

Hyperbaric Oxygen Therapy (HBOT) for Tissue Damage Including Wound Care and Treatment of Central Nervous System (CNS) Conditions

Draft Report - Public Comments

February 15, 2013

Health Technology Assessment Program (HTA)

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**Hyperbaric Oxygen Therapy (HBOT) for Tissue
Damage Including Wound Care and Treatment of
Central Nervous System (CNS) Conditions**

Response to Public Comments on First Draft

2-15-2013

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**Response to Public Comments, Draft Report
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of Central Nervous System (CNS) Conditions**

Hayes, Inc. is an independent vendor contracted to produce evidence assessment reports for the WA HTA program. For transparency, all comments received during the comments process are included in this response document.

Comments related to program decisions, process, or other matters not pertaining to the evidence report are acknowledged through inclusion only. When comments cite evidence, the information is forwarded to the vendor for consideration in the evidence report.

This document responds to comments from the following parties:

- Agency Medical Director Group (AMDG) (letter from Nobuhara, Kerilyn, MD, MHA, representing the medical directors)
- American Association for Wound Care Management (AAWCM) (letter from John Capotorto, MD)

Table 1. Public Comments on the Final Report, HBOT

Comment and Source	Response
February 4, 2013 Comments on First Draft from the HCA Agency Medical Directors	
The Hayes report confirms that hyperbaric oxygen therapy is of benefit for the incidence of healing and amputation rates for treatment of diabetic foot ulcers. This finding is in alignment with the CMS National Coverage Determination (20.29) for hyperbaric oxygen use in the treatment of diabetic foot ulcers.	
p. 5 Please clarify the definitions of “incidence of healing” and “wound size reduction.” These terms are clinically synonymous and the finding that HBO treatment substantially improves healing but does not reduce wound size needs clarification.	Thank you for your comment. “The incidence of healing,” although not always defined in each study, typically refers to the proportion of wounds completely healed at a given endpoint and is often a primary study outcome; “wound size reduction,” on the other hand, is typically an intermediate outcome expressed as a proportional reduction in wound size from baseline. The authors agree that these two terms are clinically synonymous. The report did not find that HBOT was ineffective in reducing wound size; rather, the report found just one study that reported wound size reduction as an outcome. The conclusion of insufficient evidence, therefore, reflects the lack of evidence investigating wound size reduction rather than no effect. The report has been amended to clarify the distinction.
The findings are inconsistent for the use of HBOT in graft and flap survival/take and healing. However, NCD 20.29 covers “preparation and preservation of compromised skin grafts (not for primary management of wounds).”	Thank you for your comment. The results of compromised flaps and grafts were difficult to interpret because the control groups were different across studies. Overall, the body of evidence suggests a benefit to HBOT for improved graft/flap survival, although our confidence in that evidence is low because of methodological flaws. The final document has been amended to better clarify this fact.
p. 6 Did the 2010 Cochrane Review contain risk stratification in terms of comorbid conditions and/or severity of wounds? This cannot be ascertained in the summary table on page 122.	Thank you for your comment. The 2010 Cochrane review did not stratify by severity of wound or comorbid condition. The 2012 Cochrane review set out a priori to conduct a subgroup analysis on wound severity but found there was not enough data. The review was not stratified by comorbid conditions. No

	change has been made to the document.
p. 6 Key question 1a was not addressed for skin grafts: What is the optimal frequency, dose and duration of HBOT treatment? The dose included in the summary table on page 124 states 2-3.0 ATA, 45-120 minutes, does this also apply to the skin graft cases?	Thank you for your comment. Skin grafts are not included in KQ1a because no study looked at the optimal frequency, dose, or duration of HBOT for skin grafts. However, since publication of the draft report a series of summary of findings tables have been added to both the evidence summary section and as an appendix to the report. These tables contain relevant clinical details including dose, duration, and frequency of treatment across the included studies. No change has been made to the document.
p. 8 The low to very low quality of evidence rating was given to the literature review of HBOT for refractory osteomyelitis. Was information provided regarding the length of antibiotic treatment prior to initiation of HBOT and/or the number of surgical procedures performed prior to the initiation of HBOT? NCD 20.29 covers "Chronic refractory osteomyelitis, unresponsive to conventional medical and surgical management," is there any literature which may support the definition of "chronic" in the NCD?	Thank you for your comment. In terms of failed antibiotic and surgical treatments, studies varied with regards to how they defined "refractory osteomyelitis." No study specified the length of antibiotic treatment required. Common definitions included: <ul style="list-style-type: none"> • Failed response to debridement and intravenous antibiotics (no specifics provided) • One failed surgical procedure designed to eliminate the infection • One failed surgical procedure in addition to at least 6 months of infection and a history of recurrence • 6 months duration as well as failed aggressive surgical debridement and antibiotics • 6 months duration plus recurrence after 3 surgical procedures as well as failed antibiotics "Chronic" has therefore been defined rather broadly, although most studies specify a duration of 6 months of infection coupled with failed response to antibiotics and/or surgical intervention. Appropriate text has been added to the document to reflect these definitions.
p. 8 In late radiation tissue injury, including osteoradionecrosis and soft tissue radionecrosis, did the 2012 Cochrane review	Thank you for your comment. The 2012 Cochrane review does not define 'complete resolution.' No change has been made to the

define “complete resolution of tissue damage”?	document
p. 10 Key question 1a is not addressed for late radiation tissue injury: What is the optimal frequency, dose and duration of HBOT treatment? 30 sessions is listed in the summary.	Thank you for your comment. LRTI is not included in KQ1a because no study looked at the optimal frequency, dose, or duration of HBOT for LRTI. However, since publication of the draft report a series of summary of findings tables have been added to both the evidence summary section and as an appendix to the report. These tables contain relevant clinical details including dose, duration and frequency of treatment across the included studies. No change has been made to the document.
p. 10 Were the traumatic brain injury patients stratified according to injury severity scores? Was time to enrollment comparable between HBO and control groups? Was the cause of the mortality comparable between groups? This information cannot be ascertained from the summary table on p. 144.	Thank you for your comment. No study reported stratifying patients according to severity of injury. One study stratified according to type of injury and all studies included patients classified as having severe closed head injury. Just one study reported on group differences in terms of severity of injury. Neither the cause of mortality nor the differences between groups in terms of time to enrolment were described. Text has been added to the main body of the document to reflect this information.
p. 13 Clarify if patients treated with HBOT for multiple sclerosis also received drug therapy during the clinical trials.	Thank you for your comment. Concomitant drug therapies were not described for the included studies but were not an exclusion criterion. No change has been made to the document.
p. 14 Define acute migraine and time lapse between onset of headache and initiation of hyperbaric oxygen therapy.	Thank you for your comment. Neither “acute migraine” nor “the time lapse between onset and treatment” were defined by the included studies. No change has been made to the document.
p. 16 More than one treatment session can be provided in a given day, did any of the studies address the optimal number of treatment sessions which should be delivered in a day? In addition, hyperbaric oxygen treatment is coded and reimbursed in 30 minute increments, please define the length of a	Thank you for your comment. No studies looked directly at either the optimal number of treatment sessions or the effectiveness of multiple daily sessions. Since publication of the draft report, a series of summary of findings tables have been added to both the evidence summary section and as an appendix

treatment session in minutes.	to the report. These tables contain relevant clinical details including frequency of treatment.
p. 17 Elucidate the findings of “severe pulmonary complications among 13% of TBI patients,” were these also patients with higher baseline injury severity scores?	Thank you for your comment. Severe pulmonary complication was defined as either rising oxygen requirements and infiltrates in chest x-ray or cyanosis and hyperpnoea so severe as to imply “impending hyperoxic pneumonia.” These descriptions have been added to the report.
p. 45 Specify the quantity and duration of HBOT which the patients received, for example did they have daily, twice daily, three times per week treatment sessions for 6 continuous weeks or for 1 year?	Thank you for your comment. Since publication of the draft report, a series of summary of findings tables have been added to both the evidence summary section and as an appendix to the report. These tables contain relevant clinical details including dose, duration, and frequency of treatment.
p. 48 Specify the amount of HBOT treatment received in the graft and flap survival/take and healing studies. Include number of treatment sessions and duration of therapy.	Thank you for your comment. Since publication of the draft report, a series of summary of findings tables have been added to both the evidence summary section and as an appendix to the report. These tables contain relevant clinical details including dose, duration, and frequency of treatment.
p. 51 Define “cure” for refractory osteomyelitis.	Thank you for your comment. The definition of cure varied from study to study, including such terminology as “eradication of osteomyelitis,” “resolution of drainage,” and “free of clinical signs of the disease.” The text has been amended to include these broad definitions.
p. 54 Does “wound dehiscence” reference postoperative wound dehiscence in previously radiated fields?	Thank you for your comment. Yes, the results found a significant benefit to HBOT in terms of reducing postsurgical wound dehiscence among patients previously exposed to radiation in the surgical area. The text has been amended for clarity.
p. 73 What is TCOM? This acronym does not appear to be utilized earlier in the report.	Thank you for your comment. TCOM stands for transcutaneous oxygen measurement. The term first appears on page 72 of the draft. Page 73 has been amended for further clarity.

February 7**2013 Comments on First Draft from the American Association for Wound Care Management (AAWCM)**

<p>We believe the conclusions are inconsistent with the conclusions and expert recommendations for best practice from professional societies such as the Wound Healing Society, the Undersea and Hyperbaric Medicine Society, the American College of Hyperbaric Medicine, the European Tissue and Repair Society, and the American Society for Infectious Disease.</p>	<p>Thank you for your comment. This report was carefully designed to systematically and objectively assess the available evidence for the indications under review. The included studies are based on a literature search for peer-reviewed publications that meet a set of inclusion and exclusion criteria that were determined a priori. Data from the included literature was synthesized and then carefully assessed for internal validity at the level of the individual study. This was done using well-recognized quality assessment tools aligned with GRADE, the Cochrane Collaboration and the Agency for Healthcare Research and Quality. Subsequently, the overall body of evidence was quality graded to determine the strength of the evidence (using recognized quality grading tools based primarily on the GRADE system) . In this respect, the report does not set-out to be consistent with the recommendations of societies, but rather presents an objective systematic description of the state of the science.</p> <p>Incidentally, the findings of this report largely agree with the recommendations of many stakeholder societies particularly where the quality of evidence was found to be at least of moderate quality. No change has been made to the document.</p>
<p>The TA does not offer a clear definition of a “high quality” study as there are numerous published studies that provide the highest evidence “Level I evidence” as clearly defined by Sackett and others. This is to say, rigorous, prospective, double blind randomized trials.</p>	<p>Thank you for your comment. Of 138 primary data studies referenced for key question 1, 61 were RCTs, 4 were nonrandomized controlled trials, 8 were pre-post studies (7 uncontrolled, 1 with historical controls), and 64 were other observational studies, including prospective and retrospective cohorts as well as case series. Of these, 14 were considered good quality, 64 were considered fair quality and 79 were considered to be of poor or very poor</p>

	<p>quality across 40 measured outcomes (some studies looked at multiple outcomes).</p> <p>Of the 40 outcomes measured, the overall quality of the body of evidence (i.e., the strength of evidence) varied widely. Twelve outcomes were considered to have moderate-quality evidence from which the report could draw some meaningful conclusions. On the other hand, 28 outcomes had low- or very-low-quality evidence often due to the high risk of bias in the individual studies or simply as a result of the paucity of available studies. Few meaningful conclusions could be drawn for low- and very-low-quality evidence.</p> <p>The final report includes a detailed summary of findings table for each indication. These tables, in addition to the quality assessment methods outlined in Appendix II and in the methods section of the report, should provide greater transparency with regards to the quality assessment methodology employed in the report.</p>
The TA does not take into account the reviews and conclusions of other HBOT Technology Assessments and is missing several other key references.	<p>Thank you for your comment. Unfortunately, without specific references it is difficult to provide rationale for why certain publications may have been excluded from this review. The following is a list of common reasons why any one study or review did not appear in the report:</p> <ul style="list-style-type: none">• The study or review does not meet predefined inclusion/exclusion criteria.• The date of publication falls outside the search dates detailed in the methodology.• In the case of the current report, which relied on systematic reviews supplemented by primary data studies published after release of the most current/relevant systematic review, primary data studies that were excluded from a given systematic review would not have been included in the report except

	<p>through manual searching.</p> <ul style="list-style-type: none">• Where multiple systematic reviews/HTAs, detailing the same literature, were available for a given indication, the most comprehensive and/or current review was selected for inclusion.• As described in the report, there are limitations to the methodological approach employed in so far as specific details related to individual studies may not have been captured in the original systematic reviews or may have been reported with errors. There is always risk that missing or incorrect data is mistakenly incorporated into the new review. Despite this limitation, the methodological approach was chosen because it allowed the report to cover nine indications at once and the authors were careful to look for studies that may have been relevant but excluded by earlier reviews, and when there was any doubt over the accuracy of data, the original primary data study was pulled and assessed independently. <p>No change has been made to the document.</p>
<p>The TA does not take into account the conclusion reached by impartial peer review process. For example, the European Tissue Repair Society's Joint Conference on Oxygen and Tissue Repair's Recommendations by the International Jury (Ninikoski J, 2006).</p>	<p>Thank you for your comment. Please refer to page 79 of the draft report where the recommendations from the European Tissue Repair Society's Joint Conference on Oxygen and Tissue Repair are laid out in detail. The intent of the HTA is to present guidelines from key organizations separately to the results of the systematic review of the literature; in this way, the report provides an independent analysis of the state of the science but provides the committee with the findings of other key groups for consideration in the final policy decision process.</p>

<p>UHMS Committee Report</p> <p>The TA did not take into consideration the evidence based recommendations of the “Committee Report” which is published by the Undersea and Hyperbaric Medical Society. This publication is the product of an ongoing systematic, peer review process, which provides recommendations for best practice. It is frequently cited by government agencies and payers alike as a reliable resource for “best practice” as defined by available evidence. The individual chapters of the UHMS Hyperbaric Oxygen Therapy Indications are currently being published in the peer-reviewed literature, and should be included in any HBO TA. For your convenience we have attached a copy of the Committee Report.</p>	<p>Thank you for your comment. The 12th Edition of the Hyperbaric Oxygen Therapy Indications report from the Undersea and Hyperbaric Medical Society (UHMS) was considered for inclusion under the practice guidelines section of this HTA. However, the report is not published as a set of practice guidelines and is not housed at the National Guideline Clearinghouse. It does provide a considered narrative review of the body of the literature related to HBOT and provides several accounts of best practices in the field of clinical practice. It does not however, provide a set of definitive guidelines for each indication and provides no details of a systematic search for literature. The current HTA includes results from an entire chapter of the UHMS committee report (i.e. Refractory Osteomyelitis by Brett Hart). This chapter has been published as a systematic review of the literature (with all the necessary details) and therefore met the criteria for inclusion. All other chapters were also eligible for inclusion if they met defined inclusion criteria.</p>
<p>Healing at One Year</p> <p>The conclusions of the TA rely heavily on the conclusions of the 2012 Cochrane review, which states in their analysis that the three studies included in the analysis (i.e., Abidia, Duzgun and Londahl) had significant between-study heterogeneity ($I^2 = 85\%$). The authors state that the results of the analysis should be interpreted “with caution.” Given the heterogeneity of the studies, independent analysis of the original literature can provide a clearer understanding of the questions. The Londahl and Abidia studies had the highest standard in study design (randomized, double-blinded, placebo controlled trial) while the Duzgun study was a randomized, but unblinded, controlled trial. The results of the Londahl 2011 study clearly showed improved healing in the HBOT group vs the control</p>	<p>Thank you for your comment and considered analysis of this outcome. The report does not disagree with your assessment of the 1 year findings of the 2012 Cochrane review by Kranke and colleagues. Please refer to page 45 of the draft to find the following statement “the authors caution that the 12-month pooled estimate may not be accurate because of heterogeneity among studies.” Where there is significant heterogeneity in a pooled analysis, it is wise to look to see if assessment of the individual studies can provide further insights. Following careful consideration of the three studies in question, the Londahl et al. (2010) study provides good-quality evidence of complete healing at 1 year (52% in the HBOT group versus 29% in the control group, $P=0.03$). The Abidia (2003) study also reported complete healing at 1-year follow-up in 5 of 8</p>

<p>group at 1 year (52% vs 29%, $p = 0.03$) using intention to treat analysis. When using the per-protocol analysis, the results were even stronger (61% vs 27%, $p = 0.009$). The Abidia 2003 study showed no difference in the percent of healed wounds at 6 weeks (5/8 vs 1/8, $p = \text{NS}$), but did show improved healing in the HBOT group at 1 year (5/8 vs 0/8, $p = 0.027$). The Duzgun 2008 study did not break down their results specifically at the 1 year follow-up time period, instead citing a mean duration of follow-up of 92 ± 12 weeks. They did note, however, that no patients in the control group had healing of the wound without surgery (i.e., amputation, skin grafting, or operative debridement in the OR), but 33 patients in the HBOT group had spontaneous healing (0% vs 66%, $p < 0.05$). The study did lend itself to selection bias in this regard, however, as the decision whether to operate on the wound was made by a surgeon who was unblinded to then treatment group. While the Duzgun study had the greatest number of participants ($N=100$), it had the weakest reporting of results at the one-year mark. The Abidia and Londahl, studies, while having fewer patients, had much stronger study design and reporting specifically on the healing rate at the one year mark. We feel that this detailed analysis of the source literature gives greater insight into the effects of HBOT on the diabetic foot, and we question the results found in the Cochrane report.</p>	<p>patients in the HBOT group versus 0 of 8 in the control group ($P=0.026$) and had a medium risk of bias. The Duzgun trial, as you point out, has a high risk of bias preventing us from drawing meaningful conclusions from those findings. In terms of the overall conclusions for 1-year healing, the findings of these two studies provide moderate-quality evidence that HBOT improves healing at 1-year follow-up. The results of the report have been amended to add this detail.</p>
<p>Wound Size Reduction The TA cites the 2012 Cochrane Report's analysis of the Kessler 2003 study showing that HBOT reduced wound size when compared to controls at 2 weeks (41.8% vs. 21.7%, $p=0.04$), but did not show any effects on wound size decrease at 4 weeks (48% vs. 41%, $p=\text{NS}$). Neither the TA nor the Cochrane Report commented on the fact that both</p>	<p>Thank you for your comment. This is an important observation but speaks to the internal validity of the study and does not change the findings or the overall conclusions regarding the effectiveness of HBOT to reduce wound size. No change has been made to the document.</p>

<p>HBOT and Control groups were admitted for the first 2 weeks of the study while they were receiving HBOT (while seeing a difference in wound size reduction), and then both groups were subsequently discharged on their own recognizance (after which the difference disappeared). Given that offloading of a neuropathic diabetic foot ulcer is of paramount importance in wound healing, it is just as fair to speculate that HBOT does stimulate faster decrease in wound size, but any benefits of HBOT are vastly overwhelmed by inadequately offloading of neuropathic wounds.</p>	
<p>Minor Amputations The HBO TA suggests: <i>“HBOT provided no additional benefit in the rate of minor amputation.”</i> This statement oversimplifies the complex medical decision making with regard to amputations and efforts at limb salvage. Often a minor amputation is done to prevent a major amputation. Data from other studies not included in this review have suggested that HBOT decreases MAJOR amputations perhaps in exchange for minor amputations. Further, the “limb sparing” benefit of HBO is significant in terms of cost savings and quality of life for those patients who are spared from a major amputation. Thus, the conclusion that HBOT confers no improvement in the rate of minor amputations should not be an indictment of HBOT, but instead should be viewed in light of its ability to avoid major amputations.</p>	<p>Thank you for your comment. An association between the rates of major amputations as a result of minor amputations was not measured in any study included in this review. To ensure that that your point is not missed, a sentence has been added to the report clarifying that issue.</p>
<p>Transcutaneous Oximetry We believe the data regarding transcutaneous oximetry was improperly interpreted. The TA states that low level evidence suggests that elevated oxygen breathed under normobaric conditions outside of a hyperbaric chamber can determine which patients are most likely to benefit from HBOT. The analysis of the evidence regarding transcutaneous oximetry</p>	<p>Thank you for your comment. The draft report failed to distinguish between transcutaneous oxygen measurement (TCOM) under hyperbaric and normobaric conditions. That section has been amended in the final report to reflect the distinction and to present the evidence regarding TCOM as a predictor of a response to HBOT under both conditions.</p>

<p>(PtcO₂) fails to accurately convey the value of this technology in patient selection or its proper use. The observational study included 1144 diabetic patients undergoing HBO, making it one of the largest HBO studies ever published. More importantly, while an observational study design may be inadequate to prove the efficacy of HBO, it is able to establish the accuracy of PtcO₂ in predicting HBO outcome. PtcO₂ values obtained when breathing normobaric (sea level) air or oxygen are NOT a reliable way to predict the SUCCESS of HBO. However, PtcO₂ is quite good at predicting FAILURE to benefit from HBOT, which may be a more useful way to prevent wasted resources. Specifically, when changing from breathing normobaric (sea level) air to normobaric (sea level) oxygen, if the increase in PtcO₂ is < 10 mm Hg, or if the PtcO₂ decreases, then benefit from HBO₂T is highly unlikely (at least an 89% HBO₂T failure rate). The most accurate way to predict BENEFIT from HBO is to measure PtcO₂ when breathing oxygen inside the hyperbaric chamber. In diabetic foot ulcers, if a PtcO₂ > 200 mm Hg is achieved when breathing hyperbaric oxygen, the likelihood of benefit from HBOT is >84% and the accuracy of this test is 75%. Conversely, if the in-chamber PtcO₂ value is < 100 mm Hg, benefit from HBO is unlikely. This test is 89% accurate at predicting failure of HBO. We know of no published studies which have attempted to predict the success or failure of any other advanced modalities used in the management of diabetic foot ulcers and believe the efforts of the hyperbaric community to use PtcO₂ as a guide to patient selection (including who might NOT benefit) is unique.</p>	
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Refractory Osteomyelitis

The TA indicates “*good-quality studies are necessary to determine the effectiveness of HBOT for the treatment of refractory osteomyelitis*” (page 8). This statement reflects a lack of understanding of the clinical barriers that preclude “good quality studies”. Fundamental to the scientific method is the precept of having only one variable – the treatment variable – so that clear conclusions can be drawn. The clinical complexity of osteomyelitis does not allow such a study for the following two reasons:

- **Surgical Variability** – Chronic osteomyelitis is a surgical disease. As such, it is impossible to control for variability of surgical technique among surgeons. It should also be pointed out that statistically it would be difficult using power analysis to even determine what the sample size should be
- **Antibiotic Variability** – Chronic osteomyelitis is also a medical disease and requires the use of antibiotics. In a well design trial there should only be one variable (HBO). However the practical reality is that the study subjects cannot all receive the same antibiotics for the simple reason that there will be variability in the organisms as well as the host.

However, there is high quality evidence that is available using highly controlled, well designed animal studies, which scientifically demonstrate a beneficially effect. From a practical perspective, it is unrealistic to await the “perfect” clinical study. We agree with the conclusions found in the UHMS Committee Report, which states: “while no randomized clinical trials exist, the overwhelming majority of published animal data, human case series and prospective trials support HBO2 therapy as a safe and effective adjunct to the management of refractory osteomyelitis. Further, when used appropriately, HBO2

Thank you for your comment. While not disagreeing with the basis for your argument, the challenges associated with conducting good-quality studies are not in themselves a reason to upgrade poor-quality evidence, and do not change the conclusions of this report as they relate to the need for better evidence on the use of HBOT for treating osteomyelitis. Twenty-one of the 23 included studies on osteomyelitis were case series. Well-conducted prospective cohort studies are possible and could shed important light on the effectiveness of HBOT to treat osteomyelitis. It is challenging but not impossible to account for confounders in the analysis of such a study.

<p>therapy appears to reduce the total need for surgical procedures, required antibiotic therapy and, consequently, overall health care expenditures.” provide the best guidance for the use of HBO in refractory osteomyelitis.</p>	
<p>Harms</p> <p>We do agree with the TA conclusion regarding the safety of HBO therapy. The TA states: “<i>the harms associated with HBOT are usually mild, self-limiting with most resolving after termination of treatment. The most common harms include myopia, barotrauma, claustrophobia, and oxygen toxicity. Life-threatening adverse events are rare but do occur on occasion and can include seizures and death. There is insufficient evidence to comment on specific risks for subpopulations.</i>” (page 16)</p> <p>We concur with the conclusions in the report and offer further evidence. A study with the largest reported series of hyperbaric oxygen treatments reporting adverse events supports the conclusion that hyperbaric oxygen treatment for a wide range of indications in patients with many comorbidities can be accomplished with an extremely low incidence of adverse effects.</p> <p><i>Analysis of Adverse Events Occurring in Patients Undergoing Adjunctive Hyperbaric Oxygen Treatment: 2009-2010. Beard T, Watson B, Barry R, Stewart D, Warriner R Diversified Clinical Services, Jacksonville, FL (Poster and Abstract)</i></p>	<p>Thank you for your comment. We did not include posters and abstracts in the current report but are grateful for the additional information.</p>
<p>Cost Effectiveness</p> <p>The review was incomplete in citing evidence that speaks to cost effectiveness for the use of HBO. For example it did not include the findings of the International Jury convened by the European Tissue Repair Society. For your convenience we have included a partial summary of their findings:</p> <p>1. In determining the cost-effectiveness of</p>	<p>Thank you for your comment. The National Health Service Economic Evaluation Database, as part of the UK Research Center for Reviews and Dissemination (NHS-CRD), was searched for economic evaluation. In addition, the following search string was used in PubMed to identify economic evaluation and cost-specific studies:</p> <p>((((economic analysis) OR (economic evaluation)))) OR (((((cost AND</p>

<p>HBO in the management of delayed wound healing, certain assumptions have had to be made to simplify calculations. Prospective research is recommended, but for the time being, the jury has confidence that these approaches rival the economic basis for decisions made in other fields of health care.</p> <p>2. Based on projections using the Persels formula applied to the currently available data, a significant savings can be achieved using HBO as a standard adjunct in treating necrotizing infections, diabetic ulcers, and radiation necrosis as currently recommended by the European Committee for Hyperbaric Medicine and Undersea and Hyperbaric Medical Society. The number of HBO treatments has a significant impact on cost-effectiveness ratios. Clinical guidelines are recommended to ensure optimal cost-effectiveness (type I recommendation).</p> <p>3. Based on these data, HBO for the problem wounds listed in the analysis appears to be not only clinically effective but also likely to reduce the general costs of a nation's health care, reduce the social impact of related illnesses, and offer a better quality of life.</p> <p>These findings are consistent with the technology assessment commissioned by the Canadian Government: "Adjunctive HBOT for Diabetic Foot Ulcers is cost-effective compared with standard care. The 12 year cost for patient receiving HBOT was CND \$40,695 compared with \$49,786 for standard care alone. Outcomes were 3.64 quality-adjusted life-years (QALYs) for those receiving HBOT and 3.01 QALYs for controls." Chuck AW, et al. Int J of Technology Assessment in Health Care, 24:2 (2008), 178-183. Similar conclusions were noted in the paper by Cianci et al. Here is the summary of their study: "A cohort of 41 patients with diabetes with severe, chronic foot wounds was selected</p>	<p>(analysis OR benefit OR effective* OR consequence OR minimization)))) OR ("Costs and Cost Analysis"[MeSH] OR "Cost-Benefit Analysis"[MeSH])))) AND Hyperbaric Oxygenation"[Mesh].</p> <p>The findings of the International Jury convened by the European Tissue Repair Society were included under the guidelines section of the report and the Cianci et al. study was part of the systematic review to determine the cost-effectiveness of HBOT conducted by the UK National Health Service (NHS) (Ritchie et al., 2008) and can be found in question 4.</p>
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by a neutral, blinded observer who had no knowledge of the outcomes from a group of 101 consecutive such patients who had been treated at our wound center from 1983 to 1990. All had limb-threatening lesions, scoring 3 to 4 on the Wagner scale, were treated for at least 7 days with adjunctive hyperbaric oxygen, and had photographic and medical documentation. Durability of wound repair was examined in 1991 and 1993. Initial limb salvage was 85%. Mean hospital charges were \$31,264, including average hyperbaric charges of \$15,000. At the initial review, 28 of the patients with previously salvaged limbs (80%) were contacted. Of the 28 patients, 27 remained intact (96%). The mean durability of repair was 2.6 years. At the second review, the mean duration of repair in surviving patients was 4.6 years with no further expenditures relative to the salvaged limb. In patients who died, average durability was 3.4 years, also without additional expenditure referable to the salvaged extremity. Most complex lower extremity lesions were healed by a comprehensive wound care program which included vascular surgery and hyperbaric oxygen. The results were durable, and the treatment was cost effective and humane compared with early amputation.”

<p>Evidence for Evolving Indications</p> <p>The field of hyperbaric therapy continues to evolve through scientific findings published in peer reviewed journals. There are numerous prospective, randomized, controlled studies that demonstrate the clinical benefits of HBO therapy for conditions that currently have no therapeutic solutions. The following are three such examples of “level 1” evidence that support the benefits of HBO therapy.</p> <p>Acute Sensorineural Hearing Loss</p> <p>In a recent review in the Journal of Laryngology and Otology, the authors concluded “Hyperbaric oxygen therapy has a strong scientific rationale, and improves pure tone hearing thresholds in cases of sudden sensorineural hearing loss unresponsive to medical therapy. Further research may be able to identify those patients with sudden sensorineural hearing loss for whom hyperbaric oxygen therapy would be most cost-effective.”</p> <p><i>Muzzi E, et al. J Laryngol Otol. 2010 Feb;124(2)</i></p> <p>Stroke Recovery</p> <p>A prospective, randomized, controlled trial including 74 patients (15 were excluded). All participants suffered a stroke 6-36 months prior to inclusion and had at least one motor dysfunction. After inclusion, patients were randomly assigned to “treated” or “cross” groups. Brain activity was assessed by SPECT imaging; neurologic functions were evaluated by NIHSS, ADL, and life quality. Outcome analysis found that “HBOT can lead to significant neurological improvements in post stroke patients even at chronic late stages. The observed clinical improvements imply that neuroplasticity can still be activated long after damage onset in regions where there is a brain SPECT/CT (anatomy/physiology) mismatch.”</p>	<p>Thank you for your comment. The Muzzi et al. (2010) study is included under the section on HBOT for the treatment of acute sensorineural hearing loss (page 65 of the draft).</p> <p>Stroke was not an indication under review for the current report.</p> <p>The preliminary report from the Harch et al. (2012) study was not included in this report because it did not meet the inclusion/exclusion criteria. We agree that publication of the final report will add important findings to the evidence on the use of HBOT for the treatment of TBI.</p>
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ClinicalTrials.gov NCT00715897 | Efrati S, et al. PLoS One. 2013;8(1).

Traumatic Brain Injury

This rigorously designed study is funded by the US Department of Defense. A preliminary report on the prospective, randomized, clinical trial, for the use of hyperbaric oxygen for the treatment of traumatic brain injury was recently published. The statistical analysis at this juncture indicate "Significant improvements occurred in symptoms, abnormal physical exam findings, cognitive testing, and quality-of-life measurements, with concomitant significant improvements in SPECT."

Harch PG, et al. J Neurotrauma. 2012 Jan 1;29(1):168-85.

Agency Medical Directors Comments on Draft Report:

Hyperbaric Oxygen Therapy for Tissue Damage, Including Wound Care and Treatment of Central Nervous System Conditions

Hyperbaric oxygen treatment (HBO2) is presently utilized for a wide variety of diagnoses. In certain clinical situations, such as acute carbon monoxide intoxication, cyanide poisoning, decompression illness, gas embolism, gas gangrene and progressive necrotizing infections, hyperbaric oxygen treatment is a life-saving intervention. These diagnoses were intentionally excluded from consideration for this report. For many other conditions, however, indications for hyperbaric oxygen treatment and the frequency, dose and duration of this treatment remain poorly defined.

The CMS National Coverage Determination for Hyperbaric Oxygen Therapy covers some of the diagnoses addressed in this report. The AMDG work group requested evidence to assist in the selection of conditions of coverage for these diagnoses, such as identification of patients for whom the treatment is most effective, risk stratification of different diseases, the duration and frequency of the HBOT, and cost implications. This Hayes report effectively summarizes the quality and limitations of evidence for the remaining diagnoses selected by the AMDG workgroup.

The Hayes report confirms that hyperbaric oxygen therapy is of benefit for the incidence of healing and amputation rates for treatment of diabetic foot ulcers. This finding is in alignment with the CMS national coverage determination (20.29) for hyperbaric oxygen use in the treatment of diabetic foot ulcers¹:

Diabetic wounds of the lower extremities in patients who meet the following three criteria:

- a) Patient has type I or type II diabetes and has a lower extremity wound that is due to diabetes
- b) Patient has a wound classified as Wagner grade III or higher
- c) Patient has failed an adequate course of standard wound therapy

p. 5: Please clarify the definitions of “incidence of healing” and “wound size reduction.” These terms are clinically synonymous and the finding that HBO treatment substantially improves healing but does not reduce wound size needs clarification.

The findings are inconsistent for the use of HBOT in graft and flap survival/take and healing. However, NCD 20.29 covers “preparation and preservation of compromised skin grafts (not for primary management of wounds).”

p. 6 Did the 2010 Cochrane Review contain risk stratification in terms of co morbid conditions and/or severity of wounds, this cannot be ascertained in the summary table on page 122.

¹ Centers for Medicare & Medicaid Services, National Coverage Determination for Hyperbaric Oxygen Therapy (20.29); <http://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=12&ncdver=3&bc=AAAAgAAAAA&>

p. 6 Key Question 1a was not addressed for skin grafts: What is the optimal frequency, dose and duration of HBOT treatment? The dose included in the summary table on page 124 states 2-3.0 ATA, 45-120 minutes, does this also apply to the skin graft cases?

p. 8 The low to very low quality of evidence rating was given to the literature review of HBOT for refractory osteomyelitis. Was information provided regarding the length of antibiotic treatment prior to initiation of HBOT and/or the number of surgical procedures performed prior to the initiation of HBOT? NCD 20.29 covers "Chronic refractory osteomyelitis, unresponsive to conventional medical and surgical management," is there any literature which may support the definition of "chronic" in the NCD?

p. 8 In late radiation tissue injury, including osteoradionecrosis and soft tissue radionecrosis, did the 2012 Cochrane review define "complete resolution of tissue damage?"

p. 10 Key question 1a is not addressed for late radiation tissue injury: What is the optimal frequency, dose and duration of HBOT treatment? 30 sessions is listed in the summary table on page 138.

p. 10 Were the traumatic brain injury patients stratified according to injury severity scores? Was time to enrollment comparable between HBO and control groups? Was the cause of the mortality comparable between groups? This information cannot be ascertained from the summary table on p. 144.

p. 13 Clarify if patients treated with HBOT for Multiple Sclerosis also received drug therapy during the clinical trials.

p. 14 Define acute migraine and time lapse between onset of headache and initiation of hyperbaric oxygen therapy.

p. 16 More than one treatment session can be provided in a given day, did any of the studies address the optimal number of treatment sessions which should be delivered in a day? In addition, hyperbaric oxygen treatment is coded and reimbursed in 30 minute increments, please define the length of a treatment session in minutes.

p. 17 Elucidate the findings of "severe pulmonary complications among 13% of TBI patients," were these also patients with higher baseline injury severity scores?

p. 45 Specify the quantity and duration of HBOT which the patients received, for example did they have daily, twice daily, three times per week treatment sessions for 6 continuous weeks or for 1 year?

p. 48 Specify the amount of HBOT treatment received in the graft and flap survival/take and healing studies. Include number of treatment sessions and duration of therapy.

p. 51 Define "cure" for refractory osteomyelitis.

p. 54 Does "wound dehiscence" reference postoperative wound dehiscence in previously radiated fields?

p. 73 What is TCOM? This acronym does not appear to be utilized earlier in the report.

American Association for Wound Care Management comments on the Washington State HealthCare Authority Technology Assessment Hyperbaric Oxygen Therapy (HBOT)
February 7, 2013

The American Association for Wound Care Management ("AAWCM") respectfully submits these comments regarding *Hyperbaric Oxygen Therapy (HBOT) for Tissue Damage, Including Wound Care and Treatment of Central Nervous System (CNS) Conditions*, A Health Technology Assessment ("HBO TA").

AAWCM's membership represents over 750 outpatient wound care clinics throughout the United States, most with outpatient hyperbaric oxygen therapy ("HBOT") wound care clinics. We are pleased that the authors of the Technology Assessment have solicited comments that will collectively lead to smarter health care decisions – decisions that will benefit the health and welfare of all Americans.

We are writing to express our concern with several aspect of the Technology Assessment (TA) as noted below:

- We believe the conclusions are inconsistent with the conclusions and expert recommendations for best practice from professional societies such as the Wound Healing Society, the Undersea and Hyperbaric Medicine Society, the American College of Hyperbaric Medicine, the European Tissue and Repair Society, and the American Society for Infectious Disease.
- The TA does not offer a clear definition of a "high quality" study as there are numerous published studies that provide the highest evidence "Level I evidence" as clearly defined by Sackett and others. This is to say, rigorous, prospective, double blind randomized trials.
- The TA does not take into account the reviews and conclusions of other HBOT Technology Assessments and is missing several other key references
- The TA does not take into account the conclusion reached by impartial peer review process. For example, the European Tissue Repair Society's Joint Conference on Oxygen and Tissue Repair's Recommendations by the International Jury (Ninikoski J, 2006).

The AAWCM offers several helpful observations and resources that we believe should be considered before drawing any final conclusions. We acknowledge, in advance, that the window for commentary precluded extensive analysis or comment for any given indication.

UHMS Committee Report

The TA did not take into consideration the evidence based recommendations of the "Committee Report" which is published by the Undersea and Hyperbaric Medical Society. This publication is the product of an ongoing systematic, peer review process, which provides recommendations for best practice. It is frequently cited by government agencies and payors alike as a reliable resource for "best practice" as defined by available evidence. The individual chapters of the UHMS Hyperbaric Oxygen Therapy Indications are currently being published in the peer-reviewed literature, and

should be included in any HBO TA. For your convenience we have attached a copy of the Committee Report.

Healing at One Year

The conclusions of the TA rely heavily on the conclusions of the 2012 Cochrane review, which states in their analysis that the three studies included in the analysis (*i.e.*, Abidia, Duzgan and Londahl) had significant between-study heterogeneity ($I^2 = 85\%$). The authors state that the results of the analysis should be interpreted “with caution.” Given the heterogeneity of the studies, independent analysis of the original literature can provide a clearer understanding of the questions. The Londahl and Abidia studies had the highest standard in study design (randomized, double-blinded, placebo controlled trial) while the Duzgan study was a randomized, but unblinded, controlled trial.

The results of the Londahl 2011 study clearly showed improved healing in the HBOT group vs the control group at 1 year (52% vs. 29%, $p = 0.03$) using intention to treat analysis. When using the per-protocol analysis, the results were even stronger (61% vs. 27%, $p = 0.009$).

The Abidia 2003 study showed no difference in the percent of healed wounds at 6 weeks (5/8 vs. 1/8, $p = \text{NS}$), but did show improved healing in the HBOT group at 1 year (5/8 vs. 0/8, $p = 0.027$).

The Duzgan 2008 study did not break down their results specifically at the 1 year follow-up time period, instead citing a mean duration of follow-up of 92 ± 12 weeks. They did note, however, that no patients in the control group had healing of the wound without surgery (*i.e.*, amputation, skin grafting, or operative debridement in the OR), but 33 patients in the HBOT group had spontaneous healing (0% vs. 66%, $p < 0.05$). The study did lend itself to selection bias in this regard, however, as the decision whether to operate on the wound was made by a surgeon who was unblinded to the treatment group.

While the Duzgan study had the greatest number of participants ($N=100$), it had the weakest reporting of results at the one-year mark. The Abidia and Londahl, studies, while having fewer patients, had much stronger study design and reporting specifically on the healing rate at the one-year mark. We feel that this detailed analysis of the source literature gives greater insight into the effects of HBOT on the diabetic foot, and we question the results found in the Cochrane report.

Wound Size Reduction

The TA cites the 2012 Cochrane Report’s analysis of the Kessler 2003 study showing that HBOT reduced wound size when compared to controls at 2 weeks (41.8% vs. 21.7%, $p = 0.04$), but did not show any effects on wound size decrease at 4 weeks (48% vs. 41%, $p = \text{NS}$). Neither the TA nor the Cochrane Report commented on the fact that both HBOT and Control groups were admitted for the first 2 weeks of the study while they were receiving HBOT (while seeing a difference in wound size reduction), and then both groups were subsequently discharged on their own recognizance (after which the difference disappeared). Given that offloading of a neuropathic diabetic foot ulcer is of paramount importance in wound healing, it is just as fair to speculate that HBOT does stimulate faster decrease in wound size, but any benefits of HBOT are vastly overwhelmed by inadequately offloading of neuropathic wounds.

Minor Amputations

The HBO TA suggests: *"HBOT provided no additional benefit in the rate of minor amputation."* This statement oversimplifies the complex medical decision making with regard to amputations and efforts at limb salvage. Often a minor amputation is done to prevent a major amputation. Data from other studies not included in this review have suggested that HBOT decreases MAJOR amputations perhaps in exchange for minor amputations. Further, the "limb sparing" benefit of HBO is significant in terms of cost savings and quality of life for those patients who are spared from a major amputation. Thus, the conclusion that HBOT confers no improvement in the rate of minor amputations should not be an indictment of HBOT, but instead should be viewed in light of its ability to avoid major amputations.

Transcutaneous Oximetry

We believe the data regarding transcutaneous oximetry was improperly interpreted. The TA states that low level evidence suggests that elevated oxygen breathed under normobaric conditions outside of a hyperbaric chamber can determine which patients are most likely to benefit from HBOT.

The analysis of the evidence regarding transcutaneous oximetry (PtcO₂) fails to accurately convey the value of this technology in patient selection or its proper use. The observational study included 1144 diabetic patients undergoing HBO, making it one of the largest HBO studies ever published. More importantly, while an observational study design may be inadequate to prove the efficacy of HBO, it is able to establish the accuracy of PtcO₂ in predicting HBO outcome. PtcO₂ values obtained when breathing normobaric (sea level) air or oxygen are NOT a reliable way to predict the SUCCESS of HBO. However, PtcO₂ is quite good at predicting FAILURE to benefit from HBOT, which may be a more useful way to prevent wasted resources. Specifically, when changing from breathing normobaric (sea level) air to normobaric (sea level) oxygen, if the increase in PtcO₂ is < 10 mm Hg, or if the PtcO₂ decreases, then benefit from HBO2T is highly unlikely (at least an 89% HBO2T failure rate). The most accurate way to predict BENEFIT from HBO is to measure PtcO₂ when breathing oxygen inside the hyperbaric chamber. In diabetic foot ulcers, if a PtcO₂ > 200 mm Hg is achieved when breathing hyperbaric oxygen, the likelihood of benefit from HBOT is >84% and the accuracy of this test is 75%. Conversely, if the in-chamber PtcO₂ value is < 100 mm Hg, benefit from HBO is unlikely. This test is 89% accurate at predicting failure of HBO. We know of no published studies which have attempted to predict the success or failure of any other advanced modalities used in the management of diabetic foot ulcers and believe the efforts of the hyperbaric community to use PtcO₂ as a guide to patient selection (including who might NOT benefit) is unique.

Refractory Osteomyelitis

The TA indicates *"good-quality studies are necessary to determine the effectiveness of HBOT for the treatment of refractory osteomyelitis"* (page 8). This statement reflects a lack of understanding of the clinical barriers that preclude "good quality studies". Fundamental to the scientific method is the precept of having only one variable – the treatment variable – so that clear conclusions can be drawn. The clinical complexity of osteomyelitis does not allow such a study for the following two reasons:

- **Surgical Variability** – Chronic osteomyelitis is a surgical disease. As such, it is impossible to control for variability of surgical technique among surgeons. It should also be pointed out that

statistically it would be difficult using power analysis to even determine what the sample size should be

- **Antibiotic Variability** – Chronic osteomyelitis is also a medical disease and requires the use of antibiotics. In a well design trial there should only be one variable (HBO). However the practical reality is that the study subjects cannot all receive the same antibiotics for the simple reason that there will be variability in the organisms as well as the host.

However, there is high quality evidence that is available using highly controlled, well designed animal studies, which scientifically demonstrate a beneficially effect. From a practical perspective, it is unrealistic to await the “perfect” clinical study. We agree with the conclusions found in the UHMS Committee Report, which states: “while no randomized clinical trials exist, the overwhelming majority of published animal data, human case series and prospective trials support HBO₂ therapy as a safe and effective adjunct to the management of refractory osteomyelitis. Further, when used appropriately, HBO₂ therapy appears to reduce the total need for surgical procedures, required antibiotic therapy and, consequently, overall health care expenditures.” provide the best guidance for the use of HBO in refractory osteomyelitis

Harms

We do agree with the TA conclusion regarding the safety of HBO therapy. The TA states: “the harms associated with HBOT are usually mild, self-limiting with most resolving after termination of treatment. The most common harms include myopia, barotrauma, claustrophobia, and oxygen toxicity. Life-threatening adverse events are rare but do occur on occasion and can include seizures and death. There is insufficient evidence to comment on specific risks for subpopulations.” (page 16)

We concur with the conclusions in the report and offer further evidence. A study with the largest reported series of hyperbaric oxygen treatments reporting adverse events supports the conclusion that hyperbaric oxygen treatment for a wide range of indications in patients with many co-morbidities can be accomplished with an extremely low incidence of adverse effects.

Analysis of Adverse Events Occurring in Patients Undergoing Adjunctive Hyperbaric Oxygen Treatment: 2009-2010. Beard T, Watson B, Barry R, Stewart D, Warriner R Diversified Clinical Services, Jacksonville, FL (Poster and Abstract)

Cost Effectiveness

The review was incomplete in citing evidence that speaks to cost effectiveness for the use of HBO. For example it did not include the findings of the International Jury convened by the European Tissue Repair Society. For your convenience we have included a partial summary of their findings:

1. In determining the cost-effectiveness of HBO in the management of delayed wound healing, certain assumptions have had to be made to simplify calculations. Prospective research is recommended, but for the time being, the jury has confidence that these approaches rival the economic basis for decisions made in other fields of health care.
2. Based on projections using the Persels formula applied to the currently available data, a significant savings can be achieved using HBO as a standard adjunct in treating necrotizing infections, diabetic ulcers, and radiation necrosis as currently recommended by the European Committee for Hyperbaric Medicine and Undersea and Hyperbaric Medical Society. The

number of HBO treatments has a significant impact on cost-effectiveness ratios. Clinical guidelines are recommended to ensure optimal cost-effectiveness (type I recommendation).

3. Based on these data, HBO for the problem wounds listed in the analysis appears to be not only clinically effective but also likely to reduce the general costs of a nation's health care, reduce the social impact of related illnesses, and offer a better quality of life.

These findings are consistent with the technology assessment commissioned by the Canadian Government: "Adjunctive HBOT for Diabetic Foot Ulcers is cost-effective compared with standard care. The 12 year cost for patient receiving HBOT was CND \$40,695 compared with \$49,786 for standard care alone. Outcomes were 3.64 quality-adjusted life-years (QALYs) for those receiving HBOT and 3.01 QALYs for controls." Chuck AW, et al. *Int J of Technology Assessment in Health Care*, 24:2 (2008), 178-183.

Similar conclusions were noted in the paper by Cianci et al. Here is the summary of their study: "A cohort of 41 patients with diabetes with severe, chronic foot wounds was selected by a neutral, blinded observer who had no knowledge of the outcomes from a group of 101 consecutive such patients who had been treated at our wound center from 1983 to 1990. All had limb-threatening lesions, scoring 3 to 4 on the Wagner scale, were treated for at least 7 days with adjunctive hyperbaric oxygen, and had photographic and medical documentation. Durability of wound repair was examined in 1991 and 1993. Initial limb salvage was 85%. Mean hospital charges were \$31,264, including average hyperbaric charges of \$15,000. At the initial review, 28 of the patients with previously salvaged limbs (80%) were contacted. Of the 28 patients, 27 remained intact (96%). The mean durability of repair was 2.6 years. At the second review, the mean duration of repair in surviving patients was 4.6 years with no further expenditures relative to the salvaged limb. In patients who died, average durability was 3.4 years, also without additional expenditure referable to the salvaged extremity. Most complex lower extremity lesions were healed by a comprehensive wound care program which included vascular surgery and hyperbaric oxygen. The results were durable, and the treatment was cost effective and humane compared with early amputation."

Evidence for Evolving Indications

The field of hyperbaric therapy continues to evolve through scientific findings published in peer reviewed journals. There are numerous prospective, randomized, controlled studies that demonstrate the clinical benefits of HBO therapy for conditions that currently have no therapeutic solutions. The following are three such examples of "level 1" evidence that support the benefits of HBO therapy.

Acute Sensorineural Hearing Loss

In a recent review in the *Journal of Laryngology and Otology*, the authors concluded "Hyperbaric oxygen therapy has a strong scientific rationale, and improves pure tone hearing thresholds in cases of sudden sensorineural hearing loss unresponsive to medical therapy. Further research may be able to identify those patients with sudden sensorineural hearing loss for whom hyperbaric oxygen therapy would be most cost-effective."

Muzzi E, et al. J Laryngol Otol. 2010 Feb;124(2)

Stroke Recovery

A prospective, randomized, controlled trial including 74 patients (15 were excluded). All participants suffered a stroke 6-36 months prior to inclusion and had at least one motor dysfunction. After inclusion, patients were randomly assigned to "treated" or "cross" groups. Brain activity was assessed by SPECT imaging; neurologic functions were evaluated by NIHSS, ADL, and life quality. Outcome analysis found that "HBOT can lead to significant neurological improvements in post stroke patients even at chronic late stages. The observed clinical improvements imply that neuroplasticity can still be activated long after damage onset in regions where there is a brain SPECT/CT (anatomy/physiology) mismatch."

ClinicalTrials.gov NCT00715897 | Efrati S, et al. PLoS One. 2013;8(1).

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Harch PG, et al. J Neurotrauma. 2012 Jan 1;29(1):168-85.

Conclusion

We commend the Washington Healthcare Authority for its broad-based review of hyperbaric indications and appreciate being included in the dialogue on the effectiveness of HBOT in the treatment of chronic non healing wounds. Please contact our Executive Director Jule Crider at 301-933-2200 for further discussion on any of the comments that we have provided. She will serve as the point of communication.

Respectfully,
John Capotorto, M.D.
President AAWCM