Medical Coverage Policy

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Hyperbaric and Topical Oxygen Therapies

Table of Contents

Related Coverage Resources

Autism Spectrum Disorders/Pervasive Developmental Disorders: Assessment and Treatment
Bone Growth Stimulators: Electrical (Invasive, Noninvasive), Ultrasound
Complementary and Alternative Medicine
COVID-19 Drug and Biologic Therapeutics
COVID-19: In Vitro Diagnostic Testing
Infertility Services
Lyme Disease Treatment – Antibiotic Treatment
Negative Pressure Wound Therapy/Vacuum-Assisted Closure (VAC) for Nonhealing Wounds
Compression Devices
Tissue-Engineered Skin Substitutes

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Overview

This Coverage Policy addresses the use of systemic hyperbaric oxygen (HBO) therapy (HBOT), also called hyperbaric oxygen therapy (HOT), and topical oxygen therapy (TOT) or topical HBO (THBO). Systemic HBO is proposed for the treatment of multiple conditions and involves the inhalation of 100% oxygen in a single or multiplace chamber. Topical oxygen therapy (TOT) delivers 100% oxygen to a localized area (e.g., over a wound).

Coverage Policy

Systemic hyperbaric oxygen therapy (HBO/HBOT/HOT) in single or multiplace chambers is considered medically necessary first-line treatment for ALL of the following conditions:

- acute carbon monoxide poisoning
- air or gas embolism
- decompression sickness
- exceptional blood loss when transfusion is not an option

Systemic hyperbaric oxygen therapy (HBO/HBOT/HOT) in single or multiplace chambers is considered medically necessary adjunctive treatment for ALL of the following conditions:

- acute cyanide poisoning, after administration of antidote
- acute traumatic peripheral ischemia/insufficiency (e.g., crush injuries, compartment syndrome, suturing of severed limbs)
- central retinal artery occlusion
- clostridial myositis and myonecrosis (i.e., gas gangrene)
- compromised skin grafts and flaps (i.e., preexisting grafts or flaps that are showing signs of failure or necrosis)
- delayed osteoradionecrosis, including pre- and post-dental extraction(s) from an irradiated mandible
- idiopathic sudden sensorineural hearing loss (ISSHL) within four weeks of symptom onset
- intracranial abscess
- necrotizing soft tissue infections (e.g., necrotizing fasciitis, Meleney's ulcer)
- osteomyelitis unresponsive to conventional medical and surgical interventions
- radiation-induced cystitis or hemorrhagic cystitis (i.e., resulting from chemolytic response, graft-versus-host disease [GVHD])

- soft tissue radionecrosis, delayed (e.g., radiation-induced enterocolitis, proctitis, brain necrosis)
- thermal burns, acute, requiring inpatient hospitalization
- Wagner grade III or higher diabetic wounds/ulcers of the lower extremities that have failed standard wound therapy

Systemic hyperbaric oxygen therapy in single or multiplace chambers is considered not medically necessary for ANY of the following conditions:

- actinomycosis
- acute cerebral edema
- acute coronary syndrome (ACS)/myocardial ischemia/infarction (MI), cardiogenic shock/preconditioning for coronary artery bypass graft surgery
- acute or chronic cerebral vascular insufficiency
- acute thermal and chemical pulmonary damage (i.e., smoke inhalation with pulmonary insufficiency)
- acute wound, flap, and/or graft
- anorectal disorders (e.g., chronic anal fissure [CAF], internal hemorrhoids, infectious proctitis)
- autism spectrum disorders
- avascular necrosis
- brain injury, closed head injury, traumatic brain injury (TBI), anoxic encephalopathy
- brown recluse spider bites
- cancer
- carbon tetrachloride poisoning
- cerebral palsy
- cerebral radionecrosis
- chronic fatigue syndrome
- chronic peripheral vascular insufficiency
- COVID-19
- Crohn’s disease
- cutaneous decubitus/pressure ulcers
- dementia
- epilepsy
- fractures, acute, delayed union or nonunion
- headaches (e.g., cluster, migraine)
- hepatic necrosis
- human immunodeficiency virus (HIV)–fatigue
- in vitro fertilization
- Lyme disease
- lymphedema
- malignant otitis externa (e.g., necrotizing external otitis)
- multiple sclerosis
- mycoses
- nonvascular causes of chronic brain syndrome (e.g., Pick’s disease, Alzheimer’s disease, Korsakoff’s disease)
- ophthalmologic conditions other than central retinal artery occlusion (e.g., optic neuropathy, glaucoma)
- organ storage
- organ transplantation
- pulmonary emphysema
- reflex sympathetic dystrophy/complex regional pain syndrome
- rheumatoid arthritis

- sepsis
- sickle cell disease
- soft tissue injury (e.g., delayed onset muscle soreness, sprains, strains)
- spinal cord injury
- stroke
- tetanus
- tinnitus
- venous stasis ulcers

Topical hyperbaric oxygen (THBO) is considered experimental, investigational or unproven for any indication.

General Background

Systemic hyperbaric oxygen therapy (HBO/HBOT/HOT) involves the inhalation of 100% oxygen under increased atmospheric pressure (e.g., 2 to 3 atmospheres absolute [ATA]) (Undersea and Hyperbaric Medicine Society [UHMS], 2023). A hyperbaric oxygen chamber (whether single or multiplace chamber [i.e., created to hold several people]) is a device intended to promote the movement of oxygen from the environment to the patient's tissues by means of pressurization. Forcing oxygen into the tissues, organs, brain, and fluids of the body is proposed to stimulate cell growth and regeneration, displace toxins and impurities, and stimulate the immune system. Treatment sessions may last for 30–120 minutes and may be given for up to five times per week. Some conditions may only require one or two treatments (e.g., cyanide poisoning) while others may require 10–40 treatments (e.g., osteonecrosis) depending on the severity of the illness and the clinical response of the patient (i.e., complete response occurs or no improvement is being seen).

There are two types of topical oxygen therapy (TOT), hyperbaric topical oxygen therapy (HTOT) and continuous topical oxygen therapy (CTOT). HTOT is the original mode of administering TOT. Topical oxygen therapy (TOT) is also referred to as topical hyperbaric oxygen (THBO), topical pressurized oxygen therapy (TPOT), topical oxygen wound therapy (TOWT) and topical wound oxygen. TOT has been proposed as an adjunctive therapy for the treatment of open acute and chronic wounds (e.g., on the sacrum or an extremity). With THBO, an airtight chamber or polyethylene bag (e.g., sleeve, boot, pouch) is sealed around a limb by a constriction/tourniquet device or on a part of the body with tape. High flow oxygen (usually 10 liters per minute) is introduced into the bag over the wound. These portable units can be used in a physician's office, clinic, or be self-administered in the home setting. Therapy is typically administered 90 minutes per day on four consecutive days, with a three-day break. In total, therapy may last for up to 10 weeks. The evidence in the published peer-reviewed scientific literature does not support the safety and efficacy of THBO. CTOT is a newer alternative to HTOT that does not require patient immobilization or in-clinic administration and can be used at the same time as dressings and offloading. A portable oxygen concentrator refines and delivers atmospheric (normobaric) oxygen to the wound site through a cannula.

U.S. Food and Drug Administration (FDA): Mono- and multiplace hyperbaric chambers are approved by the FDA as a Class II, 510(k) device. Examples of these chambers include the OxyHeal 1000 Monoplace Hyperbaric Chambers (OxyHeal Health Group, LaJolla, CA) and the Multiplace Hyperbaric Chambers (Makai Marine Industries, Inc., Boca Raton, Fl). The devices were approved for the treatment of the conditions recommended by the Undersea Hyperbaric Medicine Society at that time (FDA, 2005; FDA, 2004).

Topical hyperbaric oxygen systems are a Class II device approved by the FDA 510(k) process. Examples of topical systems are the Hyper-Box Topical Wound Oxygen System (Qualtech House, Gateway, Ireland) and the VHT-100 Vaporous Hyperoxia Therapy (VHT™) (formerly WHS- l000 Wound Treatment System (K050156) (Vaporox, Inc., Lone Tree, CO). Both devices are approved for the treatment of open acute or chronic wounds such as decubitus ulcers, infected stumps, skin grafts, gangrenous lesions, burns, frostbite, and skin ulcerations due to diabetes, venous stasis, and/or post-surgical infections (FDA, 2008, 2005). The O2Boot (GWR Medical, LLP, Chadds Ford, PA) is approved to provide "hyperbaric oxygen to open, chronic wounds as an adjunct therapy in wound management and treatment" (FDA, 1997).

Systemic Hyperbaric Oxygen

Literature Review - HBO as Primary Therapy: Evidence in the published peer-reviewed literature and professional society guidelines support the safety and effectiveness of HBO as a primary treatment option for acute carbon monoxide poisoning; air or gas embolism; decompression sickness; and exceptional blood loss when transfusion is not an option (Undersea & Hyperbaric Medical Society [UHMS], 2023; Bennett, et al., 2012).

Literature Review - HBO as Adjunctive Therapy: HBO has been shown to be effective and is an established adjunctive therapy used in combination with other established therapies for the treatment of acute cyanide poisoning; acute traumatic peripheral ischemia/insufficiency (e.g., crush injuries, compartment syndrome, suturing of severed limbs); central retinal artery occlusion, clostridial myositis and myonecrosis (i.e., gas gangrene); compromised skin grafts and flaps (i.e., preexisting grafts or flaps that are showing signs of failure or necrosis); intracranial abscess; necrotizing soft tissue infections such as necrotizing fasciitis or Meleney's ulcer; osteomyelitis that is unresponsive to conventional medical and surgical interventions; delayed radiation damage of non-neurologic tissue (i.e., osteoradionecrosis, including pre- and post-dental extraction in an irradiated mandible, and mandibular radionecrosis), soft tissue radionecrosis (e.g., radiation-induced enterocolitis, cystitis, proctitis; laryngeal and brain necrosis) and acute thermal burns requiring hospitalization (Lin, et. al., 2023; UHMS, 2023; Bennett, et al., 2012; Eskes, et al., 2011; Nabil and Samman, 2011; Fritz, et al., 2010; Goldman, 2009; Bennett, et al., 2008).

HBO is also a recognized adjunctive therapy for the treatment of radiation-induced cystitis or hemorrhagic cystitis resulting from chemolytic response or graft-versus-host disease, and radiation-induced enterocolitis (Cardinal, et al., 2018; Fink, 2006; Bennett, 2005; Chong, 2005; Fine, 2005; El-Zimaity, 2004; Lazzarini, 2004; Hailey, 2003; Wang, 2003; Kalayoglu-Besisik, 2003; Cesaro, 2003).

Randomized controlled trials and prospective case series support the safety and efficacy of HBO as an effective adjunctive therapy for the treatment of Wagner grades III–V diabetic wounds/ulcers of the lower extremity that are refractory to aggressive medical management including wound care, glucose control and surgical debridement or surgical revascularization. A Wagner grade III wound involves a deep ulcer that contains an abscess, osteomyelitis, or both; grade IV is an ulcer that has led to gangrene of the toes and/or forefoot; and a grade V ulcer has caused gangrene of the entire foot or enough of the foot that it cannot be salvaged. Most study protocols utilizing hyperbaric oxygen for diabetic wound healing exposed patients daily at 2–2.5 ATA for 90–120 minutes for a total of 20-40 sessions (Huang, et al., 2015; Kranke, et al., 2015; Weaver, 2014; Goldman, 2009; Roeckl-Wiedmann, et al., 2005).

Sudden sensorineural hearing loss (SSHL) is an acute hearing impairment defined as a 30 decibel (dB) or greater hearing loss occurring in at least three contiguous audiometric frequencies over 72 hours or less. With sudden hearing loss, the loss is typically defined in relation to hearing in the

opposite ear because pre-event audiometry is generally not available. Idiopathic means that there is no identifiable cause of the sudden hearing loss and 85%–90% of SHL is idiopathic. SHL is considered an emergency situation that requires immediate medical intervention. The standard treatment is systemic and/or intratympanic corticosteroids. Patients refractory to initial therapy may be given the addition of HBO as an adjuvant (Weber, 2024; UHMS, 2011). HBO is FDA approved for the treatment of "hearing loss (complete hearing loss that occurs suddenly and without any known cause)" (FDA, 2021). RCT and systematic reviews with small patient populations reported that HBO was an effective adjunctive therapy for the treatment of SSHL. Therefore, HBO has evolved into an accepted treatment option for a small subset of patients.

Tong et al. (2021) conducted a randomized control trial to assess the efficacy of hyperbaric oxygen (HBO) combined with pharmacological treatment in the treatment of idiopathic sudden sensorineural hearing loss (ISSNHL) with an additional objective of defining the subset of patients expected to benefit from HBO therapy. Patients (N=136) were included if they were > 18 years of age with unilateral ISSNHL. This was defined as more than 20 dB hearing loss occurring in three contiguous frequencies during <3 days without specific causes. Treatment was started less than 30 days from onset of symptoms and patients were instructed not to smoke or drink caffeine during the study. Excluded were patients with evidence of untreated pneumothorax, acute sinusitis, retinal detachment, claustrophobia, heart failure or renal failure, with uncontrolled hypertension (systolic blood pressure >180 mm Hg), taking anticoagulants, with middle ear disease of the ipsilateral ear, or pregnant. The intervention was HBO (17 sessions in two weeks) plus pharmacological treatment (HBO+P) compared with a control group receiving pharmacological treatment (P) only. Pharmacological treatment comprised of oral prednisone (30 mg/day for five days, followed by a 10-mg taper every five days), flunarizine tablets (5 mg/day for 14 days), vitamin A (25,000 IU/day for 14 days), vitamin E (0.1 g/day for 14 days), intramuscular injection of vitamin B1 (2 mL every other day for 14 days), mouse nerve growth factor (18 μg/day for 14 days), intravenous mecobalamin (1 mL/day for 14 days), and Shuxuetong (MuDanJiang Youbo Pharmaceutical Co. Ltd., China, 10 mL/day intravenously for 14 days), which is a traditional Chinese drug showing anticoagulation effect. Successful primary outcome was measured on day 15 as a pure tone audiometry gain larger than 15 dB. Patients were not followed past the evaluation on day 15. Hearing recovery success rate was 60.6% (40/66) in HBO+P compared to 42.9% (30/70) in the P group (p=0.038). In comparing outcomes of subgroups that received HBO + P, the following differences in success rate were noted: the degree of hearing loss (mild-moderate 75% [24/32] compared to severe-profound 47.1% [16/34]), age (≤ 50 years 71.4% [30/42] compared to > 50 years 38.5% [10/26]), time intervals (≤ 14 days 66.1% [39/59] compared to > 14 days 14.3% [1/7]), and presence of dizziness/vertigo (yes 42.3% [11/26] compared to no 72.5% [29/40]). No adverse events were noted. Author noted limitations of the study included short term follow up, not noting differences in socioeconomic levels that could have influenced etiology, using audiometric thresholds as the treatment outcome measure, not using word recognition as an outcome measure and not using intratympanic steroid administration as a comparator.

Cvorovic et al. (2013) conducted a randomized controlled trial (n=50) to compare HBO to intratympanic (IT) steroid injection in patients with ISSHL Patients who had less than a 10-dB hearing gain following systemic steroid therapy were randomized to either HBO or IT steroids. Treatment began after unsuccessful primary treatment but no later than four weeks of the onset of ISSHL. HBO was given in 20 treatments, one per day, Monday-Friday, 2ATA at 100% O2 (10 minutes of compression on air, 60 minutes of oxygen breathing, and 10 minutes of decompression on air). The IT steroid group received four intratympanic injections in 13 days. The primary outcome measure was hearing gain at 0.25, 0.5, 1, 2, and 4 kHz following treatment. Patients were classified into three subgroups: pure tone average (PTA) less than 60, PTA 61 to 81, and PTA greater than 80 dB. There were significant differences between hearing thresholds at all frequencies before and after the HBO treatment as well as, after IT steroid injections with the

exception of the 2 kHz. Patients with a PTA less than 81dB and age less than 60 years had a better response to HBO. There were no significant differences between the two groups at any of the five frequencies tested except at 2 kHz, at which HBO treatment resulted in better outcomes than IT steroids. Patients with a PTA of more than 81 dB had significantly higher hearing gain on IT steroid than on HBO treatment. Hearing recovery was significantly worse in the HBO group in patients with PTA greater than 80 dB. The majority of patients failed to improve completely. Final hearing levels were reached at one month in 78% of patients and by three months in 97% of patients. As noted by the authors a "major" limitation of the study was that the patients in the two groups were not matched and not similar. Another limitation was the small patient population and the short-term follow-up.

In a Cochrane review, Bennett et al. (2012) evaluated seven randomized controlled trials (n=392) that assessed the effectiveness of HBO for the treatment of ISSHL in adults. "The studies were small and of poor quality" and were published from 1985 to 2004. No trials were found from 2004 to 2012. Treatment regimens, outcome measures and comparators (multimodal pharmacological approach, vasodilator alone) varied between studies. Follow-ups ranged from 10 days to three months. Two studies evaluated HBO for chronic hearing loss. When the data from the two trials were pooled (n=114), no significant improvement in the chance of a 50% increase in hearing threshold on pure-tone average with HBO was seen. The data did show a significantly increased chance of a 25% increase in pure-tone average (p=0.02), a 22% greater chance of improvement with HBO, and the number needed to treat to achieve one extra good outcome was five. There was also an "absolute improvement in average pure-tone audiometric threshold following HBO (mean difference 15.6 dB greater with HBO) (p=0.03) (n=91; two studies). Although HBO improved hearing, "the clinical significance was unclear". The significance of a percentage improvement in hearing from baseline was not clear and would depend on the starting level of impairment. It was also noted that improved hearing may only be true if HBO is used within two weeks of the onset of problems. The authors noted that because of the "modest number of patients, methodological shortcomings and poor reporting, the results should be interpreted cautiously". There was "no evidence of a beneficial effect of HBO on chronic ISSHL (six months)".

Professional Societies: The American College of Emergency Physicians (ACEP) (2017) recommended the use of HBO therapy or high flow normobaric therapy for acute carbon monoxide poisoned patients. However, it remains unclear whether HBO therapy is superior to normobaric oxygen therapy for improving long-term neurocognitive outcomes.

The Society for Vascular Surgery in collaboration with the American Podiatric Medical Association and the Society for Vascular Medicine suggested HBO for the management of diabetic foot ulcers in patients who fail to respond to 4–6 weeks of conservative management. The clinical guideline noted that patients should be selected for this therapy carefully considering the cost and the burden of prolonged daily treatment (Society for Vascular Surgery, 2016).

The Undersea and Hyperbaric Medical Society (UHMS) (2023) approved the following indications for systemic HBO:

- air or gas embolism
- carbon monoxide poisoning
- carbon monoxide poisoning complicated by cyanide poisoning
- central retinal artery occlusion
- clostridial myositis and myonecrosis (gas gangrene)
- crush injury, compartment syndrome, and other acute traumatic ischemias
- decompression sickness
- enhancement of healing in select problem wounds
- exceptional blood loss (severe anemia)

- intracranial abscess
- necrotizing soft tissue infections
- osteomyelitis (refractory)
- delayed radiation injury (soft tissue and bony necrosis)
- skin grafts and flaps (compromised)
- thermal burns (acute)
- idiopathic sudden sensorineural hearing loss

The Undersea and Hyperbaric Medical Society (2011) support HBO for the treatment of ISSHL stating that patients who meet the criteria for ISSHL may benefit from HBO. Candidates for HBO include those patients with "moderate to profound ISSHL (≥ 41 dB) who present within 14 days of symptom onset". According the UHMS, patients presenting after this time may experience improvement when treated with HBO, however, the medical literature suggests that early intervention is associated with improved outcomes. The best evidence supports the use of HBO within two weeks of symptom onset.

The American Academy of Otolaryngology – Head and Neck Surgery (AAO-HNS) (2012, updated 2019) developed evidence-based clinical practice guidelines for the management of sudden hearing loss with a special emphasis on managing sudden sensorineural hearing loss (SSNHL) in adult patients (aged 18 years and older). Following a systematic review of randomized controlled trials "with methodological limitations", AAO-HNS stated that HBO, is an option when combined with steroid therapy in SSNHL as primary therapy within two weeks of onset of symptoms and as salvage therapy when used within 4 weeks of onset, with potentially more benefit noted in cases of severe to profound loss". AAO-HNS's stated that although the level of evidence was "modest and imprecise", it was "sufficient to promote greater awareness of HBO for the treatment of SSNHL". The report went on to say that the results should be interpreted with caution due to the small number of patients in the trials, methodological shortcomings, and poor reporting. The authors also noted that HBO is not recognized by many United States clinicians as an intervention for ISSNHL.

Literature Review - Other Proposed Indications for Systemic HBO: There is insufficient evidence in the published peer-reviewed scientific literature to support HBO as a primary or adjunctive treatment of the conditions discussed below (this list may not be all inclusive). HBO is not FDA approved for these other indications.

Actinomycosis: Actinomycosis is a rare chronic, indolent, suppurative, tissue-destructive infection presenting with lumps and sinus formation, usually involving the head and neck, although it can affect other parts of the body, such as the abdomen and thorax. Adjunctive HBO has been proposed as a treatment option for patients who are unresponsive to medical and surgical intervention; however, studies are primarily in the form of case reports.

Acute Cerebral Edema: Cerebral edema accompanies a wide variety of pathologic processes and may be present in head/brain injury, stroke, brain tumor, cerebral infections (e.g., brain abscess, encephalitis and meningitis), lead encephalopathy, hypoxia, disequilibrium syndrome associated with dialysis and diabetic ketoacidosis, Reye's syndrome, fulminant hepatic encephalopathy, and hydrocephalus (Rowland, 2005). HBO has not been established as a treatment option for cerebral edema.

Acute Coronary Syndrome (ACS)/Myocardial Ischemia/Infarction (MI), Cardiogenic Shock/Preconditioning for Coronary Artery Bypass Graft Surgery): ACS includes acute MI and unstable angina. HBO therapy has been proposed as an adjunct to standard therapy to improve oxygen supply to the heart and possibly decrease the amount of myocardial ischemic death that could occur and/or to prevent cardiogenic shock. HBO has also been investigated for

preconditioning coronary artery disease (CAD) patients prior to elective surgery to improve left ventricular stroke work postoperatively. However, there is insufficient evidence to support the effectiveness of HBO for these conditions.

Bennett et al. (2011) (updated 2015) conducted a systematic review of randomized controlled trials comparing the treatment of acute coronary syndrome (ACS) with HBO and without HBO. Six trials (n=665) met inclusion criteria. Overall, HBO resulted in a significant decrease in the risk of death (p=0.02), a significantly lower extent of heart muscle damage measured by lesser rise in muscle enzymes (p=0.005) and a significantly better left ventricular ejection fraction (p=0.001). Evidence from individual trials reported a reduction in the risk of major adverse coronary events (MACE) (p=0.003), re-infarction (p=0.04), dysrhythmias (p=0.01) and less time to relief of pain (P<0.00001). However, the authors warned that because of the "modest number of patients, methodological shortcomings and poor reporting, these results should be interpreted cautiously, and an appropriately powered trial of high methodological rigor is justified to define those patients (if any) who can be expected to derive the most benefit from HBOT. The routine application of HBOT to these patients cannot be justified from this review." No new trials were located in the most recent update (Bennett, et al., 2015).

Yogaratnam et al. (2010) conducted a randomized controlled trial (n=81) to determine if preconditioning coronary artery disease (CAD) patients with HBO prior to first-time, elective coronary artery bypass graft surgery (CABG) with on-pump cardiopulmonary bypass (CPB), would improve postoperative myocardial left ventricular stroke work (LVSW). Preoperatively, the study group (n=41) received HBO for two 30-minute intervals, five minutes apart. The control group (n=40) was not treated with HBO. Hemodynamic monitoring was performed on 22 HBO patients and 25 control group patients. Immediately following HBO, the study group had a significant reduction in pulmonary vascular resistance (PVD) (p=0.03), but the significant difference was not maintained. Intraoperatively, the HBO group had a significant reduction in blood loss (p=0.05). There was no significant difference in the rise in the serum troponin T level, but the rise was greater in the control group. This indicated that HBO-treated patients had less postoperative myocardial injury than the control group. Postoperatively, the HBO group had a significantly improved stroke volume (p=0.01) and LVSW (p=0.05), spent 24 minutes longer on mechanical ventilation and was intubated 36 minutes longer than the control group. The HBO group had a significantly shorter length of stay in the intensive care unit (p=0.05). The study group also had a reduction in blood loss (11.6%), blood transfusion (34%), low cardiac output syndrome (10.4%), inotrope use (8%), atrial fibrillation (11%), pulmonary complications (12.7%), and wound infections (7.6%), but the differences were not statistically significant. No renal or neurological complications were reported in the HBO group compared to 5% and 2.5%, respectively in the control group. Author-noted limitations of the study included the small patient population, recruitment of low-risk patients, and lack of comparison to patients who underwent CAPG without the use of CPB and to patients with controlled ischemia. Another limitation of the study is that all patients were not hemodynamically monitored during the postoperative period.

In a randomized controlled trial by Dekleva et al. (2004), 74 patients were assigned to HBO and streptokinase treatment versus streptokinase treatment alone within the first 24 hours after diagnosis. This study was small in sample size, showed treatment effectiveness limited to the first three days following HBO, and excluded patients with significant electrical complications. Due to these limitations, the effectiveness of HBO for the treatment of acute MI cannot be determined.

Acute or Chronic Cerebral Vascular Insufficiency: Cerebral vascular insufficiency is defined as insufficient blood flow to the brain that can lead to a stroke or transient ischemic attack (TIA). Although HBO has been proposed as a treatment option for cerebral vascular insufficiency, there is insufficient evidence in the peer-reviewed scientific literature to support its use for this indication.

Acute Thermal and Chemical Pulmonary Damage: HBO for the treatment of acute thermal and chemical pulmonary damage including smoke inhalation and pulmonary insufficiency in the absence of acute carbon monoxide poisoning is not supported by the evidence in the peer-reviewed literature.

Acute Wound, Flap and/or Graft: HBO has been proposed for the treatment of acute wounds, flaps and grafts. Published studies have included randomized controlled trials, case series and retrospective reviews. Dauwe et al. (2014) conducted a systematic review of the literature to evaluate the role of HBO in the treatment of acute wounds, flaps and grafts. Four randomized controlled trials, three prospective studies and one retrospective review met inclusion criteria. The studies included treatment of burn patients, crush injuries, postoperative ecchymosis following face lift surgery, post mastectomy and free parascapular flaps for lower extremity reconstruction. Due to the heterogeneity of the small patient populations (n=5–125), the poor methodology of the studies and conflicting outcomes, the authors concluded that the data did not support HBO for these indications.

Anorectal Disorders: HBO has been proposed as a treatment option for anorectal disorders (e.g., chronic anal fissure, internal hemorrhoids, infectious proctitis). The efficacy of HBO as primary or adjunctive treatment for anorectal disorders has not been established. Randomized controlled trials comparing HBO to standard care (e.g., non-steroidal anti-inflammatory medications, steroid enemas, cauterization or surgical excision) are lacking (Rao, 2004; Schwartz, 2004).

Autism: Autism is the most common condition in the group of developmental disorders known as autism spectrum disorders (ASD). HBO has been proposed as a potential treatment modality for improving cognitive function by increasing tissue oxygenation and improving cerebral blood flow. There are a limited number of randomized controlled trials evaluating HBO for the treatment of autism. Published studies have been primarily in the form of case series with small, heterogeneous patient populations (n=6-18) and involved various HBO treatment regimens (Sakulchit, et al., 2017; Rossignol, et al, 2007; Rossignol and Rossignol, 2006).

Xiong et al. (2016) conducted a Cochrane review of randomized and quasi-randomized controlled trials to investigate hyperbaric oxygen therapy for the treatment of autism spectrum disorder (ASD). One trial with a total of 60 children met inclusion criteria. Subjects were randomized to hyperbaric oxygen therapy or sham treatment. The quality of evidence was rated as low due to the small sample size and wide confidence intervals. Other limitations of the evidence included selection bias, short duration of treatment and short-term follow-up. Overall, there was no reported improvement in social interaction and communication, behavioral problems, communication and linguistic abilities, or cognitive function. Regarding safety of hyperbaric oxygen therapy, minor-grade ear barotrauma events were reported. The authors concluded that, there is no evidence that hyperbaric oxygen therapy improves core symptoms and associated symptoms of ASD.

In 2013 (updated 2021), the FDA posted a warning to consumers regarding HBO. The Agency stated that HBO has not been clinically proven to cure or be effective in the treatment of autism. The information warns against the use of HBO for indications that are not FDA approved.

Ghanizadeh (2012) conducted a systematic review of randomized controlled trials to evaluate the efficacy of HBO for the treatment of autism in children. Two randomized controlled trials met inclusion criteria. One study was the Rossignol et al. study discussed below. The second study (n=42) reported that HBO was not more effective than placebo.

Rossignol et al. (2009) conducted a multicenter, randomized, double-blind, controlled trial to evaluate the efficacy of HBO in the treatment of children (n=62), ages 2–7 years, diagnosed with autistic disorder. The children were randomly assigned to the study group (n=33) treated with HBO at 1.3 atmosphere and 24% oxygen or to the control group (n=29) treated with slightly pressurized room air and 21% oxygen. Forty, one-hour sessions (two sessions per day for five days) were administered over four consecutive weeks. Compared to the control group, the treatment group had significantly improved outcomes in the mean physician Clinical Global Impression (CGI) scale in overall functioning (p=0.0008), receptive language (p<0.0001), social interaction (p=0.0473), and eye contact (p=0.0102). Significantly more children in the treatment group were rated as "very much improved" (p=0.0471) or "much improved" (p=0.0024). Significant improvements were also reported by the treatment group in the parental CGI scores in overall functioning (p=0.0336), receptive language (p=0.0168), and eye contact (p=0.0322). Significant improvements were noted in total score, irritability, stereotypy, hyperactivity and speech (p<0.03 for each) on the Aberrant Behavior Checklist in the treatment group. The treatment group also showed significant improvement in the Autism Treatment Evaluation Checklist sensory/cognitive awareness score (p=0.0367) compared to the control group. Children over age five years with lower initial autism severity showed the most significant improvements. Due to the short-term duration of this study, the authors stated that studies with long-term outcomes were needed to formally validate the results. It is also unknown what the ideal HBO treatment regimen is for this patient population.

Following a review of the evidence, which included one randomized controlled trial and three case series, Undersea and Hyperbaric Medical Society (UHMS) (2009) concluded that although there is a strong case for further studies on the role of HBO in the treatment of autism, HBO cannot be recommended as a routine treatment option.

Avascular Necrosis: Avascular necrosis (AVN), also called osteonecrosis or aseptic necrosis, is a disease in which there is a lack of blood supply to the bone causing death of bone tissue. Ultimately, AVN may lead to collapse of the bone and joint surface. AVN most often occurs in the hip joint in the femoral head and usually leads to osteoarthritis. Risk factors include hip injury, alcohol abuse and/or excessive corticosteroid use. AVN may be associated with other disease entities (e.g., Gaucher disease, sickle cell disease) and in some cases there may be no underlying disease (idiopathic AVN). Treatment depends on the severity of symptoms and may include limited weight bearing, physical therapy, cessation of alcohol usage, and/or surgical intervention. HBO has been proposed for the treatment of AVN. However, there is insufficient evidence in the published peer-reviewed literature to support HBO for the treatment of AVN. Studies are primarily in the form of case series and retrospective reviews with small patient populations (n=12-109) (Camporesi et al., 2010; Reis, et al., 2003).

Uzun et al. (2016) conducted a systematic review of the literature to assess the efficacy of HBO for the treatment of osteonecrosis of the femoral head (ONFH). Two randomized controlled trials, three case series and three retrospective reviews met inclusion criteria. Four of the studies combined HBO with other treatment modalities which made it impossible to draw firm conclusions on the specific effects of HBO. Hip survivorship in studies using HBO alone was 95.5% in Steinberg Stage I lesions, 89% in Steinberg Stage II lesions and 100% in Ficat Stage II lesions. Overall, studies included small patient populations, weak methodology and heterogeneity in the number and duration of treatments and length of follow-up. Baseline disease stages were diverse and one study inappropriately included patients with advanced-stage ONFH. There is insufficient evidence to support HBO for the treatment of osteonecrosis of the femoral head.

Rollason et al. (2016) conducted a Cochrane review of randomized controlled trials to determine the efficacy and safety of any intervention aimed at treating bisphosphonate-related osteonecrosis of the jaw (BRONJ). Included studies compared the effects of any treatment for BRONJ with

another treatment or placebo. One study (n=49) at high risk of bias evaluated HBO as an adjunctive therapy to standard care and could not confirm or refute the effectiveness of HBO. There is insufficient evidence to conclude whether hyperbaric oxygen therapy is a useful add-on to standard care in the treatment of BRONJ.

Camporesi et al. (2010) conducted a randomized controlled trial (n=20) using HBO to treat Ficat stage II patients with unilateral femoral head necrosis (FHN). Patients were treated with either 30 treatments of HBO or compressed air (HBA) for six weeks. After 20 treatments, significant pain improvement ($p=0.002$) and improvement in extension, adduction and abduction ($p<0.001$) were reported for HBO-treated patients. At the end of six weeks all HBA patients were offered HBO. At the seven-year follow-up (n=17), patients were substantially pain-free and none required surgical intervention. Substantial radiographic healing of osteonecrosis was observed in seven of nine hips. Limitations of the study include the small patient population and following cross-over the study became observational.

Brain Injury, Closed Head Injury, Traumatic Brain Injury (TBI), Anoxic Encephalopathy: In patients with moderate or severe TBI, the goal is to resuscitate the patient adequately to prevent further brain injury. The available evidence on adjunctive HBO treatment for severe traumatic brain injury is limited, and patient outcomes following HBO therapy are uncertain (Rowland, 2005).

Crawford et al. (2017) conducted a systematic review to evaluate the efficacy of HBO for the treatment of traumatic brain injury (TBI). Twelve randomized controlled trials met inclusion criteria. Four studies (n=250) included patients with mild TBI suffering persistent symptoms over many months. Seven studies included patients with moderate-to-severe TBI treated acutely and one study did not clearly define the severity of the TBI. Overall, there were no statistically significant differences between HBO and sham. There were some statistical significant within group differences reporting improvement with HBO regarding cognitive performance and post-concussion symptom severity. Minor adverse events included ear pain, nausea, sinus pain, headaches, tooth pain, transient worsening of myopia and musculoskeletal pain. No serious adverse events were reported. Eight studies were rated as acceptable methodology and four as low quality methodology. Limitations of the studies included the heterogeneity of the treatment regimens and outcomes measures. Studies used various exposure times to HBO (60–117 minutes), number of sessions (3—40), length of sessions (8–10 weeks), and amount of pressure used (1.5–2.4 ATA). The types of sham arms differed in terms of pressure and oxygen levels used. Additional research is needed to support the efficacy of HBO for the treatment of TBI.

Hawkins et al. (2017) conducted a systematic review of the literature to assess the effectiveness of HBO for the treatment of concussion in subjects who suffered from mild traumatic brain injury or post-concussion syndrome. Five randomized controlled trials met inclusion criteria. Studies included 50–61 subjects and compared HBO to sham and in two studies to sham, HBO and another oxygen fraction treatment group. Four studies reported no significant improvement with HBO.

Wang et al. (2016) conducted a systematic review and meta-analysis to investigate HBO for the treatment of traumatic brain injury (TBI). Eight studies (n=519) comparing hyperbaric oxygen therapy vs. control in patients with mild (Glasgow coma scale [GCS] 13–15) to severe (GCS 3–8) TBI were included. Studies were either randomized controlled trials or prospective two-arm studies. The primary outcome was the GCS. Secondary outcomes included the Glasgow outcome score (GOS), overall mortality, and changes in post-traumatic stress disorder (PTSD) score. Mean age of the subjects ranged from 23–41 years. Meta-analysis of two studies (n=120) revealed that the change in GCS score was significantly higher in the HBO group ($p<0.001$). Analysis of three studies (n=141) showed significantly higher rate of improvement in GOS ($p=0.020$) and a lower

overall mortality rate ($p<0.001$). There was no significant change in the PTSD score between the control group and HBO group. The pooled odds ratio for the GOS improvement rate became insignificant with the removal of two studies indicating poor reliability of the meta-analysis. Limitations of the studies included: heterogeneity of pooled data; all the studies had incomplete outcome data; number of studies included in the final analysis were few (2–3); heterogeneity of treatment regimens (e.g., starting time of HBO, oxygen concentration, pressure of treatment protocol); and poor reliability of the GOS meta-analysis. A subgroup analysis of mild and severe TBI was not performed due to incomplete reporting of data and the limited number of eligible studies. The authors noted that whether HBO has a significantly favorable outcome in mild TBI patients as opposed to severe TBI patients is unknown.

Randomized controlled trials have reported that there was no significant improvement when HBO was used for the treatment of traumatic brain injury and post-concussion syndrome. Miller et al. (2015) conducted a multi-center, randomized controlled trail comparing standard care alone to standard care plus HBO or standard care plus sham for the treatment of mild traumatic brain injuries. Treatment regimens included 40 HBO sessions administered at 1.5 atmospheres absolute (ATA) or 40 sham sessions consisting of room air at 1.2 ATA. The primary outcome measure was the Rivermead Post-Concussion Symptoms Questionnaire (RPQ). The sham group and the HBO group showed improvement in the RPQ scores ($p=0.002$ and $p=0.008$, respectively) but there was no significant difference in clinical outcomes in the sham group vs. the HBO group ($p=0.70$). Cifu et al. (2014) ($n=61$) compared HBO to sham for the treatment of mild traumatic brain injury and post-concussion syndrome. Treatments included 40, once daily, 60-minute hyperbaric chamber compressions at 2.0 atmospheres absolute (ATA) at 1 of 3 randomly preassigned oxygen fractions which resulted in blinded groups. The primary outcome measure was the Rivermead Post-Concussion Questionnaire-16 (RPQ-16) taken before compressions and at one week and three months following HBO. At the three-month follow-up no significant improvements in symptoms, functional status, or cognitive or psychomotor performance were seen with HBO.

In a Cochrane review of randomized controlled trials, Bennett et al. (2012) evaluated the benefits and harms of adjunctive HBO for the treatment of patients with TBI. The authors concluded that the combined results of the studies, involving 571 patients, suggested that HBO may reduce the risk of death and improve the final Glasgow Coma Scale. However, there was little evidence of a good outcome and the routine use of HBO for this subpopulation was not supported by the evidence.

Brown Recluse Spider Bites: Brown recluse spider (i.e., loxosceles reclusa) venom contains enzymes that cause local (e.g., dermonecrosis) and systemic toxicity. There are a limited number of case studies that administered HBO as a treatment option. The studies did not show that HBO therapy produced better patient outcomes than standard aggressive wound care and antibiotic administration (Ruha, 2024; Arnold, 2018, updated 2021; Wasserman, 2005).

Cancer: HBO therapy has been proposed for use as a cure for cancer and as a means of enhancing tumor response to chemotherapeutic treatment. The American Cancer Society, the National Cancer Institute and the National Comprehensive Cancer Network® do not discuss HBO as a treatment option for any cancers. In 2013 (updated 2021), the FDA posted a warning to consumers regarding HBO. The Agency stated that HBO has not been clinically proven to cure or be effective in the treatment of cancer.

Bennett et al. (2018) conducted a Cochrane review of randomized controlled trials to assess the safety and efficacy of administering radiotherapy for the treatment of malignant tumors while breathing HBO. Nineteen trials included 2286 subjects of which 1103 were allocated to HBOT and 1153 to control groups. For head and neck cancer, there was an overall reduction in the risk of dying at one year and five years following therapy. There was also some evidence of improved

local tumor control immediately following irradiation, at year one and year five. The evidence was considered of moderate quality due to the inconsistency of outcomes between trials. No trials reported quality of life outcomes. It was noted that benefits came at the cost of an increased risk of severe local radiation reactions with HBOT (high level of evidence). There was no clear benefit of HBOT for the treatment of cervical cancer or bladder cancer. When all cancer types were combined, there was high-quality evidence for an increased risk of severe radiation tissue injury during the course of radiotherapy with HBOT and moderate quality of evidence of oxygen toxic seizures during treatment. The authors noted that given the methodological and reporting inadequacies of the studies, the results should be reviewed with caution. Additional research is needed to determine the benefits of HBO for head and neck cancer. Based on the evidence HBO is not supported for the treatment of uterine cervical or bladder cancer. There is little evidence available concerning malignancies at other anatomical sites.

Carbon Tetrachloride Poisoning: Poisoning from carbon tetrachloride, which is used in industrial solvents, grain fumigants, insecticides, and the production of fluorocarbons, may cause nausea, vomiting, abdominal pain, diarrhea, confusion, coma, respiratory depression, hypotension, convulsions and even death (Harwood-Nuss, 2001). Although HBO has been proposed as a treatment option for carbon tetrachloride poisoning, there is insufficient evidence to support its effectiveness.

Cerebral Palsy: Cerebral palsy (CP) is an umbrella term covering a group of nonprogressive, but often changing, motor-impairment syndromes secondary to lesions or anomalies of the brain arising in the early stages of development. The evidence in the peer-reviewed literature does not support HBO for the treatment of CP.

Laureau et al. (2022) conducted a systematic review (n=1008) of five randomized control trials (RCT), six observational studies and one retrospective review to evaluate the effectiveness and safety of HBO in the treatment of cerebral palsy (CP). In the RCTs, the treatment intervention was 100% O2, 1.5 to 1.75 atmospheres absolute (ATA). The comparator was pressurized air in three RCTs and physical therapy in two RCTs. Similar improvements were observed regarding motor and/or cognitive functions in the HBOT and control groups. Most common adverse event was middle ear barotrauma (up to 50% of children). Other adverse events included seizures, confinement anxiety, pulmonary disorders, nausea, hypoglycemia, hypotension, visual disorders and dizziness. Author noted study limitations include variable control intervention, heterogeneity of clinical presentation of CP, and variable length of time period of treatments. In conclusion, HBOT does not improve motor function, cognition, and functional performance in children with CP.

Lacey, et al. (2012) conducted a randomized controlled trial (n=46) to determine if HBO would improve functional abilities in children (ages 3–8 years) with spastic CP. One group received HBO (n=24), 100% oxygen at a pressure (or depth) of 1.5atm; and the second group received hyperbaric air (HBA) (n=22), a mixture of gases (14% oxygen) at 1.5atm to simulate 21% oxygen at room air. Eighty-minute sessions took place once a day for eight weeks for a total of 40 treatments. At the six month follow-up there were no changes from baseline in the Gross Motor Function Measure (GMFM)-88 and GMFM-66 or dimension A-D scores (i.e., lying and rolling, sitting, crawling and kneeling, standing) in either group. There were no significant differences between groups. The HBO group showed a significant increase in dimension E score (walking, running and jumping). Although both groups showed improvement, there was also no significant difference between the groups in the Pediatric Evaluation of Disability Inventory (PEDI) scores. The study was stopped because "the calculated conditional probability of obtaining a difference between groups if the study continued to the end was only between 0.5% and 1.6%". The results of the study do not support HBO in the treatment of this patient population.

In a 2007 systematic review including two randomized controlled trials and four observational studies evaluating the benefits and adverse effects of HBO for the treatment of CP, McDonagh et al., reported that the improvements in motor function when compared to baseline for both HBO and room air were not significantly different. The evidence to support HBO therapy for CP is insufficient at this time.

In a clinical report for the American Academy of Pediatrics (AAP) regarding the treatment of children and youth with CP, Liptak et al. (2011) listed HBO as a therapy for which some evidence exists to refute its effectiveness. "Because CP is so heterogeneous, it is unlikely that all children would improve with a single therapy; benefits have not been proven".

Cerebral Radionecrosis: Cerebral radionecrosis is a complication of radiation therapy of intracranial and extracranial tumors. Delayed radionecrosis may appear as an intracranial mass and is typically surgically removed. Although HBO has been suggested as a treatment option when surgery is not feasible, clinical trials demonstrating the efficacy of HBO for this indication are lacking.

Chronic Fatigue Syndrome: Chronic fatigue syndrome (CFS) is a disorder of unknown etiology, which may have an infectious basis. It involves a state of chronic fatigue for more than six months and can be accompanied by cognitive difficulties. Because most cases of CFS may be based on a viral infection, no effective therapy exists (Roberts, 2020). Evidence supporting HBO for the treatment of CFS is lacking.

Chronic Peripheral Vascular Insufficiency: Peripheral vascular insufficiency is most commonly a disease of the arteries and is caused by atherosclerosis which results in insufficient tissue perfusion. Although HBO has been proposed as a treatment option for peripheral vascular insufficiency, there is insufficient evidence in the peer-reviewed literature to support HBO for this indication.

COVID-19
COVID-19 is the infectious disease caused by the coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). There is insufficient evidence to support HBO for the treatment of this condition. In 2021, the FDA posted a warning to consumers regarding HBO. The Agency stated that HBO has not been clinically proven to cure or be effective in the treatment of COVID-19.

The Undersea and Hyperbaric Medical Society (UHMS) Position Statement: Hyperbaric Oxygen (HBO2) for COVID-19 Patients (jointly approved by the American College of Hyperbaric Medicine [ACHM]).(revised August 2020) states :

- "The UHMS continues to advocate strongly for well-designed IRB-approved clinical trials of hyperbaric oxygen for COVID-19. Well-designed trials are necessary to establish a proper mechanistic and clinical foundation for COVID-19 treatment and increase our understanding of this disease and the potential role of hyperbaric oxygen as part of a multidisciplinary approach.
- The UHMS recognizes the special value of Phase III randomized controlled trials in providing Level I evidence and strongly supports funding and conduct of these definitive studies.
- The UHMS now recognizes that hyperbaric oxygen treatment on an off-protocol basis for COVID-19 at the physician's discretion may be appropriate in some cases and recognizes that community centers and free-standing facilities may have limited access to IRBs (Institutional Review Boards). The UHMS strongly encourages well-documented scientific

observations of the impact, patient selection criteria, and treatment methodology for those utilizing HBO2 to treat COVID-19 patients off-protocol.
- The UHMS strongly encourages well-documented scientific observations of the impact, patient selection criteria, and treatment methodology for those utilizing HBO2 to treat COVID-19 patients. The UHMS Research Committee has published key outcome determinants and therapeutic guidance."

Literature Review: There is insufficient evidence in the published peer-reviewed scientific literature to support the effectiveness of HBO for the treatment of acute or long COVID-19. The available studies are primarily focused on the effects of HBO on hospitalized patients with pneumonia and/or on mechanical ventilation. Studies are in the form of retrospective reviews, case series, and case reports (Gorenstein, et al., 2020; Guo, et al., 2020; Thibodeaux, et al., 2020). Studies on long Covid consist of a randomized control trial by Zilberman-Itskovich et. al. (2022) and a retrospective review (n=10) by Robbins et al. (2021).

Zilberman-Itskovich et. al. (2022) conducted a randomized, sham control, double blind clinical trial (n=73) to evaluate the effects of HBO on patients with persistent symptoms of post-Covid for at least three months after confirmed infection. Patients were randomized to receive HBO daily for 40 sessions (n=37) or sham treatment (n=36). Follow-up assessments were performed at baseline and 1–3 weeks after the last treatment session. The primary outcome was the cognitive assessment as evaluated by the Mindstreams computerized cognitive testing battery. The cognitive domains assessed were memory, executive function, attention, information processing speed, and motor skills. Cognitive scores were normalized for age, gender and educational levels. Secondary outcomes were measured using self-reported questionnaires: short form-36 (SF-36) to assess quality of life, the Pittsburgh Sleep Quality Index (PSQI) to assess sleep quality, the Brief Symptom Inventory (BSI-18) to evaluate psychological distress, based on three subscales: depression, anxiety, and somatization, and the Brief Pain Inventory (BPI) to measure pain intensity and impact. Brain imaging MRI scans were performed to evaluate brain perfusion. Following HBOT, there was a significant group-by-time interaction (difference in the change over time) with a medium net effect size in global cognitive function (d=0.495, p=0.038), attention (d=0.463, p=0.05) and executive function (d=0.477, p=0.04 and) compared to the control group. Significant improvement was also demonstrated with the following net effect size in the energy domain (d=0.522, p=0.029), sleep (d=0.48, p=0.042), psychiatric symptoms (d=0.636, p=0.008), and pain interference (d=0.737, p=0.001). Increased brain MRI perfusion and microstructural changes were noted in the supramarginal gyrus, left supplementary motor area, right insula, left frontal precentral gyrus, right middle frontal gyrus, and superior corona radiate of the brain following HBO treatment. Adverse events were not reported. Study limitations include small patient population, short follow-up time, and the optimal number of sessions for maximal therapeutic effect is unknown. Hadanny et. al. (2024) reported on the results of 31 patients in the treatment arm 12 months post last treatment with HBO. The authors reported that the short-term improvements in quality of life, quality of sleep, psychiatric and pain symptoms persisted at 12 months. Additional well-designed RCTs with large patient populations and long-term follow up are needed to determine if HBO is effective in the treatment of long-Covid.

Oliaei et al. (2021) conducted a systematic review to evaluate the effects of hyperbaric oxygen therapy (HBO) on the treatment of COVID-19 pneumonia. The analysis included eight studies of which three were clinical trials and five were case reports and case series. Although the overall results reported improvement following HBOT, the limitations of the studies prevent strong conclusions to be drawn supporting HBOT for the treatment of Covid.

Crohn's Disease: Crohn's disease is a chronic inflammatory disease of the gastrointestinal tract, the cause of which remains unknown. The available evidence is limited and is considered

insufficient to determine the effect of HBO treatment on the health outcomes of patients with Crohn's disease.

Dulai et al. (2014) conducted a systematic review to evaluate the safety and efficacy of HBO for Crohn's disease (n=286) and ulcerative colitis (n=327). A total of 17 studies met inclusion criteria. One study was a randomized controlled trial. The remaining studies were case reports and case series. Known grades (n=40) of ulcerative colitis ranged from mild to severe. Of the 44 Crohn's disease patients who had disease extent reported, 40 (91%) had perineal disease and 21 (48%) had fistulas. The overall response rate for patients with irritable bowel disease (IBD) was 86%. The response rate for ulcerative colitis patients who had endoscopic follow-up (n=40) was 100%. Six patients suffered serious adverse events necessitating discontinuation of therapy (6.7/10,000 treatments). Limitations of the studies noted by the authors included: high or uncertain risk of bias; small, heterogeneous patient populations; lack of endoscopic follow-up of disease activity; missing data; unclear study designs; poorly described research methods; heterogeneity of treatment regimens; short-term follow up; and inadequate description of outcomes.

Cutaneous, Decubitus/Pressure Ulcers: Cutaneous, decubitus (pressure) ulcers are typically localized to an area of tissue necrosis that develops when soft tissue is compressed between a bony prominence and an external surface. HBO for the treatment of decubitus or pressure ulcers has generally been considered ineffective or not extensively evaluated (Javier, 2024).

Dementia: Dementia is characterized by progressive deterioration that interferes with social or occupational functions, such as: memory, orientation, abstraction, ability to learn, visuospatial perception, language function, and constructional praxis. Alzheimer's disease accounts for more than 50% of cases of dementia (Rowland, 2005). There is insufficient evidence in the peer-reviewed literature to support the treatment of dementia with HBO.

Xiao et al. (2012) conducted a Cochrane systematic review to assess HBO for the treatment of vascular dementia. One randomized controlled trial (n=64), "of poor methodological quality" met inclusion criteria. There is insufficient evidence to support HBO for the treatment of this condition.

Epilepsy: Epilepsy, or seizure disorder, is characterized by the tendency to have recurring seizures. HBO is proposed for the treatment of this condition as a means to improve cerebral circulation to the brain and decrease cerebral edema. HBO for the treatment of epilepsy has not been established.

Fractures (e.g., Acute, Delayed Union and/or Nonunion): The primary goal in the treatment of fractures is the realignment and stabilization of the fractured bone and restoration of function. HBO has been proposed to assist in improving the healing outcomes in delayed or nonunion fractures, but improvement in clinical outcomes has not been established.

In a Cochrane systematic review, Bennett et al. (2012) concluded that, although HBO has been proposed for many years for the treatment of fractures, there is insufficient evidence within the literature to support or refute that it aids in the healing of acute injuries and fractures, and/or assists in the healing process of a nonunion fracture. No studies met inclusion criteria.

Headaches (Cluster and Migraine): Cluster headaches and migraine headaches are distinct primary headaches. Both are extremely painful with cluster headaches being less common than migraine headaches. According to the International Headache Society, a cluster headache is on one side of the head and lasts 30–90 minutes. A migraine headache is a chronic condition with recurrent, episodic attacks that last hours to days. Although HBO has been proposed as a treatment option for headaches, there is insufficient evidence in the peer-reviewed literature supporting the efficacy of HBO for the treatment of these conditions.

Bennett et al. (2008) (updated 2015) conducted a systematic review and meta-analysis to evaluate the safety and efficacy of HBO compared to normobaric oxygen therapy (NBOT) used for the prevention and treatment of migraine and cluster headaches. The review included 11 randomized controlled trials (n=209) including five trials (n=103) that compared HBO to sham for acute migraines, two (n=29) that compared HBO to sham therapy for cluster headaches and one evaluated NBOT (n=56) to sham for a mixed headache group. Pooled data from three trials (n=58) suggested that HBO was effective in relieving migraines compared to sham therapy, but provided no evidence that HBO could prevent migraines or reduce nausea, vomiting or medication requirements. There was no evidence that HBO was effective for the termination of cluster headache.

Hepatic Necrosis: Hepatic necrosis is a severe and progressive form of hepatitis associated with hepatocellular death and hepatic failure. Although HBO has been proposed as a treatment option for hepatic necrosis, there is insufficient evidence in the peer-reviewed literature to support its use for this condition.

Human Immunodeficiency Virus (HIV) – Fatigue: Fatigue is often a chronic, debilitating symptom of individuals infected with HIV. It has been hypothesized that increased oxygenation by HBO may help to relieve the fatigue. However, evidence in the peer-reviewed literature supporting this hypothesis is lacking.

In Vitro Fertilization (IVF): Infertility may be the result of endometriosis, or abnormalities in tubal, uterine, endometrial, cervical, or ovulatory functions. It has been proposed that increasing oxygenation by HBO may aid in egg maturation and alignment of chromosomes during meiosis but there is insufficient evidence to report this claim.

Lyme Disease: Lyme disease is a clinical diagnosis, and currently the early use of antibiotics can prevent persistent, recurrent, and refractory conditions. The duration of therapy is determined by each individual's clinical response, but the adjuvant use of HBO therapy is not recommended as part of this treatment.

Lymphedema: Approximately 10–38% of all women who have breast-conserving surgery (BCS) or modified radical mastectomy have postsurgical irradiation to the lymph nodes, and 10% of those women develop lymphedema. HBO has not been established as an effective adjunctive treatment for the reduction of lymphedema. Studies have primarily been in the form of case series with small patient populations (n=10) and reported that the total limb volume did not change significantly from baseline measurements (Teas, et al., 2004).

Gothard et al. (2010) conducted a randomized controlled trial (n=58) to investigate the effectiveness of HBO in the treatment of patients with ipsilateral arm lymphedema, ≥ 15% increase in arm volume, following treatment for cancer. Diagnosis included breast cancer (n=56) and Hodgkin lymphoma (n=2). All patients had undergone surgery and radiation therapy. The average interval of time from radiation therapy to randomization was 2.1–21.5 years. Patients were randomized to HBO (n=38) or to the control group (n=20). The study group received 30 HBO treatments while the control group continued best standard care for lymphedema according to the 2006 Lymphoedema Framework Best Practice for the Management of Lymphoedema International Consensus. At the 12-month follow-up (n=46), there were no statistically significant differences from baseline to follow-up in the median volume of the ipsilateral limb (expressed as a percentage of contralateral limb volume) and change over time in either group. There was no clear within-patient improvement from baseline to 12 months with either group. Author-noted limitations of the study included the small patient population and the interval of time from radiation therapy to randomization.

Malignant Otitis Externa: Malignant otitis externa (i.e., necrotizing external otitis) is an uncommon, yet potentially fatal infection of the external auditory canal and may involve surrounding tissue and soft bone. HBO therapy has been proposed as an adjunct to traditional therapy (e.g., diabetic control, administration of antibiotics, repeat debridement and surgical resection). However, the efficacy of HBO for this condition has not been established.

Phillips et al. (2013) conducted a Cochrane systematic review to determine the effectiveness of HBO when used as an adjunct to the traditional treatment protocols for malignant otitis externa. The researchers could not locate any randomized controlled trials that had measured the effectiveness of HBO within this population. A small number of case reports and case series were found, but there was no clear evidence that demonstrated the effectiveness HBO therapy for this condition.

Multiple Sclerosis: Multiple sclerosis (MS) is a chronic neurological disease in which there is patchy inflammation, demyelination, and gliosis in the central nervous system. HBO has been proposed as a treatment modality for MS based on the demonstrated ability of HBO to produce vasoconstriction with increased oxygen delivery and some anecdotal evidence of efficacy.

In a Cochrane systematic review, Bennett and Heard (2011) investigated the use of HBO for the treatment of MS. Two randomized controlled trials reported generally positive results, but the remaining seven randomized trials reported no evidence of treatment effects. Due to the paucity of evidence to confirm beneficial effects of HBO, the authors did not believe that routine use of HBO was justified.

Mycoses: Mycosis is an infection or a disease caused by a fungus (e.g., candidiasis, aspergillosis, cryptoccocus). Zygomycosis (e.g., mucormycosis, phycomycosis) is an infection caused by "bread mold fungi" and can infect immunosuppresant individuals (e.g., HIV). HBO has been proposed as a treatment option for some forms of invasive mycosis (e.g., zygomycosis), but its efficacy remains unproven (McAdam and Sharpe, 2005).

Nonvascular Causes of Chronic Brain Syndrome (e.g., Pick's Disease, Alzheimer's Disease, Korsakoff's Disease): Chronic Brain Syndrome, also called dementia, is a loss of brain function. Alzheimer's disease and Pick's disease are forms of dementia. Alzheimer's is a primary degenerative dementia that typically involves diffuse atrophy of the brain, while Pick's disease is a classical frontotemporal dementia. Korsakoff's is a psychosis that results from a thiamine deficiency and is primarily a memory disorder. The efficacy of HBO for these conditions has not been established (Smith and Seirafi, 2006).

Ophthalmologic Conditions Other Than Central Retinal Artery Occlusion (e.g., Optic Neuropathy, Glaucoma): HBO has been proposed as an adjunctive treatment option for various ophthalmologic conditions, including, optic neuropathy, and glaucoma. There is insufficient evidence to determine the health outcomes of HBO for the treatment of ophthalmologic conditions other than central retinal artery occlusion.

Organ Transplant/Storage: Researchers have hypothesized that HBO may enhance the performance and growth in pancreatic islet grafts when they are subjected to high levels of oxygen prior to transplant. HBO has also been proposed for administration following organ transplantation to reduce the risk of organ rejection (e.g., liver) as well as, keeping donated organs viable for a longer period of time. However, additional research is required to establish the efficacy of HBO therapy on organ transplantation and storage (Muralidharan, et al., 2007; Juang, 2002).

Pulmonary Emphysema: Emphysema is defined as an abnormal permanent enlargement of air spaces in the distal bronchioles that is associated with chronic bronchitis. HBO has been proposed as a treatment option for emphysema, however, improvements in health outcomes have not been established in clinical trials.

Reflex Sympathetic Dystrophy (RSD)/Complex Regional Pain Syndrome (CRPS): CRPS, also known as RSD or causalgia, is a neuropathic condition that causes intense pain primarily in the arms, hands, legs, or feet. HBO has been proposed as a treatment option for the pain associated with CRPS. Evidence in the peer-reviewed literature does not support the effectiveness of HBO for the treatment of CRPS.

Kiralp et al. (2004) conducted a double-blinded, randomized, placebo-controlled study (n=71) to assess the effectiveness of HBO for treating patients with CRPS. The patients were allocated alternately to receive fifteen, 90-minute therapy sessions of HBO therapy (n=37) or normal air therapy (n=34). The visual analog scale score indicated that pain decreased starting from the first day until day 45 of treatment. An increase in wrist flexion was observed with the HBO group after 15 therapy sessions. A decrease in wrist circumference in the HBO group was also reported. There was a statistically significant difference for all variables except wrist extension. The study is limited by the small patient population and short-term follow-up. Additional studies with larger populations and long-term follow-ups are needed to validate the results of this clinical trial.

Rheumatoid Arthritis: Rheumatoid arthritis (RA) is a chronic systemic inflammatory disease of unknown cause that primarily affects the peripheral joints leading to joint destruction and limited mobility. Although HBO has been proposed for the treatment of RA to decrease pain and inflammation, there is insufficient evidence supporting its efficacy.

Sepsis: Sepsis is a group of disorders that result from infection by bacteria, viruses, fungi, or parasites or the toxic products of these microorganisms. Sepsis involves early signs of circulatory compromise to full-blown circulatory collapse with potentially multi-organ system failure and death. The role of HBO as an adjunctive therapy in the treatment of sepsis remains controversial.

Sickle-Cell Disease: Sickle-cell disease is a hereditary disorder of hemoglobin structure and function. The anemia of sickle-cell disease is due to both chronic and acute hemolysis. Several new approaches to treatment of sickle-cell disease are currently under evaluation; however, these approaches do not include HBO (Lodewijk, 2007). Studies supporting HBO for the treatment of sickle-cell anemia are lacking.

Soft Tissue Injury (e.g., Delayed Onset Muscle Soreness, Closed Soft Tissue Injury, Sprains, Strains): Soft tissue injuries can range from abrasions and bruising to disruptions of tendons, ligaments, and muscles. Muscle soreness and damage are commonly associated with athletic activity. HBO has been proposed as an adjunct to conventional therapies (e.g., rest, elevation, pharmacotherapy) to expedite the healing process, but its beneficial impact on health outcomes has not been established.

According to Bennett et al. (2010) in a Cochrane systematic review including nine randomized controlled trials (n=219), there was insufficient evidence to conclude that HBO in the treatment of delayed onset of muscle soreness or closed soft tissue injury is efficacious.

Spinal Cord Injuries: Bruising, pressure, cutting or severance of the spinal cord may result in partial or complete loss of sensation and movement below the site of injury. Studies investigating the adjunctive use of HBO for the treatment of spinal cord injuries are primarily in the form of small, uncontrolled case series with a range of spinal cord injuries. Overall, results were not

favorable. HBO therapy for the management of spinal cord injury has not been widely accepted (Rowland, 2005).

Stroke: Medical therapies for stroke are designed to minimize or prevent ischemic brain infarction, optimize functional recovery, and avert stroke recurrence. Specific therapies depend on the stroke syndrome. Xu et al. (2018) conducted a randomized controlled trial (n=79) to investigate the safety and efficacy of HBO therapy on diabetic patients who had suffered an acute intracerebral hemorrhage. Patients were randomized to 60 min of HBO daily for 30 days in a monophasic chamber or to normobaric oxygen therapy with similar protocol. No significant differences were seen between the groups at the one-month follow-up. At the six months follow-up significant improvements in the HBO group were seen in the modified Rankin Scale (p=0.045) and National Institutes of Health Stroke Scale (p=0.035), but not in the Barthel Index (p=0.080) and Glasgow Outcome Scale (p=0.73). Limitations of the study include the small patient population, short-term follow-up, and the patient population of diabetics with acute intracerebral hemorrhage preventing generalization of the results. Additional studies are needed to support HBO for this indication.

In a Cochrane review conducted by Bennett et al. (2014), the authors assessed the safety and effectiveness of adjunctive HBO therapy in the treatment of acute ischemic stroke. Eleven randomized controlled trials (n=705) met inclusion criteria. The authors concluded that there was no good evidence to show that HBO improved clinical outcomes when used for the treatment of this subpopulation. Additional research is needed to identify the benefit of HBO for these patients.

Guidelines for the early management of acute ischemic stroke (AIS) by the American Heart Association and the American Stroke Association (2018) stated HBO is not recommended for patients with AIS except when caused by air embolization. The limited available data show no benefit from HBO.

Tetanus: Tetanus is caused by the bacteria Clostridium tetani and is characterized by an acute onset of hypertonia and generalized muscle spasms. Although HBO has been proposed as a treatment option for tetanus, there is insufficient evidence in the peer-reviewed literature to support its efficacy.

Tinnitus: Tinnitus, also commonly referred to as "ringing in the ears" or "head noise," is defined as the perception of sound in the head when no external sound is present. This symptom can occur in one ear or bilaterally, as well as internal and external to the auricle. HBO has been investigated as a treatment option in order to increase the supply of oxygen to the ear and brain in an attempt to decrease the severity of hearing loss and tinnitus. Overall, improved clinical outcomes have not been reported following HBO.

Bennett, et al. (2012) conducted a systemic review of seven randomized controlled trials (n=392) to assess the benefits and harms of HBO for the treatment of tinnitus and/or sudden sensorineural hearing loss. The significance of any improvement in tinnitus could not be assessed by pooled data and the routine use of HBO for the treatment of tinnitus could not be recommended.

In a study to analyze the effectiveness of HBO treatment on tinnitus, Porubsky et al. (2007) randomized 360 patients into two HBO treatment protocols (2.2 bar vs. 2.5 bar). Twelve patients (3.3%) experienced complete remission of tinnitus, in 122 (33.9) the intensity lessened, and 44 (12.2%) had a subjectively agreeable change of noise characteristics. No change was found in 157 cases (43.6%) and 25 (6.9%) experienced deterioration. There was no statistically significant difference between the two groups (p>0.05). Out of 68 patients with a positive expectation of HBO effects, 60.3% stated that the tinnitus had improved compared to 47.2% of patients (n=271) who underwent therapy with an indifferent expectation and 19% (n=21) of patients with a

negative expectation. The influence of subjective expectation on the outcome was statistically significant ($p<0.05$).

Venous Stasis Ulcers: Venous stasis ulcers are the result of chronic venous insufficiency and can lead to life-threatening infections of the lower extremities. Although HBO therapy has been proposed for the treatment of this population, its efficacy has not been established by clinical trials. A Cochrane systematic review of randomized controlled trials evaluating HBO for the treatment of chronic wounds (Kranke, et al., 2012; updated 2015) included one trial with 16 patients who had venous ulcers. At six weeks the author reported significant reduction in the ulcer area. Large randomized controlled trials with long-term follow-ups are needed to validate the results of this study.

Keohane et al. (2023) conducted a systematic review to evaluate the efficacy of Hyperbaric Oxygen Therapy (HBO) in the complete healing or reduction in size of venous leg ulcers (VLU) when compared to control group. Six studies (n=166) met inclusion criteria. Two studies reported no statistically significant difference between HBOT and controls for the outcome of complete ulcer healing ($p=0.4478$) at 12 weeks. Four studies reported non-significant results of complete ulcer healing at 5–6 weeks follow-up ($p=0.1136$). A change is size of VLU was reported in each study ($p=0.0024$). There was significant variance across the studies, with different controls, reporting of outcomes and duration of follow-up. Additional limitations included small, heterogeneous patient populations and short-term follow-up. Although studies reported a reduction in area of VLU versus controls, this does not translate to a significant clinical benefit.

Other Indications: Studies, primarily in the form of case series (n=5-20), case reports and retrospective reviews have investigated HBO as a primary or adjunctive therapy for various other indications including: altitude sickness, avascular necrosis, Bell’s palsy, chronic non-healing wounds, comatose patients, cutaneous polyarteritis nodosa lesions, diabetes, frostbite, femoral head necrosis, fibromyalgia, gastrointestinal ulcers, heat stroke, high altitude illness, keloid recurrence, myofascial pain, Parkinson disease, chronic periodontitis, radiation-induced xerostomia, scleroderma, venomous snake bites, and to improve the success of osseointegration following maxillofacial implants. Overall, improved health outcomes following HBO for the treatment of these conditions have not been established.

The FDA issued a warning (2013, updated 2021) regarding the use of HBO for indications that are not FDA approved (”off-label”). Per the FDA, the safety and effectiveness of HBO has not been established for the following diseases and conditions: AIDS/HIV, Alzheimer's disease, autism, asthma, Bell's palsy, brain Injury, cerebral palsy, depression, diabetes, heart disease, hepatitis, migraine, multiple sclerosis, Parkinson's disease, spinal cord Injury, sport's injury, and stroke.

Fox et al. (2015) conducted a systematic review to assess the efficacy of HBO for the treatment of radiation-induced xerostomia and related quality-of-life (QOL). Studies included patients who had received radiation therapy for head and neck cancer and had not previously been treated with HBO. Seven studies met the inclusion criteria. Two studies were randomized controlled trials (n=45), four were prospective case series (n=121) and one was retrospective in design (n=80). The average number of HBO treatments ranged from 20–42.7 and the average time between radiation therapy and HBO treatment ranged from two days to 6.42 years. Overall, patients had increased stimulated saliva output, decreased sensation of dry mouth, and trends toward improvement in QOL related to dry mouth and sticky saliva. However, no significant improvement in overall QOL was demonstrated. The studies were limited by the small, heterogeneous patient populations; heterogeneity of treatment regimens; and lack of a comparator in the majority of the studies.

Wu et al. (2014) conducted a randomized controlled trial (n=80) to evaluate adjunctive HBO following autologous bone marrow mononuclear cells (BM-MNCs) infusion for the treatment of type 2 diabetes mellitus. Patients were treated with standard care for the first four months to reach optimal glycemic control. Thereafter, patients were randomized into four groups: BM-MNCs plus HBO; BM-MNC only, HBO only and standard care. The primary end point was C-peptide area under the curve (AUC) of the oral glucose tolerance test. Following 12 months of treatment, the AUC was significantly improved in the BM-MNC group and the MB-MNC plus HBO group compared to standard care ($p<0.01$, ea.) but there was no significant improvement with the use of HBO and BM-MNC compared to BM-MNC alone.

In a 2012 (updated 2016) Cochrane systematic review of the literature, Holland et al. reported that one low quality randomized controlled trial (n=79) suggested that HBO may be effective for the treatment of Bell's palsy. Further randomized controlled trials are indicated.

Esposito et al. (2013) conducted a systematic review of randomized controlled trials to investigate the effectiveness of HBO administered with dental implants. Only one randomized controlled trial with 26 patients met inclusion criteria. One year after implantation, four patients died from each group. There were no statistically significant differences for prosthesis and implant failures, postoperative complications, and patient satisfaction between the two groups.

Topical Hyperbaric Oxygen (THBO) or Topical Oxygen Therapies

Literature Review: There is insufficient evidence in the published peer-reviewed scientific literature to support the effectiveness of THBO for the treatment of acute or chronic wounds. The available studies have been primarily in the form of nonrandomized studies and case series with small patient populations and short-term follow-ups.

Frykberg et al. (2020) conducted a randomized, double blind, placebo-controlled trial to evaluate the efficacy of multimodality cyclical pressure Topical Wound Oxygen (TWO2) home care therapy (HyperBox; AOTI Ltd., Galway, Ireland) in healing refractory diabetic foot ulcers (DFUs) that had failed to heal with standard of care (SOC) alone. Seventy-three patients were included from 17 diabetic foot centers from the United States, United Kingdom, France, Germany, and Luxembourg. The average age was 63.3 years, 86% male with 68.5% White/Hispanic, 14% Black, 4.1% Asian, 1.4% American Indian, and 12.3% did not report race. Patients were included if they were 18–89 years old, had a diagnosis of Type 1 or 2 diabetes with a non-healing full-thickness, grade 1 or 2 DFU measuring ≥1 cm^2 and ≤20 cm^2 post-debridement. All ulcers included were present between four weeks and one year duration and received SOC treatment for at least four weeks. Patients were excluded if they had evidence of active severe infection, gangrene, osteomyelitis, active Charcot, uncontrolled diabetes (HgbA1c >12%), known malignancy, on renal dialysis or serum creatinine >2.5 mg/dL. All patents received concurrent SOC therapy and were randomized to receive active TWO2 therapy (n=37) or sham treatment (n=36). Patients treated themselves at home for 90 min daily five times per week with either the allocated TWO2 or sham therapy until the ulcer healed or for a total of 12 weeks. No study therapy was done at the study centers. The primary outcome was the percentage of ulcers in each group achieving 100% healing at 12 weeks. Secondary end points included wound area reduction, 12-month incidence of both recurrence and complete healing, incidence of amputation, Cardiff Wound Impact Schedule (CWIS) QOL assessment, and adverse events. At 12 weeks, TWO2 arm had a closure rate of 41.7% (15/37) compared with 13.5% (5/36) in sham arm ($p=0.010$). For open wounds at 12 weeks, the wound area reduction was 1.97 cm^2 in TWO2 arm and 0.40 cm^2 in sham arm. At 12 month follow up, 56% of ulcers in the TWO2 arm were closed versus 27% of sham treated ulcers ($p=0.013$). Recurrence occurred in 6.7% (1/15) of TWO2 arm and 40% (2/5) of sham arm. Two index limb amputations (5%) occurred in the active arm compared with three index limb amputations (8%) in the sham arm. QOL improved for those whose ulcers healed. There were equal numbers of

adverse events in the study arm and the sham arm. Serious adverse events included wound infection, osteomyelitis, hypoglycemic event, urinary tract infection, significant necrotic tissue, cardiovascular event, UTC grade 2 ulceration, severe maceration/dermatitis, and pneumonia. No device related events occurred. Author noted limitation included the small patient population.

Blackman et al. (2010) conducted a prospective controlled study to compare the efficacy of THBO (n=17) to silver-based dressing (control group, n=11) for the treatment of diabetic foot ulcers. Wounds were more severe and ulcer durations were longer in the treatment group compared to the control group. The THBO group received therapy five times per week for 90 days. Wounds were debrided in each group as indicated. The number of ulcers with complete healing in the THBO group compared to the control group was statistically significant (p=0.04). Fourteen of 17 ulcers (82.4%) in the treatment group and five of 11 ulcers (45.5%) in the control group healed after a median of 56 and 93 days, respectively. At the 24-month follow-up no ulcers had reoccurred in either group. The authors noted that there was a possible selection bias with the more serious wound patients being assigned to THBO. Limitations of the study include the small patient population and nonrandomization.

Tawfick and Sultan (2009) conducted a prospective comparative study to evaluate the safety and efficacy of THBO for the treatment of chronic venous ulcers refractory to medical management. A total of 46 ulcers were treated with THBO and debridement, and 37 ulcers were treated with dressings and debridement. Patients selected the treatment option they preferred. Treatment was continued for 12 weeks or until complete healing occurred. Compared to the control group, a significant number of ulcers in the THBO group showed a reduction in surface area by week three and complete healing by week 12 (p=0.016 and p<0.001, respectively). At 12 weeks, the mean reduction in ulcer surface area was 96% in the THBO group, compared to 61% in the control group. The median time to full healing was 45 days in the THBO group and 182 days in the control group (p<0.001). Nine of 19 methicillin resistant staphylococcus aureus (MRSA) positive ulcers in the THBO group were negative after five weeks of therapy compared to none of 17 in the control group (p=0.007). During the follow-up period none of the 37 THBO-treated healed ulcers showed signs of recurrence compared to 5 of 13 ulcers in the control group and two control group ulcers begin to deteriorate prior to complete healing. Limitations of the study include the small patient population, selection of treatment option by the patients, and nonrandomization.

Professional Societies/Organizations: Regarding topical oxygen, Undersea and Hyperbaric Medical Society (UHMS) stated (Feldmejer, et al., 2005) that topical oxygen is not hyperbaric nor is it equivalent to HBO. Outcomes from clinical studies evaluating HBO cannot be applied to topical oxygen. UHMS does not recommend the use of THBO outside of clinical trials.

Medicare Coverage Determinations

	Contractor	Determination Name/Number	Revision Effective Date
NCD	National	Hyperbaric Oxygen Therapy (20.29)	12/18/2017
LCD	CGS Administrators	Oxygen and oxygen equipment (L33797).	4/01/2023

Note: Please review the current Medicare Policy for the most up-to-date information.
(NCD = National Coverage Determination; LCD = Local Coverage Determination)

Coding Information

Notes:

1. This list of codes may not be all-inclusive since the American Medical Association (AMA) and Centers for Medicare & Medicaid Services (CMS) code updates may occur more frequently than policy updates.
2. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Systemic Hyperbaric Oxygen Therapy

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

CPT®* Codes	Description
99183	Physician or other qualified health care professional attendance and supervision of hyperbaric oxygen therapy, per session

HCPCS Codes	Description
G0277	Hyperbaric oxygen under pressure, full body chamber, per 30 minute interval

Topical Hyperbaric Oxygen

Considered Experimental/Investigational/Unproven:

HCPCS Codes	Description
A4575	Topical hyperbaric oxygen chamber, disposable
E0446	Topical oxygen delivery system, not otherwise specified, includes all supplies and accessories

ICD-10-CM Diagnosis Codes	Description
	All codes

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Revision Details

Type of Revision	Summary of Changes	Date
Annual review	No policy statement changes.	5/15/2024