different from hyperbaric oxygen. In the present reconsideration process the DMACs have accepted a statement from UMHS regarding topical oxygen that appears to have been considered in the preparation of the draft LCD. The citation is provided here. Acceptance of this position statement from an organization with a direct conflict of interest to topical oxygen technologies perpetuates a long-time competitive and biased view by this HBO focused society against topical oxygen as an alternative, effective therapy for wound treatment. The slide you see above is a letter from 1999 indicating that this hyperbaric-focused society has long held a belief that topical oxygen should not be permitted as a competitive product in the marketplace. CMS has clearly recognized that topical oxygen is distinct and not related to hyperbaric oxygen, and any statement from UMHS is irrelevant in this process and should not be considered by the DMACs.

And finally, A4575 is not an oxygen accessory. This code is erroneously listed in the respiratory oxygen accessory within this LCD. This code has historically and continues to be listed as a medical/surgical supply in all current HCPCS codes descriptions and has been considered a medical/surgical supply since 1996. The current LCD incorrectly lists A4575 as a respiratory oxygen accessory code, and I advocate that it be removed in this LCD reconsideration process. In

fact, this LCD seems to be the only location in all reimbursement documentation, both at the federal and through the local coverage determination process, that even identifies this as a respiratory or, more general, oxygen accessory. In all other locations this code is identified as a medical/surgical supply.

Thank you for considering my comments.

JODY WHITTEN

Thank you. Our next up is Dr. Anthony Iorio.

ANTHONY R. IORIO, DPM, MPH, C.Ped

Good morning doctors and thank you for the opportunity of allowing me to present to you this morning. I am Dr. Iorio, I am a Board-Certified Podiatric physician and surgeon, and also an advocate for public health. I am currently practicing in the Greater New York City area, which I am concerned about the types of care that our Medicare and Medicaid recipients are receiving. Thirty-nine years ago, I took a Hippocratic Oath to do well and to do no harm, and to help my patients, and to practice to the best of my abilities to keep them safe and, and healthy. I am proud to say that after thirty-nine years I have saved many limbs and lives, and I have been successful in treating and sharing that with my patients. I received my MPH back in the early 2000s in public health policy and management. As a result I started to articulate and to assist in quality of life

policies and commissions in the State of Connecticut with the uh State Department of Public Health in putting together the Quality Improvement Act for we taught and we've had, made and recognized to our diabetic population that this is a concern, and that 20 years later I am still saying the same thing.

What I'd like to share with you today, I'd like to keep you in mind, is nothing that you already do not know. You know doctors in the United States, diabetes, and from a diabetic point of view it is an epidemic. 30.3 million, or almost 10% of our patient population have diabetes. Two-thirds of those that have the diabetes are diagnosed while the other third is undiagnosed. We need to know, and this growth is going to happen in my generation and your generation. And as it continues to grow we need to be there to make sure that we can control it and we can work in a safe environment where we can basically take those patients and put them into the positive side. Over the years I have been recruited to a podiatric medical college in New York, where I was fortunate enough to be given a clinical appointment to where I was able to go into the field. I am now proud to say that I teach my doctors the art of doctoring and medical ethics. I was trained to keep the patients healthy and not to keep them sick. I was also training my students to be volunteers and to go into the populations which I serve. I serve the African Americans, the Latinos, the Asia-Pacific Islanders, the elderly and all of those that need it.

I'm also proud to say that we take care of the 66,000 homeless patients who live in shelters, and who have and come to me on a regular basis, that have wounds that do not heal. After trying so many places in Eastern-Central Harlem and in the Bronx with a plethora of ulcerations via diabetic foot compression, venous leg, name them, they come to me and they say, well why have I waited so long for this to heal? My students, my residents, my colleagues all perform the state-of-the-art, but we are very limited in what we have. We do with what we have and yet our patients are grateful. There is no greater joy than to see a smile on a patient who is homeless and saying, doctor, why did I wait so long for this ulcer to heal? I've been using topical oxygen for the last 12 years with success. I'm very fortunate that in the State of New York, managed Medicaid pays for this on certain people. We do our best and we fight our strongest to help the poorest of the poor to get what is needed.

By using topical oxygen, it is extremely easy to use for our patients because it is extremely safe. It is very simple. It is easy to apply. There are no risk factors. It's mobile devices; they take it on the train with them. We educate them; our students educate them; they educate each other. While educating each other, we build confidence within that patient to rehabilitate them so that that patient comes to me the following week and shows me how it to apply it -- tells me what to do. It is safe; there is no need to spend money and cost effect on nursing care. There is no additional nursing care. There is no uh adverse effects, no complications, no additional healthcare money that's needed. It's simple. It's a simple bandage the patient puts on the wound, goes home, comes

back, and gets reevaluated. There is nothing simpler than that. And it's at a fraction of the cost of what traditional hyperbaric oxygen is offering them.

Remember that it's the device that has its priority of mission. All of us here today are proponents of utilizing topical oxygen. We find that 90% of my patients who have diabetes are compliant, but it's a simple fact that they follow instructions. We care and we listen. So, my concern that the physician and the healthcare consumer today is why we are listening. I state that -

JODY WHITTEN

Thank you doctor.

ANTHONY R. IORIO, DPM, MPH, C.Ped

Thank you much, and I apologize.

JODY WHITTEN

Thank you. And our next up is Craig Kennedy, but he has um cancelled for today, so we are going to move onto Max Cavignac.

MAX CAVIGNAC, MSMHAN, MA. COM, QIDP, Doctoral Candidate

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I would like to thank the DMAC members for allowing me to talk about my firsthand knowledge of what the EOT oxygen therapy has provided me. I am honored and privileged to be here this morning and am looking forward to presenting the information in the next few minutes. I am a disabled veteran afflicted with chronic, nonhealing wound. I served in the Navy from '91 to '96 doing explosive ordinance disposal, and interior communications specialist. My initial injury occurred when I fell 20 foot down a shaft alley during my operation. Three years after that I was discharged, I was driving to a wedding and was involved in a tragic car accident. My leg was ripped off, I was thrown through the front windshield. I have been an amputee for 21 years now. This has changed my life drastically. I was living life as well as could be expected until things changed in 2015 when I decided to go through a gastric lap band to lose weight uh because I was informed that my extra weight that I had was uh causing issues with my residual limb. I spend 16 hours a day on my prosthetic. As a result, I developed a pressure ulcer. At this point what I should have done was taken time off, let my leg heal, but that wasn't an option for me at the time. Eventually I had to take the time off to see wound care physicians at the Dallas VA Clinic. The Dallas VA Hospital used a variant array of applications and products to try and provide closure to my wound. In the process of attempting to heal the wound we used wet to dry dressings every day, with a follow-up every week. This went on for about three months. Then toward the end of 2015 we advanced to the application of MEDIHONEY which only lasted a couple of weeks and gave no significant change in the size of the wound. We moved onto Prisma Dressings, wear them for the next couple of weeks, and again, no significant change. We tried application of Hydrofera

Blue, once again, no significant change in the wound. We moved onto trying different disposable wound vacs, the PICO and finally wound vac, a huge wound vac for about two months with little to no change in the size of the wound. After using the wound vac, they felt I would be able to heal enough that I could go back to wearing a prosthetic for the first part of 2016. That, however, was not the case, and we proceeded to flip back and forth with more and more collagen building dressings. Finally, fast-forward again to 2017, I was offered the opportunity try something new, something yet not approved by the Dallas VA Hospital. I met with the representatives from EO2 Oxygen Therapy and the Dallas VA physicians to see if their system would work on a tough wound like mine. All agreed, and EO2 provided this technology on a trial basis. Within a month, the opening on my wound was completely closed, as you see in the first image on the right. I would be refitted for a new prosthesis. I was in pain, and with many complications for two full years before finally getting this opportunity to use the EO2 oxygen. After finally being refitted, in the process of getting my life back and some sense of normalcy, there was to be another setback, my leg did not stay healed because there was not enough skin or fat pad left at the wound site. Consequently, in 2018 I underwent a short revision surgery where the residual end was shortened by two inches. Unfortunately, it was found there still was not enough protection. Therefore, in January 2019, I became a through knee amputee. After the surgery, EO2 Oxygen the system stepped in once again to aid with the healing of the surgical site, which helped to heal the wound thoroughly and completely, as you see uh after my second surgery. Having chronic wounds bear collective drain on family, friends and job functionality, and that burden will only increase as the

populous get older. Having the support of an organization such EO2 along with family and friends allows the patients, like myself, to get back to a functional part of society. Living with a chronic nonhealing wound leaves you feeling vulnerable, dependent on others to help with every task. The use of EO2 Oxygen Therapy on my wound has made my life become more functional and I am able to perform everyday tasks that was uh put, was not previously able to do. Quality of life has changed drastically since EO2 has come into my life. Without the EO2 providing the technology that healed my wound completely I would not be able to wear my prosthetic as I am today. I just received my final prosthesis two weeks before getting the opportunity to speak to this committee. Now I'm completely healed and able to walk. My plans are to resume my path in healthcare and to help somebody else that has gone through this chronic nonhealing wound situation. Thank you for your time.

JODY WHITTEN

Thank you. Next up we have Andres Cordova.

ANDRES CORDOVA

Okay. Good morning, ladies and gentlemen. I no where near have the education you guys have, I'm just a patient. My name is Andres Robert Cordova, here to talk about a situation I had about five years ago. I'm a diabetic Native American Hopi Indian, also a Navy veteran for six years, and I obtained a blister on my right foot, big toe, um and it became infected. Uh I tried, you know,

treating the wound at home, but it didn't, it didn't get any better. I went into the emergency room at the Phoenix Arizona IHS Hospital for uh x-rays and blood work. It was then determined that an infection um had spread to the bone on the big toe, and uh an application was needed. So, for a man who never had any medical issues, serious medical issues in the past, this was a gut punch. The - this was like something that, you know, you don't go through it you don't see it, but to lay there and have a doctor tell you that he's going to cut off your toe, it was serious. This was a small foreshadowing of my devastating news, more devastating news I was about to receive in the next few days. I went through the right foot big toe amputation and was waiting in the room to talk to my doctor. The doctor came into the room to discuss what uh they had done, and to inform me that they needed to do a second surgery to take more of the bone because it spread farther up the foot, into the tissue. So, they scheduled a second surgery. After the second surgery uh was done, um I was then sent through a vascular workup to help determine how my healing was and the post-surgery uh treatment plan. Um, They decided um the next step was to get back into a normal life. Then some more devastating news from the vascular doctor. I didn't have the strongest lower extremity, um the vascular system to receive coverage for the trauma I went through. I was not a good candidate for surgery, before working on the vascular system. I was told the few options that I had, hyperbaric chamber, but that was out of my price range, and amputation. I laid in bed remembered the days of pain, playing sports with my dad, my brother, my six years in the Navy, traveling the world and all the accomplishments I've done. But for most all of the years I went

through, special moments I had with my sons, I was going to lose them. The future of a prosthetic limb was devastating and depressing to me.

Dr. Penny came into me the following day to see if I was interested in trying a new system to help me with my wound care. It was the EO2 System he attended a seminar on, and he was um, in fact he wanted me to take a look at it and see if it would help me. Uh the group of doctors at that time had already determined that the next step was a below the knee amputation, which was already being scheduled. After all the bad news I received in the previous days, I had nothing to lose. I agreed and met with the representatives from the EO2 Systems. They applied the system to my wound on the right foot and waited a week to see the initial results. You can see the progress in the pictures there from the first one on the left was after the second surgery. Uh after the, after the initial wound I was optimistic. The first week, second week, went to 18 days, 50. Over the next few weeks the progress was amazing. My hopes were sky high. I obtained full closure and I did not receive the below the knee amputation that was actually scheduled. I currently work as an outside sales representative for a national container company in the southwest part of the United States. I would not be able to have that position today or have the remarkable life, filled with love, life, and cherished moment memories if I did, if I did have this uh limb amputated. No disrespect to anybody who has, or lack of empathy for those that have lost their limbs, but I know for myself my life would not be the same if I had my leg um amputated. So, I wholeheartedly stand by the process of the EO2 System and the Genia System to help me gain my life physically, mentally and

spiritually. You have to give other patients the opportunity. It changes lives; give them the opportunity. Thank you for your time.

JODY WHITTEN

Thank you. Next up is a teleconference presentation, it's number 8, Dr. Charles Andersen. Dr. Andersen, um please make sure you un-mute your own phone and we'll un-mute you on this end.

CHARLES ANDERSEN, MD, FACS, MAPWCS

Can you hear me okay?

JODY WHITTEN

Yes, we can.

CHARLES ANDERSEN, MD, FACS, MAPWCS

Do you have my slides up?

JODY WHITTEN

Yes, we do.

CHARLES ANDERSEN, MD, FACS, MAPWCS

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So, my name is Dr. Charles Andersen, Vascular Surgeon, currently at Madigan Army Medical Center. I have a very strong commitment to preventing amputations in patients with diabetes. I initiated a limb preservation program 24 years ago that has been very successful in preventing amputations and returning patients at risk for amputation to a high level of function. You heard from the previous presenters how traumatic the thought of amputation is. We've committed our life, our endeavors to try to prevent that morbid condition. We work as a team, we have vascular surgery, we have podiatric surgery and we have wound care. What we've found is a diabetic foot ulcer is often a precursor to a lower extremity amputation. The longer a diabetic ulcer is present the more likely it is that chronic osteomyelitis, acute foot infection will develop when amputation. What we've found in our practice is that CDO, a Continuous Diffusion Oxygen therapy, of foot ulcerations have been refractory with other therapies preventing amputations. The therapy is supported by excellent double-blind study demonstrating increased healing of chronic wounds. One unique finding of the study is that the more chronic ulcers and the larger ulcers are even more responsive to therapy. Our theory of that is that that's due to regional ischemia of the wound that can successfully be treated with CDO. I was initially very skeptical of CDO because of older devices. In my opinion, it's very important to distinguish CDO therapy from other oxygen therapies. CDO provides continuous oxygen therapy, is supported by very strong science and in our clinical experience has provided excellent outcomes and helped prevent amputations. The other advantage of this therapy is the reduction of pain, and this has been uh very, very uh evident

in our patients. This has allowed patients uh with chronic ulcers to actually stop narcotics. The finding of pain reduction is also supported by clinical studies from the company.

So, I'd like to quickly run through a case study. So, this is an ulcer, very difficult ulcer, had exposed bone, you can see bone cement. This ulcer had been present for one year and certainly put this patient at risk for developing osteomyelitis, acute infection and the possibility of amputation. So, for those of you that may not have seen the dressing, this is what the dressing looks like. Uh so it's a dressing with continuous oxygen infused into that dressing, so there is continuous oxygen into that wound. The ulcer here, again, had been present for over a year, and healed in six weeks. Uh we have good follow-up on this patient, this patient is doing well uh with no ongoing threat of amputation. In summary, at least in our experience, in a very sophisticated and long-standing limb preservation program CDO is an effective therapy, supported by an excellent double-blind study that can close foot ulcerations and help prevent amputations. Thank you for the time.

JODY WHITTEN

Thank you. Our next up is um Sean Geary.

SEAN M. GEARY

Good morning, I'm Sean Geary, President and CEO of GWR Medical. I'd like to share with you a timeline for GWR and topical oxygen. In 1997 GWR received device approval. In 2000-2001

the Federal Supply Schedule and the Federal Employee Program began coverage for topical oxygen. In 2006 FDA proposed reclassifying topical oxygen devices based upon adequate experience in the clinical community and effectiveness information. In 2008 New York State Medicaid approved GWR topical oxygen devices for its members. In 2011 FDA finalized its reclassification. Not shown in this slide, but in 2016, GWR presented the CMS Coverage Analysis Group unpublished data for real world patient use of GWR Medical's topical oxygen devices. This data was subsequently published in 2017 as a nine-and-a-half-year retrospective study in advances in wound care. That same year CMS removed its longstanding coverage um statement for topical oxygen. Contrary to the conclusion of the panel of invited experts at the October 29th CAC meeting in San Francisco the topical oxygen is not generally accepted as a standard of care for chronic wounds. As of this year GWR's topical oxygen devices have been utilized for almost 25 years, and for more than 10,000 patients.

In 2016 CMS published a quality strategy that included these stated goals for Medicare beneficiaries. One, increasing safety by reducing harm caused in the delivery of care. Two, strengthening patient and family engagement as partners in their care. And three, promoting treatment of chronic wounds. Topical oxygen squarely aligns with all three of these CMS quality strategies for Medicare patients. Regarding safety, a review of the MAUDE database dating back to 1997 reports not a single adverse event for topical oxygen. CMS covers alternative chronic wound therapies for systemic HBO and negative pressure wound therapy as safe and effective, but

for which the MAUDE database confirmed significant reporting of malfunction, injury and death over the same time period. Regarding family engagement, in addition to its safety record topical oxygen allows patients to treat independently at home or with the help of a family member, and with no need for transportation or a professional caregiver. Regarding effective prevention and treatment of chronic disease, topical oxygen promotes a significant treatment alternative for Medicare patients, especially for elderly patients contraindicated or who cannot travel for systemic HBO and who are unable to remain connected 24/7 for negative pressure wound therapy.

Additionally, CMS's Center for Clinical Standards and Quality published Quality Initiatives seeking evidence-based care, patient-centered interactions and state-of-the-art results linked care, and challenges industry to go beyond the traditional gold standard of published clinical trials alone. The outcomes in GWR's retrospective study demonstrate successful patient-centered interaction to treat independently at home with topical oxygen. And when possible, GWR has utilized wound imaging and planimetry measurement software validated in a study published by Johns Hopkins in 2007. Planimetry can supplement traditional manual wound measurements and supports evidence-based care. The stated goals of safety, family engagement and promoting treatment for chronic disease as listed in CMS's 2016 Quality Strategy are demonstrated in GWR's retrospective study over a nine-and-a-half-year period. Patients treated safely with topical oxygen have experienced no adverse events, patients treated independently or with the help of a family member at home, and thirdly patients were provided an alternative form for treatment for their chronic

wound. Additionally, this study offers a dataset of 4127 wounds treated with topical oxygen with no more than - with more than 50% Medicare eligible or covered patients, and the results confirm the low amputation rate of 2.4% published in other controlled clinical trials for patients treated with topical oxygen.

In closing, CMS has historically relied on controlled clinical trials as its benchmark for approving new treatments for CMS beneficiaries. Topical oxygen has been utilized for over 30 years and cannot be viewed strictly as a new treatment. CMS states that it is working to achieve its objectives through multiple drivers and policy levers of quality, including the adoption of evidence-based coverage determinations. GWR's nine-and-a- half years of published outcomes for topical oxygen in the real-world setting provides CMS with evidence-based information to help determine a positive coverage decision for topical oxygen as reasonable and necessary for Medicare patients. Thank you. I yield any of my remaining time to Angie Purvis.

JODY WHITTEN

Thank you. Right at five minutes, good job. Our next up is Dr. Tunde Osofisan.

TUNDE OSOFISAN, DPM

Good morning and thank you. Good morning, thank you Dr. Tunde Osofisan, um and thank you for your time. I do want to thank Dr. De Meo, who is actually my Assistant Residency Director.

So, it's always good to see that Dr. Iorio, who was one of the instructors when I was in med school as well. So, thank you guys. I practice in Brooklyn; I am the Assistant Program Director now at Brooklyn Hospital. We do have a pretty huge um wound care program there. For me, I think uh the most important thing when I consider topical oxygen is looking at patients that are not able to physically come to the hospital and just trying to have the coverage for patients who need to be in the society or able to go to work, and still have the same or similar treatment in terms of wound healing with less risk of amputations. So, a big um part of that for me is uh patients who are working compared to hyperbaric therapy where you have to physically come to the hospital, spend about two hours in the chamber every day, five days a week. It's almost impossible um, you know, to have a full-time job, have a family and still be able to do that. Um also a lot of our elderly patients who rely on some kind of transportation. I practice in New York, I'm sure a lot of people have the same issues where they have transportation schedules. If the transportation is late, they don't show up, they have to drop off the patient, and end up showing up late for treatments, or are not able to make treatments, and it's not consistent or it's very inconvenient for them. Or their home health aides who are there to help them have to leave now because the time is out. So, this topical oxygen treatment allows them to actually treat at home four consecutive days a week, and they are able to monitor and be more compliant with that, without having to rely on traveling to the hospital.

Um another big group of patients that we see are patients on dialysis, who have to, you know, go to the dialysis center three days a week, every week. They spend four to five hours there, without considering, you know, their travel time. So, imagine if you have to go to dialysis five, six hours of your day, then travel back to the hospital to sit in another machine for another two to three hours. That's an eight, nine, ten-hour day that you need to do five days a week. I think that uh it becomes very uncomfortable um for patients like that.

Uh also patients uh who have contractures, cannot lay flat, they are not able to go in the machine, like Dr. De Meo mentioned earlier, patients with COPD, that's a big concern, patients with pacemakers. Um, you know, we have a group of people who our goal as physicians is to save their limbs, save their life and help them incorporate back into the society, be able to function in the society, have a job, have a family and be able to spend more time with their family and go do what they like to do besides just sitting with us in the hospital. Um I think that's a huge advantage of this type of treatment where they can monitor themselves at home, and they can still be able to be productive with their day.

Um like I said, I do practice in Brooklyn, a heavy Medicaid population. And again, being able to have coverage for their treatment is something that's very important. Uh I do have a lot of patients, like I said, probably in the last five years or so over 500 prescriptions I've done with a great success. But it's unfortunate where you see patients who can benefit from it and I have to tell them, you

know, your insurance doesn't cover it, um sorry. I think that's not a great factor. So overall, I think it's uh important like as uh Elliott mentioned just being able to have an option to be productive, to use your time wisely and still get good treatment that works, and that's worked over several years. Thank you.

JODY WHITTEN

All right, thank you. Um our next one is uh another teleconference, and that would be Dr. Mark Couture. Are you there?

MARK COUTURE, DPM

Good morning. Can you hear me?

JODY WHITTEN

We certainly can.

MARK COUTURE, DPM

Okay, good morning. Thank you for having me. My name is Mark Couture, I'm a staff podiatrist at the Central Texas VA in Temple. Um I've had over seven years of clinical experience with the continuous diffusion oxygen device by EO2 Concepts at the VA. In that time, I've used it on multiple foot and ankle wounds. I see the majority of the foot and ankle wounds in our service,

uh having three-plus days of uh wound care a week. Um I use it as a uh very effective advanced wound healing modality uh in order to not only get these patients better but to actually heal wounds, which is very significant in our uh limb salvage attempts for these veterans. Uh I've used the device both as a stand-alone treatment, and at times in conjunction with a um biologic tissue. Um I've published a 25 patient uh retrospective study back in 2015 in Podiatry Today, in which I listed the first 16 months that I utilized the uh technology and had a 68% heal rate with 17 of the 25%, excuse me, 17 of the 25 patients healing. Um which was a very significant uh heal rate, this is not just something that improves the wounds but actually will uh close wounds. And in uh trying to uh save uh people's feet or their legs uh you need to have the technologies available to you that are able to uh not just improve wounds but actually close them. And because of this closure rate, we've actually been able to reduce our lower extremity amputation uh rate in both major and minor amputations in our facility for the last several years. We are fortunate at our facility to have a uh LUNA fluorescent angiography device, and um this is a device that can uh show perfusion uh down to the foot in a very short period of time after injecting a uh dye. Um with this technology I was able to uh show that two patients had visual evidence of an increased angiogenic response uh to their foot, after utilizing the continuous diffusion of oxygen technology in which um there were uh studies that were done uh pre use of the continuous diffusion oxygen device, and then post. And we showed an increased uh angiogenic response once again to uh the areas, that was only due to use of the uh continuous diffusion oxygen technology.

Um I believe that this is uh a technology that has several advantages, one is that it's a portable device. Uh patients come once a week for weekly debridements and dressing changes uh to my clinic. Uh they uh very rarely will do dressing changes at home. Um we also uh have veterans that uh will often say that they can't make it to hyperbaric oxygen treatments Monday through Friday, and so this device allows us to treat the patients and have them come in on a regular basis. And, again, the best advantage is that this heals wounds. My concern is that if there is no coverage given to this technology, which is a unique technology out on the market, that um this will not be available for my patients, and that uh the company won't be able to sustain the business uh due to lack of coverage. So, I'm a strong supporter of this device, I utilize it in my practice on a uh weekly basis and uh I appreciate your time this morning. Thank you.

JODY WHITTEN

All right, our next up is Dr. Amit Shah.

AMIT SHAH, MD

Good morning. My name is Amit Shah, I'm one of the vascular surgeons. I just want to thank the committee for the opportunity to speak this morning. A little bit about myself, I'm a Board Certified vascular general surgeon, I work with Azura Uh Vascular Care, which I'm on the Medical Board for. Uh they are a uh partnered corporation with Fresenius, which is a large dialysis corporation. I'm the Chief of Vascular Surgery at North Bronx Health Network, which uh is part

of the Health and Hospitals Corporation, which is one of the largest public healthcare systems, and uh an active uh researcher and ah clinician. Uh really I'm here to kind of, once again, drive home the physician perspective, uh specifically, uh as mentioned before, I work in a somewhat challenged uh area, uh socioeconomically, uh medically these patients really present to uh me and my partners uh in healthcare uh at a very end stage. So, it's very difficult to treat some of these patients because they are not uh really uh able to get to healthcare early enough to kind of get to the beginning stages. So, when we get to see them, they, they already have chronic wounds somewhere at the uh limb loss stage, so we really have to work quickly and diligently to try to fix some of these patients. Some of the demographics that are very important, we have 38,000 patients that are uh within the Medicare guidelines of age, uh and also a huge dialysis population, 8500 uh patients and growing. Uh and to put that into perspective that's nearly 10% of the dialysis population of the United States is actually concentrated in the Bronx. Uh we have the highest number of diabetics in New York, and roughly we see about 100,000 wounds, so that's a lot of patients.

Uh the patients that I usually see in my practice are, like I mentioned before, very uh at the end stage of their healthcare, so they are very elderly, they are very frail. Oftentimes they have a lot of mobility issues, they've either had previous surgery, amputations, uh and they have uh what I do, uh which is vascular insufficiency. So, a lot of these patients need uh a lot of acute therapy and some long-term chronic therapy. Uh and mobility is a big deal for us because we have to work

around their uh handicaps, their age, their amputations. A lot of them have significant other comorbidities that require them to go to the, uh to the hospital or other physicians, so there is a big-time commitment on their end that needs to be accommodated for. So uh, and I think mentioned before, I deal with a lot of dialysis patients. And dialysis is three and a half hours on the machine three times a week. Uh these patients oftentimes are very tired afterwards; they are uh not really in the best mental or physical shape to go to other physician appointments. So, we have to take that into account when we have to deal with lifestyle, and that's a big take home point, lifestyle. This is a therapy that offers back patient's lifestyle.

So hyperbaric versus topical, not so much about the science but just more about, like I mentioned, lifestyle, the commitment of not only resources, which is transportation, uh nursing care, physician care. You get to get patients to uh buy into their own wound care, which is really important because that leads to compliance. So, with topical oxygen, which I've used for many years, I think that we have increased compliance and certainly a lot more uh, you know, satisfaction in patients' healthcare. So, I've done it for uh, for the past ten years, I've had myself over 450 patients. Uh the partners I work with in my facility, a lot of burn care, wound care surgeons, my other vascular partners. We've treated over 750 patients, and we really have seen pretty amazing results. Uh I think it's important to stress uh compliance, which is a big thing for us, especially for our patients; uh pain relief, which is also a big thing; uh and, you know, participation from every aspect. When you see good results, you want to keep going, and that's big. So, in summary, topical oxygen is

uh necessary, it's a necessary part of the armamentarium for wound care. And I think it's important to uh really be a good partner with the patient, and this helps us. Thank you.

JODY WHITTEN

Thank you. Our next up is Dr. Gayle Gordillo.

GAYLE GORDILLO, MD, FACS

Thank you. My name is Gayle Gordillo, I'm the Chief of Plastic Surgery at Indiana University, and I'm also an NIH funded ah surgeon/scientist. I've been using topical oxygen clinically for the last 18 years. I'm just going to go over, I've got a bunch of slides, I'm going to skip through some of these pretty quickly. Just a reminder, there is a clear rationale why oxygen therapy is effective. I want you to take a look at these numbers. Uh 20 to 25 mm of mercury is the average rate of, uh or the average OT tension you need for collagen formation. And if you think about wounds, many of those are less than that. It also helps us with resistance to infection, where again the average rate of functioning for the enzymes responsible for clearing bacteria require a PO2 of 75 mm of mercury, again frequently the wounds are less than that. And if the tissue oxygen tension is less than 20 mm of mercury you lose the ability to fight infection.

Um I'm going to skip, I'm going to talk about uh our concept that, you know, the first question is does topical oxygen really improve the wound oxygenation? And this was a preclinical model that

we did in pigs. Um this is just an example, where we put the topical oxygen device on the pigs, we gave them some treatment and we measured um their uh wound oxygenation beneath the surface of the wound. So topical oxygen is able to penetrate the surface of the wound and raise the wound PO2, and we could get it up as high as 70 mm of mercury. So, keep that in mind with the numbers that I gave you. This is an important proof of concept. The other thing that we found is that it helped promote closure, again in our pig model, um and that is compared to pigs that got sham treatment with room air. And then finally, this data is from pig burn wound biopsies, these bio-punch biopsies, at 15 days. So after they completed their um oxygen therapy they have, as you can see, as you can see here much more elevated level of PO2, increased levels of vessel formation, and this is a sustained response after the completion of topical oxygen therapy. And so, we were very pleased with that.

We did also do a prospective human study where we looked specifically at uh O2 naïve wounds and the production of vascular endothelial growth factor at time 0, midpoint of healing and end stage healing. And I'm going to skip through some of these slides just to basically get you to the end, to show you that uh here. Uh if you look at this ratio of the baseline to the end of treatment you can see that basically all the patients have an increased ratio of VEGF expression, so it confirms essentially what we saw in the pigs.

And then, finally, um just our, my clinical case experience. So, one of the things that's a little different as a surgeon is uh we've heard about using topical oxygen to take patients to complete healing, I also find it extremely useful as an adjunct to prepare patients for healing. It makes it an easier case uh to close, and I'll give you an example here. So, this was the first patient that we ever treated. Uh this was a 17-year-old girl who had spinal hardware for her entire spine. As you can see, this is a huge wound with a very challenging problem, and she was treated with topical oxygen therapy. So, this was really a life-threatening situation. And we got it down to that. And then from that we were able to close it surgically. So, another important role of topical oxygen is as an adjunct, so particularly for large wounds not to take it to end healing, but to prepare for surgery.

I'm going to skip here, basically the podiatrist mentioned that he had a 68% heal rate, um this was uh a retrospective review but all comers, as pragmatic as it comes. So, we didn't exclude anybody. We looked at our eight-month experience at when we first started using topical oxygen back in 2003, and we had a 75% heal rate with a topical oxygen. So, we felt we had a good experience. And as a result of this retrospective review I've continued to use it throughout my practice. We had had, everyone had a response to topical oxygen, we looked at wound acuity, which really didn't make a difference whether it was acute or chronic. Um And then we looked at the location, um and basically found, again, 75% overall healing rate. Our average length of time was 10 weeks, which is consistent with what the podiatrist had reported. Um and again when I have a really large wound, I think about using oxygen as an adjunct to therapy and not as a stand-alone treatment.

So, in conclusion, um my experience has been the topical oxygen raises wound tension, it induces angiogenesis in experimental models, um and it increases VEGF expression in humans. It can be used as a primary or adjunctive therapy for wounds, and as I said I like to consider it as an adjunct for larger wounds. Thank you.

JODY WHITTEN

Thank you. Our next is a teleconference um attendee, it's Dr. David Armstrong. Are you there? Again, Dr. David Armstrong, are you there, sir?

DAVID R. ARMSTRONG, DPM, MD, PhD

Hello, can you hear me?

JODY WHITTEN

I can year you.

DAVID R. ARMSTRONG, DPM, MD, PhD

Oh, I can hear my echo in the back of the hall, it sounds very mellifluous. Anyway, it's a pleasure to join you from uh Los Angeles, uh and our clinic actually. Um I am uh David Armstrong, I'm a Professor of Surgery and uh I direct the Southwestern Academic Limb Salvage Alliance, or

SALSA, here at University of Southern California and CAC Hospital. Um I was recruited out here with the big idea to eliminate uh preventable amputations uh over the next uh generation, and so it's kind of rather apropos that we are talking uh about this area uh right now in terms of topical oxygen. And I'll be extremely brief, you've already heard from some spectacular people, including Dr. Gordillo who just preceded me. But I was an early and extremely vocal critic uh of this, of topical oxygen and this therapy, um and including, by the way, a lot of the things that Dr. Gordillo was talking about. And I'm, I'm on record and was on record as saying that unless we have evolved gills on our legs, I'm not certain how this product and this technology is going to work. It was, it struck me as quackery, frankly. So, and I was therefore pretty surprised by the consistent, early basic science data that came out from not only Gayle's lab but uh Chandan Sen's lab when they were at Ohio State, or excuse me, The Ohio State University, uh which showed some positive physiologic signal. Um and this kind of caused me to sort of evolve on this, at least to challenge it, uh and put our money where our mouth is. And to my surprise when we started using this we started, we saw early and very, very consistent pain relief in people with limb threatening wounds, which is the majority of patients that we treat here at SALSA at USC. Um And this exact mechanism is inexplicable to me still, um but it is clear and consistent. This was followed now by ah two different well controlled, sham controlled trials now, including by the way one which I was the senior author, and another you are going to hear from in a minute, I think, on which Bob Frykberg was the first author, a multinational, uh multicenter study that showed a real clear signal favoring topical oxygen with two different uh form factors. Um and so at this point there are data

um I think that are clearly stronger to support this therapy than to many of the other things that we use, I use, and will use in five minutes here when I leave this call, every day.

Um And so, this technology I think right now um has too much data to allow it to just languish. And the small companies I think that have worked on this, along with academic medical centers, have really done this the right way. I think they've tried to work within the goal posts to address this problem, um and it has been consistent uh discussions between CMS and uh some of these, some of these companies, and I find it kind of heartening. Um and so I look forward to your consideration for this because I think it may have a chance to help uh a number of patients now uh that don't have anything else to help them, other than our good wishes and our best intentions. Uh so, ladies and gentlemen, I thank you very much for your consideration, and your reconsideration uh of what I think may be um a promising therapy. Thank you.

JODY WHITTEN

Next up we have Joe Moffett um and Dr. Mark Niederauer.

JOE MOFFETT

Good morning, my name is Joe Moffett, I'm President of EO2 Concepts. I have a financial interest in the company, and I'm here to provide commentary regarding the proposed LCD, uh and my comments are limited to continuous diffusion of oxygen for CDO therapy as EO2 is a subject

matter expert. Our first contact with CMS was in January 2010, to start a process for coding, coverage and payment for the company's innovative and effective product. The company has been working diligently on the process for ten years and has conducted over 70 meetings and communications with CMS and now the DME MACs. The reconsideration request submitted to DME MAC in December of 2018 was a request for coverage of CDO for nonhealing ulcers. EO2 provided justification for a positive coverage decision for its CDO including new peer-reviewed published evidence which was not part of the October 2017 request for information; and a detailed explanation of how the new evidence addressed the agency's coverage and analysis groups, concerns, inaccuracies and inconsistencies of the 2017 CMS Decision Memo that remain uncorrected to this day. There are a number of critical issues with the proposed LCD. The DME MAC's evaluation of the technology includes all forms of topical oxygen, including all delivery mechanisms. This suggests there is no reasonable way to newer innovation nor improved study design as suggested in the HRQ Negative Pressure Recommendations to overcome the marginal, older technology and less rigorous study designs. Specifically, inclusion of the study data from Driver et all in an LCD for DME should not be considered in this process. This device used in the Driver study is a disposal non-DME device and can indicate it is working even though it's not producing oxygen at all. And neither the physician nor the patient would know it was working. Low humidity environments will also stop the oxygen production.

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The Underwater Hyperbaric Medical Society has a conflict of interest with regards to coverage of CDO. This organization represents facilities and physicians who provide HBO and have a vested interest in maintaining their reimbursement and eliminating competition, which are significant conflicts in a fee for service system. The proposed LCD limits innovation and competition in supporting hypoxic wounds. HBO does not have a study with the design and full closure outcomes of CDO and should be held to the same standard. The CAC meeting did not have the benefit of a complete literature review, not the history of EO2's open cooperation communication with the CAC through the incomplete process resulting in a 2017 CMS Decision Memo. This process was incomplete because only the interim and per protocol publications were available at the time of the release of the Decision Memo. The completed ITT data was submitted to CMS and the DME MAC in the request for reconsideration, which was submitted after the Decision Memo. The uniqueness and rigor of the CDL RCT was a first of its kind placebo control all blinded study with a patient lead-in which wasn't addressed. The CAC focused on revisiting the 2017 CMS Decision Memo, continuing the errors and incomplete assessment of the EO2 RCT. The ITT CDO publication addressed the criticisms raised in both the 2017 Decision Memo and the CAC low confidence discussions of the study issues like standard of care, blinding and quality of life measures. With so many of the non-consensus discussions and unanswered questions on the definition of standard of care, quality of uh life metrics, generalization of Medicare population and even full closure wounds one’s confidence as to how the CAC members could vote confidently on the questions is uncertain.

From the very beginning EO2 has been diligent working with CMS and asking what the agency wanted to prove efficacy and change to coverage status. The company has devoted itself to providing exactly what the agency recommended in clinical outcome study design, blinding rigor and attention to detail to successfully complete the goal to be removed from NCD 2029, and to obtain coverage for beneficiaries who can clinically benefit from CDO. We believe the proposed LCD is incorrect, and that CDO is reasonable and necessary based on a complete and informed assessment of the ITT paper and supportive pain and debridement papers. We ask for DME MACs to judge the strength of the data and remedy the misunderstandings and inaccuracies of the 2017 Decision Memo -

JODY WHITTEN

Thank you doctor. Our next up is Chandan.

CHANDAN K. SEN, PhD

Good morning, I'm Chandan Sen. I am the Executive Director of the Indiana University Health Comprehensive Wound Center, and uh I'm also the Editor of the top ranked journal in wound care, Advances in Wound Care. Our group has been studying the effect of oxygen in wound healing for over 20 years. And during all of this time we have NIH funded with multiple grants. There was a review that we wrote a few years ago that remains heavily cited in the literature that sums up the

various aspects of how oxygen plays a role in different aspects of wound healing. As Dr. Gordillo pointed out, uh this was the first evidence that topical oxygen, or oxygen applied topically can directly raise PO2 of the wound tissue. This has been seen in preclinical models, since then it has been seen clinically, so this was one of the early event data showing that direct application of oxygen over the wound can increase wound PO2, wound tissue PO2. Now a big problem in wound healing, as we all know, is the recurrence of wound. And a wound recurs because even after it was closed the tensile strength of the wound is not maintained. And this happens because collagen production and maturation does not happen adequately. The process of collagen production and maturation requires a reaction called hydroxylation, that directly requires molecular oxygen. And in the superficial part of the wound, therefore wound PO2 plays a key role in maintaining um the wound tensile strength, which directly plays into wound recurrence.

In this article we summarized that it is not just molecular oxygen but reactive derivatives of oxygen such as superoxides, hydrogen peroxide, nitric oxide and a range of other non-molecular concentration of oxygen that's essential for wound healing. If you have molecular oxygen but if you disable the ability of the body to convert this molecular oxygen into its corresponding free radical form, such as superoxide, which is done using an enzyme called (inaudible) oxidase, which as we know is key in uh killing pathogens or managing wound infection. What we have addressed in this article is the fact that once you have infection, which is common in uh chronic wounds, each and every pocket of infection acts as an oxygen sink, and you have a deep hypoxia around

those pockets. And because most chronic wounds suffer from underlying vasculopathy, blood is not a reliable mode of bringing oxygen to those particular sites. And we have found that topical oxygenation of wound and by increasing the PO2 of the topical wound tissue these types are infection-related oxygen sink can be corrected, resulting in improved healing.

Dr. Gordillo mentioned that of the many mechanisms by which topical oxygen can improve wound healing, one is that um topical oxygen induces VEGF. And by the way, there are dozens of papers in the literature demonstrating that oxygen derivatives such as hydrogen peroxide, which I just mentioned, and these are not hydrogen peroxide delivered from the outside, these are hydrogen peroxide produced endogenously by the body, are a significant inducer of angiogenic factors such as VEGF.

There was also the study that came out of a group several years ago, and in this study over nine months seven surgeons treated 58 wounds, and 75% or so went on to close their wounds. That was a very encouraging result. More recently we had this work from Dr. Armstrong's group, and I would pause to recognize Dr. Armstrong as one of the key uh scientists and experts in the area of wound closure, and I'm thrilled that this work has come out. It's a very well-done work, and worth a lot in what the field has to offer, uh showing in a very confident manner uh the effect of topical oxygen in improving wound closure. Following that, in the fall of 2019, last year, this study with a group sequential design came out to show that adjunctive cyclical pressurized topical

oxygen is superior in healing, as healing chronically diffuse or diabetic foot ulcers compared with optimal standard of care alone. Now the interesting part here is the cyclical part of the topical oxygen. We are not going to parse out the different modes of topical oxygen, but I would just want to note that when you apply topical oxygen you provide the oxygen. When you withdraw the topical oxygen, you elicit the hypoxic response during which numerous hypoxic changes will factor that generated. Then when you put back the oxygen those factors taken together with oxygen actually enable the type of healing that we get to see. And there is plenty of literature, mechanistic literature to support this statement. With that, I would like to close by saying that topical oxygen delivery is effective and uh I would like to advocate in favor of using it as a standard of care. Thank you.

JODY WHITTEN

Thank you. Next up is a teleconference attendee, Eric Greig.

ERIC GREIG

Hello, can you hear me?

JODY WHITTEN

We can hear you.

ERIC GREIG

Okay, thank you. Um my name is Eric Greig, I'm a partner in the Healthcare and Life Sciences Practice at Latham and Watkins, and my comments today are made on behalf of my client, Innotech AMB Limited. Innotech manufactures the Natrox Oxygen Wound Therapy System, which is an FDA cleared medical device that applies continuous topical oxygen therapy to wound sites to enhance the healing process. Uh we respectfully request that the medical directors reverse the proposed noncoverage determination and provide coverage of topical oxygen therapy for the specific wound types where this therapy has been shown to be effective. Uh with all the great clinical discussion we've been hearing and feedback from physicians, I'm certainly going to stay in my lane and focus on a procedural aspect of the LCD that I would like to confirm in the couple of minutes I have. Uh looking at the proposed LCD, uh the language certainly suggests that the medical directors have analyzed the evidence with respect to specific wound types and reached different determinations on the level of evidence available for diabetic foot ulcers, for venous leg ulcers and for pressure ulcers.

My concern relates more to the transcript and consideration of the uh CAC's October 2019 meeting, where there was discussion among several members uh whether they should consider particular subtypes of wound in the coverage determination, or whether there needed to be some determination for all chronic nonhealing wounds, or all Medicare beneficiaries. And it seems the latter group uh sort of won the day in that discussion. Uh we believe the LCD summary uh pretty

clearly shows that there are different levels of available evidence in these different wound types, most notably with studies of diabetic foot ulcers providing a consistent and notable signal of efficacy.

Uh in related coverage context, we would note that NCDs and LCDs have been narrowly tailored uh to cover certain types of wounds or conditions where uh the evidence at that time supported coverage, and uh, you know, over time that coverage can expand to other wound types as further evidence was available. For instance, looking at the HBO LCD there are different criteria and coverage limitations applied for uh diabetic wounds of the lower extremities, versus other types of ulcers. And so consistent with that prior procedure and policy, we would support the continuation of the policy as it appears to be in the proposed LCD, which is to not force a wholesale coverage decision on all chronic nonhealing wounds, but to analyze the available evidence uh specifically by wound type. And we appreciate the director, the medical directors' examination of this treatment area and look forward to further discussion. Thank you.

JODY WHITTEN

Next, we have um Dr. Matthew um Garoufalis please?

MATTHEW G. GAROUFALIS, DPM, FASPS, FACFAOM, CWS, FFMP, RCPS

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Thank you for allowing me to present, and we've had some wonderful speakers so far. Um I am going to talk about how to accurately assess the impact of topical wound therapy on wound healing. A little bit about myself. I am the past President of the American Podiatric Medical Association, uh Co-Chair of the Alliance Wound Care Stakeholders, Associate Chief of the Podiatry Section Surgery Service at Jesse Brown and Heinz VA Medical Centers in Chicago, as well as my private practice in Chicago, and also Clinical Associate Professor of Podiatric Medicine and Surgery, Western University of Health Sciences. It's amazing we are talking about oxygen because, in this past year, the Nobel Prize in Medicine was awarded in research on how cells manage oxygen. So, it's a very important topic, and a topic we've heard a lot about today, and um we are going to continue to hear more about this as we proceed.

My background and position on assessing topical oxygen is that I'm a recognized diabetic foot ulcer and topical oxygen clinical expert. I've treated over 500 patients suffering from diabetic foot ulcers with the multimodality AOTI Cyclical Intermittent Pressure Device. The majority of these patients are of Medicare age. Our experience is that we see the clinical outcomes and patient complaints consistent with that scene in the recently published AOTI diabetic foot ulcer RCT that has been reported at several leading clinical conferences already, and that is about 64% complete closure at 12 weeks. It should be noted that all topical oxygen devices are not equal as their oxygen delivery approaches greatly vary, and this clearly impacts the clinical efficacy as demonstrated by the various studies on the different manufacturers' devices. That is the AOTI Cyclical Intermittent

Pressure unique multimodality approach that provides both higher oxygen diffusion, radiant or humidified oxygen to penetrate into the wound tissue with noncontact cyclical compression to reduce edema.

Topical Oxygen Efficacy for Wound Healing. All chronic wounds are not equal, and they have different etiologies and standards of care. Clinical efficacy can only be fairly assessed based upon the evidence presented for a specific oxygen delivery approach and wound type. Combining different wound types and delivery approaches into a single study would make it impossible to draw confident conclusions about the effects of any specific approach on each type of wound. It is of course completely appropriate and consistent with previous LCD decisions to delineate coverage criteria to a specific approach within a broader category.

Limitations of the Proposed LCD for Topical Oxygen. The draft LCD does not accurately incorporate the outcomes from the most recent AOTI RCT on diabetic foot ulcers, as it was only published in Diabetes Care on November 16, 2019, after the reconsideration process had commenced. The study was incorrectly summarized in the draft LCD. The study addresses the concerns raised by the CAC, specifically, the need for an adequate number of Medicare age patients, a good standard of care comparator, reporting quality of life and a one-year follow-up. All of the Professional Society Recommendations and Guidelines and External Assessment cited were conducted prior to the publication of the AOTI Diabetic Foot randomized clinical trial on

October 16, 2019, so did not incorporate this pivotal new evidence in this delivery approach. Thank you very much.

JODY WHITTEN

Thank you. Next up we have Dr. Robert Frykberg.

ROBERT G. FRYKBERG, DPM, MPH, MAPWCA, FFPM

Good morning. I'm here to present data on a recently completed trial that uh several people mentioned already. I'll try to get through this as quickly as I can. Uh I've been in the wound healing space, diabetic foot space for many, many years, conducted a number of trials, trained many persons in this regard, and have great interest in management of diabetic foot ulcers. I wanted to present data on our trial. And I want to refer back to this 2017 Decision Memo which identified a number of deficiencies in diabetic foot ulcer trials as well as specifically topical wound oxygen trials. As we can see here, lack of effective blinding, randomization, uh incomplete wound healing measures, etc. They also in this same Decision Memo uh looked at the need for blinding, and they specifically mentioned one trial that was undergoing uh patient enrollment at the time and recommended that this design should be encouraged to use for further designs. And this uh publication, or this report that they mentioned was actually the trial that I'm going to present now, which we have uh completed.

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This was published in October of 2019 in a leading diabetes journal in the world, and this is specifically on the use of intermittent uh cyclical uh pressurized topical wound oxygen for chronic diabetic foot ulcers. And this protocol intentionally addressed the deficiencies previously annotated in a number of diabetic foot ulcer studies as well as uh topical oxygen studies. We used a group sequential design with three predetermined analyses points, using appropriate Pocock trial uh data stopping points, and as you can see, we used a PO2 of a P of 0.22, .022 rather than the typical .05 because of the three predetermined analyses. We used the two-week optimal uh standard of care, with gold standard offloading and sharp debridement. And we only enrolled patients who achieved less than 30% healing during that two-week run-in period. This was a randomized, double blind uh sham controlled uh trial, uh with two treatment arms, 90 minutes a day, five days per week. Our primary endpoint as indicated is ulcers achieving 100% healing at 12 weeks. We only uh used intention to treat analysis in this regard. Secondary endpoints, of course, wound area reduction, and specifically, 12-month incidence of both healing and recurrence as a measure of durability. We also measured quality of life.

This is one of the tables that we used. I just wanted to point out here that uh the average age in the TW02 arm was Medicare population, in fact the majority of patients in this trial were of the Medicare uh population.

Our results, uh complete healing at 12 weeks was our primary endpoint. We found very strong statistical significance in this regard with the active group about 42% and compared to the sham group at 13.5%. When we adjusted for the University of Texas Grade Measure of Severity, we found that the odds ratio actually increased uh to a six. And remember, this is a confidence interval of 97.8, not 95% confidence interval.

This Kaplan-Meier graph really tells the tale as far as I'm concerned. You can see the separation right from week one here, and this was uh associated with a positive uh Cox proportional hazard modeling also adjusted for University of Texas Grade, which showed a 4.5 times likelihood to heal DFUs over the uh 12-week time point.

Now also we wanted to show ah durable healing, so we also not just looked at the 12 weeks, the trial was also a 12-month outcome where we still saw a positive effect in this regard, 52% margin of effect and a 207% relative performance. We also saw uh only 7% of active patients recurred, compared to 40% in the sham arm. Because of uh small numbers in this regard, it didn't quite reach statistical significance. But by this very robust trial, we think that we have corroborated all the other evidence that you've already heard in a very robust, double blinded, sham controlled trial that proves our mind that the use of this therapy adjunctive to standard of care for diabetic foot ulcers certainly uh deserves consideration for uh approval. Thank you.

JODY WHITTEN

Thank you. Next up we have Dr. Michael Griffiths.

MICHAEL GRIFFITHS

Okay, thank you. Uh I'm Dr. Michael Griffiths, I am the CEO and Medical Director of Advanced Oxygen Therapy AOTI. We are one of the reconsideration requesters. Um and what I want to do is deal on the study data presented by Professor Frykberg relative to our reconsideration request. And you can see uh our product there in the corner. It's a little bit different to other topical true devices. And we want to outline a little bit what's unique about our approach, because I think it's important that all the topical devices are not the same. Firstly, we fit into the intermittent category, which means we are not continuous diffusion, we are not connected to the patient all the time. The patient uses our therapy, as you saw in the study, commonly for five days a week, 90 minutes per treatment, that they apply at home. What's also unique about our approach is that we are the only FDA cleared device that allows us to use cyclical pressure. And the benefit of that cyclical pressure is we are able to provide a higher diffusion gradient of humidified oxygen, with the multimodality of noncontact compression, which we believe has additional benefits of reducing edema and, as Professor Sen mentioned earlier, um signaling mechanisms in the wound.

Now the benefit that impacts all phases of wound healing, as you've seen for that very robust randomized study just presented, this includes a very high healing efficacy at 12 weeks, which has

been the established benchmark. And we show, in refractory DFU ulcers, proven non-failures of good standard of care up to six times more likely to heal at 12 weeks from that study. But also, when we looked at 12 months we showed a six-fold reduction in reoccurrence, which talks to the durability of the healing with topical oxygen where you have greater angiogenesis, more blood supply feeding the wound and by the quality collagen tissue.

And then additionally we've treated over 15,000 patients in both New York Medicaid and the Veterans Administration across the U.S. as well. So, you know, relative to the decision that the DME Medical Directors have to make relative to the statute and whether the therapy is reasonable and necessary, you know, part of the criteria for that is that it's, you know, effective and nonexperimental. And we believe that's demonstrated clearly by the randomized study just presented. You know, in that study we have appropriately powered the study to get significance. Um we had a optimized controlled standard of care, which used gold standard offloading, um equivalent toe to contact casting, and sharp debridement with simple dressings. Uh we ran those patients in to make sure that they had failed standard of care before they were randomized in the study; and then we had a predominant Medicare population; we looked at 12 weeks efficacy of healing, but also 12 months reoccurrence; and we looked at patient's quality of life. So, all of the components outlined as deficiencies in previous studies we believe we addressed. And then we have secondary studies that have been published that support those outcomes, and other

publications including the Yuma document that you cite that gives positive recommendations for topical oxygen.

You know, we also believe that our therapy is appropriate, and that, you know, it functions in accordance with accepted standards in appropriate clinical setting. Um we believe it should be used as a therapy once standard of care has been tried, like most adjunctive, and failed for 30 days um in diabetic foot ulcers. And this is supported I think by the peer reviewed evidence from the studies and the guidelines. And what's important in our study, also the point that we looked at University of Texas one and two ulcers, stages A through D. So, these are ulcers that are penetrating down to maximum tendon, not just superficial wounds. And also, a good number of them were infected and all with ischemia. So real world, hard to hit ulcers that have failed standard of care. And, very important, this is a home care therapy, very high compliance, easily applied by the patient at home.

Then again, we believe it's been, you know, ordered by qualified personnel and meets the beneficial need, you know, of those patients, as is evidenced again, you know, by the fact of prescription device from the FDA. The fact that it is, you know, used as we believe should be used as an adjunctive post failure of standard of care. And as we said in the study, as was demonstrated, um you know it looks at very robustly at wounds that have failed, that we then apply the therapy to as an adjunctive to that standard of care. Um and finally, if we move on then, you know, the

fact that only randomized patients that were in that study were ones that failed standard of care, so it's not easy to heal ulcers.

So, our recommendation and our request is a update to the LCD for coverage that would be specific, like other presenters have mentioned, to the evidence and the devices that are being um examined in those studies. So we believe the evidence for our device per the latest RCT supports that, you know, cyclical uh pressurized topical oxygen that cycles between 10 and 14 millibars, 15 millibars should be covered specifically for diabetic foot ulcers, because that's the level of evidence that currently exists. And could be incorporated in a bundle payment, like it is in New York Medicaid, in a similar structure. And some of the guidance then would also go further that there are criteria that could be established that they have to be failure of standard of care, on adequate nutritional diabetic maintenance plans, so that it is clear these patients are being managed appropriately and have failed standard of care before a more expensive modality is used. We believe that's the most appropriate way uh to delineate coverage for any of the devices. Thank you.

JODY WHITTEN

Thank you. Next up we have Dr. Angie Purvis.

ANGIE PURVIS, PhD

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Thank you very much for the opportunity to speak today. I'm here to present a retrospective chart review of chronic wound patients treated with topical oxygen therapy. I'm the senior author of the study. A little bit about the authors. My name is Angie Purvis, I have a PhD from Washington University. My expertise is in basic research, including uh work in regulatory affairs and clinical research. I worked with Dr. Karen Copeland, an esteemed mathematician, with a PhD from Clemson University. Uh she focuses on statistical analysis, specifically in clinical studies.

A little bit of background on the study. So, the purpose here was to assess the effectiveness of topical oxygen therapy under real world use conditions. To that end, we used a retrospective chart review design from data, uh using data on wounds treated with the O2 boot, or the O2 cycle devices. These wounds had been treated previously with a different modality. Um our study was conducted under exempt status granted by the IRB uh company.

For the study we extracted data from the GWR Medical Database. Um the total number of wounds included in that database at the time of extraction was 10,980 wounds. Um all of these records were reviewed against the inclusion criteria for the study, and a total of 3,462 patients were included in the study, which represented a total of 4,127 total wounds. For this study, we imposed the following inclusion criteria. These data accumulated over a 9-1/2-year period of time, between 2007 and 2016, all of the patients included in this study were treated with at least one separate modality prior to treatment with topical oxygen therapy. All of the patients had at least one chronic

wound that was at least one cm squared in area. Um the patients and their wounds were treated with topical oxygen therapy for a minimum of two weeks. The data excluded from the study included any, any data which had an incomplete data set, or any patients who were still receiving topical oxygen therapy at the time of uh the study.

The participants in the study were both male and female and ranged in age from four years old to 105 years old. When we look at the breakdown of patients included in the study you can see that there was a predominance of patients in the 65 plus age group, at almost 52%, and a total of 42% of patients included in the study listed Medicare as their primary insurance. For the wounds included in this study, the majority, approaching 60%, um experienced healing. When we looked at reasons for discontinuing topical oxygen therapy in this study, the predominant, the prominent reason was the wounds were healed, approaching 40%. When we looked at wound size, before and after treatment with topical oxygen therapy, you can see there was an even distribution at the beginning, and following treatment with topical oxygen therapy there was a rise in the smaller wound size for these patients.

When we look at chronic wounds from patients of all age groups, you can clearly see here that patients from all age groups experience some benefit from topical oxygen treatment. However, when we look at the 65 plus group, um this group experienced significant healing across the board. Um over 50% experienced at least some healing in the study, and when you look at patients who

um experienced 100% healing of their wounds, greater than 50% of those patients were from the 65 plus age group. Overall, the patients included in this study um had a low amputation rate after treatment with topical oxygen therapy. The rate was 2.4%.

Our key findings here include uh treatment. Wounds treated with topical oxygen therapy had a rate of healing similar to what we've seen um in controlled clinical studies. Uh chronic wounds treated with topical oxygen therapy have a low rate of amputation, regardless of their site, the age of the wound, the size of the wound at the beginning of treatment, and other clinical variables. Um these patients had increased quality of life -

JODY WHITTEN

Thank you. We are going to try to circle back and see if we have on the line Dr. Serena. Dr. Serena, if you are available can you please make sure your phone is un-muted? Okay, I'm being told that they are not there. Thank you. We'll turn it back over to Dr. Mamuya.

THOMAS E. SERENA, MD FACS FACHM MAPWCA

Hello. I'm here.

JODY WHITTEN

Dr. Serena?

THOMAS E. SERENA, MD FACS FACHM MAPWCA

Yeah, it is, someone had muted me, I had to un-mute myself. Sorry about that.

JODY WHITTEN

Oh, awesome, thank you. We can hear you.

THOMAS E. SERENA, MD FACS FACHM MAPWCA

All right, so I want to thank you very much for letting me present uh today, and it's really an area of tremendous interest and we've been studying topical oxygen for uh quite some time. I'm anxious just to put in my two cents. So, I'm Tom Serena, I run uh two organizations. One, the uh Serena Group, a family of wound and hyperbaric centers, and we have uh 30 some centers that do wound and hyperbaric medicine across the U.S. And a number of those uh are in, will be covered by this LCD. So, I basically have a large number, probably thousands of patients, that will be affected by the decisions uh made today. So that's one of the reasons I'm here. In addition, we have our foundation associated with this company, the Serena Group Research Foundation, uh that does clinical, uh clinical trials. And we run six to eight clinical trials uh at any given uh time during a year. And at present uh we have just completed a clinical trial, not presented here because the results are not done, uh analyzed yet, on topical oxygen.

Uh now you notice when I first started this introduction that I said uh wound and hyperbaric center, so I've been doing hyperbaric medicine for 30 years as well. So I must say that in the beginning I was a naysayer for topical oxygen, uh I think if you grew up in the world of hyperbaric medicine, uh topical oxygen uh doesn't seem like it's going to have positive effects. Uh I will tell you that I've learned a lot since then. Uh I've reviewed the EO2 trial with Dave Armstrong, who has already presented today. Very good data, a very well-run trial, and David is just a super investigator. I've had the pleasure of working with him for a couple of decades. So, uh we, uh so I've come over uh from uh to the topical oxygen side, if you will. I'm now - I now believe that uh the mechanistic actions as outlined by Dr. Sen and Dr. Gordillo uh clearly give us a reason for using topical oxygen. And now we have evidence in, in several clinical trials that demonstrate uh that there is efficacy of this modality. And speaking on behalf of our centers and the doctors and nurses and clinicians that work in those centers, we'd like to have this as an available modality. I mean one of the things that's still true in our centers, as good as we think we are, is that, you know, if you look at healing at 12 weeks in a patient, who is not in a clinical trial but just coming to the center, it still ranges around 40 to 50%. The patients need more modal - we need more. We need more arrows in the quiver in order to treat these patients and get them healed, particularly diabetic foot ulcer patients. The longer they are open, the longer they have this wound is exposed the more likely they are to develop osteomyelitis or even go on to amputation. And we've been able to show that in numerous clinical studies, and it's really a matter of time. The more rapidly I can get them healed, the better. And we need modalities that are efficacious uh in the treatment of these patients, um and

particularly those diabetic foot ulcers so we can get them healed and prevent amputation and long-term sequelae from that, from that uh, from the diabetic foot ulceration. So, uh I think with that I'll end. I was going to go over mechanism as well; I can't do a better job than Drs. Sen and Gordillo. Uh I will uh offer uh my email if anyone else, anyone on the committee would like to get a hold of me. I apologize, uh I had trouble getting on. I didn't uh note my disclosures, I have no disclosures, I'm here on behalf of my group. And thank you very much.

JODY WHITTEN

Thank you, sir. And with that, that's all we have. Uh Dr. Mamuya?

DR. FRED MAMUYA

Well, we would like to thank all the members of the public and stakeholders who came here to Dallas today, and gave us your thoughtful comments. I think the first is a reminder, please send them in writing. And if you have any uh full text, peer reviewed articles to help uh support your comments that are not included in the bibliography, please send them along. Uh process wise, the comment period ends I believe on February the 10th for this particular LCD. And then after that there is really no official timeline. I think we will carefully consider all the comments, carefully consider anything that is sent along with the comments, think about whether we are going to change any of the proposed language, and at some point, uh post the final LCD. Uh I tell everyone please don't email us because we will give you the same response, just watch our website, because

there is not a timeline other than that. Actually, that kind of is, there is a year at a um point where we have to do something if we haven't finalized it. I don't think that will be the case. I think we will get to it way before then. So once again, thank you everyone for coming, and uh we will formally adjourn and get ready for the next um open meeting. Thank you very much.