02.01.13 Hyperbaric Oxygen Therapy (HBOT) Systemic* and Topical Hyperbaric Oxygen Therapy (THOT)

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Related Policies:

- None

Summary

Description

Hyperbaric oxygen therapy (HBOT) involves breathing 100% oxygen at pressures between 1.5 and 3.0 atmospheres. It is generally applied systemically with the patient inside a hyperbaric chamber. HBOT can also be applied topically i.e., the body part to be treated is isolated (e.g., in an inflatable bag and exposed to pure oxygen). HBOT has been investigated for various conditions that have potential to respond to increased oxygen delivery to tissue.

Summary of Evidence

Systemic Hyperbaric Oxygen Therapy

For individuals with bisphosphonate-related osteonecrosis of the jaw who receive systemic HBOT, the evidence includes a randomized control trial (RCT). Relevant outcomes are symptoms and change in disease status. The RCT was unblinded and reported initial benefits at 3-month follow-up; however, there were no significant benefits of HBOT for most health outcomes compared with standard care in the long-term (6 months to 2 years). The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with acute coronary syndrome who receive systemic HBOT, the evidence includes RCTs and a systematic review. Relevant outcomes are OS, symptoms, change in disease status, and functional outcomes. A Cochrane review identified 6 RCTs. There were 2 pooled analyses, 1 found significantly lower rates of death with HBOT and the other reported inconsistent results in left ventricular function. Additional RCT data are needed. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with acute ischemic stroke who receive systemic HBOT, the evidence includes RCTs and a systematic review. Relevant outcomes are OS, symptoms, change in disease status, and functional outcomes. Cochrane reviewers could only pool data for a single outcome for acute ischemic stroke (mortality at 3 to 6 months), and for that outcome, there was no significant difference between active and sham HBOT treatments. An RCT found that HBOT combined with DAPT may enhance neurological recovery, and support daily living activities in elderly acute cerebral infarction patients; larger, multicenter studies with standardized HBOT protocols and extended follow-up are needed to confirm these findings. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with motor dysfunction associated with stroke who receive systemic HBOT, the evidence includes an RCT. Relevant outcomes are symptoms and functional outcomes. The RCT, which used a crossover design, found better outcomes with HBOT at 2 months than with delayed treatment. However, the trial had a number of methodologic limitations (e.g., lack of patient blinding, heterogeneous population, high dropout rate) that make it difficult to evaluate the efficacy of HBOT. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with Bell palsy who receive systemic HBOT, the evidence includes a systematic review. Relevant outcomes are symptoms, change in disease status, and functional outcomes. A Cochrane review did not identify any RCTs meeting selection criteria; the single RCT found did not have a blinded outcome assessment. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with traumatic brain injury who receive systemic HBOT, the evidence includes RCTs and systematic reviews. Relevant outcomes are OS, symptoms, change in disease status, and functional outcomes. RCTs were heterogeneous regarding intervention protocols, patient populations, and outcomes reported. Systematic reviews conducted pooled analyses only on a minority of the published RCTs, and these findings were inconsistent. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with inflammatory bowel disease who receive systemic HBOT, the evidence includes RCT, observational studies, and a systematic review. Relevant outcomes are symptoms, change in disease status and functional outcomes. RCTs have reported mixed findings in patients with ulcerative colitis, with one study terminated early due to futility. A systematic review including the RCT and observational studies found a high rate of bias in the literature due to attrition and reporting bias. Another systematic review

found that HBOT appears to be a safe and effective adjunctive therapy for UC, with potential benefits for CD requiring further investigation. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with delayed-onset muscle soreness who receive systemic HBOT, the evidence includes RCTs and a systematic review. Relevant outcomes are symptoms and functional outcomes. A Cochrane review of RCTs found worse short-term pain outcomes with HBOT than with control and no difference in longer-term pain or other outcomes (e.g., swelling). The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with autism spectrum disorder who receive systemic HBOT, the evidence includes an RCT and systematic reviews. Relevant outcomes are symptoms and functional outcomes. A Cochrane review identified a single RCT on HBOT for autism spectrum disorder and this trial did not find significantly better parental-assessed or clinician-assessed outcomes with HBOT compared with sham. A controlled trial (Rizzato 2018) reached the same conclusion. A subsequent systematic review by Tu et al (2025) evaluated the effectiveness of HBOT in children and adolescents with autism spectrum disorders. Although their meta-analysis found potential benefits of HBOT, including a significant reduction in the core symptoms of autism [SMD = -0.66, 95 % CI (-1.04, -0.28), P = 0.0006], significant limitations such as poor methodological quality and high heterogeneity precluded drawing strong conclusions about these findings. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with cerebral palsy who receive systemic HBOT, the evidence includes 2 RCTs and an observational study. Relevant outcomes are symptoms and functional outcomes. One RCT was stopped early due to futility, and the other did not find significantly better outcomes with HBOT than with a sham intervention. The observational study focused on sleep disorders in children with cerebral palsy and reported improvements with the HBOT treatment. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with vascular dementia who receive systemic HBOT, the evidence includes an RCT and a systematic review. Relevant outcomes are symptoms and functional outcomes. The Cochrane review identified only a single RCT with methodologic limitations. Well-conducted controlled trials are needed. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with idiopathic femoral neck necrosis who receive systemic HBOT, the evidence includes RCT. Relevant outcomes are symptoms, change in disease status, and functional outcomes. The RCT, which had a small sample, only reported short-term (i.e., 6-week) outcomes. Larger well-conducted RCTs reporting longer-term outcomes are needed. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with a migraine who receive systemic HBOT, the evidence includes RCTs and a systematic review. Relevant outcomes are symptoms, change in disease status, and functional outcomes. The Cochrane review conducted a pooled analysis including 3 of the 11 trials. Meta-analysis of these 3 RCTs found significantly greater relief of migraine symptoms with HBOT than with a comparator intervention within 45 minutes of treatment. Longer-term data are needed. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with herpes zoster who receive systemic HBOT, the evidence includes an RCT. Relevant outcomes are symptoms and change in disease status. The RCT was unblinded and only reported short-term (i.e., 6-week) outcomes. Additional well-conducted RCTs with longer follow-up are needed. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with fibromyalgia who receive systemic HBOT, the evidence includes RCTs. Relevant outcomes are symptoms, change in disease status, and functional outcomes. Only 2 RCTs were identified, and both reported positive effects of HBOT on tender points and pain. However, the trials had relatively small samples and methodologic limitations (e.g., quasi-randomization, no or uncertain sham control for a condition with subjective outcomes susceptible to a placebo effect). Moreover, the HBOT protocols varied. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with multiple sclerosis who receive systemic HBOT, the evidence includes RCTs and a systematic review. Relevant outcomes are symptoms and functional outcomes. A Cochrane review of RCTs did not find a significant difference in Expanded Disability Status Scale scores when patients with multiple sclerosis were treated with HBOT versus a comparator intervention. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with radiotherapy adverse events to include radiation induced cystitis or arm lymphedema who receive systemic HBOT, the evidence includes RCTs, nonrandomized comparator trials, case series, and systematic reviews. Relevant outcomes are symptoms and functional outcomes. Two systematic reviews included few RCTs and provided limited evidence on the effect of HBOT. Two RCTs had inconsistent findings. One reported no short-term benefit with HBOT, but some benefits 12 months after radiotherapy; the other did not find a significant benefit of HBOT at 12-month follow-up. Another RCT assessed HBOT for radiation-induced cystitis and found significant benefit by some measures but not others. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with cancer and are undergoing chemotherapy who receive systemic HBOT, the evidence includes an RCT and a systematic review. Relevant outcomes are OS and change in disease status. While the systematic review reported improvements in tumor control in patients with head and neck cancer who received HBOT, the adverse events accompanying the treatment (e.g., radiation tissue injury, seizures) were significant. The single RCT did not find a significant difference in survival for cancer patients who received HBOT before chemotherapy compared with usual care. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with various indications listed in Policy section below who receive systemic HBOT, the evidence includes systematic reviews, RCTs and observational studies. Relevant outcomes are OS, symptoms, change in disease status, and functional outcomes. The current evidence search did not find that systemic HBOT consistently significantly improved outcomes versus sham or other comparators for the indications listed below, see Policy. The evidence is insufficient in determining the effects of the technology on net health outcomes.

Topical Hyperbaric Oxygen Therapy

For individuals with wounds, burns or infections who receive topical hyperbaric oxygen therapy (HBOT), the evidence includes a systematic review, case series, and a randomized controlled trial (RCT). Relevant outcomes are overall survival (OS), symptoms, change in disease status, and functional outcomes. The systematic review identified 3 RCTs including patients with sacral pressure ulcers, ischial pressure ulcers, and refractory venous ulcers. All trials reported that healing improved significantly after topical HBOT than after standard of care. Pooling of results was not possible due to heterogeneity in patient populations and treatment regimens. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Additional Information

Not applicable.

OBJECTIVE

The objective of this evidence review is to determine whether the use of topical or systemic hyperbaric oxygen pressurization improves net health outcomes for a variety of indications.

PRIOR APPROVAL

Prior approval required.

Note: *Refer to Wellmark Authorization Table for medical necessity clinical coverage criteria using InterQual® criteria related to systemic hyperbaric oxygen therapy.*

POLICY

Systemic Hyperbaric Oxygen Therapy (HBOT)

Systemic hyperbaric oxygen therapy (HBOT) is considered **investigational,** including but not limited to the following indications because the evidence is insufficient in determining the effects of the technology on net health outcomes:

- When the medical necessity InterQual® criteria is not met, see Prior Approval
- Acute carbon tetrachloride poisoning
- Acute cerebral edema
- Acute coronary syndromes and as adjunct to coronary artery interventions including but not limited to percutaneous coronary interventions and cardiopulmonary bypass
- Acute frost bite
- Acute ischemic stroke
- Acute osteomyelitis (for refractory osteomyelitis, see Prior Approval)
- Acute surgical and traumatic wounds not meeting medically necessary InterQual® criteria related to compromised graft or flap, see Prior Approval
- AIDS/HIV
- Alzheimer's disease/Dementia
- Anorectal disorders (e.g., chronic anal fissure, internal hemorrhoids, infections proctitis)
- Asthma
- Autism spectrum disorder (ASD)
- Bell's palsy
- Bisphosphonate-related osteonecrosis of the jaw
- Bone graft
- Brain injury, acute and traumatic brain injury (TBI)
- Brown recluse spider bite (necrotizing arachnoidism)
- Cerebral palsy
- Cerebrovascular disease, acute (thrombotic or embolic) or chronic
- Chronic arm lymphedema following radiotherapy for cancer

- Chronic fatigue syndrome
- Chronic wounds, other than those individuals with diabetic foot ulcer or diabetic lower extremity wound that meet the criteria specified as medically necessary per InterQual® criteria, see Prior Approval
- Delayed onset muscle soreness
- Demyelinating disease including but not limited to multiple sclerosis (MS) and amyotrophic lateral sclerosis (ALS)
- Early treatment (beginning at the completion of radiation therapy) to reduce side effects of radiation therapy
- Epilepsy
- Fibromyalgia
- First-degree thermal burns (for second and/or third-degree thermal burns see Prior Approval)
- Fracture healing
- Heart disease
- Hepatitis/Hepatic necrosis
- Herpes zoster
- Hydrogen sulfide poisoning
- Idiopathic femoral head necrosis
- Inflammatory bowel disease (Crohn's disease to include fistulizing Crohn's' disease and ulcerative colitis)
- Intra-abdominal abscesses
- In-vitro fertilization
- Lepromatous leprosy
- Meningitis
- Mental illness (i.e., post-traumatic stress disorder, generalized anxiety disorder or depression)
- Migraine headaches/headaches
- Motor dysfunction associated with stroke
- Neurologic conditions
- Parkinson's disease
- Preconditioning to improve myocardial function and/or reduce postoperative complications in patients undergoing coronary artery bypass grafting (CABG)
- Pseudomembranous colitis (antimicrobial agent-induced colitis)
- Pyoderma gangrenosum
- Radiation induced injury of head and neck, except for osteoradionecrosis or prophylactic pre and post treatment for individuals undergoing dental surgery (non-implant related) of irradiated jaw per InterQual® criteria, see Prior Approval
- Radiation myelitis
- Refractory mycoses: mucormycosis, actinomycosis, conidiobolus coronato
- Retinopathy, adjunct to scleral buckling procedures in patients with sickle cell peripheral retinopathy and retinal detachment
- Sickle cell crisis and/or hematuria
- Spinal cord injury
- Sports injury
- Tumor sensitization for cancer treatments including but not limited to radiotherapy or chemotherapy
- Vascular dementia

Topical Hyperbaric Oxygen Therapy (THOT)

Topical hyperbaric oxygen therapy is considered **investigational** for all indications because the evidence is insufficient in determining the effects of the technology on net health outcomes.

POLICY GUIDELINES

There is limited comparative evidence for HBOT. The policy is based on the best available evidence, and is largely informed by clinical input and guidelines.

Systemic Hyperbaric Oxygen Therapy

Systemic hyperbaric oxygen therapy refers to treatment at pressures greater than 1.4 atmosphere absolute, administered in a hard-sided hyperbaric chamber that meets applicable safety standards.

Topical Hyperbaric Oxygen Therapy

HCPCS code A4575 is used to describe a disposable topical hyperbaric oxygen appliance that creates a "chamber" around the wound area which is pressurized with "hyperbaric oxygen." Conventional oxygen tanks, typically gas, are used to supply the oxygen. An example of such a device is the AOTI Hyper-Box™.

This policy addresses topical hyperbaric oxygen therapy (HBOT) but not topical oxygen wound care.

Topical HBOT may be performed in the office, clinic, or may be self-administered by the patient in the home. Typically, the therapy is offered for 90 minutes per day for 4 consecutive days. After a 3-day break, the cycle is repeated. The regimen may last for 8 to 10 weeks.

Timing and Duration of HBOT Treatment

While broad indications are given above, the decision to treat with HBOT and timing of HBOT should be made on a case-by-case basis. For example, acute arterial ischemia have a spectrum of times that vary by tissue type: minutes for neurological tissues, hours for muscle, days for skin and bone, and even longer for relatively avascular connective tissues, cartilage, and adnexal structures. Even for indications with guideline-based time periods there are case studies showing improvement outside of such windows. For example, the Undersea and Hyperbaric Medical Society Committee recommends HBOT treatment for central retinal artery occlusion (CRAO) within 24 hours of onset, as studies demonstrate the outcome of HBOT is improved with early treatment. However, successful cases have been reported in which treatment began later, sometimes up to weeks later. Given the safety of HBOT, the lack of successful alternative medical treatments, the debilitating impact of vision loss, and the challenges faced in getting a patient to a hyperbaric facility, it is difficult to provide a specific time cutoff after which HBOT should not be tried for CRAO.

As such, no broad statements or specific statements as to timing of HBOT can be provided.

Recommended treatment dose and number of treatment sessions per the UHMS Hyperbaric Oxygen Therapy Committee (15th edition, 2023) include:

- **Acute traumatic ischemia** – there are 3 stages of wound healing. Treatment recommended varies based on stage, and ranges from 2-3 times per day for 2-3 days for acute inflammatory stage, 14 days for repair stage, and up to a month for remodeling.
- **Carbon monoxide poisoning** – Use up to 3 ATA for 1 to 3 sessions or to clinical plateau.
- **Central Retinal Artery Occlusion(CRAO)**– Recommend 2 to 2.8 ATA or U.S. Navy Table 6 or equivalent. Treat twice daily to clinical plateau, which typically occurs in less than a week, plus 3 days. Hyperbaric treatments 2-3 times daily may be necessary until the angiogram normalizes or the patient has no further improvement for 3 treatments.
- **Clostridial myositis, Clostridial myonecrosis (Gas gangrene)-** Recommend 3 ATA pressure for 90 minutes, 2-3 times in the first 24 hours, and then 2 times daily for the next 2-5 days. Review is indicated after 10 treatments.
- **Chronic refractory osteomyelitis –** Typically, once daily, 5-7 days per week for 90-120 minutes using 2-3 ATA, and continued for 4-6 weeks. 20-40 sessions typically needed, although might be situations where up to 60 sessions are needed. Patients with refractory stage 3 or 4 osteomyelitis are most likely to benefit from adjunctive hyperbaric oxygen therapy, especially when complicated by adverse local or systemic factors.
- **Compartment syndrome** – Use 2 to 2.4 ATA, usually twice a day for 2 days but sometimes might need 3 times a day. After fasciotomy, twice a day for 7-14 days.
- **Compromised skin grafts and flaps –** Use 2 to 2.5 ATA twice daily for up to 20 sessions.
- **Crush injury** – similar to acute traumatic ischemia above. The UHMS notes that HBOT should be started as close as possible to the time of injury; 3 or more treatments during the first 24 to 72 hours are recommended; 1-2 times per day for 14 days if in the repair phase; daily use for 3-6 weeks during remodeling.
- **Cyanide poisoning** – Patients with cyanide poisoning frequently present with simultaneous carbon monoxide poisoning. Treatment protocol recommended is the same as for carbon monoxide poisoning.
- **Decompression sickness** – Use U.S. Navy Treatment Table 6 or equivalent, typically up to 2.8 ATA, for 1 session up to a clinical plateau. Typically, no more than 1 to 2 treatment sessions are needed.
- **Diabetic lower extremity wounds, selected individuals and healing of other problem wounds** –Use 2 to 2.5 ATA daily, should see effects by 2-3 weeks; course of outpatient therapy is typically 30 sessions but might require up to 40 sessions. For HBOT to continue, reevaluation at 30-day intervals must show continued progress in healing.
- **Necrotizing soft-tissue infections** – Use 2 to 2.5 ATA twice daily until stabilization occurs, often occurs within 7-10 treatments. If differential diagnosis includes the possibility of Clostridial myositis and/or myonecrosis and/or remains unclear, 2.8-3 ATA pressures are warranted with 3 treatments in the first 24-48 hours. Avoidance of premature cessation of HBOT is advised, and once extension of necrosis has been halted then once daily treatments over an extended period until the infection is well controlled is recommended. This might require 30 treatments. Review after 30 treatments.
- **Radiation Necrosis** –Most treatments range from 2-2.5 ATA for 40-60 treatments, and review should occur after 60 treatments.
    1. **Mandibular osteoradionecrosis, laryngeal necrosis, other soft tissue head and neck, chest wall necrosis, radiation cystitis, radiation proctitis, miscellaneous abdominal pelvic injuries, cutaneous necrosis** – 2 to 2.4 ATA daily for 90 minutes.
    2. **Neoadjuvant hyperbaric oxygen therapy before dental extractions** – 2 to 2.4 ATA, typically 20 treatments before extraction and 10 treatments after.
- **Sudden sensorineural heating loss** – Recommend 2 to 2.5 ATA for 10 to 20 sessions.
- **Severe Anemia** – Use 2 to 3 ATA for 3 or 4 times a day until there is replacement of red blood cells by regeneration or transfusion.

Coding

See the Codes table for details.

BACKGROUND

Hyperbaric Oxygen Therapy

Hyperbaric oxygen therapy (HBOT) is a technique for delivering higher pressures of oxygen to tissue. Two methods of administration are available: topical and systemic.

Systemic Hyperbaric Oxygen Therapy

In systemic or large hyperbaric oxygen chambers, the patient is entirely enclosed in a pressure chamber and breathes oxygen at a pressure greater than 1 atmosphere (the pressure of oxygen at sea level). Thus, this technique relies on systemic circulation to deliver highly oxygenated blood to the target site, typically a wound. Treatment may be carried out either in a monoplace chamber pressurized with pure oxygen or in a larger, multiplace chamber pressurized with compressed air, in which case the patient receives pure oxygen by mask, head tent, or endotracheal tube.

Topical Hyperbaric Oxygen Therapy

Topical hyperbaric oxygen therapy (THOT) is a technique of delivering 100% oxygen directly to an open, moist wound at a pressure slightly higher than atmospheric pressure. It is hypothesized that the high concentrations of oxygen diffuse directly into the wound to increase the local cellular oxygen tension, which in turn promotes wound healing. Devices consist of an appliance to enclose the wound area (frequently an extremity) and a source of oxygen; conventional oxygen tanks may be used. The appliances may be disposable and may be used without supervision in the home by well-trained patients. THOT/CTOT has been investigated as a treatment of skin ulcerations resulting from diabetes, venous stasis, postsurgical infection, gangrenous lesion, decubitus ulcers, amputations, skin graft, burns, or frostbite.

Adverse Events

HBOT is a generally safe therapy, with an estimated adverse side effect rate of 0.4%. Adverse events may occur either from pressure effects or the oxygen. The pressure effect (barotrauma) may affect any closed air-filled cavity such as ears, sinus, teeth, and lungs. Pain and/or swelling may occur at these sites as pressure increases during the procedure and decreases as the procedure is ending. Oxygen toxicity may affect the pulmonary, neurologic, or ophthalmologic systems. Pulmonary symptoms include a mild cough, substernal burning, and dyspnea. Neurologic effects include tunnel vision, tinnitus, nausea, and dizziness. Ophthalmologic effects include retinopathy in neonates, cataract formation, and transient myopic vision changes.

Note: *This evidence review does not address topical oxygen therapy in the absence of pressurization.*

Regulatory Status

Since 1979, the U.S. Food and Drug Administration (FDA) has cleared multiple topical and systemic hyperbaric oxygen administration devices through the 510(k) pathway. In 2013, the FDA published a statement warning that non-FDA approved uses of HBOT may endanger the health of patients. If patients mistakenly believe that HBOT devices have been proven safe for uses not cleared by the FDA, they may delay or forgo proven medical therapies.

The FDA issued a warning (2013) 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."

As of July 2021, the FDA has cleared hyperbaric chambers for the following disorders:

- Air and gas bubbles in blood vessels
- Anemia (severe anemia when blood transfusions cannot be used)
- Burns (severe and large burns treated at a specialized burn center)
- Carbon monoxide poisoning
- Crush injury
- Decompression sickness (diving risk)
- Gas gangrene
- Hearing loss (complete hearing loss that occurs suddenly and without any known cause)
- Infection of the skin and bone (severe)
- Radiation injury
- Skin graft flap at risk of tissue death
- Vision loss (when sudden and painless in one eye due to blockage of blood flow)
- Wounds (non-healing, diabetic foot ulcers).

RATIONALE

This evidence review was created in September 1999 and has been updated regularly with a search of the PubMed database. The most recent literature search was conducted through February 2026.

Evidence reviews assess the clinical evidence to determine whether the use of technology improves the net health outcome. Broadly defined, health outcomes are length of life, quality of life, and ability to function - including benefits and harms. Every clinical condition has specific outcomes that are important to patients and managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of technology, 2 domains are examined: the relevance, and quality and credibility. To be relevant, studies must represent one or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. RCTs are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

Evidence for a majority of the indications consists of Cochrane systematic reviews, which focus on summarizing RCTs, and when possible, conducting pooled analyses of results.

Systemic Hyperbaric Oxygen Therapy for Bisphosphonate-Related Osteonecrosis of the Jaw

Clinical Context and Therapy Purpose

The purpose of systemic HBOT is to provide a treatment option that is an alternative to or an improvement on existing therapies in patients with bisphosphonate-related osteonecrosis of the jaw.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with bisphosphonate-related osteonecrosis of the jaw

Interventions

The therapy being considered is systemic HBOT.

Comparators

Comparators of interest include medication and surgical therapy. Medications prescribed may consist of systemic antibiotics and systemic or topical antifungals. Systemic HBOT may be used as an adjunct to these comparators

Outcomes

The general outcomes of interest are symptoms and change in disease status. The existing literature evaluating systemic HBOT as a treatment for bisphosphonate-related osteonecrosis of the jaw analyzed follow-up to 18 months. Though follow-up to 3-months showed initial benefits, the RCT reported below recommended longer term follow-up to analyze outcomes compared with standard of care. Therefore, at least 1 year of follow-up is considered necessary to demonstrate efficacy and superiority to comparators.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess longer term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

Review of Evidence

An unblinded RCT by Freiberger et al (2012) evaluated the use of HBOT as an adjunct therapy for patients with bisphosphonate-related osteonecrosis of the jaw (see Tables 1 and 2). The investigators did a per-protocol analysis (actual treatment received) due to crossovers between the treatment groups. Participants were evaluated at 3, 6, 12, and 18 months. At 3 months, significantly more patients receiving HBOT as an adjunct to standard care experienced improvements in lesion size and number compared with patients receiving only standard care. When the change from baseline to 6, 12, or 18 months was examined, there were no statistically significant differences between groups in the proportion of patients with improvement or in the proportion of those who healed completely at any time point. This trial had a number of methodologic limitations (e.g., unblinded, crossover, per-protocol analysis rather than intention-to-treat). A disadvantage of the per-protocol analysis is that randomization is not preserved, and the 2 groups may differ on characteristics that affect outcomes.

Table 1. Characteristics of Trials Assessing Hyperbaric Oxygen Therapy for Bisphosphonate-Related Osteonecrosis of the Jaw

					Treatment	
Study (Year)	**Countries**	**Sites**	**Dates**	**Participants**	**Active (n=25)**	**Comparator (n=21)**
Freiberger et al (2012)	United States	NR[a]	2006-2010	Patients with bisphosphonate-related osteonecrosis of the jaw	• Hyperbaric oxygen plus standard oral care • 100% oxygen at 2 ATA • 40 treatments	Standard oral care (antiseptic rinses, surgery, and antibiotics)

ATA: atmospheres absolute; HBOT: hyperbaric oxygen therapy; NR: not reported.
[a] Number of sites not reported, though all oncologists, dentists, and oral-maxillofacial surgeons in the referral area of central North Carolina, southern Virginia, and northern South Carolina were eligible to participate.

Table 2. Results of Trials Assessing Hyperbaric Oxygen Therapy for Bisphosphonate-Related Osteonecrosis of the Jaw

	Improved, % (n)				Healed, % (n)		
Study (Year)	**3 Months**	**Between-Group P-Value**	**18 Months**	**Between-Group P-Value**	**3 Months**	**Between-Group P-Value**	**Between-Group P-Value**
Freiberger et al (2012)[23,]	46		46		46		
HBOT	68.0 (25)	.03	58.3 (12)	.31	36.0 (25)	.04	1.0
Control	35.0 (20)		33.3 (6)		10.0 (20)		

HBOT: hyperbaric oxygen therapy.

Section Summary: Systemic Hyperbaric Oxygen Therapy for Bisphosphonate-Related Osteonecrosis of the Jaw

One RCT evaluated HBOT for patients with bisphosphonate-related osteonecrosis of the jaw. This unblinded study reported initial benefits at the 3-month follow-up; however, there were no significant benefits of HBOT for most health outcomes compared with standard care in the long-term (6 months to 2 years). Additional evidence from RCTs is needed to permit conclusions on the impact of HBOT on health outcomes in patients with bisphosphonate-related osteonecrosis of the jaw.

Systemic Hyperbaric Oxygen Therapy for Acute Coronary Syndrome

Clinical Context and Therapy Purpose

The purpose of systemic HBOT is to provide a treatment option that is an alternative to or an improvement on existing therapies in individuals with acute coronary syndrome.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with acute coronary syndrome.

Interventions

The therapy being considered is systemic HBOT.

Comparators

Comparators of interest include medication and surgical therapy. Medication prescribed for the treatment of acute coronary syndrome may include thrombolytics, nitroglycerin, antiplatelet drugs, beta-blockers, angiotensin-converting enzyme inhibitors, angiotensin receptor blocks, and statins. Surgical therapy can include angioplasty and stenting and coronary bypass surgery. Systemic HBOT may be used as an adjunct to these comparators.

Outcomes

The general outcomes of interest are OS, symptoms, change in disease status, and functional outcomes. The existing literature evaluating systemic HBOT as a treatment for acute coronary syndrome has varying lengths of follow-up. However, longer-term follow-up does provide a better opportunity for analyses of outcomes. Therefore, at least 1 year of follow-up is considered necessary to demonstrate efficacy.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess longer term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

Review of Evidence

A Cochrane review by Bennett et al (2015) identified 6 trials (N=665) evaluating HBOT for acute coronary syndrome (see Table 3). Included studies were published between 1973 and 2007. All studies included patients with acute myocardial infarction; a study also included individuals with unstable angina. Additionally, all trials used HBOT, administered between 2 and 3 ATA, for 30 to 120-minute sessions, as an adjunct to standard care. Control interventions varied; only a trial described using a sham therapy to blind participants to treatment group allocation. In a pooled analysis of data from 5 trials, there was a significantly lower risk of mortality in patients who received HBOT compared with a control intervention. Due to the variability of outcome reporting across studies, few other pooled analyses could be conducted. Three trials reported outcomes related to left ventricular function. One did not find a statistically significant improvement in contraction with HBOT, while 2 trials showed left ventricular ejection fraction improved significantly with HBOT. Reviewers noted that, although some evidence from small trials correlated HBOT with a lower risk of death, larger trials with high-quality methods were needed to determine which patients, if any, could be expected to derive benefit from HBOT.

Table 3. Systemic Reviews of Trials Assessing Hyperbaric Oxygen Therapy for Acute Coronary Syndrome

Study (Year)	Literature Search	Studies	Participants	N	Design	Results
Bennett et al (2015)	Jun 2010	6	Adults with acute coronary syndrome, with or	665	RCTs	• Pooled analyses of 5 trials (n=614) reported a lower mortality rate for patients in the HBOT group vs.

Study (Year)	Literature Search	Studies	Participants	N	Design	Results
			without S-T segment elevation			the control (RR, 0.58; 95% CI, 0.36 to 0.92) • Left ventricular outcomes, 3 trials total: 1 trial reported no difference in contraction (RR, 0.09; 95% CI, 0.01 to 1.4) and pooled analyses of 2 trials (n=190) found significant improvements in LVEF with HBOT (MD, 5.5%; 95% CI, 2.2% to 8.8%)

CI: confidence interval; HBOT: hyperbaric oxygen therapy; LVEF: left ventricular ejection fracture; MD: mean difference; RCT: randomized controlled trial; RR: relative risk.

Section Summary: **Systemic Hyperbaric Oxygen Therapy for Acute Coronary Syndrome**

A Cochrane review of 6 RCTs found insufficient evidence that HBOT is safe and effective for acute coronary syndrome. One pooled analysis of data from 5 RCTs found a significantly lower rate of death with HBOT than with a comparison intervention; however, larger, higher-quality trials are needed. Three trials measuring left ventricular function report inconsistent results.

Systemic Hyperbaric Oxygen Therapy for Acute Ischemic Stroke

Clinical Context and Therapy Purpose

The purpose of systemic HBOT is to provide a treatment option that is an alternative to or an improvement on existing therapies in patients with acute ischemic stroke.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with acute ischemic stroke.

Interventions

The therapy being considered is systemic HBOT.

Comparators

Comparators of interest include administration of tissue plasminogen activator and endovascular procedures. Systemic HBOT may be used as an adjunct to these comparators.

Outcomes

The general outcomes of interest are OS, symptoms, change in disease status, and functional outcomes. The existing literature evaluating systemic HBOT as a treatment for acute ischemic stroke has varying lengths of follow-up, ranging from none to 6 months. In the systematic review described below, all

studies reported at least 1 outcome of interest, but longer follow-up was necessary to fully observe outcomes. Therefore, 6 months to 1 year or more of follow-up is considered necessary to demonstrate efficacy.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess longer term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

Review of Evidence

Systematic Reviews

In a Cochrane systematic review of RCTs, Bennett et al (2014) evaluated HBOT for acute ischemic stroke (see Table 4). Reviewers identified 11 RCTs (N=705) that compared HBOT with sham HBOT or no treatment. Reviewers could pool study findings for only 1 outcome (mortality at 3 to 6 months), and no difference was detected between the treatment groups for that outcome. There was heterogeneity in the participants enrolled and in the clinical and functional outcomes measured across the studies.

Table 4. Systemic Reviews of Trials Assessing Hyperbaric Oxygen Therapy for Acute Ischemic Stroke

Study (Year)	Literature Search	Studies	Participants	N	Design	Results
Bennett et al (2014)	Apr 2014	11	Patients with acute ischemic stroke, defined as sudden neurologic deficit of vascular origin for which hemorrhage was excluded by CT or MRI	705	RCTs	Pooled analyses of 4 trials (n=144) found no difference in mortality at 3 to 6 mo (RR, 0.97; 95% CI, 0.34 to 2.75)

CI: confidence interval; CT: computed tomography; HBOT: hyperbaric oxygen therapy; MRI: magnetic resonance imaging; RCT: randomized controlled trial; RR: relative risk.

Randomized Controlled Trials

Wang et al (2025) published an RCT subsequent to the Cochrane review evaluating the efficacy of HBOT combined with dual antiplatelet therapy (DAPT) in elderly patients with acute cerebral infarction (Table 5 and 6). A total of 122 patients (≥60 years, first onset within 72 hours) were randomized 1:1 to either DAPT alone or HBOT plus DAPT; HBOT was administered in 30 sessions over three courses, starting at admission, alongside standard aspirin and clopidogrel therapy. After treatment, the HBOT+DAPT group demonstrated a significantly higher overall clinical efficacy rate (90.16% vs. 75.41%, p<.05) and greater

improvements in NIH Stroke Scale (NIHSS), Chinese Stroke Scale (CSS), serum neuron-specific enolase (NSE), and plasma β-amyloid-42 levels compared with the control group. Limitations include modest sample size, lack of long-term follow-up, and absence of biomarker validation. Larger, multicenter studies with standardized HBOT protocols and extended follow-up are needed to confirm these finding.

Table 5. Characteristics of Trials Assessing Hyperbaric Oxygen Therapy for Acute Ischemic Stroke

					Treatment	
Study (Year)	**Countries**	**Sites**	**Dates**	**Participants**	**Active (n=61)**	**Comparator (n=61)**
Wang et al (2025)	China	1	2023-2024	Patients ⩾60 years with acute ischemic stroke (onset of disease ⩽72 hours)	HBOT plus DAPT	DAPT alone

DAPT, dual antiplatelet therapy; HBOT: hyperbaric oxygen therapy

Table 6. Results of Trials Assessing Hyperbaric Oxygen Therapy for Acute Ischemic Stroke

Study (Year)	**Clinical Efficacy***	**NIHSS**	**CSS**
Wang et al (2025)			
HBOT + DAPT n(%)	55 (90.16)	NR	NR
DAPT alone n(%)	46 (75.41)	NR	NR
OR or Cohen's d (95% CI)	OR, 0.335 (95% CI, 0.120 to 0.932)	Cohen's d=0.610 (95% CI, 1.211 to 4.658)	Cohen's d=1.392 (95% CI=4.565 to 7.730)

*Clinical efficacy defined as (1) basic cure: 91%−100% reduction in functional deficit score; (2) notable progress: 46%−90% reduction in functional deficit score; (3) progress: 18%−45% reduction in functional deficit score; (4) ineffectiveness: 0–17% reduction in functional deficit score. The clinical efficacy rate was calculated using the following formula: (number of "basic cure" patients + number of "notable progress" patients + number of "progress" patients)/total number of patients × 100%
CI: confidence interval; CSS:China Stroke Scale; DAPT, dual antiplatelet therapy; HBOT: hyperbaric oxygen therapy; NIHSS: National Institutes of Health Stroke Scale; NR: not reported OR: odds ratio

Section Summary: Systemic Hyperbaric Oxygen Therapy for Acute Ischemic Stroke

A Cochrane review of RCTs conducted a pooled analysis of 4 RCTs and found no significant difference in mortality rates at 3 to 6 months when patients with acute ischemic stroke were treated with HBOT or a sham intervention. Additional RCT data are needed to permit conclusions on the impact of HBOT on the health outcome in patients with acute ischemic stroke.

Systemic Hyperbaric Oxygen Therapy for Motor Dysfunction Associated with Stroke

Clinical Context and Therapy Purpose

The purpose of systemic HBOT is to provide a treatment option that is an alternative to or an improvement on existing therapies in individuals with motor dysfunction associated with stroke.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with motor dysfunction associated with stroke.

Interventions

The therapy being considered is systemic HBOT.

Comparators

Comparators of interest include physical therapy. Systemic HBOT may be used as an adjunct to these comparators.

Outcomes

The general outcomes of interest are symptoms and functional outcomes. The existing literature evaluating systemic HBOT as a treatment for motor dysfunction associated with stroke had a treatment-group follow-up time of 2 months. In the RCT described below, longer follow-up was recommended to fully observe outcomes. Therefore, 3 months to 1 year or more of follow-up is considered necessary to demonstrate efficacy.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess longer term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

Review of Evidence

Efrati et al (2013) published an RCT evaluating HBOT for the treatment of neurologic deficiencies associated with a history of stroke (see Tables 7 and 8). Patients in the treatment group were evaluated at baseline and 2 months. For patients in the delayed treatment control group, outcomes were evaluated at 4 months after crossing over and receiving HBOT. Outcome measures included the National Institutes of Health Stroke Scale, which was measured by physicians blinded to the treatment group, and several patient-reported QOL and functional status measures. At the 2-month follow-up, there was a statistically significant improvement in function in the HBOT group compared with the control group, as measured by the National Institutes of Health Stroke Scale, QOL scales, and the ability to perform activities of daily

living. These differences in outcome measures were accompanied by improvements in single-photon emission computed tomography imaging in the regions affected by stroke. For the delayed treatment control group, there was a statistically significant improvement in function after HBOT compared with before HBOT. This RCT raises the possibility that HBOT may induce improvements in function and QOL for post-stroke patients with motor deficits. However, the results are not definitive, as the RCT was small and enrolled a heterogeneous group of post-stroke patients. The trial was not double-blind and most outcome measures, except for National Institutes of Health Stroke Scale, were patient-reported and prone to the placebo effect. Also, there was a high total dropout rate (20%) at the 2-month follow-up. Larger, double-blind studies with longer follow-up are needed to corroborate these results.

Table 7. Characteristics of Trials Assessing Hyperbaric Oxygen Therapy for Motor Dysfunction Associated with Stroke

					Treatment	
Study (Year)	**Countries**	**Sites**	**Dates**	**Participants**	**Active (n=30)**	**Comparator (n=29)**
Efrati et al (2013)	Israel	1	2008-2010	Patients ⩾18 y with ischemic or hemorrhagic stroke 6 to 36 mo prior to inclusion with ⩾1 motor dysfunction	• Hyperbaric oxygen • 100% oxygen at 2 ATA • 40 times over 2 mo	Same as active, delayed after 2 mo

ATA: atmospheres absolute; HBOT: hyperbaric oxygen therapy.

Table 8. Results of Trials Assessing Hyperbaric Oxygen Therapy for Motor Dysfunction Associated with Stroke

	National Institutes of Health Stroke Scale			Activities of Daily Living[a]		
Study (Year)	**Baseline**	**2 Months**	**Between-Group P-Value**	**Baseline**	**2 Months**	**Between-Group P-Value**
Efrati et al (2013)[29,]	50	50		50	50	
Mean HBOT (SD)	8.5 (3.6)	5.5 (3.6)	.004	16.1 (6.5)	12.8 (7.3)	.02
Mean control (SD)	8.7 (4.1)	8.3 (4.3)		17.4 (9.5)	17.5 (9.5)	

HBOT: hyperbaric oxygen; SD: standard deviation.

[a] Activities of Daily Living: 16 functions scored across a range whether patient was independent to did not perform at all. Range: 0 (best) to 51 (worst).

Section Summary: Systemic Hyperbaric Oxygen Therapy for Motor Dysfunction Associated with Stroke

One crossover RCT evaluated HBOT in patients with a recent history of stroke. The RCT reported better outcomes at 2 months with HBOT than with delayed treatment. However, the trial had a number of methodologic limitations, making it difficult to draw conclusions about the efficacy of HBOT for this indication. Double-blind RCTs that address potential bias in subjective outcomes and studies with adequate follow-up are needed.

Systemic Hyperbaric Oxygen Therapy for Bell Palsy

Clinical Context and Therapy Purpose

The purpose of systemic HBOT is to provide a treatment option that is an alternative to or an improvement on existing therapies in individuals with Bell palsy.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with Bell palsy.

Interventions

The therapy being considered is systemic HBOT.

Comparators

Comparators of interest include self-care (e.g., artificial tears, eyepatch) and medication. Medications prescribed for Bell palsy may include steroids and antiviral drugs. Systemic HBOT may be used as an adjunct to these comparators.

Outcomes

The general outcomes of interest are symptoms, change in disease status, and functional outcomes. There is a lack of published information analyzing the efficacy of systemic HBOT in individuals with Bell palsy. However, in order to analyze long-term outcomes of function, symptoms, and change in disease status, follow-up ranging from 3 months or 1 year or more is considered necessary to demonstrate efficacy.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess longer term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.

- Studies with duplicative or overlapping populations were excluded.

Review of Evidence

Holland et al (2012) published a Cochrane review evaluating HBOT in adults with moderate-to-severe Bell palsy. The literature search, conducted through January 2012, identified 1 RCT with 79 participants, but this trial did not meet reviewers' prespecified selection standards because the outcome assessor was not blinded to treatment allocation. The trial was therefore excluded with no further analysis

Section Summary: Systemic Hyperbaric Oxygen Therapy for Bell Palsy

There is a lack of evidence on use of HBOT for Bell palsy. A Cochrane review did not identify any eligible RCTs; the single RCT identified lacked blinded outcome assessment. Well-conducted RCTs are needed.

Systemic Hyperbaric Oxygen Therapy for Traumatic Brain Injury

Clinical Context and Therapy Purpose

The purpose of systemic HBOT is to provide a treatment option that is an alternative to or an improvement on existing therapies in individuals with traumatic brain injury (TBI).

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with TBI.

Interventions

The therapy being considered is systemic HBOT.

Comparators

Comparators of interest include medication, surgical therapy, and rehabilitation protocols. Medications prescribed for TBI may include diuretics, anti-seizure drugs, and coma-inducing drugs. Emergency surgery is used to minimize damage to brain tissues and can follow on the removal of hematomas, repairing skull fractures, stopping bleeding in the brain, and opening a window in the skull. Systemic HBOT may be used as an adjunct to these comparators.

Outcomes

The general outcomes of interest are OS, symptoms, change in disease status, and functional outcomes. The existing literature evaluating systemic HBOT as a treatment for TBI has varying lengths of follow-up. In the systematic reviews described below, all studies reported at least 1 outcome of interest, but longer follow-up was necessary to fully observe outcomes. Therefore, at least 1 year of follow-up is considered necessary to demonstrate efficacy.

Table 9 summarizes key measurement tools for assessing severity of brain injury.

Table 9. Brain Injury Assessment Scales Outcome Measures

Outcome	Description	Administration	Scoring	MCID
Glasgow Coma Scale (GCS)	Assesses impairment of conscious level in response to stimuli	Physician-administered	Likert-type scale; lower numbers, more severe TBI: • eye opening (0 [not testable]–4) • verbal response (0–5) • motor response (0–6) Total Score: • Severe: ⩽ 8 • Moderate: 9–12 • Mild: 13–15	NR
Glasgow Outcome Scale (GOS)	Categorizes outcomes of patients after TBI	Physician-administered	1. Death 2. Persistent vegetative state: minimal responsiveness 3. Severe disability: conscious but disabled; dependent on others for daily support 4. Moderate disability: disabled but independent; can work in sheltered setting 5. Good recover: resumption of normal life despite minor deficits	Unfavorable outcome: 1-3
PTSD Checklist (PCL)	A 17-item measure that reflects the DSM-IV symptoms of PTSD	Self-administered	• Likert-type scale (0: not at all–4: extremely) • Total score range: 17–85 • PTSD cut point score for DoD screening: 31–33	• Response to treatment: ⩾ 5 points • Clinically meaningful: ⩾ 10 points

Outcome	Description	Administration	Scoring	MCID
Rivermead Post-Concussion Symptoms Questionnaire (RPQ)	Assesses severity of somatic, cognitive, and emotional symptoms for mTBI	Self-administered or by interviewer	• 16 Likert-type questions • Score range: 0–84 • Higher values indicate more several symptoms	10% improvement

DoD: Department of Defense; DSM-IV: Diagnostic and Statistical Manual of Mental Disorders Fourth Edition; MCID: minimum clinically important difference; mTBI: mild traumatic brain injury; NR: not reported; PTSD: posttraumatic stress disorder; TBI: traumatic brain injury.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess longer term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

Review of Evidence

Systematic Reviews

A meta-analysis by Wang et al (2016) assessed HBOT for TBI (see Table 10). Eight studies (N=519) met the eligibility criteria. HBOT protocols varied across studies in the levels of oxygen and the length and frequency of treatments. The primary outcome was change in the Glasgow Coma Scale score. A pooled analysis of 2 studies found a significantly greater improvement in the mean Glasgow Coma Scale score in the HBOT group compared with control groups. Mortality (a secondary outcome) was reported in 3 of the 8 studies. Pooled analysis of these 3 studies found a significantly lower overall mortality rate in the HBOT group than in the control group.

Another systematic review, by Crawford et al (2016), did not conduct pooled analyses (see Table 8). Reviewers identified 12 RCTs evaluating HBOT for patients with TBI. Using the Scottish Intercollegiate Guidelines Network (SIGN) 50 criteria, 8 trials were rated acceptable and 4 rated low. Four trials, all rated as having acceptable quality, addressed patients with mild TBI and compared HBOT with sham. None found statistically significant differences between groups on outcomes (i.e., postconcussive symptom severity, psychological outcomes). Seven trials evaluated HBOT for the acute treatment of patients with moderate-to-severe TBI. Four were rated as acceptable quality and 3 as low quality. Study protocols and outcomes varied and none used a sham control. Three acceptable quality studies with standard care controls reported the Glasgow Outcome Scale score and mortality rate. In 2 of them, outcomes were better with HBOT than with standard care; in the third study, outcomes did not differ significantly.

A Cochrane review by Bennett et al (2012) evaluated HBOT as adjunctive therapy for acute TBI (see Table 8). Reviewers identified 7 RCTs comparing a standard intensive treatment regimen with the same treatment regimen plus HBOT. Reviewers did not include studies with interventions in specialized acute care settings. The HBOT regimens varied among studies; e.g., the total number of individual sessions varied from 3 to 40. None of the trials used sham treatment or blinded staff treating patients, and only 1 had blinding of outcome assessment. Allocation concealment was inadequate in all studies. The primary outcomes of the review were mortality and functional outcomes. A pooled analysis of data from 4 trials showed that adding HBOT to standard care decreased mortality, but did not improve functional outcome at final follow-up. The unfavorable functional outcome was commonly defined as a Glasgow Outcome Scale score of 1, 2, or 3, which are described as “dead,” “vegetative state,” or “severely disabled,” respectively. Studies were generally small and judged to have a substantial risk of bias.

The systematic review and pooled analysis by Hart et al (2019) evaluated HBOT for mild traumatic brain injury (mTBI)-associated post-concussive symptoms (PCS) and posttraumatic stress disorder (PTSD). Data were aggregated from 4 Department of Defense (DoD) studies that included participant-level data on 254 patients assigned to either HBOT or sham intervention. An additional 3 studies with summary-level participant data were summarized (n=135). The authors assessed changes from baseline to post-intervention on PCS, PTSD, and neuropsychological measures (Table 8). The DoD data analyses indicated improvements with HBOT for PCS, measured by the Rivermead Total Score. Statistically significant improvements were seen for PTSD based on the PTSD Checklist Total Score, as well as for verbal memory based on the California Verbal Learning Test (CVLT) -II Trial 1-5 Free Recall.

Table 10. Systematic Reviews of Trials Assessing Hyperbaric Oxygen Therapy for Traumatic Brain

Study (Year)	Literature Search	Studies	Participants	N	Design	Results
Hart et al (2019)		7 (4 by DoD)	Patients (primarily US Service personnel) with mild traumatic brain injury	389		DoD Analysis: • Improvement in mean Rivermead Total Score (-2.3 points; 95% CI, -5.6 to 1.0; p=.18) • Improvement in mean PTSD Checklist Total Score (-2.7 points; 95% CI, -5.8 to 0.4; p=.089) • Improvement in mean verbal memory based on CVLT-II Trial 1-5 Free Recall (mean=3.8; 95% CI, 1.0 to 6.7; p=.01)
Wang et al (2016)	Dec 2014	8	Patients with mild or severe traumatic brain injury	519	RCTs and 2-arm prospective studies	• Pooled analyses of 2 trials (n=120) found significant improvements in GCS score change (3.1; 95% CI, 2.3 to 3.9) in HBOT vs. control • Pooled analyses of 3 trials (n=263) found lower risk of mortality among patients

Study (Year)	Literature Search	Studies	Participants	N	Design	Results
						treated with HBOT vs. controls (OR, 0.3; 95% CI, 0.2 to 0.6)
Crawford et al (2017)	Aug 2014	12	Military and civilian patients with traumatic brain injury		RCTs	• Pooled analyses not performed • Among 3 trials with GCS outcomes, 2 reported improvements with HBOT and 1 found no difference • 4 trials assessed as acceptable quality did not find significant differences in symptom severity or psychological outcomes
Bennett et al (2012)	Mar 2012	7	Patients with acute traumatic brain injury following blunt trauma	571	RCTs	• Pooled analyses of 4 trials (n=385) found that adding HBOT to standard care decreased mortality vs standard care alone (RR, 0.7; 95% CI, 0.5 to 0.9) • Pooled analyses of 4 trials (n=380) reported no difference in functional status at final follow-up between groups (RR, 1.9; 95% CI, 0.9 to 4.1)

CI: confidence interval; CVLT: California Verbal Learning Test; DoD: Department of Defense; GCS: Glasgow Coma Scale; HBOT: hyperbaric oxygen therapy; OR: odds ratio; PTSD: posttraumatic stress disorder; RCT: randomized controlled trial; RR: relative risk.

Clinical Trials

The DoD-sponsored RCT, “Brain Injury and Mechanisms of Action in Hyperbaric Oxygen for Persistent Post-Concussive Symptoms after Mild Traumatic Brain Injury (mTBI) (BIMA),” completed in 2016, was the first to include post-intervention follow-up beyond 3 to 6 months. Hart et al (2019) described BIMA, which assessed HBOT for U.S. service members with mTBI. BIMA was initially planned for a 12-month follow-up, but was amended to include PCS and PTSD, QOL, pain, depression, anxiety, and alcohol use assessments at 24 and 36 months. Investigators saw no significant differences at 24 or 36 months between the HBOT and sham groups, and group mean scores had returned to near pre-intervention values. Churchill et al (2019) reported on the chamber- and protocol-related adverse events (AEs) in the HOPPS and BIMA trials. In addition to AEs, they assessed the success of maintaining the blind with a low-pressure sham control group. Of the total 4245 chamber sessions, AEs were rare, at 1.1% in the HOPPS study and 2.2% in BIMA. Most AEs were minor, non-limiting barotrauma, and headaches. Results of a questionnaire that followed the intervention showed that the sham group blind was adequately maintained in both trials.

Weaver et al (2019) evaluated BIMA and a second RCT of U.S. service members for the efficacy of HBOT in treating persistent PCS after mTBI. The second study, titled "A Pilot Phase II Study of Hyperbaric Oxygen for Persistent Post-concussive Symptoms After Mild Traumatic Brain Injury (HOPPS)," was completed in 2012. The 3 outcomes assessed in the pooled analyses of the 2 studies were symptoms, cognitive impairment, and functional impairment; they were weighted and grouped into different domains to calculate the composite outcome score. A total of 143 service members were randomized to receive either HBOT (1.5 ATA, > 99% oxygen) or sham therapy (1.2 ATA, room air). In HOPPS, composite total scores improved from baseline for HBOT (mean, -2.9 ± 9.0) and sham treatment (-2.9 ± 6.6), but the groups did not differ significantly from each other (p=.33). The BIMA trial results showed a greater improvement from baseline in the HBOT group (-3.6 ± 6.4) versus sham (-0.3 ± 5.2; p=.02). The authors concluded that composite total scores in HOPPS and BIMA were consistent with primary study results.

Harch et al (2020) published a RCT evaluating HBOT for persistent post-concussion syndrome (PPCS) following mild TBI. Sixty-three civilian and military participants with chronic PPCS were randomized to either 40 HBOT sessions (150 kPa for 60 minutes, 5 days/week for 8 weeks) or a no-treatment control period, after which the control group crossed over to HBOT. Fifty participants completed the protocol. At the end of the initial treatment period, the HBOT group demonstrated a 26.3-point reduction in Neurobehavioral Symptom Inventory scores compared to a 2.5-point reduction in controls. Significant improvements were also observed in memory index, cognitive efficiency (ANAM composite score), depression (HAM-D), anxiety (HAM-A), sleep quality (PSQI), quality of life (QOLIBRI), and PTSD symptom checklist scores, all favoring HBOT over control.

Hadanny et al (2022) published results of a randomized, double-blind, sham-controlled trial evaluating HBOT in children aged 8 to 15 years with PPCS following mild-to-moderate TBI. Twenty-five participants were randomized to receive either 60 daily HBOT sessions (n=15) or sham treatment (n=10). The HBOT group showed a significant improvement in general cognitive scores, increasing from 90.2 ± 10.3 to 96.1 ± 10.3 (p = .01), whereas the sham group remained unchanged (95.1 ± 7.5 to 94.9 ± 7.7; p=.96). This corresponded to a moderate effect size of 0.598. The most notable improvement was in the memory domain, with a mean increase of 11.5 ± 12.5 (p=.017) and an effect size of 0.480 following HBOT, compared to a smaller, non-significant change of 3.4 ± 8.8 (p=.39) in the sham group. No other cognitive domains demonstrated statistically significant changes. Participants also demonstrated behavioral improvements showed reductions in (effect size=0.244, p=.03), along with better global executive functioning (effect size=0.528, p=.001) and enhanced planning/organization skills (effect size=1.09, p<.001). Neuroimaging revealed significant microstructural changes in brain regions associated with cognition, including the insula, supramarginal gyrus, and inferior frontal gyri, which correlated with cognitive improvements.

Zhang et al (2025) published a retrospective study evaluating long-term outcomes (5 to 8 years post-injury) in patients with moderate-to-severe TBI treated with HBOT.[,] A total of 133 patients (median age 49 years) who initiated HBOT within 90 days of injury were analyzed. The primary outcome was the Disability Rating Scale (DRS), dichotomized as favorable (scores 0–3) or unfavorable (scores 4–30); the secondary outcome was the Glasgow Outcome Scale (GOS). At follow-up, 62.4% of patients achieved a favorable outcome (DRS 0–3), including 30.8% with full recovery (DRS 0). Mortality was 6.8%, and 82.7% of survivors were living independently (GOS ≥ 4). Severe TBI patients (GCS 3–8) had worse outcomes than moderate TBI patients (GCS 9–12): mortality 7.8% vs. 3.2%, favorable outcome 60.8% vs. 67.7%. Logistic regression identified age at injury, ICU stay length, and number of HBOT sessions as independent predictors of long-term prognosis.

Section Summary: Systemic Hyperbaric Oxygen Therapy for Traumatic Brain Injury

A number of RCTs and systematic reviews have been published. Pooled analyses were only conducted on a minority of the published RCTs, and these analyses had inconsistent findings.

Additionally, there was overlap in RCTs included in the reviews. There is a lack of consistent evidence from well-conducted trials that HBOT improves the health outcome for patients with TBI.

Systemic Hyperbaric Oxygen Therapy for Inflammatory Bowel Disease

Clinical Context and Therapy Purpose

The purpose of systemic HBOT is to provide a treatment option that is an alternative to or an improvement on existing therapies in individuals with inflammatory bowel disease (IBD).

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with IBD.

Interventions

The therapy being considered is systemic HBOT.

Comparators

Comparators of interest include medication and surgical therapy. Medications prescribed for IBD may include anti-inflammatory drugs, immune systems suppressors, antibiotics, anti-diarrheal medications, pain relievers, iron supplements, and calcium and vitamin D supplements. Surgical therapy can include ileal pouch anal anastomosis. Systemic HBOT may be used as an adjunct to these comparators.

Outcomes

The general outcomes of interest are symptoms, change in disease status, and functional outcomes. The existing literature evaluating systemic HBOT as a treatment for IBD has varying lengths, though many of the studies in the systematic review reported below only followed patients during treatment or for a short time after. Nearly all studies reported at least 1 outcome of interest, but longer follow-up was necessary to fully observe outcomes. Therefore, at least 1 year of follow-up is considered necessary to demonstrate efficacy.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess longer term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

Review of Evidence

You et al (2022) conducted a systematic review and meta-analysis evaluating the adjunctive role of HBOT for IBD management (Table 17). The review included 16 RCTs and 13 non-randomized trials/case series. For ulcerative colitis, HBOT plus usual care significantly improved clinical response compared to usual care alone (risk ratio [RR], 1.24; 95% CI, 1.17 to 1.31; p<.001). Recurrence rates were lower with HBOT (RR, 0.35; 95% CI, 0.24 to 0.53; p<.001). HBOT also reduced serum TNF-α levels (standardized mean difference, −2.13; 95% CI, −3.09 to −1.18; p<.001). For Crohn disease, non-RCT data suggested HBOT may aid healing of refractory disease, but no meta-analysis was performed due to lack of randomized trials.

A systematic review by McCurdy et al (2022) examined the evidence on HBOT for a range of IBD phenotypes (Crohn disease, ulcerative colitis; see Table 11). The review was not limited by study design, and included 3 small RCTs (N=40) and 16 case series. All 3 of the RCTs were conducted in patients with ulcerative colitis. The included case series generally enrolled less than 30 patients each, with the exception of one study, conducted in Russia, that enrolled 519 patients. Overall, a total sample size for the systematic review across phenotypes was 844. Pooled response rates are reported in Table 9. Results from the individual RCTs were mixed. Two RCTs found a benefit for HBOT compared with standard medical care, but they were small studies (n=10 and 20) and were likely underpowered to detect between-group differences. In addition, one of the trials only included prior HBOT responders and one was stopped early due to enrollment difficulties. The third RCT found no benefit of HBOT compared with standard care, and was also stopped early due to futility. Quality assessment of the included studies judged 2 of the 3 included RCTs to be at high risk of bias. Study authors concluded that although HBOT was associated with high response rates across phenotypes, high-quality evidence was very limited, and well-designed RCTs are needed to confirm the effect of HBOT in patients with IBD.

Table 11. Systematic Reviews of Studies Assessing Hyperbaric Oxygen Therapy for Inflammatory Bowel Disease

Study (Year)	Literature Search	Studies	Participants	N	Design	Response Rate (95% CI)
You et al (2022)	Mar 2022	29	Patients with ulcerative colitis or Crohn disease	• Ulcerative colitis (n=2071) • Crohn disease (n=80)	• 16 RCTs • 11 non-randomized trials • 2 case series	• Ulcerative colitis (n=1075): HBOT plus usual care was more effective than usual care alone (RR, 1.24; 95% CI, 1.17 to 1.31; p<.001) • Ulcerative colitis (n=584): HBOT plus usual care had a lower recurrence rate than those who received usual care

Study (Year)	Literature Search	Studies	Participants	N	Design	Response Rate (95% CI)
						only; (RR 0.35; 95% CI, 0.24 to 0.53, p <0.001) • Ulcerative colitis (n= 360) results indicated that HBOT significantly reduced TNF-α levels in patients with ulcerative colitis: SMD, -2.13 (95% CI, -3.09 to -1.18; p<0.001) • Crohn disease: no meta-analysis was performed due to lack of randomized trials
McCurdy et al (2022)	Nov 2020	19	Patients with various IBD phenotypes	• Ulcerative colitis (n=383); • Crohn disease (n=250) • Perianal fistula (n=118) • Enterocutaneous fistula (n=21) • Inflammatory pouch disorders (n=60) • Dermatologic manifestation of IBD (n=12)	3 RCTs 16 case series	• Ulcerative colitis (5 studies): 86% (66% to 95%) • Crohn disease (2 studies): 86% (81% to 90%) • Perianal fistula (10 studies): 75% (66% to 83%) • Pouch disorder (2 studies): 65% (52% to 76%) • Enterocutaneous fistula (3 studies): 85% (61% to 95%)

CI: confidence interval; HBOT: hyperbaric oxygen therapy; IBD: inflammatory bowel disease; RCT: randomized controlled trial.

Section Summary: Systemic Hyperbaric Oxygen Therapy for Inflammatory Bowel Disease

A systematic review of RCTs and observational studies found heterogeneity in HBOT protocols and high rates of bias in the literature (e.g., attrition, reporting bias). Another systematic review found that HBOT appears to be a safe and effective adjunctive therapy for ulcerative colitis, with potential benefits for Crohn disease requiring further investigation.

Systemic Hyperbaric Oxygen Therapy for Delayed-Onset Muscle Soreness

Clinical Context and Therapy Purpose

The purpose of systemic HBOT is to provide a treatment option that is an alternative to or an improvement on existing therapies in individuals with delayed-onset muscle soreness.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with delayed-onset muscle soreness.

Interventions

The therapy being considered is systemic HBOT.

Comparators

Comparators of interest include conservative care (eg, massage) and medication (eg, pain relief). Systemic HBOT may be used as an adjunct to these comparators.

Outcomes

The general outcomes of interest are symptoms and functional outcomes. The existing literature evaluating systemic HBOT as a treatment for delayed-onset muscle soreness has varying lengths of follow-up. In the systematic review described below, all studies reported at least 1 outcome of interest, but longer follow-up was necessary to fully observe outcomes. Therefore, at least 1 month of follow-up is considered necessary to demonstrate efficacy.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;

- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess longer term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

Review of Evidence

In a Cochrane review, Bennett et al (2005; updated 2010) identified 9 small RCTs on HBOT for delayed-onset muscle soreness and closed soft tissue injury (see Table 12). Included trials were published between 1996 and 2003. Methodologic quality was assessed as fair to high. Pooled analysis showed significantly higher pain in the group receiving HBOT compared with control. There were no between-group differences in long-term pain outcomes or other measures (e.g., swelling, muscle strength).

Table 12. Systematic Reviews of Trials Assessing Hyperbaric Oxygen Therapy for Delayed-Onset Muscle Soreness

Study (Year)	Literature Search	Studies	Participants	N	Design	Results
Bennett et al (2010)	Feb 2010	9	Patients with acute closed soft tissue injuries or DOMS	219	RCTs	• 2 trials on closed soft tissue injuries: no significant difference in time to recovery, functional outcomes, or pain • 7 DOMS trials, pooled: significantly higher pain at 48 and 72 h in HBOT group, 0.9 (95% CI, 0.09 to 1.7); no differences in long-term pain, swelling, or muscle strength

CI: confidence interval; DOMS: delayed-onset muscle soreness; HBOT: hyperbaric oxygen therapy; RCT: randomized controlled trial.

Section Summary: Systemic Hyperbaric Oxygen Therapy for Delayed-Onset Muscle Soreness

A Cochrane review of RCTs with fair to high methodologic quality found worse short-term pain outcomes with HBOT than with a control condition and no difference in longer term pain or other outcomes (eg, swelling).

Systemic Hyperbaric Oxygen Therapy for Autism Spectrum Disorder

Clinical Context and Therapy Purpose

The purpose of systemic HBOT is to provide a treatment option that is an alternative to or an improvement on existing therapies in individuals with autism spectrum disorder.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with autism spectrum disorder.

Interventions

The therapy being considered is systemic HBOT.

Comparators

Comparators of interest include behavioral therapy and medication. Behavioral therapy may include anger management, family therapy, applied behavior analysis, etc. Medications prescribed may include antipsychotics. Systemic HBOT may be used as an adjunct to these comparators.

Outcomes

The general outcomes of interest are symptoms and functional outcomes. The existing literature evaluating systemic HBOT as a treatment for autism spectrum disorder had a follow-up of 10 weeks. However, longer term follow-up may show difference between the intervention and comparators. Therefore, at least 6 months of follow-up is considered necessary to demonstrate efficacy.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess longer term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

Review of Evidence

Tu et al (2025) conducted a systematic review and meta-analysis evaluating HBOT for autism spectrum disorder in children and adolescents; 17 studies (11 RCTs and 6 quasi-experimental; N=890) were included (Table 23). In pooled analyses, HBOT significantly reduced core ASD symptoms (SMD=0.66; 95% CI, 0.28 to 1.04; p=.0006) and improved communication (SMD=0.88; 95% CI, 0.04 to 1.71; p=.04), cognitive awareness (SMD=0.93; 95% CI, 0.35 to 1.51; p=.002), and behavior (SMD=0.80; 95% CI, 0.13 to 1.46; p=.02). Sociability showed no significant improvement (SMD=0.29; p=.33). Adverse events were mild (e.g., ear discomfort, sinus congestion) and did not require special treatment. Limitations included high heterogeneity in included studies (I^2 up to 94%), low methodological quality, and lack of standardized HBOT protocols.

A Cochrane review by Xiong et al (2016) identified 1 RCT evaluating systemic HBOT for people with autism spectrum disorder that met eligibility criteria (see Table 13). Criteria included a hyperbaric oxygen intervention using 100% oxygen at more than 1 atm. The trial, published by Sampanthaviat et al (2012), was considered low-quality evidence as assessed by the GRADE approach. The trial randomized children with autism to receive 20 1-hour sessions with HBOT or sham air (n=30 per group). The primary outcome measures were change in Autism Treatment Evaluation Checklist and Clinical Global Impression scores, evaluated separately by clinicians and parents. There were no statistically significant differences between groups for either primary outcome. Post-treatment clinician-assessed mean scores on Autism Treatment Evaluation Checklist were 52.4 in the HBOT group and 52.9 in the sham air group.

Table 13. Systematic Reviews of Trials Assessing Hyperbaric Oxygen Therapy for Autism Spectrum Disorder

Study (Year)	Literature Search	Studies	Participants	N	Design	Results
Tu et al (2025)	Mar 2024	17	Children and adolescents diagnosed with autism spectrum disorder	890	11 RCTs, 6 non-randomized trials	• Effect of HBOT on core symptoms of autism (15 studies): significant reduction in core symptoms compared to control (SMD, -0.66; 95% CI, -1.04 to -0.28; p=.0006) • Effect of HBOT on communication (8 studies): significant improvement compared to control (SMD, -0.88; 95% CI, -1.71 to -0.04; p=.04) • Effect of HBOT on sociability (8 studies): no effect in improving sociability compared to control (SMD, -0.29; 95% CI, -0.88 to 0.30; p=.33) • Effect of HBOT on cognitive awareness (7 studies): significant improvement compared to control (SMD, -0.93; 95% CI, -1.51 to -0.35; p=.002) • Effect of HBOT on behavior (10 studies): significant improvement compared to control (SMD, -0.80; 95% CI, -1.46 to -0.13; p=.02)
Xiong et al (2016)	Dec 2015	1	Children aged 3-9 y with autism spectrum disorder	60	RCT	• Parental assessed ATEC: 1.2 (95% CI, -2.2 to 4.6) • Clinician assessed ATEC: 1.5 (95% CI, -1.3 to 4.5)

ATEC: Autism Treatment Evaluation Checklist; CI: confidence interval; HBOT: hyperbaric oxygen therapy; RCT: randomized controlled trial.

In their controlled trial, Rizzato et al (2018) examined the effect of HBOT on children diagnosed with autism. The children in the HBOT group (n=8; mean age=7 y ± 2.33 y) and control group (n=7; mean age=6.6 y ± 2.7 y) completed the Aberrant Behavior Checklist-Community (ABC) before intervention (T0), after 40 sessions (1), and 1 months after the end of treatment (T2). The HBOT was also assessed with the Childhood Autism Rating Scale at T0 and T2. Total ABC scores had improved between T0 and T2 in both the intervention and control groups. The HBOT group mean score at T0 was 57.5 ± 19.01 and 50.38 ± 18.55 at T2 ($p<.001$). The control group's mean score at T0 was 103.6 ± 20.38 and 59 ± 25.25 at T2 (p <.05). The investigators concluded that their results do not support the use of HBOT in children diagnosed with autism.

Section Summary: **Systemic Hyperbaric Oxygen Therapy for Autism Spectrum Disorder**

A systematic review reported that HBOT appears promising for reducing core ASD symptoms and enhancing functional outcomes, but further high-quality, multicenter trials are needed to confirm efficacy and establish optimal treatment parameters. A Cochrane review identified a single small low-quality RCT on HBOT for autism spectrum disorder, and that trial did not find significantly improved outcomes with HBOT versus sham. A subsequent controlled trial reached the same conclusion, stating results do not support the use of HBOT for autism spectrum disorder.

Systemic Hyperbaric Oxygen Therapy for Cerebral Palsy

Clinical Context and Therapy Purpose

The purpose of systemic HBOT is to provide a treatment option that is an alternative to or an improvement on existing therapies in individuals with cerebral palsy (CP).

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with CP.

Interventions

The therapy being considered is systemic HBOT.

Comparators

Comparators of interest include physical therapy and medication. Medications directed at isolated (e.g., onabotulinumtoxin A) and generalized spasticity (e.g., diazepam, dantrolene, and baclofen) may be prescribed for CP. Systemic HBOT may be used as an adjunct to these comparators.

Outcomes

The general outcomes of interest are symptoms and functional outcomes. The existing literature evaluating systemic HBOT as a treatment for CP has varying lengths of follow-up. In the trials described below, all studies reported at least 1 outcome of interest, but longer follow-up was necessary to fully observe outcomes. Therefore, at least 1 year of follow-up is considered necessary to demonstrate efficacy.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess longer term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

Review of Evidence

Two published RCTs were identified on use of HBOT for CP (see Tables 14 and 15). Lacey et al (2012) published a double-blind RCT that included 49 children ages 3 to 8 years with spastic CP. Participants were randomized to 40 treatments with HBOT or hyperbaric air to simulate 21% oxygen at room air. The primary efficacy outcome was change in the Gross Motor Function Measure global score. The trial was stopped early due to futility when an interim analysis indicated that there was less than a 2% likelihood that a statistically significant difference between groups would be found.

Collet et al (2001) randomized 111 children with CP to 40 treatments over a 2-month period of HBOT or slightly pressurized room air. Investigators found similar improvements in outcomes such as gross motor function and activities of daily living in both treatment groups.

An observational study by Long et al (2017) evaluated the effects of HBOT as a treatment for sleep disorders in children with CP (N=71). Children, ages 2 to 6 years, underwent 60-minute sessions of 100% oxygen, at 1.6 ATA, for 15 to 20 sessions total. Results showed improvements in average time to fall asleep, average hours of sleep duration, and an average number of night awakenings after 10 HBOT sessions compared with pretreatment.

Table 14. Characteristics of Randomized Trials Assessing Hyperbaric Oxygen Therapy for Cerebral Palsy

					Treatment	
Study (Year)	**Countries**	**Sites**	**Dates**	**Participants**	**Active**	**Comparator**
Lacey et al (2012)	United States	2	2005-2009	Children age 3-8 y with spastic CP	• n=25 • Hyperbaric oxygen • 100% oxygen at 1.5 ATA • 40 times over 2 mo	• n=24 • Hyperbaric air • 14% oxygen at 1.5 ATA • 40 times over 2 mo
Collet et al (2001)	Canada	17	NR	Children age 3-12 y with CP	• n=57 • Hyperbaric oxygen • 100% oxygen at 1.75 ATA • 40 times over 2 mo	• n=54 • Slightly pressurized air • 100% oxygen at 1.3 ATA • 40 times over 2 mo

ATA: atmospheres absolute; CP:cerebral palsy; HBOT: hyperbaric oxygen therapy; NR: not reported.

Table 15. Results of Trials Assessing Hyperbaric Oxygen Therapy for Cerebral Palsy

Study (Year)	**Mean Change GMFM[a] (95% CI)**	**Between-Group Difference (95% CI)**	**Mean Change Functional Skill**	**Between-Group Difference (95% CI)**
Lacey et al (2012)	46		46	
HBOT	1.5 (-0.3 to 3.3)	0.9 (-1.5 to 3.3)	4.4 (2.3 to 6.5)	1.1 (-1.5 to 3.7)
HBAT	0.6 (-1.0 to 2.2)		3.3 (1.6 to 5.0)	
Collet et al (2001)			Mean Change, PEDI Self Care	
HBOT	2.9 (1.9 to 3.9)	-0.4 (-1.7 to 0.9)	2.8 (1.6 to 4.0)	0.1 (-1.8 to 2.0)
Slight pressure	3.0 (2.1 to 3.9)		2.7 (1.3 to 4.0)	

CI: confidence interval; GMFM: Gross Motor Function Measure; HBAT: hyperbaric air therapy; HBOT: hyperbaric oxygen therapy; PEDI: Pediatric Evaluation of Disability Inventory.

[a] Positive score represents improvement in function from baseline.

Section Summary: Systemic Hyperbaric Oxygen Therapy for Cerebral Palsy

Two RCTs and an observational study were identified. One RCT was stopped early due to futility and the other did not find significantly better outcomes with HBOT than with a sham intervention. The observational study, which focused on improving sleep in patients with CP, reported improvements following HBOT.

Systemic Hyperbaric Oxygen Therapy for Vascular Dementia

Clinical Context and Therapy Purpose

The purpose of systemic HBOT is to provide a treatment option that is an alternative to or an improvement on existing therapies in individuals with vascular dementia.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with vascular dementia.

Interventions

The therapy being considered is systemic HBOT.

Comparators

Comparators of interest are rehabilitation and medication (eg, cognition-enhancing medication). Systemic HBOT may be used as an adjunct to these comparators.

Outcomes

The general outcomes of interest are symptoms and functional outcomes. The existing literature evaluating systemic HBOT as a treatment for vascular dementia reported follow-up at 12 weeks. However, longer follow-up is necessary to fully observe outcomes. Therefore, at least 1 year of follow-up is considered necessary to demonstrate efficacy.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess longer term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

Review of Evidence

A Cochrane review (2012) identified a small RCT evaluating HBOT for vascular dementia (see Table 16). This 2009 RCT, conducted in China, compared HBOT (30-day cycles of 1 hour/day for 24 days and 6 days of rest) plus donepezil to donepezil-only in 64 patients. The HBOT plus donepezil group had significantly improved cognitive function after 12 weeks of treatment, though the confidence intervals were wide due to the small sample size. Reviewers judged the trial to be of poor quality because it was not blinded and the methods of randomization and allocation concealment were not discussed.

Table 16. Systematic Reviews of Trials Assessing Hyperbaric Oxygen Therapy for Vascular Dementia

Study (Year)	Literature Search	Studies	Participants	N	Design	Results
Xiao et al (2012)	Dec 2011	1	Patients with vascular dementia, according to DSM- IV criteria	64	RCT	• WMD of MMSE score: 3.5 (95% CI, 0.9 to 6.1) • WMD of HDS score: 3.1 (95% CI, 1.2 to 5.0)

CI: confidence interval; DSM-IV: Diagnostic and Statistical Manual for Mental Disorders Fourth Edition; HBOT: hyperbaric oxygen therapy; HDS: Hasegawa's Dementia Rating Scale; MMSE: Mini-Mental State Examination; RCT: randomized controlled trial; WMD: weighted mean difference.

Section Summary: Systemic Hyperbaric Oxygen Therapy for Vascular Dementia

A Cochrane review identified an RCT judged to be of poor quality. This trial provided insufficient evidence to permit conclusions on the impact of HBOT on health outcomes in patients with vascular dementia.

Systemic Hyperbaric Oxygen Therapy for Idiopathic Femoral Neck Necrosis

Clinical Context and Therapy Purpose

The purpose of systemic HBOT is to provide a treatment option that is an alternative to or an improvement on existing therapies in individuals with idiopathic femoral neck necrosis.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with idiopathic femoral neck necrosis.

Interventions

The therapy being considered is systemic HBOT.

Comparators

Comparators of interest include physical therapy, medication, and surgical therapy. Medications prescribed to treat idiopathic femoral neck necrosis may include non-steroidal anti-inflammatory drugs, osteoporosis drugs, cholesterol-lowering drugs, and blood thinners. Systemic HBOT may be used as an adjunct to these comparators.

Outcomes

The general outcomes of interest are symptoms, change in disease status, and functional outcomes. The existing literature evaluating systemic HBOT as a treatment for idiopathic femoral neck necrosis analyzed HBOT therapy at 6 weeks of follow-up. Longer follow-up is necessary to fully observe outcomes. Therefore, at least 1 year of follow-up is considered necessary to demonstrate efficacy.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess longer term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

Review of Evidence

A double-blind RCT evaluating HBOT for the treatment of femoral head necrosis was published by Camporesi et al (2010) (see Tables 17 and 18). The trial included 20 adults with idiopathic unilateral femoral head necrosis. Patients received HBOT or a sham treatment of hyperbaric air. The mean severity of pain on a 0-to-10 scale was significantly lower in the HBOT group than in the control group after 30 sessions ($p<.001$) but not after 10 or 20 sessions. The trial did not report exact pain scores. Several range-of-motion outcomes were reported. At the end of the initial treatment period, extension, abduction, and adduction, but not flexion, was significantly greater in the HBOT group than in the control group. Longer-term comparative data were not available because the control group was offered HBOT after the initial 6-week treatment period.

Table 17. Characteristics of Trials Assessing Hyperbaric Oxygen Therapy for Femoral Neck Necrosis

					Treatment	
Study (Year)	**Countries**	**Sites**	**Dates**	**Participants**	**Active (n=10)**	**Comparator (n=10)**

Camporesi et al (2010)	United States	1	NR	Patients with unilateral femoral neck necrosis	• HBOT • 100% oxygen at 2.5 ATA • 30 sessions over 6 wk	• Hyperbaric air • 30 sessions over 6 wk

ATA: atmospheres absolute; HBOT: hyperbaric oxygen therapy; NR: not reported.

Table 18. Results of Trials Assessing Hyperbaric Oxygen Therapy for Femoral Neck Necrosis

Study (Year)	Median (Range) Extension, After 10 Sessions	Between-Group Difference P Value	Median (Range) Extension, After 30 Sessions	Between-Group Difference P Value
Camporesi et al (2010)				
HBOT	7.5 (4.0-20.0)	NS	20.0 (15.0-20.0)	<.001
HBAT	4.0 (3.0-6.0)		3.0 (0.0-5.0)	

HBAT: hyperbaric air therapy; HBOT: hyperbaric oxygen therapy; NS: not significant.

Section Summary: Systemic Hyperbaric Oxygen Therapy for Idiopathic Femoral Neck Necrosis

One small RCT (n=20) was identified. Six-week outcomes and results were mixed, with improvements reported in extension, abduction, and adduction, but not flexion. Significant improvements in pain were reported after 30 sessions, though no differences were detected after 10 or 20 sessions. This RCT does not provide sufficient data to permit conclusions about the efficacy of HBOT for femoral head necrosis.

Systemic Hyperbaric Oxygen Therapy for Migraine Headache

Clinical Context and Therapy Purpose

The purpose of systemic HBOT is to provide a treatment option that is an alternative to or an improvement on existing therapies in individuals with migraine headache.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with migraine headache.

Interventions

The therapy being considered is systemic HBOT.

Comparators

Comparators of interest include medication. Medications prescribed to treat migraines may include antipsychotics, analgesics, non-steroidal anti-inflammatory drugs, stimulants, nerve pain relievers, Triptan, and neurotoxins. Systemic HBOT may be used as an adjunct to these comparators.

Outcomes

The general outcomes of interest are symptoms, change in disease status, and functional outcomes. The existing literature evaluating systemic HBOT as a treatment for migraine has varying lengths of follow-up. In the systematic reviews described below, nearly all studies reported at least 1 outcome of interest, but longer follow-up was necessary to fully observe outcomes. Therefore, at least 1 month of follow-up is considered necessary to demonstrate efficacy.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess longer term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

Review of Evidence

A Cochrane review by Bennett et al (2015) identified 11 RCTs (N=209) comparing the effectiveness of systemic HBOT for preventing or treating migraine headache or cluster headaches with another treatment or a sham control see Table 19). A pooled analysis of 3 trials focusing on migraine headaches (n=58) found a statistically significant increase in the proportion of patients with substantial relief of migraine within 45 minutes of HBOT. No other pooled analyses were conducted due to variability in outcomes reported across trials. The meta-analysis did not report data on treatment effectiveness beyond the immediate post-treatment period, and the methodologic quality of selected trials was moderate to low (e.g., randomization was not well-described in any trial).

Table 19. Systemic Reviews of Trails Assessing Hyperbaric Oxygen Therapy for Migraine or Cluster Headaches

Study (Year)	Literature Search	Studies	Participants	N	Design	Results
Bennett et al (2015)	Jun 2015	11	Patients with migraine or cluster headaches	209	RCT	• For 3 trials focusing on migraine headaches (n=58) of low quality, HBOT was effective in relieving migraine (RR, 6.21; 95% CI, 2.4 to 16.0)

						• No evidence that HBOT can prevent migraine, reduce nausea or vomiting, or reduce the need for rescue medication

CI: confidence interval; HBOT: hyperbaric oxygen therapy; RCT: randomized controlled trial; RR: relative risk.

Section Summary: Systemic Hyperbaric Oxygen Therapy for Migraine

A Cochrane review identified 11 RCTs on HBOT for a migraine headache. However, only a single pooled analysis was conducted including 3 of the 11 trials. The pooled analysis found significantly greater relief of migraine symptoms with HBOT than with a comparator intervention within 45 minutes of treatment. Limitations included the availability of outcomes specific to the immediate post-treatment period, the variability of outcomes across trials, and generally low methodologic quality of trials.

Systemic Hyperbaric Oxygen Therapy for Herpes Zoster

Clinical Context and Therapy Purpose

The purpose of systemic HBOT is to provide a treatment option that is an alternative to or an improvement on existing therapies in patients with herpes zoster.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with herpes zoster.

Interventions

The therapy being considered is systemic HBOT.

Comparators

Comparators of interest include medication. Medications prescribed to treat herpes zoster may include anti-viral drugs, anesthetics, non-steroidal anti-inflammatory drugs, analgesics, and nerve pain relievers. Systemic HBOT may be used as an adjunct to these comparators.

Outcomes

The general outcomes of interest are symptoms and functional outcomes. The existing literature evaluating systemic HBOT as a treatment for herpes zoster described below, reported outcomes of interest, but longer follow-up are necessary to fully observe outcomes. Therefore, at least 1 year of follow-up is considered necessary to demonstrate efficacy.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess longer term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

Review of Evidence

Peng et al (2012) in China published an RCT evaluating HBOT for herpes zoster (see Tables 20 and 21). Sixty-eight patients with herpes zoster were randomized to HBOT with medication or medication treatment alone. The following outcomes were measured after 3 weeks of treatment: therapeutic efficacy, days to blister resolution, days to scar formation, and pain. Patients receiving HBOT experienced significantly improved outcomes compared with patients receiving medication alone. Limitations of the trial included a lack of blinding and long-term follow-up

Table 20. Characteristics of Trials Assessing Hyperbaric Oxygen Therapy Herpes Zoster

					Treatment	
Study (Year)	**Countries**	**Sites**	**Dates**	**Participants**	**Active (n=36)**	**Comparator (n=32)**
Peng et al (2012)	China	NR	2008-2010	Patients diagnosed with herpes zoster within 2 wk	• HBOT • 100% oxygen at 2.2 ATA • 2 sessions/day for 5 d • Thirty 120-min sessions; plus medications that the control group received	Medication alone, including antiviral, nerve nutritive, pain relief, and antidepressives

ATA: atmospheres absolute; HBOT: hyperbaric oxygen therapy; NR: not reported.

Table 21. Results of Trials Assessing Hyperbaric Oxygen Therapy Herpes Zoster

Study (Year)	**Efficacy[a,b]**	**Mean Days to Blister Resolution[b]**	**Mean Days to Scar Formation[b]**	**NPRS Score[b]**	
				Pretreatment	**Posttreatment**
Peng et al (2012)	68	68	68	68	68

Mean HBOT and medication (SD)	97.2%	2.8 (1.5)	11.1 (4.0)	8.0 (1.8)	1.8 (2.7)
Mean medication alone (SD)	81.3%	3.3 (1.4)	13.9 (4.3)	8.1 (1.7)	3.5 (4.1)

HBOT: hyperbaric oxygen therapy; NPRS: Numeric Pain Rating Scale; SD: standard deviation.
[a] Calculation: (number cases with healing + number cases with improvement)/(total number cases × 100).
[b] Between-group difference p<.05.

Section Summary: Systemic Hyperbaric Oxygen Therapy for Herpes Zoster

One RCT was identified. Only short-term outcomes were reported. Outcomes at the end of treatment were significantly better in the HBOT group than in the medication group. Trial limitations included a lack of blinding and long-term outcomes.

Systemic Hyperbaric Oxygen Therapy for Fibromyalgia

Clinical Context and Therapy Purpose

The purpose of systemic HBOT is to provide a treatment option that is an alternative to or an improvement on existing therapies in individuals with fibromyalgia.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with fibromyalgia.

Interventions

The therapy being considered is systemic HBOT.

Comparators

Comparators of interest include medication. Medications prescribed for fibromyalgia may include selective serotonin reuptake inhibitors, analgesics, non-steroidal anti-inflammatory drugs, nerve pain relievers, and muscle relaxants. Systemic HBOT may be used as an adjunct to these comparators.

Outcomes

The general outcomes of interest are symptoms, change in disease status, and functional outcomes. The existing literature evaluating systemic HBOT as a treatment for fibromyalgia has varying lengths of follow-up. In the systematic reviews described below, all studies reported at least 1 outcome of interest, but longer follow-up was necessary to fully observe outcomes. Therefore, at least 1 year of follow-up is considered necessary to demonstrate efficacy.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess longer term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

Review of Evidence

One delayed treatment RCT and a quasi-randomized trial on HBOT for fibromyalgia were identified.

Efrati et al (2015) published an RCT that included 60 symptomatic women who had fibromyalgia for at least 2 years (see Tables 21 and 22). Patients were randomized to an immediate 2-month course of HBOT or delayed HBOT after 2 months. Forty-eight (80%) of 60 patients completed the trial. After the initial 2 months, outcomes including a number of tender points, pain threshold, and QOL (SF-36) were significantly improved in the immediate treatment group than in the delayed treatment group. After the delayed treatment group had undergone HBOT, outcomes were significantly improved compared with scores in the 2 months before HBOT treatment. These findings are not only consistent with the clinical benefit of HBOT but also with a placebo effect. A sham control trial is needed to confirm the efficacy of HBOT in the treatment of fibromyalgia and other conditions where primary endpoints are pain and other subjective outcomes.

Yildiz et al (2004) assessed 50 patients with fibromyalgia (see Tables 22 and 23). On an alternating basis, patients were assigned to HBOT or a control group. After HBOT treatment, the mean standard deviation, number of tender points, and mean visual analog scale scores were improved in patients receiving HBOT compared with controls. It is unclear whether the control group received a sham intervention that would minimize any placebo effect (i.e., whether the control intervention was delivered in a hyperbaric chamber). The authors stated that the trial was double-blind, but did not provide details of patient blinding.

Table 22. Characteristics of Trails Assessing Hyperbaric Oxygen Therapy for Fibromyalgia

					Treatment	
Study (Year)	**Countries**	**Sites**	**Dates**	**Participants**	**Active**	**Comparator**
Efrati et al (2015)	Israel	1	2010-2012	Patients with fibromyalgia based on: (1) widespread pain and (2) at least 11 of 18 tender points	• n=24 • HBOT	• n=26 • No treatment for 2 mo, then same

					Treatment	
					• 100% oxygen at 2 ATA • 1 session/day for 5 d • Forty 90-min sessions	treatment as the active group
Yildiz et al (2004)	Turkey	NR	NR	Patients meeting ACR criteria for fibromyalgia, with persistent symptoms despite medical therapy and PT	• n=26 • HBOT • 100% oxygen at 2.4 ATA • 1 session/day for 5 d • Fifteen 90-min sessions	• n=24 • Air • 1 ATA • 1 session/day for 5 d • Fifteen 90-minute sessions

ACR: American College of Rheumatology; ATA: atmospheres absolute; HBOT: hyperbaric oxygen therapy; NR: not reported; PT: physical therapy.

Table 23. Results of Trials Assessing Hyperbaric Oxygen Therapy for Fibromyalgia

	Tender Points			Pain Threshold		
Study (Year)	**Baseline**	**After HBOT**	**Between-Group P-Value**	**Baseline**	**After HBOT**	**Between-Group P-Value**
Efrati et al(2015)	50			50		
Mean HBOT (SD)	17.3 (1.4)	8.9 (6.0)	<.001	0.5 (1.2)	1.7 (0.8)	<.001
Mean control (SD)	17.7 (0.7)	17.2 (1.1)		0.7 (0.5)	0.6 (0.5)	
Yildiz et al (2004)	50			50		
Mean HBOT (SD)	15.0 (1.5)	6.0 (1.2)	<.001	0.7 (0.1)	1.3 (0.1)	<.001
Mean air (SD)	15.3 (1.2)	12.5 (1.1)		0.7 (0.1)	0.8 (0.1)	

HBOT: hyperbaric oxygen therapy; SD: standard deviation.

Section Summary: Systemic Hyperbaric Oxygen Therapy for Fibromyalgia

Two RCTs assessing HBOT for fibromyalgia were identified. Both had relatively small sample sizes and methodologic limitations (e.g., quasi-randomization, no or uncertain sham control for a condition with subjective outcomes susceptible to a placebo effect). Moreover, the HBOT protocols varied. Thus, the

evidence is insufficient to permit conclusions on the impact of HBOT on health outcomes for patients with fibromyalgia.

Systemic Hyperbaric Oxygen Therapy for Multiple Sclerosis

Clinical Context and Therapy Purpose

The purpose of systemic HBOT is to provide a treatment option that is an alternative to or an improvement on existing therapies in individuals with multiple sclerosis (MS).

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with MS.

Interventions

The therapy being considered is systemic HBOT.

Comparators

Comparators of interest include medication. Medications prescribed to treat MS include chemotherapy, anti-inflammatory drugs, immunosuppressive drugs, and steroids. Systemic HBOT may be used as an adjunct to these comparators.

Outcomes

The general outcomes of interest are symptoms and functional outcomes. The existing literature evaluating systemic HBOT as a treatment for MS has varying lengths of follow-up, ranging from 4 weeks to 6 months. In the systematic review described below, nearly all studies reported at least 1 outcome of interest, but longer follow-up was necessary to fully observe outcomes. Therefore, at least 1 year of follow-up is considered necessary to demonstrate efficacy.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess longer term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

Review of Evidence

Bennett et al (2010) published a systematic review on the use of HBOT for treatment of MS (see Table 24). Nine RCTs (N=504) were identified that compared the effects of HBOT with placebo or no treatment. All trials used an initial course of 20 sessions over 4 weeks, although dosages among studies varied from 1.75 ATA for 90 minutes to 2.5 ATA for 90 minutes. The primary outcome of the review was the Expanded Disability Status Scale score. A pooled analysis of data from 5 trials (n=271) did not find a significant difference in mean Expanded Disability Status Scale score change after 20 HBOT treatments versus control or after 6 months of follow-up.

Table 24. Systematic Reviews of Trials Assessing Hyperbaric Oxygen Therapy for Multiple Sclerosis

Study (Year)	Literature Search	Studies	Participants	N	Design	Results
Bennett et al (2010)	Jul 2009	9	Patients with multiple sclerosis, at any state or course of the condition	504	RCT	EDSS score difference between groups: • At 4-wk follow-up: 0.07 (95% CI, -0.09 to 0.23) • At 6-mo follow-up: 0.22 (95% CI, -0.09 to 0.54)

CI: confidence interval; EDSS: Expanded Disability Status Scale; HBOT: hyperbaric oxygen therapy; RCT: randomized controlled trial.

Section Summary: Systemic Hyperbaric Oxygen Therapy for Multiple Sclerosis

A Cochrane review of RCTs did not find a significant difference in outcomes when patients with MS were treated with HBOT versus a comparison intervention.

Systemic Hyperbaric Oxygen Therapy for Individuals with Cancer who are Undergoing Radiotherapy or Chemotherapy

Clinical Context and Therapy Purpose

The purpose of systemic HBOT is to provide a treatment option that is an alternative to or an improvement on existing therapies in individuals with cancer who are undergoing radiotherapy or chemotherapy.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with cancer who are undergoing radiotherapy or chemotherapy.

Interventions

The therapy being considered is systemic HBOT.

Comparators

Comparators of interest include radiotherapy or chemotherapy without HBOT. Systemic HBOT may be used as an adjunct to these comparators.

Outcomes

The general outcomes of interest are OS and change in disease status. The existing literature evaluating systemic HBOT as a treatment for cancer who are undergoing radiotherapy or chemotherapy has varying lengths of follow-up, 6 months to 5 years. In the systematic review and RCT described below, nearly all studies reported at least 1 outcome of interest, but longer follow-up was necessary to fully observe outcomes. Therefore, at least 1 year of follow-up is considered necessary to demonstrate efficacy.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess longer term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

Review of Evidence

In a Cochrane review (2005), which was updated in 2012, Bennett et al (2012) identified 19 randomized and quasi-randomized trials (N=2286) comparing outcomes following radiotherapy with and without HBOT in patients with solid tumors (see Table 25). The latest trial identified in the Cochrane search was published in 1999. Reviewers did not find any ongoing RCTs in this area. Results from the review reported that HBOT given with radiotherapy might be useful in tumor control in head and neck cancer. However, reviewers expressed caution because significant adverse events, such as severe radiation tissue injury (relative risk, 2.3; p<.001) and seizures (relative risk, 6.8; p=.03) occurred more frequently in patients treated with HBOT.

Table 25. Systematic Review of Trials Assessing Hyperbaric Oxygen Therapy for Tumor Sensitization During Cancer Treatment with Radiotherapy

Study (Year)	Literature Search	Studies	Participants	N	Design	Results
Bennett et al (2012)	Sep 2017	19, some including multiple cancer sites	• Head and neck: 10 trials • Uterine: 7 trials • Urinary bladder: 5 trials • Bronchus: 1 trial • Rectum: 1 trial • Brain: 1 trial • Esophagus: 1 trial	2286	RCT and quasi-RCT	Head and neck: • 1-y mortality: RR, 0.8 (p=.03) • 5-year mortality: RR, 0.8 (p=.03) • 5-y recurrence: RR, 0.8 (p=.01) Uterine: • 2-y recurrence: RR, 0.6 (p=.04)

HBOT: hyperbaric oxygen therapy; RCT: randomized controlled trial; RR: relative risk.

In an RCT of 32 patients, Heys et al (2006) found no increase in 5-year survival for patients treated with HBOT to increase tumor vascularity before chemotherapy for locally advanced breast carcinoma.

Section Summary: Systemic Hyperbaric Oxygen Therapy for Tumor Sensitization During Cancer Treatment Radiotherapy or Chemotherapy

A Cochrane review on the use of HBOT with radiotherapy and an RCT on the use of HBOT with chemotherapy were identified. While the Cochrane review found improvements in tumor control in patients with head and neck cancer, the adverse events accompanying HBOT treatment (eg, radiation tissue injury, seizures) were significant. The RCT did not find a significant difference in survival in cancer patients who received HBOT before chemotherapy.

Systemic Hyperbaric Oxygen Therapy for Radiotherapy Adverse Events

Clinical Context and Therapy Purpose

The purpose of systemic hyperbaric oxygen therapy (HBOT) is to provide a treatment option that is an alternative or an improvement on existing therapies in individuals with radiotherapy adverse events.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with radiotherapy adverse events.

Interventions

The therapy being considered is systemic HBOT.

Comparators

Comparators of interest include medication. Medications to treat cardiovascular and pulmonary adverse events (e.g., pentoxifylline), gastrointestinal toxicity (e.g., amifostine, antidiarrheals), radiation-induced emesis (5-HT3), radiation cystitis (e.g., phenazopyridine, oxybutynin, and flavoxate), and sexual dysfunction (e.g., sildenafil and tadalafil) may be prescribed. Systemic HBOT may be used as an adjunct to these comparators.

Outcomes

The general outcomes of interest are symptoms and functional outcomes. The existing literature evaluating systemic HBOT as a treatment for radiotherapy adverse events has varying lengths of follow-up. In the systematic reviews and RCTs described below, nearly all studies reported at least 1 outcome of interest, but longer follow-up was necessary to fully observe outcomes. Therefore, at least 1 year of follow-up is considered necessary to demonstrate efficacy.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess longer term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

Review of Evidence

Systematic Reviews

Ravi et al (2017) conducted a systematic review assessing the effect of HBOT on patients with head and neck cancer who had received radiotherapy (see Table 26). Pooled analyses were not performed.

Villeirs et al (2020) conducted a systematic review on the effect of HBOT on cystitis following pelvic radiotherapy. The review included 20 studies, only one of which was an RCT; the remaining studies were cohort studies. The number of HBOT sessions ranged widely from 1 to 179 (mean or median number of sessions was not reported). The review broadly assessed cystitis response across studies, generally based on the absence of hematuria. Complete response was achieved in a weighted mean of 63.6% of patients receiving HBOT (range, 20% to 100%) while 35.2% of patients showed no response. In 11 studies reporting follow-up greater than 1 year, recurrence ranged from 0% to 40.7%. Other pooled outcomes were not reported.

Table 26. Systematic Reviews of Studies Assessing Hyperbaric Oxygen Therapy for Radiotherapy Adverse Events

Study (Year)	Literature Search	Studies	Participants	N	Design	Results
Ravi et al (2017)	Dec 2016	10	Patients who have received RT for head and neck cancer	375	Prospective case series and prospective comparative studies	• Salivary gland function: 2 case series (n=96) reported that patients receiving HBOT experienced improvements in salivary flow rates • QOL: 3 case series (n=106) administered various QOL instruments (eg, SF-36, EORTC, HADS), reporting that many subsets of the questionnaires (e.g., swallowing, pain, salivary quantity) showed significant improvements with HBOT
Villeirs et al (2020)	May 2018	20	Patients with RT-induced cystitis	815	RCTs, cohort studies, and case series	• Based on evidence from 18 studies, HBOT was associated with 63.6% (range 20% to 100%) of patients achieving complete cystitis response; 35.2% of patients had no response to HBOT.

EORTC: European Organization for Research and Treatment of Cancer; HADS: Hospital Anxiety and Depression Scale; HBOT: hyperbaric oxygen therapy; QOL: quality of life; RCT: randomized controlled trial; RT: radiotherapy; SF-36: 36-Item Short-Form Health Survey.

Randomized Controlled Trials

Trials not included in one of the systematic reviews are described below.

Gothard et al (2010) in the U.K. published findings of an RCT using HBOT for arm lymphedema occurring after radiotherapy for cancer. Fifty-eight patients with arm lymphedema (at least a 15% increase in arm volume) following cancer treatment were randomized in a 2:1 ratio to HBOT (n=38) or usual care without HBOT (n=20). Fifty-three patients had baseline assessments, and 46 (79%) of 58 had 12-month assessments. At the 12-month follow-up, there was no statistically significant difference in the change from baseline in arm volume. Median change from baseline was -2.9% in the treatment group and -0.3% in the control group. The study protocol defined response as at least an 8% reduction in arm volume relative to the contralateral arm. By this definition, 9 (30%) of 30 patients in the HBOT group were considered responders compared with 3 (19%) of 16 in the control group (p=not significant). Other outcomes (eg, QOL scores on the 36-Item Short-Form Health Survey [SF-36]) also did not differ significantly between groups.

A phase 2/3 RCT by Oscarsson et al (2019) not included in the Villiers systematic review assessed HBOT for late radiation-induced cystitis in adult cancer patients who had received pelvic radiotherapy. Eighty-seven patients were randomized to either HBOT (n=42) or standard care (n=45). Eight patients withdrew consent directly after randomization, so 79 were included in the intention-to-treat analysis. The primary outcome was change in the urinary domain of the Expanded Prostate Index Composite Score, which is a patient-reported outcome measurement tool with 12 questions covering a range of urinary tract symptoms; each answer is given on a Likert scale, and the totals are calculated on a 0 to 100 score. A

post hoc analysis determined the minimal clinically important difference to be 9 points. Patients were required to have a baseline score of less than 80 to participate in the study. Patients in the HBOT group received 30 to 40 treatments within 60 to 80 days. No study-specific treatment was administered to the standard care group. The trial included 4 visits, and at the fourth visit, the mean Expanded Prostate Index Composite urinary total score in the HBOT group had increased by 17.8 points (standard deviation [SD]=18.4), whereas the standard care group increased by 7.7 points (SD=15.5). The difference between the group means in the analysis was 10.1 points (95% CI, 2.2 to 18.1; p=.013). Possible confounding factors that could have influenced the total score were invasive surgery, body mass index, sex, age, and time from radiotherapy to inclusion. A secondary outcome was change in SF-36 total and domain scores. No significant differences in SF-36 scores were seen either from baseline or between groups, with the exception of the domain of "General Health," which showed a significant improvement for the HBOT group (p=.0012).

Section Summary: **Systemic Hyperbaric Oxygen Therapy for Radiotherapy Adverse Events**

Two systematic reviews included few RCTs and provided limited evidence evaluating HBOT for radiotherapy adverse events. One review focused on salivary gland function, osteonecrosis prevention, dental implant survival, and QOL. An RCT not included in the reviews focused on arm lymphedema; it found no significant differences between study groups. Another RCT assessed HBOT for radiation-induced cystitis and found significant benefit by some measures but not others.

Other Indications

Clinical Context and Therapy Purpose

The purpose of systemic hyperbaric oxygen therapy (HBOT) is to provide a treatment option that is an alternative or an improvement on existing therapies.

The following PICO was used to select literature to inform this review.

Populations

Individuals with various conditions that have the potential to respond to increased oxygen delivery to tissue.

Interventions

The therapy being considered is systemic HBOT.

Comparators

Comparators of interest may include physical therapy, medication(s) and surgical therapy. Systemic HBOT may be used as an adjunct to these comparators.

Outcomes

The general outcomes of interest are symptoms, change in disease status and functional outcomes. Depending on the indication systemic HBOT as a treatment has varying lengths of follow-up. Therefore, at least 1 year of follow-up is considered necessary to demonstrate efficacy.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess longer term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

Review of Evidence

For the indications listed below, literature searches did not identify sufficient evidence to support the use of HBOT, such as systematic reviews and/or multiple well-conducted randomized controlled trials directly relevant to U.S. settings, assessing:

- Acute frost bite
- Acute osteomyelitis
- Acute surgical and traumatic wounds except related to compromised graft or flap
- AIDS/HIV
- Alzheimer's disease/Dementia
- Anorectal disorders (e.g., chronic anal fissure, internal hemorrhoids, infections proctitis)
- Asthma
- Amyotrophic lateral sclerosis;
- Bone grafts;
- Brown recluse spider bites;
- Carbon tetrachloride poisoning, acute;
- Cerebrovascular disease, acute (thrombotic or embolic) or chronic;
- Chronic fatigue syndrome
- Chronic wounds except for other than those individuals with diabetic foot ulcer or diabetic lower extremity wound
- Epilepsy
- First degree thermal burns
- Fracture healing;
- Hepatitis/Hepatic necrosis

- Hydrogen sulfide poisoning;
- In vitro fertilization;
- Lepromatous leprosy;
- Meningitis;
- Mental illness (i.e., post-traumatic stress disorder, generalized anxiety disorder or depression)
- Parkinson's disease
- Pseudomembranous colitis (antimicrobial agent-induced colitis);
- Pyoderma gangrenosum;
- Radiation induced injury of head and neck, except for osteoradionecrosis or prophylactic pre and post treatment for individuals undergoing dental surgery (non-implant related) of irradiated jaw
- Radiation myelitis;
- Refractory mycoses: mucormycosis, actinomycosis, conidiobolus coronato;
- Retinopathy, adjunct to scleral buckling procedures in patients with sickle cell peripheral retinopathy and retinal detachment;
- Sickle cell crisis and/or hematuria;
- Spinal cord injury.

Topical Hyperbaric Oxygen Therapy for Wounds, Burns, or Infections

Clinical Context and Therapy Purpose

The purpose of topical hyperbaric oxygen therapy (THOT) is to provide a treatment option that is an alternative or an improvement on existing therapies in treating wounds, burns or infections.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with wounds, burns, or infections.

Interventions

The therapy being considered is THOT.

Comparators

Comparators of interest include dressings, debridement, and medication. Medications prescribed may include topical antibiotics and antiseptics. Pain and anxiety management medication may also be used. THOT.

Outcomes

The general outcomes of interest are overall survival, (OS), symptoms, change in disease status, and functional outcomes. Based on the site and severity of the wound, burn, or infection, patients may require prolonged physical and occupational support to evaluate symptoms. Additionally, the existing evidence on the use of topical hyperbaric oxygen therapy involves studies that treat patients for 12 weeks, but information on follow-up was limited. Therefore, follow-up should be determined based on the site and severity of the wound, burn or infection and can range from months to a year after starting treatment.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess longer term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

Review of Evidence

de Smet et al (2017) conducted a systematic review of various oxygen therapies (oxygen dressing therapy, topical oxygen therapy, HBOT, inspired oxygen therapy). Three RCTs evaluating topical oxygen therapy for chronic wound healing were identified (see Table 27). One RCT (n=100) administered treatment for 20 minutes 3 times per day for 12 days to the treatment group and standard care to the control group. The number of patients experiencing complete wound healing, defined as complete epithelialization of the wound without drainage, was 16 in the experimental group and 1 in the control group (p<.001). Two of the RCTs, which had overlapping populations with refractory venous ulcers (n=83 in one and n=132 in the other) administered treatment for 180 minutes 2 times per day for 12 weeks to the treatment group and conventional compression dressing to the control group. In all trials, patients in the treatment group experienced significantly higher proportions of healed ulcers and significantly faster healing times.

Table 27. **Systematic Reviews of Trials Assessing Topical Hyperbaric Oxygen for Wounds**

Study (Year)	Literature Search	Studies	Participants	N (Range)	Design	Results
de Smet et al (2017)	Feb 2016	3	Stage II-IV sacral or ischial pressure ulcers (1 RCT) Refractory venous ulcers (2 RCTs)	315[a] (83-132)	RCT	• Results not pooled • In all trials, patients in the treatment group experienced significantly higher wound healing rates

RCT: randomized controlled trial.
[a] Two of the trials had overlapping populations, so there were not 315 unique patients.

Section Summary: Topical Hyperbaric Oxygen Therapy (THOT)

A systematic review identified 3 RCTs on the use of topical HBOT for chronic wound healing. The results showed topical oxygen therapy improved wound healing, but there was heterogeneity in the trial populations and treatment regimens. There is a small RCT on topical HBOT for diabetic foot ulcers; it showed no differences in outcomes between the treatment and control group. No controlled studies on topical HBOT for patients with burns or infections were identified. The data are insufficient to draw conclusions about the effect on the net health outcome.

SUPPLEMENTAL INFORMATION

The purpose of the following information is to provide reference material. Inclusion does not imply endorsement or alignment with the evidence review conclusions.

Practice Guidelines and Position Statements

Guidelines or position statements will be considered for inclusion in ‘Supplemental Information' if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

American College of Cardiology/American Heart Association

In 2026 the American Heart Association and American Stroke Association updated the guideline for early management of acute ischemic stroke. The guidelines were endorsed by the Society for Academic Emergency Medicine, the Neurocritical Care Society, the American Association of Neurological Surgeons, and the Congress of Neurological Surgeons. The Guideline included the following statements relevant to this evidence review:

- "In patients with AIS due to arterial air embolism, hyperbaric oxygen (HBO) may be reasonable to improve clinical outcome.” (Class of Strength of Recommendation 2b [Weak]/Level (Quality) of Evidence: B-R [Randomized, Moderate Quality Evidence])
- "In patients with AIS not associated with air embolism, HBO is not recommended to improve functional outcomes.” (Class Strength of Recommendation 3: No benefit/Level (Quality) of Evidence: B-R [Randomized, Moderate Quality Evidence])

The 2021 American Heart Association and American Stroke Association scientific statement on the primary care of adult patients after stroke did not mention use of HBOT.

American College of Hyperbaric Medicine

In 2015, the following indications are approved by the American College of Hyperbaric Medicine and are reimbursable through CMS:

- Air or gas embolism
- Acute carbon monoxide intoxication
- Clostridial myositis and myonecrosis (gas gangrene)
- Crush injury, compartment syndrome or other acute traumatic ischemia’s

- Decompression illness
- Enhancement of healing in select problem wounds
- Extreme anemia
- Intracranial abscess
- Necrotizing soft tissue infections
- Osteomyelitis (refractory)
- Delayed radiation injury (soft tissue and bony necrosis)
- Skin flaps and grafts (compromised)

If sufficient data demonstrates that hyperbaric oxygen therapy is associated with a favorable risk-benefit ratio for an indication, which is not currently on the approved list from the Centers of Medicare and Medicaid, The Undersea and Hyperbaric Medical Society or a Commercial Insurance Carrier, the ACHM will endorse the application of hyperbaric therapy for the supported indication. Indications that meet these criteria and are supported by the ACHM as appropriate for hyperbaric oxygen therapy include:

- Acute thermal burns
- Acute central retinal artery occlusion
- Acute frost bite
- Actinomycosis (refractory and recalcitrant)
- Brown recluse spider bites
- Idiopathic sudden sensorineural hearing loss

The ACHM supports the treatment of patients with non-approved indications only in a research setting using a protocol that has been approved by an Institutional Review Board. The ACHM supports the continued performance of well-designed clinical trials in these areas, especially those that are prospective, randomized, controlled trials. The ACHM does not support the treatment of non-approved conditions for financial gain, without investigational treatment protocols. College members who intentionally mislead the patient or family into believing that hyperbaric therapy is an approved indication or is supported by peer reviewed literate will be dismissed from the ACHM.

Tenth European Consensus Conference on Hyperbaric Medicine

In 2016, the tenth European Consensus Conference on Hyperbaric Medicine issued recommendations for accepted and non-accepted clinical indications of hyperbaric oxygen treatment that included the following:

Condition	Level of Evidence	Strength of Recommendation
Carbon monoxide (CO) poisoning	B	Level 1
Open fractures with crush injury	B	Level 1
Prevention of osteoradionecrosis after dental extraction	B	Level 1
Osteoradionecrosis (mandible)	B	Level 1
Soft tissue radionecrosis (cystitis, proctitis)	B	Level 1
Decompression illness	C	Level 1
Gas embolism	C	Level 1

Condition	Level of Evidence	Strength of Recommendation
Anerobic or mixed bacterial infections	C	Level 1
Sudden deafness	B	Level 1
Diabetic foot lesions	B	Level 2
Femoral head necrosis	B	Level 2
Compromised skin grafts and musculocutaneous flaps	C	Level 2
Central retinal artery occlusion (CRAO)	C	Level 2
Crush injury without fracture	C	Level 2
Osteoradionecrosis (bones other than mandible)	C	Level 2
Radio-induced lesions of soft tissues (other than cystitis and proctitis)	C	Level 2
Surgery and implant in irradiated tissue (preventative treatment)	C	Level 2
Ischemic ulcers	C	Level 2
Refractory chronic osteomyelitis	C	Level 2
Burns 2nd degree more than 20% BSA	C	Level 2
Pneumatosis cystoides intestinalis	C	Level 2
Neuroblastoma, Stage IV	C	Level 2
Brain injury (acute and chronic TBI, chronic stroke, post anoxic encephalopathy) in highly selected patients	C	Level 3
Radio-induced lesions of larynx	C	Level 3
Radio-induced lesions of the CNS	C	Level 3
Post-vascular procedure reperfusion syndrome	C	Level 3
Limb replantation	C	Level 3
Selected non-healing wounds secondary to systemic processes	C	Level 3
Sickle cell disease	C	Level 3
Interstitial cystitis	C	Level 3

Recommendations on the non-accepted indications for hyperbaric oxygen therapy

Condition	Level of Evidence	Strength of Recommendation
Post sternotomy	D	No recommendation
Mediastinitis	D	No recommendation
Malignant otitis externa	D	No recommendation
Acute myocardial infarction	D	No recommendation
Retinitis pigmentosa	D	No recommendation
Facial (Bell's) palsy	D	No recommendations

Recommendations on those indications for which hyperbaric oxygen therapy should not be used

Condition	Level of Evidence	Strength of Recommendation
Autism spectrum disorders	B	Level 2
Placental insufficiency	C	Level 3
Multiple sclerosis	B	Level 2
Cerebral Palsy	B	Level 2
Tinnitus	B	Level 2
Acute phase stroke	C	Level 3

Level of Evidence: Grade A = High level of evidence; Grade B = Moderate level of evidence; Grade C = Low level of evidence; Grade D = Very low level of evidence.

Strength of Recommendation: Level 1 = strong recommendation (we recommend); Level 2 = weak recommendation (we suggest); Level 3 = neutral recommendation (would be reasonable); no recommendation = no agreement was reached by the group of experts.

American College of Surgeons

In 2024, the American College of Surgeons released best practice guidelines on the management of traumatic brain injury (TBI). Utilization of HBOT is not mentioned.

American College of Gastroenterology

In 2024, the American Gastroenterological Association (AGA) released a clinical guideline update on the management of moderate-to-severe ulcerative colitis in adults; the guidelines did not mention use of HBOT.

In 2025, the AGA released a clinical guideline update on the management on the management of moderate-to-severe Crohn's disease; the guidelines did not mention use of HBOT.

Department of Veterans Affairs and Department of Defense

In 2021, the U.S. VA/DoD released a clinical practice guideline on the management of post-acute mild TBI. Regarding HBOT, the guideline states "We recommend against the use of hyperbaric oxygen therapy for the treatment of patients with symptoms attributed to mild traumatic brain injury."

Undersea & Hyperbaric Medical Society (UHMS)

In 2023, the Undersea and Hyperbaric Medical Society (UHMS) issued the 15th edition for hyperbaric oxygen therapy that included the following recommendations:

Indications for Hyperbaric Oxygen Therapy:

- Air or gas embolism
- Carbon monoxide poisoning and carbon monoxide poisoning complicated by cyanide poisoning
- Clostridial myositis and myonecrosis (gas gangrene)
- Crush injury, compartment syndrome and other acute traumatic ischemia's
- Decompression sickness
- Arterial insufficiencies
    - Cranial retinal artery occlusion
    - Enhancement of healing in selected problem wounds
- Severe anemia
- Intracranial abscess
- Necrotizing soft tissue infections
- Osteomyelitis (refractory)
- Delayed radiation injury (soft tissue and bony necrosis)
- Compromised grafts and flaps
- Acute thermal burn injury
- Idiopathic sudden sensorineural hearing loss

In 2015, the Undersea and Hyperbaric Medical Society (UHMS) issued a clinical practice guideline for the use of hyperbaric oxygen therapy in the treatment of diabetic foot ulcers, that included the following recommendations:

- In patients with Wagner Grade 2 or lower diabetic foot ulcers, we suggest against using hyperbaric oxygen therapy (very low-level evidence in support of HBO_2, conditional recommendation)
- In patients with Wagner Grade 3 or higher diabetic foot ulcers that have not shown significant improvement after 30 days of treatment, we suggest adding hyperbaric oxygen therapy to the standard of care to reduce the risk of major amputation and incomplete healing (moderate-level evidence, conditional recommendation)
- In patients with Wagner Grade 3 or higher diabetic foot ulcers who have just had surgical debridement of an infected foot (e.g. partial toe or ray amputation; debridement of ulcer with underlying bursa, cicatrix or bone; foot amputation; incision and drainage of deep space abscess; or necrotizing soft tissue infection), we suggest adding acute post-operative hyperbaric oxygen therapy to the standard of care to reduce the risk of major amputation and incomplete healing (moderate -level of evidence, conditional recommendation)

In 2009, the Undersea and Hyperbaric Medical Society (UHMS) issued a position paper on the treatment of autism spectrum disorder (ASD) with hyperbaric oxygen therapy which states: There are few data upon which to base firm conclusions regarding the use of hyperbaric oxygen therapy for the treatment of ASD. “At this time, the UHMS cannot recommend the routine treatment of ASD with hyperbaric oxygen therapy outside appropriate comparative research protocols”.

The Undersea and Hyperbaric Medical Society (UHMS) issued a position paper on the treatment of multiple sclerosis with hyperbaric oxygen therapy: The synthesis of data presented suggests there is little evidence for the efficacy of hyperbaric oxygen therapy from trials with a low potential for bias. Most randomized controlled trials have failed to show any clinical benefit, while a minority have suggested some benefit. “At this time, the UHMS cannot recommend the routine treatment of multiple sclerosis with hyperbaric oxygen therapy outside appropriate comparative research protocols”.

In 2018, the Undersea and Hyperbaric Medical Society (UHMS) updated their position statement on topical oxygen for chronic wounds which states:

Topical oxygen may be a promising treatment based on some recent studies, but it cannot be recommended for routine clinical care at this time due to a restricted volume and quality of supporting scientific evidence. More investigation is necessary to determine if topical oxygen can be used in the clinical setting for wound care. In particular, we need better information on precise indications for use, optimal dosing regimens and standardized outcomes. Future clinical studies should address these issues.

Before topical oxygen therapy can be recommended for non-healing wounds, its application should be subjected to additional scientific scrutiny to better establish indications for use, dosing and response to treatment.

Ongoing and Unpublished Clinical Trials

Some currently ongoing and unpublished trials that might influence this review can be located at clinicaltrials.gov.

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CODES

To report provider services, use appropriate CPT codes, HCPCS codes, Revenue codes, and/or ICD diagnosis codes.

Codes	Number	Description
CPT		
	99183	Physician or other qualified health care professional, attendance, and supervision of hyperbaric oxygen chamber, per session
HCPCS		
	A4575	Topical hyperbaric oxygen chamber, disposable
	G0277	Hyperbaric oxygen under pressure, full body chamber, per 30-minute interval
Type of Service	Medical	
Place of Service	Inpatient/Outpatient/Home	

POLICY HISTORY

Date	Action	Action
February 2026	Annual Review	Policy Revised
November 2025	Annual Review	Policy Renewed
September 2024	Annual Review	Policy Revised
March 2024	Annual Review	Policy Revised
March 2023	Annual Review	Policy Revised
March 2022	Annual Review	Policy Revised
March 2021	Annual Review	Policy Renewed
March 2020	Annual Review	Policy Revised
March 2019	Annual Review	Policy Revised

Date	Action	Action
March 2018	Annual Review	Policy Revised
March 2017	Annual Review	Policy Revised
March 2016	Annual Review	Policy Revised
April 2015	Annual Review	Policy Revised
May 2014	Annual Review	Policy Revised
July 2013	Annual Review	Policy Revised
August 2012	Annual Review	Policy Revised
August 2011	Annual Review	Policy Revised

New information or technology that would be relevant for Wellmark to consider when this policy is next reviewed may be submitted to:

Wellmark Blue Cross and Blue Shield
Medical Policy Analyst
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