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Medical Policy

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Title: Hyperbaric Oxygen Therapy (HBOT)

Professional	Institutional
Original Effective Date: November 2, 1989	Original Effective Date: June 3, 2004
Revision Date(s): June 10, 2003; August 29, 2003; July 20, 2004; March 14, 2011; October 11, 2011; January 1, 2012; January 30, 2012: March 27, 2014; January 23, 2015; February 5, 2015; November 12, 2015; November 19, 2015; October 1, 2016; February 15, 2017; October 1, 2017; February 15, 2018; April 26, 2019; June 19, 2019; October 1, 2019; March 16, 2021; February 22, 2022	Revision Date(s): July 20, 2004; March 14, 2011; October 11, 2011; January 1, 2012; January 30, 2012; March 27, 2014; January 23, 2015; February 5, 2015; November 12, 2015; November 19, 2015; October 1, 2016; February 15, 2017; October 1, 2017; February 15, 2018; April 26, 2019; June 19, 2019; October 1, 2019; March 16, 2021; February 22, 2022
Current Effective Date: April 26, 2019	Current Effective Date: April 26, 2019

Archived Date: August 23, 2022 **Archived Date: August 23, 2022**

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Populations	Interventions	Comparators	Outcomes
Individuals: • With wounds, burns, or infections	Interventions of interest are: • Topical hyperbaric oxygen therapy	Comparators of interest are: • Dressings • Débridement • Medication	Relevant outcomes include: • Overall survival • Symptoms • Change in disease status • Functional outcomes
Individuals: • With chronic diabetic ulcers	Interventions of interest are: • Systemic hyperbaric oxygen therapy	Comparators of interest are: • Standard wound care • Advanced wound therapy	Relevant outcomes include: • Symptoms • Change in disease status
Individuals: • With carbon monoxide poisoning	Interventions of interest are: • Systemic hyperbaric oxygen therapy	Comparators of interest are: • Breathing oxygen at standard pressure	Relevant outcomes include: • Overall survival • Symptoms
Individuals: • With radionecrosis, osteoradionecrosis, and treatment of irradiated jaw	Interventions of interest are: • Systemic hyperbaric oxygen therapy	Comparators of interest are: • Débridement • Medication	Relevant outcomes include: • Symptoms • Change in disease status
Individuals: • With chromic refractory osteomyelitis	Interventions of interest are: • Systemic hyperbaric oxygen therapy	Comparators of interest are: • Medication • Surgical therapy	Relevant outcomes include: • Symptoms • Change in disease status
Individuals: • With acute thermal burns	Interventions of interest are: • Systemic hyperbaric oxygen therapy	Comparators of interest are: • Cooling therapy • Medication	Relevant outcomes include: • Overall survival • Symptoms • Change in disease status
Individuals: • With acute surgical and traumatic wounds	Interventions of interest are: • Systemic hyperbaric oxygen therapy	Comparators of interest are: • Dressings • Débridement • Medication	Relevant outcomes include: • Overall survival • Symptoms • Change in disease status
Individuals: • With bisphosphonate-related osteonecrosis of the jaw	Interventions of interest are: • Systemic hyperbaric oxygen therapy	Comparators of interest are: • Medication • Surgical therapy	Relevant outcomes include: • Symptoms • Change in disease status
Individuals: • With necrotizing soft tissue infections	Interventions of interest are: • Systemic hyperbaric oxygen therapy	Comparators of interest are: • Medication • Surgical therapy	Relevant outcomes include: • Overall survival • Symptoms • Change in disease status

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Populations	Interventions	Comparators	Outcomes
Individuals: • With acute coronary syndrome	Interventions of interest are: • Systemic hyperbaric oxygen therapy	Comparators of interest are: • Medication • Surgical therapy	Relevant outcomes include: • Overall survival • Symptoms • Change in disease status • Functional outcomes
Individuals: • With acute ischemic stroke	Interventions of interest are: • Systemic hyperbaric oxygen therapy	Comparators of interest are: • Tissue plasminogen activator • Endovascular procedure	Relevant outcomes include: • Overall survival • Symptoms • Change in disease status • Functional outcomes
Individuals: • With motor dysfunction associated with stroke	Interventions of interest are: • Systemic hyperbaric oxygen therapy	Comparators of interest are: • Physical therapy	Relevant outcomes include: • Symptoms • Functional outcomes
Individuals: • With Bell's palsy	Interventions of interest are: • Systemic hyperbaric oxygen therapy	Comparators of interest are: • Self-care (eg, artificial tears, eyepatch) • Medication	Relevant outcomes include: • Symptoms • Change in disease status • Functional outcomes
Individuals: • With traumatic brain injury	Interventions of interest are: • Systemic hyperbaric oxygen therapy	Comparators of interest are: • Medication • Surgical therapy • Rehabilitation	Relevant outcomes include: • Overall survival • Symptoms • Change in disease status • Functional outcomes
Individuals: • With inflammatory bowel disease	Interventions of interest are: • Systemic hyperbaric oxygen therapy	Comparators of interest are: • Medication • Surgical therapy	Relevant outcomes include: • Symptoms • Change in disease status • Functional outcomes
Individuals: • With idiopathic sudden sensorineural hearing loss	Interventions of interest are: • Systemic hyperbaric oxygen therapy	Comparators of interest are: • Medication • Surgical therapy	Relevant outcomes include: • Symptoms • Change in disease status • Functional outcomes
Individuals: • With delayed-onset muscle soreness	Interventions of interest are: • Systemic hyperbaric oxygen therapy	Comparators of interest are: • Conservative care (eg, massage) • Medication	Relevant outcomes include: • Symptoms • Functional outcomes

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Populations	Interventions	Comparators	Outcomes
Individuals: • With autism spectrum disorder	Interventions of interest are: • Systemic hyperbaric oxygen therapy	Comparators of interest are: • Behavioral therapy • Medication	Relevant outcomes include: • Symptoms • Functional outcomes
Individuals: • With cerebral palsy	Interventions of interest are: • Systemic hyperbaric oxygen therapy	Comparators of interest are: • Physical therapy • Medication	Relevant outcomes include: • Symptoms • Functional outcomes
Individuals: • With vascular dementia	Interventions of interest are: • Systemic hyperbaric oxygen therapy	Comparators of interest are: • Rehabilitation • Medication	Relevant outcomes include: • Symptoms • Functional outcomes
Individuals: • With radiotherapy adverse events	Interventions of interest are: • Systemic hyperbaric oxygen therapy	Comparators of interest are: • Medication	Relevant outcomes include: • Symptoms • Functional outcomes
Individuals: • With idiopathic femoral neck necrosis	Interventions of interest are: • Systemic hyperbaric oxygen therapy	Comparators of interest are: • Physical therapy • Medication • Surgical therapy	Relevant outcomes include: • Symptoms • Change in disease status • Functional outcomes
Individuals: • With migraine	Interventions of interest are: • Systemic hyperbaric oxygen therapy	Comparators of interest are: • Medication	Relevant outcomes include: • Symptoms • Change in disease status • Functional outcomes
Individuals: • With herpes zoster	Interventions of interest are: • Systemic hyperbaric oxygen therapy	Comparators of interest are: • Medication	Relevant outcomes include: • Symptoms • Change in disease status
Individuals: • With fibromyalgia	Interventions of interest are: • Systemic hyperbaric oxygen therapy	Comparators of interest are: • Medication	Relevant outcomes include: • Symptoms • Change in disease status • Functional outcomes
Individuals: • With multiple sclerosis	Interventions of interest are: • Systemic hyperbaric oxygen therapy	Comparators of interest are: • Behavioral therapy • Medication	Relevant outcomes include: • Symptoms • Functional outcomes
Individuals: • With cancer who are undergoing radiotherapy or chemotherapy	Interventions of interest are: • Systemic hyperbaric oxygen therapy	Comparators of interest are: • Chemotherapy without hyperbaric oxygen therapy	Relevant outcomes include: • Overall survival • Change in disease status

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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.

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.

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.

Topical Hyperbaric Oxygen Therapy

Topical hyperbaric therapy 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. Topical hyperbaric therapy 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.

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. Systemic HBOT can be used to treat systemic illness, such as air or gas embolism, carbon monoxide poisoning, or clostridial gas gangrene. 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.

Adverse Events

HBOT is a generally safe therapy, with an estimated adverse side effect rate of 0.4%.[1,] 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

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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 that 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.[2,] 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.

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POLICY

A. Systemic hyperbaric oxygen pressurization may be considered **medically necessary** in the treatment of any of the following conditions:
   1. Acute traumatic ischemia (eg, crush injuries, reperfusion injury, compartment syndrome); **OR**
   2. Carbon monoxide poisoning, acute; **OR**
   3. Cyanide poisoning, acute; **OR**
   4. Non-healing diabetic wounds of the lower extremities in patients who meet the following criteria:
      a. Patient has type 1 or type 2 diabetes and has a lower extremity wound due to diabetes;
      b. Patient has a wound classified as Wagner grade 3 or higher (see Policy Guidelines); and
      c. Patient has no measurable signs of healing after 30 days of an adequate course of standard wound therapy; **OR**
   5. Chronic refractory osteomyelitis; **OR**
   6. Decompression sickness; **OR**
   7. Soft tissue radiation necrosis (eg, radiation enteritis, cystitis, proctitis) and osteoradionecrosis; **OR**
   8. Gas embolism, acute; **OR**
   9. Gas gangrene (ie, clostridial myonecrosis); **OR**
   10. Pre and post treatment for individuals undergoing dental surgery (non-implant related) of an irradiated jaw; **OR**
   11. Profound anemia with exceptional blood loss: only when blood transfusion is impossible or must be delayed.

B. Systemic hyperbaric oxygen pressurization is considered **experimental / investigational** in all other situations including, but not limited to, the treatment of the following conditions:
   1. Acute osteomyelitis;
   2. Acute surgical and traumatic wounds;
   3. Spinal cord injury;
   4. Traumatic brain injury;
   5. Inflammatory bowel disease (Crohn's disease or ulcerative colitis);
   6. Brown recluse spider bites;
   7. Bone grafts;
   8. Carbon tetrachloride poisoning, acute;
   9. Cerebrovascular disease, acute (thrombotic or embolic) or chronic;
   10. Fracture healing;
   11. Hydrogen sulfide poisoning;
   12. Intra-abdominal and intracranial abscesses;
   13. Lepromatous leprosy;
   14. Meningitis;
   15. Pseudomembranous colitis (antimicrobial agent-induced colitis);
   16. Radiation myelitis;

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17. Sickle cell crisis and/or hematuria;
18. Demyelinating diseases, eg, multiple sclerosis, amyotrophic lateral sclerosis;
19. Retinopathy, adjunct to scleral buckling procedures in patients with sickle cell peripheral retinopathy and retinal detachment;
20. Pyoderma gangrenosum;
21. Acute coronary syndromes and as an adjunct to coronary interventions, including, but not limited to, percutaneous coronary interventions and cardiopulmonary bypass;
22. Idiopathic sudden sensorineural hearing loss;
23. Refractory mycoses: mucormycosis, actinomycosis, conidiobolus coronato;
24. Cerebral edema, acute;
25. Migraine;
26. In vitro fertilization;
27. Cerebral palsy;
28. Tumor sensitization for cancer treatments, including, but not limited to, radiotherapy or chemotherapy;
29. Delayed onset muscle soreness;
30. Idiopathic femoral neck necrosis;
31. Chronic arm lymphedema following radiotherapy for cancer;
32. Radiation-induced injury in the head and neck (except as noted in Item A10 above);
33. Early treatment (beginning at completion of radiotherapy) to reduce adverse effects of radiotherapy;
34. Autism spectrum disorders;
35. Bisphosphonate-related osteonecrosis of the jaw;
36. Acute ischemic stroke;
37. Motor dysfunction associated with stroke;
38. Herpes zoster;
39. Vascular dementia;
40. Fibromyalgia;
41. Compromised skin grafts or flaps;
42. Necrotizing soft tissue infections;
43. Acute thermal burns;
44. Chronic wounds, other than those in patients with diabetes who meet the criteria specified in the medically necessary statement above);
45. Acute arterial peripheral insufficiency;
46. Mental illness (ie, posttraumatic stress disorder, generalized anxiety disorder, or depression);
47. Bell's palsy; and
48. Retinal artery insufficiency, acute

C. Topical hyperbaric oxygen therapy is considered **experimental / investigational**.

POLICY GUIDELINES

A. Topical Hyperbaric Oxygen

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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, but not topical oxygen wound care.

Topical hyperbaric oxygen 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.

B. **Systemic Hyperbaric Oxygen**

The Wagner classification system of wounds is defined as follows: grade 0, no open lesion; grade 1, superficial ulcer without penetration to deeper layers; grade 2, ulcer penetrates to tendon, bone, or joint; grade 3, lesion has penetrated deeper than grade 2 and there is abscess, osteomyelitis, pyarthrosis, plantar space abscess, or infection of the tendon and tendon sheaths; grade 4, wet or dry gangrene in the toes or forefoot; grade 5, gangrene involves the whole foot or such a percentage that no local procedures are possible and amputation (at least at the below the knee level) is indicated.

Following are recommended indications from the Undersea and Hyperbaric Medical Society's (UHMS) 2019 Hyperbaric Oxygen Therapy Committee report on utilization of HBOT (14th edition):

1. Air or gas embolism
2. Carbon monoxide poisoning and carbon monoxide complicated by cyanide poisoning
3. Clostridial myositis and myonecrosis (gas gangrene)
4. Crush injury, compartment syndrome, and other acute traumatic ischemias
5. Decompression sickness
6. Central retinal artery occlusion
7. Diabetic foot ulcer
8. Healing of other problem wounds
9. Severe anemia
10. Intracranial abscess
11. Necrotizing soft tissue infections
12. Refractory osteomyelitis
13. Delayed radiation injury (soft tissue and bony necrosis)
14. Compromised grafts and flaps
15. Acute thermal burn injury
16. Sudden sensorineural hearing loss.

C. **Treatment duration recommendations:**

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1. Enhancement of healing in problem wounds: Treatments are performed for 90 to 120 minutes. The initial treatment schedule depends on the severity of disease. More serious conditions may require twice daily treatments; when stabilized, this can decrease to once daily. Utilization review is required after the initial 30 days of treatment and at least once every additional 30 days.
2. Crush injury, compartment syndrome, and other acute traumatic ischemias:
    a. Reperfusion injury: 1 treatment.
    b. Crush injury: 8-12 treatments (three times per day for 2 days, then twice a day for 2 days, and daily for 2 days).
    c. Compartment syndrome: 3-4 treatments (twice a day for 1 day and one treatment on day 2).
3. Decompression sickness: The majority of cases respond to a single treatment. Patients with residual defects after the initial session should receive additional treatments until they achieve clinical stability (generally no more than 5-10 treatments). Utilization review is recommended after 10 treatments.
4. Gas embolism, acute: It is recommended that treatments continue until there is no additional improvement; this typically occurs after 1-2 treatments but occasionally up to 5-10. Utilization review is recommended after 10 treatments.
5. Acute carbon monoxide poisoning and carbon monoxide poisoning complicated by cyanide poisoning: Some patients improve after a single treatment. Patients who fail to demonstrate a full recovery should receive additional treatments. In patients with persistent neurologic dysfunction after the initial treatment, further treatment can occur within 6-8 hours and can be continued once or twice daily until there is no additional improvement in cognitive function. Utilization review is mandatory after the fifth treatment.
6. Soft-tissue radiation necrosis (eg, radiation enteritis, cystitis, proctitis) and osteoradionecrosis: Most treatment courses for radiation injury will be 30-60 treatments (once daily for 90 to 120 minutes). Utilization review is recommended after 60 treatments.
7. Mandibular osteoradionecrosis: The initial course of treatment for patients with stage I osteoradionecrosis is 30 sessions, followed by only minor bony debridement. If response is adequate, an additional 10 treatments are given. If patients are not responding they are considered stage II and they receive more extensive surgical debridement, followed by 10 additional treatments. Patients who present as stage III patients receive 30 treatments followed by mandibular segmental resection and then an additional 10 treatments.
8. Gas gangrene (ie, clostridial myonecrosis): Recommended are three 90-minute treatments during the first 24 hours and then 2 treatments per day for the next 2-5 days, depending on the patient's initial response. Utilization review is indicated after 10 treatments.
9. Severe anemia: HBOT can be considered for severe anemia when patients cannot receive blood products due to medical, religious, or strong personal preference reasons. Treatment can occur for periods of up to 3 or 4 hours 3 to 4 times a day if patients receive intra-treatment air breaks. HBOT treatment should be continued with taper of

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both time and frequency until red blood cells have been satisfactorily replaced by patient regeneration or the patient can undergo transfusion.

10. Chronic refractory osteomyelitis: No recommendations were made for the total number of treatments required. For patients who respond to initial treatment with antibiotics, surgical debridement, and HBOT, therapy should be continued for approximately 4-6 weeks. Utilization review is indicated after 30-40 sessions.

Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

RATIONALE

This evidence review has been updated regularly with a search of the PubMed database. The most recent literature search was conducted through November 30, 2021.

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.

TOPICAL HYPERBARIC OXYGEN THERAPY FOR WOUNDS, BURNS, OR INFECTIONS

Clinical Context And Therapy Purpose

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

The question addressed in this evidence review is: Does the use of topical hyperbaric oxygen as a treatment for wounds, burns, or infections improve net health outcomes?

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 topical HBOT.

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. Topical HBOT may be used as an adjunct to these comparators. Patients with wounds, burns, or infections are actively managed by emergency care providers, dermatologists, wound care specialists, and primary care providers in a clinical setting.

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 HBOT 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:

a. To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
b. In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
c. To assess longer term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
d. 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).[3,] Three RCTs

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evaluating topical oxygen therapy for chronic wound healing were identified (see Table 1). 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 1. 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)[3,]	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 for Wounds, Burns, or Infections

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.

SYSTEMIC HYPERBARIC OXYGEN THERAPY FOR CHRONIC DIABETIC ULCERS

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 chronic diabetic ulcers.

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The question addressed in this evidence review is: Does the use of systemic hyperbaric oxygen as a treatment for chronic diabetic ulcers improve net health outcomes?

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

Populations
The relevant population of interest is individuals with chronic diabetic ulcers.

Interventions
The therapy being considered is systemic HBOT.

Comparators
Comparators of interest include standard wound care and advanced wound therapy. Standard wound care can include offloading of the wound with appropriate therapeutics, dressings, debridement antibiotic therapy, and blood glucose control. Advanced wound therapy can include the application of recombinant growth factors and wound coverage with dressings. 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 chronic diabetic ulcers has varying lengths of follow-up, ranging from none to 22 months. While studies included in the systematic reviews described below all reported at least 1 outcome of interest, 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
Sharma et al (2021)[4,] conducted a systematic review and meta-analysis of 14 studies (N=768) comparing the effect of HBOT with standard care on diabetic foot ulcers (Table 2). Study authors noted that various modalities can be considered standard care including, but not limited to, debridement, antibiotics and blood sugar control. However, the specific standard care modality in each included study was not reported. HBOT duration ranged from 45 to 120 minutes (median 90

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minutes). All included studies had methodological limitations, including selection, performance, detection, attrition and reporting bias. The review found those treated with standard care were less likely to have complete ulcer healing versus HBOT, based on pooled analysis of 11 studies (odds ratio [OR], 0.29; 95% confidence interval [CI], 0.14 to 0.61; I^2=62%). Results were consistent when stratified according to duration of follow up of less than 1 year (7 studies; OR, 0.63; 95% CI, 0.39 to 1.02; I^2=1%) and at 1 year (4 studies; OR, 0.16; 95% CI, 0.03 to 0.82; I^2=83%), although the risk estimate wasn't statistically significant for studies with less than one year follow-up. A funnel plot analysis for this outcome was asymmetrical, suggesting publication bias. Risk of major amputation was also significantly lower with HBOT compared to standard care based on pooled analysis of 7 studies (OR, 0.60; 95% CI, 0.39 to 0.92; I^2=24%). There were no clear differences between groups in minor amputation (9 studies; OR, 0.89; 95% CI, 0.71 to 1.12) or mortality (3 studies; OR, 0.55; 95% CI, 0.25 to 1.24). Standard care was associated with an increased risk of adverse events compared with HBOT (7 studies; OR, 1.68; 95% CI, 1.07 to 2.65).

A Cochrane review of RCTs on HBOT for chronic wounds was published by Kranke et al (2015) (see Table 2).[5,] Reviewers identified 12 RCTs (N=577 participants) comparing the effect of HBOT on chronic wound healing with an alternative treatment approach that did not use HBOT. Ten of the 12 trials evaluated HBOT in patients with diabetes (n=531). The trials were assessed as moderate quality using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) system. HBOT regimens varied across studies, ranging from 3.0 atmospheres absolute (ATA) for 45 minutes to 2.2 ATA for 120 minutes. In a pooled analysis of 5 trials, a significantly higher proportion of ulcers had healed at the end of treatment (i.e., 6 weeks) in the group receiving HBOT than in the group not receiving HBOT, but there was no statistically significant difference in the risk of major amputations between groups.

A systematic review by Elraiyah et al (2016) evaluated adjunctive therapies (HBOT, arterial pumps, and pharmacologic agents) used to treat diabetic foot ulcers (see Table 2).[6,] RCTs and nonrandomized cohort studies were included. The RCTs were rated as low-to-moderate quality using the GRADE system. A pooled analysis of 6 RCTs found a significantly higher healing rate and a significantly lower major amputation rate (OR, 0.30; 95% CI , 0.10 to 0.89) with HBOT than with control.

Table 2. Systematic Reviews of Trials Assessing HBOT for Chronic Diabetic Foot Ulcers

Study (Year)	Literature Search	Studies	Participants	N	Design	Results
Kranke et al (2015)[5,]	Feb 2015	12	Patients with chronic wounds associated with venous or arterial	577	RCTs	• 10 of 12 trials focused on patients with diabetic foot ulcers (n=531) • Pooled analysis of 5 of 10 trials (n=205) reported higher heal rates with HBOT (RR=2.3; 95%

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Study (Year)	Literature Search	Studies	Participants	N	Design	Results
			disease, diabetes, or external pressure			CI, 1.2 to 4.6) and no difference in amputation risk (RR=0.4; 95% CI, 0.1 to 2.2)
Elraiyah et al (2016)[6,]	Oct 2011	18	Patients with diabetic foot ulcers	1526	RCTs, cohort	• 16 of 18 trials included HBOT as a treatment option and 6 of those were RCTs • Pooled analysis of the 6 RCTs (n=340) reported higher heal rate with HBOT (OR=14.3; 95% CI, 7.1 to 28.7) and lower amputation risk (OR=0.3; 95% CI, 0.1 to 0.9)
Sharma et al (2021)[4,]	Sep 2020	14	Patients with diabetic foot ulcers	768	RCTs, CCTs	• 12 RCTs and 2 CCTs compared HBOT with undefined standard care • Pooled analysis found HBOT significantly associated with complete ulcer healing (ST vs. HBOT: OR 0.29, 95% CI 0.14 to 0.61) and lower risk of major amputation (HBOT vs. ST: OR 0.60, 95% CI 0.39 to 0.92) when compared with standard care.

CCT: controlled clinical trial; CI: confidence interval; HBOT: hyperbaric oxygen therapy; OR: odds ratio; RCT: randomized controlled trial; RR: relative risk; ST: standard care.

Section Summary: Systemic Hyperbaric Oxygen Therapy for Chronic Diabetic Ulcers
Three systematic reviews have been published that included trials and cohort studies.. Pooled analyses of RCTs found significantly higher wound healing rates with HBOT than with control conditions. One of the 2 meta-analyses found that HBOT was associated with a significantly lower rate of major amputation.

SYSTEMIC HYPERBARIC OXYGEN THERAPY FOR CARBON MONOXIDE POISONING

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 carbon monoxide poisoning.

The question addressed in this evidence review is: Does the use of systemic hyperbaric oxygen as a treatment for carbon monoxide poisoning improve net health outcomes?

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

Populations
The relevant population of interest is individuals with carbon monoxide poisoning.

Interventions
The therapy being considered is systemic HBOT.

Comparators
Comparators of interest include breathing oxygen at standard pressure and other supportive measures such as a ventilator. Systemic HBOT may be used as an adjunct to these comparators.

Outcomes
The general outcomes of interest are OS and symptoms. The existing literature evaluating systemic HBOT as a treatment for carbon monoxide poisoning has varying lengths of follow-up. In the systematic review described below all 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
A Cochrane review by Buckley et al (2011) included 6 RCTs evaluating HBOT for carbon monoxide poisoning (see Table 3).[7,] Four of the 6 trials were assessed as having a high risk of bias due to nonblinding of treatment allocation. The trials had substantial methodologic and statistical heterogeneity. The outcome of interest was dichotomous, presence or absence of signs or symptoms indicative of neurologic injury at 4 to 6 weeks after study inclusion. Two of the 6 RCTs found that HBOT reduced the likelihood of neurologic sequelae at 1 month and 4 others did not find a significant effect. A pooled analysis of the 6 trials did not find a significant effect of HBOT on neurologic injury. Reviewers concluded that there was insufficient evidence to determine whether HBOT reduces the risk of adverse neurologic outcomes after carbon monoxide poisoning. Quality of the evidence was deemed very low, using the GRADE system.

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Table 3. Systematic Reviews of Trials Assessing HBOT for Carbon Monoxide Poisoning

Study (Year)	Literature Search	Studies	Participants	N	Design	Results
Buckley et al (2011)[7,]	Jun 2010	6	Nonpregnant adults with acute carbon monoxide poisoning	1361	RCTs	• Studies extremely heterogeneous in: severity of CO poisoning, HBOT regimens, and comparators· Pooled analyses of 6 trials (N=1361) reported no statistical difference in neurologic deficits between treatment groups (OR=0.78; 95% CI, 0.54 to 1.12)

CI: confidence interval; CO: carbon monoxide; HBOT: hyperbaric oxygen therapy; OR: odds ratio; RCT: randomized controlled trial.

Nonrandomized Comparative Studies

Nakajima et al (2020) conducted a retrospective cohort study comparing the effect of HBOT versus control (no HBOT) on mortality and morbidity in patients with carbon monoxide poisoning.[8,] The median number of HBOT sessions was 3 (range 2 to 5). After propensity score matching of study participants (N=4 068) the study found no significant difference between groups in in-hospital mortality (mean rate difference -0.4%, 95% CI -1.0 to 0.2%). Results were consistent across subgroups according to severity of carbon monoxide poisoning, age and number of HBOT sessions. However, the study found HBOT associated with lower rates of depressed mental status (mean difference -3.2%, 95% CI -4.9% to -1.5%) and reduced activities of daily living (mean difference -5.3%, 95% CI -7.8% to -2.7%) relative to no HBOT.

Section Summary: Systemic Hyperbaric Oxygen Therapy for Carbon Monoxide Poisoning

A Cochrane review identified 6 RCTs, the majority of which did not find a significant effect of HBOT on health outcomes. A pooled analysis of the RCT data did not find a significant effect of HBOT on neurologic injuries and the quality of the evidence was considered very low. Evidence from a large cohort study also found no clear benefit of HBOT on in-hospital mortality.

SYSTEMIC HYPERBARIC OXYGEN THERAPY FOR RADIONECROSIS, OSTEORADIONECROSIS, AND TREATMENT OF IRRADIATED 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 radionecrosis, osteoradionecrosis, and treatment of irradiated jaw.

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The question addressed in this evidence review is: Does the use of systemic hyperbaric oxygen as a treatment for radionecrosis, osteoradionecrosis and treatment of irradiated jaw improve net health outcomes.

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

Populations
The relevant population of interest is individuals with radionecrosis, osteoradionecrosis, and treatment of irradiated jaw.

Interventions
The therapy being considered is systemic HBOT.

Comparators
Comparators of interest include debridement and medication. Medications prescribed for radionecrosis may include corticosteroids and anticoagulants. For osteoradionecrosis, medications include vasodilators. Medication for the treatment of irradiated jaw can include antibiotics. 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 radionecrosis, osteoradionecrosis, and treatment of irradiated jaw has varying lengths of follow-up, ranging from 3 weeks to 18 months. 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 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
Bennett et al (2016) published a Cochrane review on HBOT for late radiation tissue injury (see Table 4).[9,] Reviewers identified 14 RCTs. There was a moderate level of evidence for 2 pooled analyses. In a pooled analysis of 3 studies, a significantly higher proportion of patients with osteoradionecrosis achieved complete mucosal cover after HBOT compared with control

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treatments, and in a pooled analysis of 2 trials, a significantly lower risk of wound dehiscence after surgery to repair mandibular osteoradionecrosis with HBOT than with control treatments was reported. A single trial found a significantly higher likelihood of successful healing with HBOT than with antibiotics for tooth extraction in irradiated jaws (absolute risk reduction, 25%; p=.02). There were insufficient data to conduct meta-analyses on other outcomes.

Borabet al (2017) published a systematic review focusing on the use of HBOT to treat the subgroup of patients with late radiation tissue injury had skin necrosis (see Table 4).[10,] Reviewers identified 8 studies, including a large observational cohort and several case series. No RCTs were identified. The risk of bias was high due to the design of the included studies. The studies reported improved healing, though, without a comparator, interpretation of the results is limited.

Ravi et al (2017) published a systematic review on the use of HBOT to treat patients who had received radiotherapy for head and neck cancer.[11,] Ten prospective case series and comparative studies were identified. Qualitative summaries of outcomes were provided, but pooled analyses were not performed. Outcomes of interest included osteonecrosis and dental implant survival (see Table 4). Other outcomes of interest included salivary gland function and quality of life, which are discussed in the Radiotherapy Adverse Events section.

Table 4. Systematic Reviews of Studies Assessing HBOT for Radionecrosis, Osteoradionecrosis, and Treatment of Irradiated Jaw

Study (Year)	Literature Search	Studies	Participants	N	Design	Results
Bennett et al (2016)[9,]	Dec 2015	14	Patients with late radiation tissue injury (including necrosis) and patients treated with large-dose radiotherapy likely to induce early necrosis	753	RCTs	• Pooled analyses of 3 trials of patients with osteoradionecrosis (n=246) found a higher rate of complete mucosal cover after HBOT vs control (RR=1.3; 95% CI, 1.1 to 1.5) • Pooled analyses of 2 trials (n=264) found a lower risk of wound dehiscence following surgery to repair mandibular osteoradionecrosis in patients treated with HBOT vs control (RR=4.2; 95% CI, 1.1 to 16.8)

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Study (Year)	Literature Search	Studies	Participants	N	Design	Results
Borab et al (2017)[10],	May 2016	8	Patients with radiation-induced skin necrosis	720	Observational cohort and case series	• Adding across the studies, 80% reported complete healing and 86% reported symptom improvement • Studies had no comparators
Ravi et al (2017)[11],	Dec 2016	10	Patients who received radiotherapy for head and neck cancer	375	Prospective case series and prospective comparative studies	• Osteonecrosis prevention: 1 case series and 1 comparative study (n=77) reported low osteonecrosis rates with HBOT • Dental implant survival: 1 case series and 2 comparative studies (n=122) report mixed results, with 2 studies finding implant survival improved with HBOT and another finding no difference in survival

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

Section Summary: Systemic Hyperbaric Oxygen Therapy for Radionecrosis, Osteoradionecrosis, and Treatment of Irradiated Jaw

A Cochrane review of RCTs found that HBOT improved some radionecrosis and osteoradionecrosis outcomes and resulted in better outcomes before tooth extraction in an irradiated jaw. Observational studies focused on skin necrosis and reported high rates of healing with HBOT, though with no comparators, interpretation of results is limited. Prospective observational studies using HBOT for treatment on patients with head and neck cancer receiving HBOT, have reported low osteonecrosis rates and inconsistent results for dental implant survival. The number of RCTs evaluating HBOT for these indications, especially in irradiated jaws, is limited.

SYSTEMIC HYPERBARIC OXYGEN THERAPY FOR CHRONIC REFRACTORY OSTEOMYELITIS

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 chronic refractory osteomyelitis.

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The question addressed in this evidence review is: Does the use of systemic hyperbaric oxygen as a treatment for chronic refractory osteomyelitis improve net health outcomes?

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

Populations
The relevant population of interest is individuals with chronic refractory osteomyelitis.

Interventions
The therapy being considered is systemic HBOT.

Comparators
Comparators of interest include medication and surgical therapy. Medications prescribed for chronic refractory osteomyelitis may include intravenous antibiotics. Surgery can include debridement. 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 chronic refractory osteomyelitis report follow-up times ranging from 34 to 60 months, suggesting that extensive follow-up up to or more than 5 years 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
No prospective clinical trials on chronic or refractory osteomyelitis were identified in literature searches. The evidence for the use of HBOT in chronic osteomyelitis has been primarily based on case series.

Among the larger case series, Maynor et al (1998) reviewed the records of all patients with chronic osteomyelitis of the tibia seen at a single-institution.[12,] Follow-up data were available on 34 patients who had received a mean of 35 adjunctive HBOT sessions (range, 6 to 99 sessions). Of the 26 patients with at least 24 months of follow-up after treatment, 81% (21/26) remained drainage-free. At 60 months of follow-up, 80% (12/15), and at 84 months, 63% (5/8) remained drainage-free.

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Davis et al (1986) reviewed outcomes for 38 patients with chronic refractory osteomyelitis treated at another U.S. institution.[13,] Patients received HBOT until the bone was fully recovered with healthy vascular tissue; this resulted in a mean of 48 daily treatments (range, 8 to 103 treatments). After a mean post-treatment follow-up of 34 months, 34 (89%) of 38 patients remained clinically free of infection (i.e., drainage-free and no tenderness, pain, or cellulitis). Success rates from several smaller case series (N range, 13 to 15 patients), all conducted in Taiwan (1998 through 2000), ranged from 79% to 92%.[14,15,16,] A high percentage of refractory patients in these series had successful outcomes.

Section Summary: Systemic Hyperbaric Oxygen Therapy for Chronic Refractory Osteomyelitis
Only case series data are available; no RCTs or comparative nonrandomized trials were identified. Case series tended to find high rates of successful outcomes in patients with chronic refractory osteomyelitis treated with HBOT. However, controlled studies are needed to determine conclusively that HBOT improves health outcomes in patients with chronic refractory osteomyelitis compared with other interventions.

SYSTEMIC HYPERBARIC OXYGEN THERAPY FOR ACUTE THERMAL BURNS

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 thermal burns.

The question addressed in this evidence review is: Does the use of systemic hyperbaric oxygen as a treatment for acute thermal burns improve net health outcomes?

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

Populations
The relevant population of interest is individuals with acute thermal burns.

Interventions
The therapy being considered is systemic HBOT.

Comparators
Comparators of interest include cooling therapy and medication. Medications prescribed for acute thermal burns may include antibiotics. Pain and anxiety medication may also be used. Systemic HBOT may be used as an adjunct to these comparators.

Outcomes
The general outcomes of interest are OS, symptoms, and change in disease status. The existing literature evaluating systemic HBOT as a treatment for acute thermal burns does not report follow-up time. However, given that patients may require prolonged occupational and physical

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therapy based on the site and severity of the acute thermal burn, 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 2004, a Cochrane review assessed HBOT for thermal burns (see Table 5).[17,] Two RCTs were identified, published in 1974 and 1997. Sample sizes were 16 and 125. Both trials were judged by reviewers to have poor methodologic quality. Reviewers concluded that the evidence was insufficient to permit conclusions on whether HBOT improves health outcomes in patients with acute thermal burns. No additional trials have been identified in updated literature searches.

Table 5. Systematic Reviews of Trials Assessing HBOT for Acute Thermal Burns

Study (Year)	Literature Search	Studies	Participants	N	Design	Results
Villanueva et al (2009)[17,]	Jun 2009	5	Patients with thermal injuries to the epidermis, subcutaneous tissues, vessels, nerve, tendons, or bone	141	RCTs	• 1 trial (N=125) reported no difference in length of stay, mortality, or number of surgeries between HBOT and control groups • 1 trial (N=16) reported shorter healing times (19.7 days vs 43.8 days; p<.001) with HBOT vs control, and an RR for failed graft without HBOT of 2.0 (95% CI 0.5 to 8.0)

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

Section Summary: Systemic Hyperbaric Oxygen Therapy for Acute Thermal Burns

A Cochrane review identified 2 RCTs on HBOT for thermal burns. Both were judged to have poor methodologic quality. There is insufficient evidence from well-conducted controlled studies to permit conclusions on the impact of HBOT on health outcomes in patients with acute thermal burns.

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SYSTEMIC HYPERBARIC OXYGEN THERAPY FOR ACUTE SURGICAL AND TRAUMATIC WOUNDS

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 surgical and traumatic wounds.

The question addressed in this evidence review is: Does the use of systemic hyperbaric oxygen as a treatment for acute surgical and traumatic wounds improve net health outcomes?

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

Populations

The relevant population of interest is individuals with acute surgical and traumatic wounds.

Interventions

The therapy being considered is systemic HBOT.

Comparators

Comparators of interest include dressings, debridement, and medication. Medications prescribed for acute surgical and traumatic wounds may include antibiotics and pain management. Systemic HBOT may be used as an adjunct to these comparators.

Outcomes

The general outcomes of interest are OS, symptoms, and change in disease status. The existing literature evaluating systemic HBOT as a treatment for acute surgical and traumatic wounds has varying lengths of follow-up, though many had short follow-up period of 6 to 7 days. Depending on the severity of the wounds, 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 of RCTs on HBOT for acute surgical and traumatic wounds was published by Eskes et al (2013) (see Table 6).[18,] HBOT was administered at pressures above 1 atmosphere

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(atm). To be included, studies had to compare HBOT with a different intervention or compare 2 HBOT regimens; also, studies had to measure wound healing objectively. Four RCTs met reviewers' inclusion criteria. Trials ranged in size from 10 to 135 participants. Due to differences among trials regarding patient population, comparison intervention, and outcome measurement, results could not be pooled. The primary outcome examined by Cochrane reviewers (wound healing) was not reported in either of the 2 trials comparing HBOT with usual care and was not reported in the trial comparing HBOT with dexamethasone or heparin. Complete wound healing was reported in the RCT comparing active HBOT with sham HBOT. In this study (n=36), there was a statistically higher rate of wound healing in the group, though the time point for outcome measurement in this trial was unclear. Also, there was no statistically significant difference between groups in the meantime to wound healing.

A systematic review of studies on HBOT for acute wounds, published by Dauwe et al (2014), included RCTs and controlled nonrandomized studies (see Table 6).[19,] Reviewers included 8 studies, with sample sizes ranging from 5 to 125 patients. Four studies were randomized, 3 were prospective observational studies, and 1 was a retrospective observational study. As in the Eskes et al (2013) systematic review, data were not pooled. Reviewers noted that 7 of the 8 studies reported statistically significant findings for their primary endpoints, but the endpoints differed among studies (e.g., graft survival, hospital length of stay, wound size). Moreover, the studies were heterogeneous regarding treatment regimens, patient indications (e.g., burns, facelifts), and study designs making it difficult to draw conclusions about the effect of HBOT on acute wound treatment.

Table 6. Systematic Reviews of Trials Assessing HBOT for Acute Surgical and Traumatic Wounds

Study (Year)	Literature Search	Studies	Participants	N	Design	Results
Eskes et al (2013)[18,]	Aug 2013	4	Patients with acute wounds (skin injuries occurring due to surgery or trauma)	229	RCTs	• 3 of 4 trials did not include wound healing as an outcome measure • A small trial (N=36) reported patients receiving HBOT had significantly higher wound healing rate vs sham; however, no difference in time to healing
Dauwe et al (2014)[19,]	Oct 2012	8	Patients with acute wounds, grafts, and flaps	256	RCTs and nonrandomized studies	• HBOT may augment healing of acute wounds • Not indicated for routine wound management

HBOT: hyperbaric oxygen therapy; RCT: randomized controlled trial.

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Section Summary: Systemic Hyperbaric Oxygen Therapy for Acute Surgical and Traumatic Wounds

Two systematic reviews identified 4 RCTs; 1 of the reviews also included nonrandomized studies. Heterogeneity among studies (e.g., in patient population, treatment regimen, comparison group, outcomes) prevented pooling of study findings and limited the ability to draw conclusions about the impact of HBOT on health outcomes in patients with acute and traumatic wounds. Additional evidence from high-quality RCTs is needed.

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 question addressed in this evidence review is: Does the use of systemic hyperbaric oxygen as a treatment for bisphosphonate-related osteonecrosis of the jaw improve net health outcomes?

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-month 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

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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 7 and 8).[20,] 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 7. Characteristics of Trials Assessing HBOT for Bisphosphonate-Related Osteonecrosis of the Jaw

					Treatment	
Study (Year)	**Countries**	**Sites**	**Dates**	**Participants**	**Active (n=25)**	**Comparator (n=21)**
Freiberger et al (2012)[20,]	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 8. Results of Trials Assessing HBOT for Bisphosphonate-Related Osteonecrosis of the Jaw

	Improved, % (n)	**Healed, % (n)**

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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)[20],	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 Necrotizing Soft Tissue Infections

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 necrotizing soft tissue infections.

The question addressed in this evidence review is: Does the use of systemic hyperbaric oxygen as a treatment for necrotizing soft tissue infections improve net health outcomes?

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

Populations

The relevant population of interest is individuals with necrotizing soft tissue infections.

Interventions

The therapy being considered is systemic HBOT.

Comparators

Comparators of interest include medication and surgical therapy. Medications prescribed for necrotizing soft tissue infection may include antibiotics. Surgical therapy can include debridement. Systemic HBOT may be used as an adjunct to these comparators.

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Outcomes

The general outcomes of interest are OS, symptoms, and change in disease status. The existing literature evaluating systemic HBOT as a treatment for necrotizing soft tissue infections has varying lengths of follow-up. However, given the severity of the infection, 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 Levett et al (2015) evaluated the literature on HBOT as adjunctive therapy for necrotizing fasciitis.[21,] No RCTs were identified. A 2021 systematic review conducted by Hedetoft et al included 31 retrospective cohort studies assessing the effect of adjunctive HBOT for treating necrotizing soft-tissue infections (necrotizing fasciitis, Fournier's gangrene and gas gangrene).[22,] Ten studies assessed to have critical (very high) risk of bias were excluded from meta-analyses. Pooled results from the remaining 21 studies found HBOT associated with a reduced risk of in-hospital mortality (OR, 0.44; 95% CI, 0.33 to 0.58; I^2=8%), but duration of follow-up for mortality was not reported. Results were consistent when studies were stratified according to moderate (5 studies; OR, 0.39; 95% CI, 0.28 to 0.55; I^2=0%) and serious (high) risk of bias (16 studies; OR, 0.51; 95% CI, 0.33 to 0.80; I^2=17%). Publication bias favoring HBOT was present for this outcome based on funnel plot analysis. For other outcomes, including major amputation and length of hospital stay, there were no statistically significant differences between HBOT use and non-use. Evidence on adjunctive HBOT and need for surgical debridement was mixed. One study with low/moderate risk of bias reported a higher number of debridement's with HBOT use versus non-use (mean difference, 1.8; 95% CI, 1.15 to 2.45), but the mean difference between HBOT use and non-use in a pooled analysis of 5 studies with methodological flaws was not statistically significant (mean difference, 0.63; 95% CI, -0.49 to 1.75).

Section Summary: Systemic Hyperbaric Oxygen Therapy for Necrotizing Soft Tissue Infections

No RCTs have evaluated HBOT for necrotizing soft tissue infection. A systematic review of retrospective cohort studies with methodological limitations suggested that HBOT use may reduce risk of in-hospital mortality, but these results were subject to publication bias.

SYSTEMIC HYPERBARIC OXYGEN THERAPY FOR ACUTE CORONARY SYNDROME

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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 coronary syndrome.

The question addressed in this evidence review is: Does the use of systemic hyperbaric oxygen as a treatment for acute coronary syndrome improve net health outcomes?

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 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 patients) evaluating HBOT for acute coronary syndrome (see Table 9).[23,] Included studies were published between 1973 and 2007. All studies included patients with acute myocardial infarction; a study also included

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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 9. Systematic Reviews of Trials Assessing HBOT for Acute Coronary Syndrome

Study (Year)	Literature Search	Studies	Participants	N	Design	Results
Bennett et al (2015)[23,]	Jun 2010	6	Adults with acute coronary syndrome, with or without S-T segment elevation	665	RCTs	• Pooled analyses of 5 trials (n=614) reported a lower mortality rate for patients in the HBOT group vs 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

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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 question addressed in this evidence review is: Does the use of systemic hyperbaric oxygen as a treatment for acute ischemic stroke improve net health outcomes?

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
In a Cochrane systematic review of RCTs, Bennett et al (2014) evaluated HBOT for acute ischemic stroke (see Table 10).[24,] Reviewers identified 11 RCTs (N=705 participants) 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.

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Table 10. Systematic Reviews of Trials Assessing HBOT for Acute Ischemic Stroke

Study (Year)	Literature Search	Studies	Participants	N	Design	Results
Bennett et al (2014)[24,]	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.

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 patients with motor dysfunction associated with stroke.

The question addressed in this evidence review is: Does the use of systemic hyperbaric oxygen as a treatment for motor dysfunction associated with stroke improve net health outcomes?

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

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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 treatment of neurologic deficiencies associated with a history of stroke (see Tables 11 and 12).[25,] 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 treatment group, and several patient-reported quality of life (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 11. Characteristics of Trials Assessing HBOT for Motor Dysfunction Associated With Stroke

					Treatment	
Study (Year)	**Countries**	**Sites**	**Dates**	**Participants**	**Active (n=30)**	**Comparator (n=29)**
Efrati et al (2013)[25,]	Israel	1	2008-2010	Patients ≥18 y with ischemic or hemorrhagic stroke 6 to 36 mo prior to	• Hyperbaric oxygen • 100% oxygen at 2 ATA	Same as active, delayed after 2 mo

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				inclusion with ≥1 motor dysfunction	• 40 times over 2 mo	

ATA: atmospheres absolute; HBOT: hyperbaric oxygen therapy.

Table 12. Results of Trials Assessing HBOT 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)[25],	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 patients with Bell palsy.

The question addressed in this evidence review is: Does the use of systemic hyperbaric oxygen as a treatment for Bell palsy improve net health outcomes?

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

Populations

The relevant population of interest is individuals with Bell palsy.

Interventions

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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.[26,] 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 patients with traumatic brain injury (TBI).

The question addressed in this evidence review is: Does the use of systemic hyperbaric oxygen as a treatment for TBI improve net health outcomes?

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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 13 summarizes key measurement tools for assessing severity of brain injury.

Table 13. 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	Unfavorable outcome: 1-3

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Outcome	Description	Administration	Scoring	MCID
			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	
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
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; RPQ: Rivermead Post-Concussion Symptoms Questionnaire; 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

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Systematic Reviews

A meta-analysis by Wang et al (2016) assessed HBOT for TBI (see Table 14).[27,] Eight studies (N=519 participants) 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 14).[28,] 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., post concussive 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 14).[29,] 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).[30,] 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 14). The DoD data analyses indicated improvements with HBOT for PCS, measured by the Rivermead Total Score. Statistically significant improvements

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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 14. Systematic Reviews of Trials Assessing HBOT for Traumatic Brain Injury

Study (Year)	Literature Search	Studies	Participants	N	Design	Results
Hart et al (2019)[30,]		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)[27,]	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 treated with HBOT vs controls (OR=0.3; 95% CI, 0.2 to 0.6)
Crawford et al (2016)[28,]	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

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Study (Year)	Literature Search	Studies	Participants	N	Design	Results
						severity or psychological outcomes
Bennett et al (2012)[29,]	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

Several trials on mild TBI in military populations have been published; they did not find significant benefits of HBOT compared with sham treatment.[31,32,33,] Miller et al (2015) evaluated HBOT in 72 military service members with symptoms continuing at least 4 months after mild TBI in the "Hyperbaric Oxygen Therapy (HBO2) for Persistent Post-concussive Symptoms After Mild Traumatic Brain Injury (mTBI) (HOPPS)" trial.[33,] Patients were randomized to 40 daily HBOT sessions at 1.5 atm, 40 sham sessions consisting of room air at 1.2 atm or standard care with no hyperbaric chamber sessions. The primary outcome was change in Rivermead Post-Concussion Symptoms Questionnaire score. A cutoff of 15% improvement was deemed clinically important, which translates to a change score of at least 2 points on the Rivermead Post-Concussion Symptoms Questionnaire-3 subscale. The proportion of patients who met this prespecified change on the Rivermead questionnaire was 52% in the HBOT group, 33% in the sham group, and 25% in the standard care-only group. The difference between rates in the HBOT and sham groups was not statistically significant (p=.24). None of the secondary outcomes significantly favored the HBOT group. A criticism of this trial, as well as the other military population studies, was that patient response in the sham group was not due to a placebo effect but to an intervention effect of slightly increased atmospheric pressure (1.2 atm).[34,] Other researchers have noted that room air delivered at 1.2 atm would not be considered an acceptable therapeutic dose for any indication, and especially for a condition with persistent symptoms like PCS.

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),"

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completed in 2016,[35] 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.[36] BIMA initially planned for 12-month follow-up but was amended to include PCS and PTSD, quality of life, 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.[37] 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.[38] 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.[39] 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.

Section Summary: Systemic Hyperbaric Oxygen Therapy for Traumatic Brain Injury
A number of RCTs and systematic reviews have been published. Several RCTs focused on U. S. service members with mild TBI and found that the HBOT and sham group results did not differ significantly. In addition, pooled analyses were only conducted on a minority of the published RCTs, and these analyses had inconsistent findings. Additionally, there was some 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 patients with inflammatory bowel disease (IBD).

The question addressed in this evidence review is: Does the use of systemic hyperbaric oxygen as a treatment for IBD improve net health outcomes?

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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
A systematic review by Dulai et al (2014) examined the evidence on HBOT for IBD (Crohn disease, ulcerative colitis; see Table 15).[40,] The review was not limited by study design. One RCT identified was published in 2013; it was open-label and included 18 patients with ulcerative colitis.[41,] Patients were randomized to standard medical therapy only (n=8) or medical therapy plus HBOT (n=10). The hyperbaric oxygen intervention consisted of 90 minutes of treatment at 2.4 atm, 5 days a week for 6 weeks (total of 30 sessions). The primary outcome was the Mayo score, which has a potential range of 0 to 12, consisting of 4 components (bleeding, stool frequency, physician assessment, and endoscopic appearance) rated from 0 to 3, and added for a final score.[42,] Patients with a score of 6 or more are considered to have moderate-to-severe active disease. At follow-up, there was no significant difference between groups in the Mayo score; the median score at 6 months was 0.5 in the HBOT group and 3 in the control group (p-

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value not reported). Also, there were no significant differences in any secondary outcomes, including laboratory tests and fecal weight. This small trial might have been underpowered. Overall, reviewers found that the selected studies had a high risk of bias, due to attrition and reporting bias.

Table 15. Systematic Reviews of Studies Assessing HBOT for Inflammatory Bowel Disease

Study (Year)	Literature Search	Studies	Participants	N	Design	Results
Dulai et al (2014)[40]	Dec 2013	17	Patients with ulcerative colitis or Crohn disease	• Ulcerative colitis (n=327); • Crohn disease (n=286)	• 11 case reports • 3 case series • 2 case-control • 1 RCT	• Overall HBOT response rate across studies: 86% • 1 RCT (N=18) reported no difference in outcomes among patients with ulcerative colitis treated with HBOT vs HBOT plus medical therapy

HBOT: hyperbaric oxygen therapy; RCT: randomized controlled trial.

Section Summary: Systemic Hyperbaric Oxygen Therapy for Inflammatory Bowel Disease

Only 1 small RCT has been published, and it did not find a significant improvement in health outcomes when HBOT was added to standard medical therapy. 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).

SYSTEMIC HYPERBARIC OXYGEN THERAPY FOR IDIOPATHIC SUDDEN SENSORINEURAL HEARING LOSS

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 for individuals with idiopathic sudden sensorineural hearing loss(ISSNHL).

The question addressed in this evidence review is: Does the use of systemic hyperbaric oxygen as a treatment for ISSNHL improve net health outcomes?

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

Populations
The relevant population of interest is individuals with ISSNHL.

Interventions
The therapy being considered is systemic HBOT alone or as an adjunct to medical therapy.

Comparators
Comparators of interest include medical therapy. Medications prescribed for ISSNHL may include systemic and intratympanic steroids, antiviral and hemodilution agents and, mineral, vitamin, and herbal supplements.

Outcomes
The general outcomes of interest are symptoms, change in disease status, and functional outcomes. Follow-up for the evaluation of systemic HBOT as a treatment for ISSNHL would be weeks to months after early intervention. Longer follow-up of at least 1 year is 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
A Cochrane review by Bennett et al (2012) on HBOT for ISSNHL and/or tinnitus identified 7 RCTs (N=392; see Table 16).[43,] Treatment of tinnitus is covered in evidence review 8.01.39. Studies were small and generally of poor quality. Randomization procedures were only described in 1 study, and only 1 study stated they blinded participants to treatment group assignment using sham therapy. Six studies included time-based entry criteria for hearing loss and/or tinnitus (48 hours in 3 studies, 2 weeks in 2 studies, 6 months in 1 study). The dose of oxygen per treatment session and the treatment protocols varied across studies (e.g., the total number of treatment sessions ranged from 10 to 25). All trials reported on the change in hearing following treatment, but specific outcomes varied. Two trials reported the proportion of participants with more than 50% and more than 25% return of hearing at the end of therapy. A pooled analysis of these studies did not find a statistically significant difference in outcomes between the HBOT and the

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control groups at the level of 50% or higher but did find a significantly higher rate of improvement at the level of 25% or higher (see Table 16). A pooled analysis of 4 trials found a significantly greater mean improvement in hearing over all frequencies with HBOT compared with control. Reviewers stated that, due to methodologic shortcomings of the trials and the modest number of patients, results of the meta-analysis should be interpreted cautiously; they did not recommend the use of HBOT for treating ISSNHL.

Rhee et al (2018) performed a systematic review and meta-analysis through February 2018 for patients comparing HBOT plus medical therapy (MT) with medical therapy alone for ISSNHL treatment.[44,] Randomized clinical trials and nonrandomized studies were included. The main outcomes considered were complete hearing recovery, any hearing recovery, and absolute hearing gain. Nineteen studies (3 randomized and 16 nonrandomized) with a total of 2401 patients (mean age, 45.4 years; 55.3% female) were included. In the HBOT+MT group, rates of complete hearing recovery and any hearing recovery were 264/897 (29.4%) and 621/919 (67.6%), respectively, and in the MT alone group were 241/1167 (20.7%) and 585/1194 (49.0%), respectively. Pooled HBOT+MT also showed favorable pooled results from random-effects models for both complete hearing recovery (OR, 1.61; 95% CI, 1.05 to 2.44) and any hearing recovery (OR, 1.43; 95% CI, 1.20 to 1.67). The study was limited by the following: (1) differences in clinical and methodological characteristics of selected studies, (2) considerable heterogeneity, (3) the possibility of measure or unmeasured confounder effects, and (4) difficulty in evaluating the benefit of treatment due to a substantial proportion of patients experiencing spontaneous recovery.

A third systematic review, conducted by Joshua et al (2021)[45,] included 3 RCTs comparing HBOT with medical treatment, all published in 2018 and none of which were included in either the Bennett or Rhee systematic reviews. Inclusion criteria for studies in the Joshua review differed from the previous reviews in that: 1) only randomized studies were included and 2) diagnosis of ISSNHL was based on American Academy of Otolaryngology Head and Neck Surgery criteria. In addition, the literature search was limited to studies published beginning in January 2020. HBOT interventions were 60 or 90 minutes in duration, for time periods ranging from 10 to 20 days and medical treatment included a use of steroids (oral and/or intravenous) alone or in combination with antiviral medications and/or hemorheologic therapy. The patients included in the studies were clinically heterogenous, with baseline hearing loss ranging from moderate to profound in 2 studies and was unreported in the third study. The proportion of patients with hearing recovery, based on a ≥10 point audiometric gain, was significantly higher with HBOT compared with control based on pooled analysis of 2 studies (OR, 4.32; 95% CI, 1.60 to 11.68; I^2=0%). Limitations of these results include the fact that the included studies were judged to have moderate (2 studies) and high (1 study) risk of bias and the small number of participants in both HBOT (n=88) and medical treatment (n=62) groups.

Table 16. Systematic Reviews and Meta-Analyses of Trials Assessing HBOT for Idiopathic Sudden Sensorineural Hearing Loss

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Study (Year)	Literature Search	Studies	Participants	N	Design	Results
Bennett et al (2012)[43]	May 2012	7	Patients with idiopathic SSNHL and/or tinnitus	392	RCTs	• Pooled analyses of 2 RCTs (n=114) showed HBOT did not result in >50% improvement in pure tone average threshold (RR=1.5; 95% CI, 0.9 to 2.8), but was able to achieve >25% improvement (RR=1.4; 95% CI, 1.1 to 1.8) • Pooled analyses of 4 trials (n=169) found a significantly greater mean improvement in hearing over all frequencies with HBOT vs control (mean difference, 15.6 dB; 95% CI, 1.5 to 29.8 dB)
Rhee et al (2018)[44]	Feb 2018	19	Patients with SSNHL	2401	3 RCTs, 16 non-RCTs	• Pooled results significantly favored the HBOT and MT group over MT alone group for complete hearing recovery (pooled OR: 1.61; CI: 1.05-2.44) and for hearing recovery (pooled OR: 1.43, CI: 1.20-1.67)
Joshua et al (2021)[45]	Apr 2020	3	Patients with SSNHL	150	3 RCTs	• Pooled results from 2 RCTs favored HBOT over MT for hearing recovery, defined as ≥10 point audiometric gain (OR 4.32, 95% CI 1.60 to 11.68)

CI: confidence interval; HBOT: hyperbaric oxygen therapy; MT: medical therapy; OR: odds ratio; RCT: randomized controlled trial; RR: relative risk; SSNHL: sudden sensorineural hearing loss.

In their qualitative systematic review, Eryigit et al (2018) assessed the effectiveness of HBOT to treat patients with ISSNHL.[46] Sixteen clinical trials were included, with a total of 1759 operative ears, 580 of which received HBOT. All patients also received steroid treatment—either systemic, intravenous, or intratympanic injection. Most studies found that patients with severe or profound hearing loss who received steroids (any route of administration) plus HBOT saw statistically significant improvements (specified *p*-value range across studies:.0014 to.012), whereas those with a lower level of hearing loss did not see these improvements. Several studies reported no significant difference between case and control groups, but the studies that broke down the results by levels of hearing loss all showed that profound (or severe and profound) loss benefited from the addition of HBOT to steroid treatment.

Section Summary: Systemic Hyperbaric Oxygen Therapy for Idiopathic Sudden Sensorineural Hearing Loss

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A Cochrane review of RCTs had mixed findings from studies that included individuals with tinnitus. Some outcomes (i.e., improvement in hearing of all frequencies, >25% return of hearing) were better with HBOT than with a control intervention, but more than 50% return of hearing did not differ significantly between groups. There was important variability in the patients enrolled in the studies. A subsequent systematic review had similarly limited conclusions due to the inclusion of non-randomized studies. A third review that had stricter inclusion criteria found HBOT increased rate of hearing recovery, but the analysis was limited to 2 trials with methodological limitations.

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 patients with delayed-onset muscle soreness.

The question addressed in this evidence review is: Does the use of systemic hyperbaric oxygen as a treatment for delayed-onset muscle soreness improve net health outcomes?

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 (e.g., massage) and medication (e.g., 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.

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- 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 17).[47,] 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 17. Systematic Reviews of Trials Assessing HBOT for DOMS

Study (Year)	Literature Search	Studies	Participants	N	Design	Results
Bennett et al (2010)[47,]	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 (e.g., 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 patients with autism spectrum disorder.

The question addressed in this evidence review is: Does the use of systemic hyperbaric oxygen as a treatment for autism spectrum disorder improve net health outcomes?

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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
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 18).[48,] 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).[49,] 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 18. Systematic Reviews of Trials Assessing HBOT for Autism Spectrum Disorder

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Study (Year)	Literature Search	Studies	Participants	N	Design	ResultsMean Difference
Xiong et al (2016)[48,]	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.[50,] 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 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 patients with cerebral palsy (CP).

The question addressed in this evidence review is: Does the use of systemic hyperbaric oxygen as a treatment for CP improve net health outcomes?

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.

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Comparators

Comparators of interest include physical therapy and medication. Medications directed at isolated (e.g., onabotulinumtoxinA) 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 19 and 20). Lacey et al (2012) published a double-blind RCT that included 49 children ages 3 to 8 years with spastic CP.[51,] 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.[52,] 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).[53,] Children, aged 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 19. Characteristics of Trials Assessing HBOT for Cerebral Palsy

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					Treatment	
Study (Year)	**Countries**	**Sites**	**Dates**	**Participants**	**Active**	**Comparator**
Lacey et al (2012)[51,]	United States	2	2005-2009	Children aged 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)[52,]	Canada	17	NR	Children aged 3-2 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 20. Results of Trials Assessing HBOT 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)[51,]	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)[52,]			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

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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 patients with vascular dementia.

The question addressed in this evidence review is: Does the use of systemic hyperbaric oxygen as a treatment for vascular dementia improve net health outcomes?

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 (e.g., 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

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A Cochrane review (2012) identified a small RCT evaluating HBOT for vascular dementia (see Table 21).[54,] 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 21. Systematic Reviews of Trials Assessing HBOT for Vascular Dementia

Study (Year)	Literature Search	Studies	Participants	N	Design	Results
Xiao et al (2012)[54,]	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 RADIOTHERAPY ADVERSE EVENTS

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 radiotherapy adverse events.

The question addressed in this evidence review is: Does the use of systemic hyperbaric oxygen as a treatment for radiotherapy adverse effects improve net health outcomes?

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

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

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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.

This indication covers adverse events of radiotherapy other than osteoradionecrosis and treatment of irradiated jaw, which was covered in an earlier indication.

REVIEW OF EVIDENCE

Systematic Reviews
Spiegelberg et al (2010) conducted a systematic review of studies on HBOT to prevent or treat radiotherapy-induced head and neck injuries associated with the treatment of malignant tumors (see Table 22).[55,] Reviewers identified 20 studies. Protocols and conclusions varied across the studies. Eight studies included control groups; their sample sizes ranged from 19 to 78 subjects. Four studies with a control group concluded that HBOT was effective; the other 4 did not. Reviewers noted a paucity of RCTs, though they did not state how many RCTs were included in the review, because studies were only identified only as prospective or retrospective.

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 22).[11,] Pooled analyses were not performed; however, summary results were discussed for the following outcomes: salivary gland

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function, osteonecrosis prevention, dental implant survival, and QOL. Osteonecrosis prevention and dental implant survival outcomes were discussed previously (see the Radionecrosis, Osteoradionecrosis, and Treatment of Irradiated Jaw section).

Villeirs et al (2020) conducted a systematic review on the effect of HBOT on cystitis following pelvic radiotherapy.[56,] 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 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 22. Systematic Reviews of Studies Assessing HBOT for Radiotherapy Adverse Events

Study (Year)	Literature Search	Studies	Participants	N	Design	Results
Spiegelberg et al (2010)[55,]	Jun 2009	20	Patients who have received RT for malignant tumors in the head and neck	695	Prospective and retrospective studies	• Due to the heterogeneity among studies, pooled analysis was not possible • 8 studies had control groups and 4 concluded that HBOT was effective and 4 concluded that HBOT was not
Ravi et al (2017)[11,]	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 • Quality of life: 3 case series (n=106) administered various QOL instruments (e.g., SF-36, EORTC, HADS), reporting that many subsets of the questionnaires (e.g., swallowing, pain, salivary quantity) showed

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Study (Year)	Literature Search	Studies	Participants	N	Design	Results
						significant improvements with HBOT
Villeirs et al (2020)[56,]	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

Several RCTs were identified in literature searches. A trial by Teguh et al (2009), included in the reviews, evaluated 17 patients with oropharyngeal or nasopharyngeal cancer who were treated with radiotherapy; the trial was conducted in the Netherlands.[57,] HBOT was used to prevent adverse events following radiotherapy. Eight patients were randomized to 30 sessions of HBOT, administered within 2 days of completing radiotherapy, and 9 patients to no additional treatment. QOL outcomes were assessed, and the primary outcome was xerostomia at 1 year. QOL measures did not differ significantly between groups in the acute phase (first 3 months). One month after treatment, the mean visual analog scale score (0-to-10 scale) for xerostomia was 5 in the HBOT group and 6 in the control group. However, at 1 year, there was a statistically significant difference between groups in mean QOL score (0-to-100 scale) for swallowing, (7 in the HBOT group and 40 in the control group, p<.001). The trial is limited by its small sample size and wide fluctuations over the follow-up in QOL ratings.

In a trial not included in the reviews, Gothard et al (2010) in the U.K. published findings of an RCT using HBOT for arm lymphedema occurring after radiotherapy for cancer.[58,] Fifty-eight patients with arm lymphedema (at least 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 of patients in the HBOT group were considered responders compared with 3 (19%) of 16 in the control group (p=not significant). Other outcomes (e.g., QOL scores on the 36-Item Short-Form Health Survey [SF-36]) also did not differ significantly between groups.

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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.[59,]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 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).

Prospective Clinical Trials

A prospective cohort study by Sherlock et al (2018) evaluated HBOT for managing radiation-induced xerostomia (dry mouth).[60,] They compared saliva volume (objective),QOL scoring, and visual analog scale of discomfort (subjective) measurements taken before HBOT treatment, and after 30 90-minute sessions completed over 6 weeks, and a review at 12 weeks from the start of HBOT. Fifty-three treatment courses in 51 patients were eligible for inclusion in the statistical analysis, 78.4% of whom had been treated for oral cancer (2 patients repeated the treatment due to symptom relapse). All domains had improved significantly at the end of treatment: saliva volume, p=.016; visual analog scale score, p<.001; QOL score, p<.001. The only adverse reactions were minor middle ear barotrauma, occurring in 21% of patients (1.4% of all compression cycles). The authors concluded that HBOT may be a safe and effective option for treating symptoms of xerostomia after radiation therapy.

Section Summary: Systemic Hyperbaric Oxygen Therapy for Radiotherapy Adverse Events

Three systematic reviews included few RCTs and provide limited evidence evaluating HBOT for radiotherapy adverse events. One review focused on salivary gland function, osteonecrosis prevention, dental implant survival, and QOL. The available RCTs had mixed findings. One found no short-term benefit and some benefits of HBOT 12 months after radiotherapy, while the other did not find a significant benefit of HBOT 12 months after radiotherapy. 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

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by some measures but not others. An observational study for dry mouth (xerostomia) caused by radiotherapy found some benefit to HBOT.

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 patients with idiopathic femoral neck necrosis.

The question addressed in this evidence review is: Does the use of systemic hyperbaric oxygen as a treatment for femoral neck necrosis improve net health outcomes?

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.

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Review of Evidence

A double-blind RCT evaluating HBOT for treatment of femoral head necrosis was published by Camporesi et al (2010) (see Tables 23 and 24).[61,] The trial included 20 adults with idiopathic unilateral femoral head necrosis. Patients received HBOT or a sham treatment of hyperbaric air. 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 23. Characteristics of Trials Assessing HBOT for Femoral Neck Necrosis

					Treatment	
Study (Year)	**Countries**	**Sites**	**Dates**	**Participants**	**Active (n=10)**	**Comparator (n=10)**
Camporesi et al (2010)[61,]	United States	1	NR	Patients with unilateral femoral neck necrosis	• Hyperbaric oxygen • 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 24. Results of Trials Assessing HBOT 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**	
Camporesiet al (2010)[61,]					
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.

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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 patients with migraine headache.

The question addressed in this evidence review is: Does the use of systemic hyperbaric oxygen as a treatment for migraine headache improve net health outcomes?

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

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A Cochrane review by Bennett et al (2015) identified 11 RCTs (N=209 patients) comparing the effectiveness of systemic HBOT for preventing or treating migraine headache or cluster headaches with another treatment or a sham control (see Table 25).[62,] A pooled analysis of 3 trials focusing on migraine headaches (n=58 patients) found a statistically significant increase in the proportion of patients with substantial relief of a 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 25. Systematic Reviews of Trials Assessing HBOT for Migraine or Cluster Headaches

Study (Year)	Literature Search	Studies	Participants	N	Design	Results
Bennett et al (2015)[62,]	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 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 question addressed in this evidence review is: Does the use of systemic hyperbaric oxygen as a treatment for herpes zoster infection improve net health outcomes?

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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 26 and 27).[63,] 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. Patient 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 26. Characteristics of Trials Assessing HBOT for Herpes Zoster

					Treatment	
Study (Year)	**Countries**	**Sites**	**Dates**	**Participants**	**Active (n=36)**	**Comparator (n=32)**

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Peng et al (2012)[63,]	China	NR	2008-2010	Patients diagnosed with herpes zoster within 2 wk	• Hyperbaric oxygen • 100% oxygen at 2.2 ATA • 2 sessions/day for 5 d • Thirty 120-min sessions; plus medications that control group received	Medication alone, including: antiviral, nerve nutritive, pain relief, and antidepressives

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

Table 27. Results of Trials Assessing HBOT for 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)[63,]	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 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 patients with fibromyalgia.

The question addressed in this evidence review is: Does the use of systemic hyperbaric oxygen as a treatment for fibromyalgia improve net health outcomes?

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

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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.

Efratiet al (2015) published an RCT that included 60 symptomatic women who had fibromyalgia for at least 2 years (see Tables 28 and 29).[64,] 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 a 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 end points are pain and other subjective outcomes.

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Yildizet al (2004) assessed 50 patients with fibromyalgia (see Tables 28 and 29).[65,] 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 28. Characteristics of Trials Assessing HBOT for Fibromyalgia

					Treatment	
Study (Year)	**Countries**	**Sites**	**Dates**	**Participants**	**Active**	**Comparator**
Efrati et al (2015)[64,]	Israel	1	2010-2012	Patients with fibromyalgia based on: (1) widespread pain and (2) at least 11 of 18 tender points	• n=24 • Hyperbaric oxygen • 100% oxygen at 2 ATA • 1 session/day for 5 d • Forty 90-min sessions	• n=26 • No treatment for 2 mo, then same treatment as active group
Yildiz et al (2004)[65,]	Turkey	NR	NR	Patients meeting ACR criteria for fibromyalgia, with persistent symptoms despite medical therapy and PT	• n=26 • Hyperbaric oxygen • 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 29. Results of Trials Assessing HBOT 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)[64,]	50			50		
Mean HBOT (SD)	17.3 (1.4)	8.9 (6.0)	<.001	0.5 (1.2)	1.7 (0.8)	<.001

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Mean control (SD)	17.7 (0.7)	17.2 (1.1)		0.7 (0.5)	0.6 (0.5)	
Yildiz et al (2004)[65,]	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 patients with multiple sclerosis (MS).

The question addressed in this evidence review is: Does the use of systemic hyperbaric oxygen as a treatment for MS improve net health outcomes?

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

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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 30).[66,] Nine RCTs (N=504 participants) 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 Expanded Disability Status Scale score. A pooled analysis of data from 5 trials (n=271 patients) 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 30. Systematic Reviews of Trials Assessing HBOT for Multiple Sclerosis

Study (Year)	Literature Search	Studies	Participants	N	Design	Results
Bennett et al (2010)[66,]	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.

SYSTEMATIC HYPERBARIC OXYGEN THERAPY FOR INDIVIDUALS WITH CANCER WHO ARE UNDERGOING RADIOTHERPY OR CHEMOTHERAPY

Clinical Context and Therapy Purpose

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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 cancer who are undergoing radiotherapy or chemotherapy.

The question addressed in this evidence review is: Does the use of systemic hyperbaric oxygen as a treatment for individuals with cancer who are undergoing radiotherapy or chemotherapy improve net health outcomes?

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),[67,] which was updated in 2012,[68,] Bennett et al (2018) identified 19 randomized and quasi-randomized trials (N=2286 patients) comparing outcomes following radiotherapy with and without HBOT in patients with solid tumors (see Table 31). The latest trial identified in the Cochrane search was published in 1999. Reviewers did not find any ongoing

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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 31. Systematic Reviews of Trials Assessing HBOT for Tumor Sensitization during Cancer Treatment With Radiotherapy

Study (Year)	Literature Search	Studies	Participants	N	Design	Results
Bennett et al (2018)[68,]	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.[69,]

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 (e.g., radiation tissue injury, seizures) were significant. The RCT did not find a significant difference in survival in cancer patients who received HBOT before chemotherapy.

Other Indications

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 US-settings, assessing:

- bone grafts;
- carbon tetrachloride poisoning, acute;

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- cerebrovascular disease, acute (thrombotic or embolic) or chronic;
- fracture healing;
- hydrogen sulfide poisoning;
- intra-abdominal and intracranial abscesses;
- lepromatous leprosy;
- meningitis;
- pseudomembranous colitis (antimicrobial agent-induced colitis);
- radiation myelitis;
- sickle cell crisis and/or hematuria;
- amyotrophic lateral sclerosis;
- retinal artery insufficiency, acute;
- retinopathy, adjunct to scleral buckling procedures in patients with sickle cell peripheral retinopathy and retinal detachment;
- pyoderma gangrenosum;
- compromised skin grafts and flaps;
- brown recluse spider bites;
- spinal cord injury;
- refractory mycoses;
- acute peripheral arterial insufficiency;
- in vitro fertilization; or
- mental illness.

Summary of Evidence

For individuals with wounds, burns or infections who receive topical HBOT, the evidence includes a systematic review, case series, and an RCT. Relevant outcomes are 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 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.

For individuals with chronic diabetic ulcers who receive systemic HBOT, the evidence includes RCTs and systematic reviews. Relevant outcomes are symptoms and change in disease status. Meta-analyses of RCTs found significantly higher diabetic ulcer healing rates with HBOT than with control conditions. Two of the 3 meta-analyses found that HBOT was associated with a significantly lower rate of major amputation. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with carbon monoxide poisoning who receive systemic HBOT, the evidence includes RCTs and a systematic review. Relevant outcomes are OS and symptoms. A meta-analysis in a Cochrane review of low-quality RCT data did not find HBOT to be associated with a significantly lower risk of neurologic deficits after carbon monoxide poisoning. The evidence is

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insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with radionecrosis, osteoradionecrosis, or treatment of irradiated jaw who receive systemic HBOT, the evidence includes RCTs and a systematic review. Relevant outcomes are symptoms and change in disease status. A meta-analysis in a Cochrane review of RCTs found evidence that HBOT improved radionecrosis and osteoradionecrosis outcomes and resulted in better outcomes before tooth extraction in an irradiated jaw. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome

For individuals with chronic refractory osteomyelitis who receive systemic HBOT, the evidence includes case series. Relevant outcomes are symptoms and change in disease status. The case series reported high rates of successful outcomes (no drainage, pain, tenderness, or cellulitis) in patients with chronic refractory osteomyelitis treated with HBOT. However, controlled studies are needed to determine conclusively the impact of HBOT on health outcomes compared with other interventions. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with acute thermal burns who receive systemic HBOT, the evidence includes a systematic review of 2 RCTs. Relevant outcomes are OS, symptoms, and change in disease status. Both RCTs were judged to have poor methodologic quality. Evidence from well-conducted controlled trials is needed. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with acute surgical and traumatic wounds who receive systemic HBOT, the evidence includes RCTs, controlled nonrandomized studies, and systematic reviews. Relevant outcomes are OS, symptoms, change in disease status, and functional outcomes. There was considerable heterogeneity across the 4 RCTs identified (e.g., patient population, comparison group, treatment regimen, outcomes). This heterogeneity prevented pooling of trial findings and limits the ability to conclude the impact of HBOT on health outcomes for patients with acute surgical and traumatic wounds. Additional evidence from high-quality RCTs is needed. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with bisphosphonate-related osteonecrosis of the jaw who receive systemic HBOT, the evidence includes an 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 necrotizing soft tissue infections who receive systemic HBOT, the evidence includes systematic reviews. Relevant outcomes are OS, symptoms, and change in disease status. A Cochrane review did not identify any RCTs. Another systematic review of retrospective

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cohort studies with methodological limitations did not find consistent benefit of adjunctive HBOT use. 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 (mortality at 3 to 6 months), and for that outcome, there was no significant difference between active and sham HBOT treatments. 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 heterogenous regarding intervention protocols, patient populations, and outcomes reported. Multiple RCTs of US military service members showed no statistical difference in outcomes between HBOT groups and those that received sham treatment. 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 an RCT, observational studies, and a systematic review. Relevant outcomes are symptoms, change in disease status and functional outcomes. One small RCT has been

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published, and this trial did not find a significant improvement in health outcomes when HBOT was added to standard medical therapy. A systematic review including the RCT and observational studies found a high rate of bias in the literature due to attrition and reporting bias. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with idiopathic sudden sensorineural hearing loss who receive systemic HBOT, the evidence includes systematic reviews. Relevant outcomes are symptoms, change in disease status, and functional outcomes. A Cochrane review of RCTs had mixed findings from studies that included individuals with tinnitus. Some outcomes (i.e., improvement in hearing of all frequencies, >25% return of hearing) were better with HBOT than with a control intervention, but more than 50% return of hearing did not differ significantly between groups. There was important variability in the patients enrolled in the studies. A subsequent systematic review had similarly limited conclusions due to the inclusion of non-randomized studies. A third review found a higher proportion of patients with hearing recovery with HBOT compared to medical treatment alone, but the analysis was limited to 2 RCTs with methodological limitations. 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 a systematic review. 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 subsequent controlled trial reached the same conclusion. 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

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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 radiotherapy adverse events who receive systemic HBOT, the evidence includes RCTs, nonrandomized comparator trials, case series, and systematic reviews. Relevant outcomes are symptoms and functional outcomes. Three systematic reviews included few RCTs and provide limited evidence on the effect of HBOT. Two RCTs identified 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. An observational study for dry mouth (xerostomia) caused by radiotherapy found some benefit with HBOT. 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 an 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.

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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 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.

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.

Clinical Input From Physician Specialty Societies and Academic Medical Centers

While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

2010 Input

In response to requests, input was received from 6 physician specialty societies and 5 academic medical centers while this policy was under review in 2010. Clinical input varied by condition. There was consensus that topical hyperbaric oxygen therapy (HBOT) and systemic HBOT for autism spectrum disorder and headache/migraine are investigational. There was also wide support for adding acute carbon monoxide poisoning, compromised skin grafts or flaps, chronic refractory osteomyelitis, and necrotizing soft tissue infections to the list of medically necessary indications for HBOT. Several reviewers acknowledged that there is a paucity of clinical trials on HBOT for compromised skin grafts/flaps, necrotizing soft tissue infections, and chronic refractory osteomyelitis. These reviewers commented on the support from basic science, animal studies, and retrospective case series, as well as lack of effective alternative treatments for these conditions. Based on the available evidence and clinical input, acute carbon monoxide poisoning, and chronic refractory osteomyelitis were changed in 2010 to medically necessary indications for HBOT. However, despite the clinical input and given the limited published evidence, compromised skin grafts and flaps and necrotizing soft tissue infections are still considered investigational.

Practice Guidelines and Position Statements

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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.

Society of Vascular Surgery et al

In 2016, the Society of Vascular Surgery in collaboration with the American Podiatric Medical Association and the Society for Vascular Medicine published guidelines on the management of the diabetic foot.[70,] According to the guidelines, for diabetic foot ulcers that fail to demonstrate improvement (>50% wound area reduction) after a minimum of 4 weeks of standard wound therapy, adjunctive therapy such as HBOT is recommended (grade 1B). Also, for diabetic foot ulcers with adequate perfusion that fail to respond to 4 to 6 weeks of conservative management, HBOT is suggested (grade 2B).

Undersea and Hyperbaric Medical Society

In 2015, the Undersea and Hyperbaric Medical Society (UHMS) published guidelines on the use of HBOT for treating diabetic foot ulcers.[71,] Recommendations in the current version include:

- Suggest against using HBOT in patients with "Wagner Grade 2 or lower diabetic foot ulcers..."
- Suggest adding HBOT in patients with "Wagner Grade 3 or higher diabetic foot ulcers that have not shown significant improvement after 30 days of [standard of care] therapy..."
- Suggest "adding acute post-operative hyperbaric oxygen therapy to the standard of care" in patients with "Wagner Grade 3 or higher diabetic foot ulcers" who have just had foot surgery related to their diabetic ulcers.

The 2019 UHMS Hyperbaric Oxygen Therapy Indications (14th edition) included the following indications as recommended:[72,]

1. Air or Gas Embolism
2. Carbon Monoxide Poisoning and carbon monoxide complicated by cyanide poisoning
3. Clostridial Myositis and Myonecrosis (Gas Gangrene)
4. Crush Injury, Compartment Syndrome and Other Acute Traumatic Ischemias
5. Decompression Sickness
6. Central retinal artery occlusion
7. Diabetic foot ulcer
8. Healing of other problem wounds
9. Severe anemia
10. Intracranial abscess
11. Necrotizing soft tissue infections
12. Refractory osteomyelitis
13. Delayed radiation injury (soft tissue and bony necrosis)
14. Compromised grafts and flaps
15. Acute thermal burn injury
16. Sudden Sensorineural hearing loss.

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American Academy of Otolaryngology-Head and Neck Surgery
In 2018, the American Academy of Otolaryngology-Head and Neck Surgery updated clinical guidelines on treatment of sudden hearing loss.[73,] They give the following options regarding HBOT:

"Clinicians may offer, or refer to a physician who can offer, hyperbaric oxygen therapy (HBOT) combined with steroid therapy within 2 weeks of onset of SSNH."

"Clinicians may offer, or refer to a physician who can offer, hyperbaric oxygen therapy (HBOT) combined with steroid therapy as salvage within 1 months of onset of SSNHL."

U.S. Preventive Services Task Force Recommendations
Not applicable.

Ongoing and Unpublished Clinical Trials
Some currently unpublished trials that might influence this review are listed in Table 32.

Table 32. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT04472780	Effect of Hyperbaric Oxygen Therapy (HBOT) in Children With Autism Spectrum Disorder (ASD)	80	Oct 2021
NCT02407028	Hyperbaric Oxygen Brain Injury Treatment (HOBIT) Trial	200	Jun 2023
NCT04316702	Hyperbaric Oxygen Therapy vs. Pharmaceutical Therapy in Patients Suffering From Fibromyalgia That Was Induced by Emotional Trauma: Prospective, Randomized, Two Active Arms Clinical Trial	60	Mar 2023
NCT04193722	The Effect of Hyperbaric Oxygen Therapy on Breast Cancer Patients With Late Radiation Toxicity	120	Sep 2023
NCT04049721	Use of Hyperbaric Oxygen Therapy for the Treatment of Crush Injuries	30	Sep 2023
NCT01986205	A Double-blind Randomized Trial of Hyperbaric Oxygen Versus Sham for Persistent Symptoms After Brain Injury	150	Dec 2023
NCT04975867	Targeted Temperature Management Combined With Hyperbaric Oxygen Therapy in Acute Severe Carbon Monoxide Poisoning: Multicenter Randomized Controlled Clinical Trial (TTM-COHB Trial)	46	Jul 2025
Unpublished			

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NCT No.	Trial Name	Planned Enrollment	Completion Date
NCT02085330	Hyperbaric Oxygen Therapy for Mild Cognitive Impairment	60	Feb 2017 (unknown; last updated 10/02/14)
NCT03147352	Pro-Treat - Prognosis and Treatment of Necrotizing Soft Tissue Infections: a Prospective Cohort Study	310	Jan 2018 (completed; last updated 06/24/19)
NCT02089594	Hyperbaric Oxygen Therapy Treatment of Chronic Mild Traumatic Brain Injury (mTBI)/Persistent Post-Concussion Syndrome (PCCS)	59	Mar 2019 (status unknown; last updated 4/18/17)
NCT03325959	Hyperbaric Oxygen versus Standard Pharmaceutical Therapies for Fibromyalgia Syndrome - Prospective, Randomized, Crossover Clinical Trial	70	Nov 2019 (status unknown; last updated 10/30/17)

NCT: national clinical trial.

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CODING

The following codes for treatment and procedures applicable to this policy are included below for informational purposes. This may not be a comprehensive list of procedure codes applicable to this policy.

Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

The code(s) listed below are medically necessary ONLY if the procedure is performed according to the "Policy" section of this document.

CPT/HCPCS	
99183	Physician or other qualified health care provider attendance and supervision of hyperbaric oxygen therapy, per session
A4575	Topical hyperbaric oxygen chamber, disposable
G0277	Hyperbaric oxygen under pressure, full body chamber, per 30 minute interval

ICD-10 DIAGNOSIS	
A48.0	Gas gangrene
D62	Acute posthemorrhagic anemia
E08.621	Diabetes mellitus due to underlying condition with foot ulcer (Note: Use additional code to identify site of ulcer L97.4-, L97.5-)
E08.622	Diabetes mellitus due to underlying condition with other skin ulcer (Note: Use additional code to identify site of ulcer L97.1-L97.9)
E09.621	Drug or chemical induced diabetes mellitus with foot ulcer(Note: Use additional code to identify site of ulcer L97.4-, L97.5-)
E09.622	Drug or chemical induced diabetes mellitus with other skin ulcer (Note: Use additional code to identify site of ulcer L97.1-L97.9)
E10.621	Type 1 diabetes mellitus with foot ulcer (Note: Use additional code to identify site of ulcer L97.4-, L97.5-)
E10.622	Type 1 diabetes mellitus with other skin ulcer (Note: Use additional code to identify site of ulcer L97.1-L97.9)
E11.621	Type 2 diabetes mellitus with foot ulcer (Note: Use additional code to identify site of ulcer L97.4-, L97.5-)

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ICD-10 DIAGNOSIS	
E11.622	Type 2 diabetes mellitus with other skin ulcer (Note: Use additional code to identify site of ulcer L97.1-L97.9)
E13.621	Other specified diabetes mellitus with foot ulcer (Note: Use additional code to identify site of ulcer L97.4-, L97.5-)
E13.622	Other specified diabetes mellitus with other skin ulcer (Note: Use additional code to identify site of ulcer L97.1-L97.9)
K52.0	Gastroenteritis and colitis due to radiation
M27.2	Inflammatory conditions of jaws (includes osteoradionecrosis, osteomyelitis, etc.) (Note: sequelae due to exposure to ionizing radiation would also be reported, when applicable, using code W88.0xxS, W88.1xxS or W88.8xxS depending on the radiation source)
M46.20-M46.28	Osteomyelitis of vertebra, code range
M86.40-M86.69	Chronic osteomyelitis, code range
N30.40-N30.41	Irradiation cystitis, code range
T58.01xA-T58.94xD	Toxic effect of carbon monoxide, code range (Note: 7th character "S" for sequelae is defined as after the acute stage has ended so codes ending in S would not be applicable to acute poisoning)
T65.0x1A-T65.0x4D	Toxic effect of cyanides, code range (see note regarding 7th character "S" above)
T79.0xxA-T79.0xxD	Air embolism (traumatic), code range (see note regarding 7th character "S" above)
T79.6xxA-T79.6xxD	Air embolism (traumatic), code range (see note regarding 7th character "S" above)

REVISIONS	
03-14-2011	Description section updated
	In Policy section: ▪ Revised policy to current policy language from: "Covered Conditions: Benefits are available for hyperbaric oxygen (HBO) therapy that is administered in a chamber (whole body - single or multiple chamber).

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REVISIONS	
	HBO therapy is a valuable adjunctive treatment to be used in combination with accepted standard therapeutic measures when loss of function, limb or life is threatened for the following conditions: 1. Acute carbon monoxide poisoning (986); smoke inhalation (987.9); cyanide poisoning (987.7 and 989.0). 2. Decompression sickness (993.2 – 993.3). 3. Cerebral arterial gas embolism (958.0 and 999.1). 4. Clostridial gas gangrene (040.0). 5. Acute traumatic peripheral ischemia (902.53, 903.01, 903.1, 904.0 and 904.41). 6. Crush injuries and suturing of severed limbs (925.1 - 929.9, 996.90 – 996.99). 7. Pyoderma gangrenosum (686.01) Note: The use of hyperbaric oxygen in any other type of cutaneous ulcer is not covered (problem wounds may be submitted for individual consideration). 8. Osteoradionecrosis as an adjunct to conventional treatment/osteoradionecrosis prevention and prophylactic treatments prior to dental extraction(s) involving areas of previously irradiated bone (526.89). 9. Soft tissue radionecrosis as an adjunct to conventional treatment (990). 10. Acute peripheral arterial insufficiency (444.21, 444.22, 444.81). 11. Preparation and preservation of compromised skin grafts (996.52). 12. Chronic refractory osteomyelitis, unresponsive to conventional medical and surgical management (730.00 – 730.29, 730.80 – 730.89). 13. Actinomycosis, only as an adjunct to conventional therapy when the disease process is refractory to antibiotics and surgical treatment (039.0 – 039.4, 039.8 – 039.9). Conditions for Review: 1. Selected problem wounds 2. Anaerobic septicemia (038.3) and infection other than clostridial (nonclostridial gas gangrene) 3. Acute thermal burns/radiation tissue injury (940 – 949). Conditions Not Medically Necessary: All other diagnosis not previously listed. Conditions Experimental/Investigational: 1. Multiple Sclerosis (340) 2. Topical Application of Oxygen (THBO) -- does not meet the definition of hyperbaric oxygen therapy as stated above. Also, its clinical efficacy has not been established. Therefore, use of topical oxygen is investigational and therefore non-covered. 3. Claims for Partial Body Hyperbaric Oxygen Therapy should be denied as investigational and therefore non-covered."
	Rationale section added
	In Coding section: ▪ Removed HCPCS Code: G0167 ▪ Added HCPCS Code: A4575 ▪ Removed Diagnosis Codes: 686.01, 987.9 ▪ Added Diagnosis Codes: 111.0-111.9, 112.0-112.3, 117.7, 117.9, 249.00-250.93, 285.1, 324.0, 362.31, 383.20-383.22, 443.89, 443.9, 459.9, 526.4, 595.82, 686.00-686.9, 707.00-707.19, 707.20-707.25, 707.8-707.9, 728.86, 728.9, 729.71-729.79, 903.01-903.9, 904.1, 904.51, 904.53, 904.6-904.9, 906.0-906.1, 906.4, 909.2, 941.20-941.59,

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REVISIONS	
	942.20-942.59, 943.20-943.59, 944.20-944.58, 945.20-945.59, 946.2-946.5, 948.00-948.99, 949.2-949.5, 958.8, 958.90-958.99, 998.83
	References section updated
10-11-2011	In the Policy title, removed "(HBO2) Therapy" and inserted "Pressurization (HBO)" to read "Hyperbaric Oxygen Pressurization (HBO)"
	Updated the Description section.
	In the Policy section: • In Item A, #5, removed "(CRAO)" • In Item C, removed "all other conditions" and inserted "the following conditions" • In Item C, added the following conditions: 1. acute osteomyelitis, refractory to standard medical management; 2. acute surgical and traumatic wounds; 3. spinal cord injury; 4. traumatic brain injury; 5. severe or refractory Crohn's disease;
	6. acute brown recluse spider bites; 7. bone grafts; 8. carbon tetrachloride poisoning, acute; 9. cerebrovascular disease, acute (thrombotic or embolic) or chronic; 10. fracture healing; 11. hydrogen sulfide poisoning; 12. intra-abdominal abscesses; 13. lepromatous leprosy; 14. meningitis; 15. Pseudomembranous colitis (antimicrobial agent-induced colitis); 16. radiation myelitis; 17. sickle cell crisis and/or hematuria; 18. demyelinating diseases, e.g., multiple sclerosis, amyotrophic lateral sclerosis; 19. retinopathy, adjunct to scleral buckling procedures in patients with sickle cell peripheral retinopathy and retinal detachment; 20. pyoderma gangrenosum; 21. acute coronary syndromes and as an adjunct to coronary interventions, including but not limited to, percutaneous coronary interventions and cardiopulmonary bypass; 22. idiopathic sudden sensorineural hearing loss; 23. refractory mycoses: mucormycosis, actinomycosis, canidiobolus coronato; 24. cerebral edema, acute; 25. migraine; 26. in vitro fertilization; 27. cerebral palsy; 28. tumor sensitization for cancer treatments, including but not limited to, radiotherapy or chemotherapy; 29. delayed onset muscle soreness; 30. idiopathic femoral neck necrosis; 31. chronic arm lymphedema following radiotherapy for cancer; 32. radiation-induced injury in the head and neck;

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REVISIONS	
	33. early treatment (beginning at completion of radiation therapy) to reduce adverse effects of radiation therapy; and 34. autism spectrum disorders." Updated the Rationale section. Updated the References section.
01-01-2012	In the Coding section: ▪ Added HCPCS code A9272
01-30-2012	In the Coding section: ▪ Removed HCPCS code A9272
03-27-2014	In Policy section: ▪ In Item A, #3, added "e.g., crush injuries, reperfusion injury, compartment syndrome" to read "Acute traumatic ischemia (e.g., crush injuries, reperfusion injury, compartment syndrome); or" ▪ In Item A, removed #11, crush injuries was incorporated into Item A, #3. ▪ In Item C, added #36, "bisphosphonate-related osteonecrosis of the jaw" ▪ In Item C, added #37, "acute ischemic stroke; and" ▪ In Item C, added #38. "Bell's palsy." Rationale section updated. In Coding section: ▪ Added ICD-10 Diagnosis *(Effective October 1, 2014)* Reference section updated.
01-23-2015	In Policy title: ▪ Changed title from, "Hyperbaric Oxygen-Pressurization (HBO)" In Policy section: ▪ In Item A, #7, removed the word "treatments" and changed to "days" to read, "Chronic non-healing wounds which have not responded to 30 days of appropriate conservative treatment and which show continued response when evaluated at 30 day intervals;" Updated Rationale section. In Coding section: ▪ Added HCPCS code G0277. ▪ Removed HCPCS code C1300. ▪ Updated effective date for ICD-10 to October 1, 2015. Update References section.
02-05-2015	In Policy section: ▪ In Item C, removed wording "conditions, but limited to," and corrected to, "Hyperbaric oxygen pressurization is considered experimental / investigational in the treatment of the following conditions including, but not limited to:"
11-12-2015	Updated Description section. In Policy section: ▪ In Item A 1, removed "when performed in accordance with Undersea and Hyperbaric Medical Society (UHMS) guidelines". ▪ In Item A 4, added "acute" to read, "Carbon monoxide poisoning, acute;" ▪ In Item A 6, added "acute" to read, "Cyanide poisoning, acute;" ▪ Removed Item A 9 "Compartment syndrome," as this is stated in Item A 3. ▪ In Item A 13, added "acute" to read, "Gas or air embolism, acute;"

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REVISIONS	
	▪ In Item C, removed "in the treatment of the following conditions" and added "in all other situations" to read, "Hyperbaric oxygen pressurization is considered experimental/investigational in all other situations including, but not limited to:" ▪ In Item C 5, removed "severe or refractory Crohn's disease" and added "irritable bowel syndrome (Crohn's disease or ulcerative colitis)" ▪ In Item C 32, added "(except as noted in Item A 11 above)" to read, "radiation-induced injury in the head and neck (except as noted in Item A 11 above);" ▪ Added Items C 37-41. ▪ In Policy Guidelines, added section on Topical Hyperbaric Oxygen.
	In Coding section: ▪ Revised nomenclature to CPT code 99183.
	Updated Rationale section.
	Updated References section.
11-19-2015	Updated References section of revision on 11-12-2015 ("In Policy Guidelines, added section on Topical Hyperbaric Oxygen.").
10-01-2016	In Coding section: ▪ Removed ICD-10 codes: A18.01, A18.03, A42.0, A42.1, A42.81, A42.82, A43.0, E08.00, E08.01, E08.10, E08.11, E08.21, E08.22, E08.29, E08.311, E08.319, E08.36, E08.39, E08.40, E08.41, E08.42, E08.43, E08.44, E08.49, E08.51, E08.610, E08.618, E08.630, E08.638, E08.641, E08.649, E08.65, E08.69, E08.8, E08.9, E09.00, E09.01, E09.10, E09.11, E09.21, E09.22, E09.29, E09.311, E09.319, E09.36, E09.39, E09.40, E09.41, E09.42, E09.43, E09.44, E09.49, E09.51, E09.610, E09.618, E09.630, E09.638, E09.641, E09.649, E09.65, E09.69, E09.8, E09.9, E10.10, E10.11, E10.21, E10.22, E10.29, E10.311, E10.319, E10.36, E10.39, E10.40, 310.41, 310.42, E10.43, 310.44, E10.49, E10.51, E10.610, E10.618, E10.630, E10.638, E10.641, E10.649, E10.65, E10.69, E10.8, E10.9, E11.00, E11.01, E11.21, E11.22, E11.29, E11.311, E11.319, E11.36, E11.39, E11.40, E11.41, E11.42, E11.43, E11.44, E11.49, E11.51, E11.610, E11.618, E11.630, E11.638, E11.641, E11.649, E11.65, E11.69, E11.8, E11.9, E13.00, E13.01, E13.10, E13.11, E13.21, E13.22, E13.29, E13.311, E13.319, E13.36, E13.39, E13.40, E13.41, E13.42, E13.43, E13.44, E13.49, E13.51, E13.610, E13.618, E13.630, E13.638, E13.641, E13.649, E13.65, E13.69, E13.8, E13.9, E83.2 ▪ Termed ICD-10 codes effective 09-30-2016: E08.321, E08.329, E08.331, E08.339, E08.341, E08.349, E08.351, E08.359, E09.321, E09.329, E09.331, E09.339, E09.341, E09.349, E09.351, E09.359, E10.321, 310.329, 310.331, E10.339, E10.341, E10.349, E10.351, E10.359, E11.321, E11.329, E11, 331, E11.339, E11.341, E11.349, E11.351, E11.359, E13.321, E13.329, E13.331, E13.339, E13.341, E13.349, E13.351, E13.359
02-15-2017	Updated Description section.
	Updated Rationale section.
	In Coding section: ▪ Updated coding bullet.
	Updated References section.
10-01-2017	In Coding section: ▪ Added ICD-10 codes: L97.125, L97.126, L97.128, L97.215, L97.216, L97.218, L97.225, L97.226, L97.228, L97.315, L97.316, L97.318, L97.325, L97.326, L97.328, L97.415, L97.416, L97.418, L97.425, L97.426, L97.428, L97.515, L97.516, L97.518, L97.525, L97.526, L97.528, L97.815, L97.816, L97.818, L97.825, L97.826, L97.828,

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REVISIONS	
	L97.915, L97.916, L97.918, L97.925, L97.926, L97.928, L98.415, L98.416, L98.418, L98.425, L98.426, L98.428, L98.495, L98.496, L98.498
02-15-2018	Updated Description section.
	Updated Rationale section.
	In Coding section: ▪ Removed ICD-9 codes.
	Updated References section.
04-26-2019	The policy published to the bcbsks.com website on 03-27-2019 with an effective date of 04-26-2019.
	Updated Description section.
	In Policy section: ▪ Removed previous Item A 1, "Acute peripheral arterial insufficiency; OR". ▪ Removed previous Item A 2, "Acute thermal burns: deep second degree or third degree in nature; OR". ▪ Removed previous Item A 5, "Central retinal artery occlusion; OR". ▪ In Item A 4 (previous Item A 7), removed "chronic" and "and which show continued response when evaluated at 30 day intervals" and added "diabetic" and "of the lower extremities in patients who meet the following criteria" to read, "Non-healing diabetic wounds of the lower extremities in patients who meet the following criteria". ▪ Added new Item A 4 a, "Patient has type 1 or type 2 diabetes and has a lower extremity wound due to diabetes". ▪ Added new Item A 4 b, "Patient has a wound classified as Wagner grade 3 or higher (see Policy Guidelines)". ▪ In Item A 5 (previous Item A 8), removed "(refractory osteomyelitis)" to read, "Chronic refractory osteomyelitis". ▪ Removed previous Item A 9, "Compromised skin graft or flaps (enhancement of healing in selected wounds); OR". ▪ In Item A 7 (previous Item A 11), removed "delayed radiation injury, including osteoradionecrosis" and "and radiation cystitis" to read, "Soft tissue radiation necrosis". ▪ In Item A 8 (previous Item A 12), removed "or air" to read, "Gas embolism, acute". ▪ In Item A 9 (previous Item A 13), removed "myositis and" to read, "Gas gangrene (ie, clostridial myonecrosis)". ▪ Removed previous Item A 14, "Intracranial abscess; OR". ▪ Removed previous Item A 15, "Necrotizing soft tissue infections; OR" ▪ In Item A 10 (previous Item A 16", removed "prophylactic" and added "(non-implanted related)" to read, "Pre and post treatment for individuals undergoing dental surgery (non-implant related) of an irradiated jaw". ▪ In Item A 11 (previous Item A 17), added "profound", "only", "blood", and "must be" to read, "Profound anemia with exceptional blood loss: only when blood transfusion is impossible or must be delayed." ▪ In Item B, added "the treatment of the following conditions" to read, "Hyperbaric oxygen pressurization is considered experimental / investigational in all other situations including, but not limited to, the treatment of the following conditions:". ▪ In Item B 1, removed "refractory to standard medical management" to read, "Acute osteomyelitis".

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<table>
<tr><th colspan="2">REVISIONS</th></tr>
<tr><td></td><td>▪ In Item B 5, removed “irritable” and “syndrome” and added “inflammatory” and “disease” to read, “Inflammatory bowel disease (Crohn’s disease or ulcerative colitis)”.
▪ In Item B 12, added “and intracranial” to read, “Intra-abdominal and intracranial abscesses”.
▪ Added new Item B 41, “Compromised skin grafts or flaps”.
▪ Added new Item B 42, “Necrotizing soft tissue infections”.
▪ Added new Item B 43, “Acute thermal burns”.
▪ Added new Item B 44, “Chronic wounds, other than those in patients with diabetes who meet the criteria specified in Item A 4 above”.
▪ Added new Item B 45, “Acute arterial peripheral insufficiency”.
▪ In Item B 48 (previous Item B 43), removed “insufficiency, acute” and added “central” and “occlusion” to read, “Central retinal artery occlusion.”
▪ Updated Policy Guidelines.</td></tr>
<tr><td></td><td>Updated Rationale section.</td></tr>
<tr><td></td><td>Updated References section.</td></tr>
<tr><td>06-19-2019</td><td>In Policy section:
▪ Policy Guidelines updated to include treatment session recommendations.</td></tr>
<tr><td>10-01-2019</td><td>In Coding section:
▪ Added ICD-10 Codes: L89.006, L89.016, L89.026, L89.106, L89.116, L89.126, L89.136, L89.146, L89.156, L89.206, L89.216, L89.226, L89.306, L89.316, L89.326, L89.46, L89.506, L89.516, L89.526, L89.606, L89.616, L89.626, L89.816, L89.896, L89.96</td></tr>
<tr><td>03-16-2021</td><td>Updated Description section</td></tr>
<tr><td></td><td>In the Policy section
• Added
Item A 7- (eg, radiation enteritis, cystitis, proctitis) and osteoradionecrosis;
Item B 49 Retinal artery insufficiency, acute.
• Deleted
Item B 48 Central retinal artery occlusion</td></tr>
<tr><td></td><td>In Coding section
▪ Deleted ICD 10 codes:
<table>
<tr><td>A42.2</td><td>E10.620</td><td>I70.333</td><td>I70.638</td><td>L89.013</td><td>L89.212</td></tr>
<tr><td>A42.89</td><td>E10.628</td><td>I70.334</td><td>I70.639</td><td>L89.014</td><td>L89.213</td></tr>
<tr><td>A42.9</td><td>E11.52</td><td>I70.335</td><td>I70.641</td><td>L89.016</td><td>L89.214</td></tr>
<tr><td>A43.1</td><td>E11.59</td><td>I70.338</td><td>I70.642</td><td>L89.020</td><td>L89.216</td></tr>
<tr><td>A43.8</td><td>E11.620</td><td>I70.339</td><td>I70.643</td><td>L89.021</td><td>L89.220</td></tr>
<tr><td>A43.9</td><td>E11.628</td><td>I70.341</td><td>I70.644</td><td>L89.022</td><td>L89.221</td></tr>
<tr><td>B36.0</td><td>E13.52</td><td>I70.342</td><td>I70.645</td><td>L89.023</td><td>L89.222</td></tr>
<tr><td>B36.1</td><td>E13.59</td><td>I70.343</td><td>I70.648</td><td>L89.024</td><td>L89.223</td></tr>
<tr><td>B36.2</td><td>E13.620</td><td>I70.344</td><td>I70.649</td><td>L89.026</td><td>L89.224</td></tr>
<tr><td>B36.3</td><td>E13.628</td><td>I70.345</td><td>I70.65</td><td>L89.029</td><td>L89.226</td></tr>
<tr><td>B36.8</td><td>G06.0</td><td>I70.348</td><td>I70.731</td><td>L89.101</td><td>L89.306</td></tr>
<tr><td>B36.9</td><td>H34.11</td><td>I70.349</td><td>I70.732</td><td>L89.102</td><td>L89.310</td></tr>
<tr><td>B37.0</td><td>H34.12</td><td>I70.35</td><td>I70.733</td><td>L89.103</td><td>L89.311</td></tr>
<tr><td>B37.2</td><td>H34.13</td><td>I70.431</td><td>I70.734</td><td>L89.104</td><td>L89.312</td></tr>
<tr><td>B37.3</td><td>H70.201</td><td>I70.432</td><td>I70.735</td><td>L89.106</td><td>L89.313</td></tr>
<tr><td>B37.41</td><td>H70.202</td><td>I70.433</td><td>I70.738</td><td>L89.110</td><td>L89.314</td></tr>
<tr><td>B37.42</td><td>H70.203</td><td>I70.434</td><td>I70.739</td><td>L89.111</td><td>L89.316</td></tr>
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</table>

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REVISIONS

B37.49	H70.209	I70.435	I70.741	L89.112	L89.320
B37.83	H70.211	I70.438	I70.742	L89.113	L89.321
B46.0	H70.212	I70.439	I70.743	L89.114	L89.322
B46.1	H70.213	I70.441	I70.744	L89.116	L89.323
B46.2	H70.221	I70.442	I70.745	L89.120	L89.324
B46.3	H70.222	I70.443	I70.748	L89.121	L89.326
B46.4	H70.223	I70.444	I70.749	L89.122	L89.41
B46.5	H70.229	I70.445	I70.75	L89.123	L89.42
B46.8	I70.231	I70.448	I73.89	L89.124	L89.43
B46.9	I70.232	I70.449	I73.9	L89.126	L89.44
B47.1	I70.233	I70.45	I74.2	L89.130	L89.45
B47.9	I70.234	I70.531	I74.3	L89.131	L89.46
B48.3	I70.235	I70.532	I74.5	L89.132	L89.506
B48.8	I70.238	I70.533	I87.9	L89.133	L89.510
B49	I70.239	I70.534	I99.9	L89.134	L89.511
B78.1	I70.241	I70.535	K52.0	L89.136	L89.512
E08.52	I70.242	I70.538	L08.0	L89.140	L89.513
E08.59	I70.243	I70.539	L08.1	L89.141	L89.514
E08.620	I70.244	I70.541	L08.81	L89.142	L89.516
E08.628	I70.245	I70.542	L08.82	L89.143	L89.520
E09.59	I70.248	I70.543	L08.89	L89.144	L89.521
E09.620	I70.249	I70.544	L08.9	L89.146	L89.522
E09.628	I70.25	I70.545	L88	L89.150	L89.523
E10.52	I70.331	I70.548	L89.001	L89.151	L89.524
E10.59	I70.332	I70.549	L89.002	L89.152	L89.526
		I70.55	L89.003	L89.153	L89.606
		I70.631	L89.004	L89.154	L89.610
		I70.632	L89.006	L89.156	L89.611
		I70.633	L89.010	L89.206	L89.612
		I70.634	L89.011	L89.210	L89.613
		I70.635	L89.012	L89.211	L89.614
L89.616	L97.222	L97.522	L98.421	M79.A12	M86.8X0
L89.620	L97.223	L97.523	L98.422	M79.A19	M86.8X1
L89.621	L97.224	L97.524	L98.423	M79.A21	M86.8X2
L89.622	L97.225	L97.525	L98.424	M79.A22	M86.8X3
L89.623	L97.226	L97.526	L98.425	M79.A3	M86.8X4
L89.624	L97.228	L97.528	L98.426	M79.A9	M86.8X5
L89.626	L97.229	L97.529	L98.428	M86.30	M86.8X6
L89.810	L97.311	L97.811	L98.429	M86.311	M86.8X7
L89.811	L97.312	L97.812	L98.491	M86.312	M86.8X8
L89.812	L97.313	L97.813	L98.492	M86.321	M86.8X9
L89.813	L97.314	L97.814	L98.493	M86.322	M90.811
L89.814	L97.315	L97.815	L98.494	M86.331	M90.812
L89.816	L97.316	L97.816	L98.495	M86.332	M90.821
L89.890	L97.318	L97.818	L98.496	M86.341	M90.822
L89.891	L97.319	L97.819	L98.498	M86.342	M90.831
L89.892	L97.321	L97.821	L98.499	M86.351	M90.832
L89.893	L97.322	L97.822	M27.0	M86.352	M90.841
L89.894	L97.323	L97.823	M27.8	M86.361	M90.842
L89.896	L97.324	L97.824	M46.20	M86.362	M90.851
L89.91	L97.325	L97.825	M46.21	M86.371	M90.852
L89.92	L97.326	L97.826	M46.22	M86.372	M90.861

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REVISIONS

L89.93	L97.328	L97.828	M46.23	M86.38	M90.862
L89.94	L97.329	L97.829	M46.24	M86.39	M90.871
L89.95	L97.411	L97.911	M46.25	M86.419	M90.872
L89.96	L97.412	L97.912	M46.26	M86.429	M90.88
L92.8	L97.413	L97.913	M46.27	M86.329	M90.89
L97.111	L97.414	L97.914	M46.28	M86.449	N30.40
L97.112	L97.415	L97.915	M62.9	M86.459	N30.41
L97.113	L97.416	L97.916	M63.80	M86.469	S07.0XXA
L97.114	L97.418	L97.918	M63.811	M86.479	S07.0XXD
L97.119	L97.419	L97.919	M63.812		S07.0XXS
L97.121	L97.421	L97.921	M63.821		S07.1XXA
L97.122	L97.422	L97.922	M63.822		S07.1XXD
L97.123	L97.423	L97.923	M63.831		S07.1XXS
L97.124	L97.424	L97.924	M63.832		S07.8XXA
L97.125	L97.425	L97.925	M63.841		S07.8XXD
L97.126	L97.426	L97.926	M63.842		S07.8XXS
L97.128	L97.428	L97.928	M63.851		S07.9XXA
L97.129	L97.429	L97.929	M63.852		S07.9XXD
L97.211	L97.511	L98.0	M63.861		S07.9XXS
L97.212	L97.512	L98.411	M63.862		S17.0XXA
L97.213	L97.513	L98.412	M63.871		S17.0XXD
L97.214	L97.514	L98.413	M63.872		S17.0XXS
L97.215	L97.515	L98.414	M63.88		S17.8XXA
L97.216	L97.516	L98.415	M63.89		S17.8XXD
L97.218	L97.518	L98.416	M72.6		S17.8XXS
L97.219	L97.519	L98.418	M79.A11		S17.9XXA
L97.221	L97.521	L98.419			S17.9XXD
M86.8X1	S28.0XXA	S45.102A	S45.392A	S47.2XXA	S55.201A
M86.8X2	S28.0XXD	S45.102D	S45.392D	S47.2XXD	S55.201D
M86.8X3	S28.0XXS	S45.102S	S45.392S	S47.2XXS	S55.201S
M86.8X4	S35.511A	S45.111A	S45.801A	S47.9XXA	S55.202A
M86.8X5	S35.511D	S45.111D	S45.801D	S47.9XXD	S55.202D
M86.8X6	S35.511S	S45.111S	S45.801S	S47.9XXS	S55.202S
M86.8X7	S35.512A	S45.112A	S45.802A	S55.001A	S55.211A
M86.8X8	S35.512D	S45.112D	S45.802D	S55.001D	S55.211D
M86.8X9	S35.512S	S45.112S	S45.802S	S55.001S	S55.211S
M90.811	S38.001A	S45.191A	S45.811A	S55.002A	S55.212A
M90.812	S38.001D	S45.191D	S45.811D	S55.002D	S55.212D
M90.821	S38.001S	S45.191S	S45.811S	S55.002S	S55.212S
M90.822	S38.002A	S45.192A	S45.812A	S55.011A	S55.291A
M90.831	S38.002D	S45.192D	S45.812D	S55.011D	S55.291D
M90.832	S38.002S	S45.192S	S45.812S	S55.011S	S55.291S
M90.841	S38.01XA	S45.201A	S45.891A	S55.012A	S55.292A
M90.842	S38.01XD	S45.201D	S45.891D	S55.012D	S55.292D
M90.851	S38.01XS	S45.201S	S45.891S	S55.012S	S55.292S
M90.852	S38.02XA	S45.202A	S45.892A	S55.019A	S55.801A
M90.861	S38.02XD	S45.202D	S45.892D	S55.019D	S55.801D
M90.862	S38.02XS	S45.202S	S45.892S	S55.019S	S55.801S
M90.871	S38.03XA	S45.211A	S45.899A	S55.091A	S55.802A
M90.872	S38.03XD	S45.211D	S45.899D	S55.091D	S55.802D
M90.88	S38.03XS	S45.211S	S45.899S	S55.091S	S55.802S
M90.89	S38.1XXA	S45.212A	S45.901A	S55.092A	S55.811A

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REVISIONS

N30.40	S38.1XXD	S45.212D	S45.901D	S55.092D	S55.811D
N30.41	S38.1XXS	S45.212S	S45.901S	S55.092S	S55.811S
S07.0XXA	S45.001A	S45.291A	S45.902A	S55.101A	S55.812A
S07.0XXD	S45.001D	S45.291D	S45.902D	S55.101D	S55.812D
S07.0XXS	S45.001S	S45.291S	S45.902S	S55.101S	S55.812S
S07.1XXA	S45.002A	S45.292A	S45.911A	S55.102A	S55.891A
S07.1XXD	S45.002D	S45.292D	S45.911D	S55.102D	S55.891D
S07.1XXS	S45.002S	S45.292S	S45.911S	S55.102S	S55.891S
S07.8XXA	S45.011A	S45.301A	S45.912A	S55.109A	S55.892A
S07.8XXD	S45.011D	S45.301D	S45.912D	S55.109D	S55.892D
S07.8XXS	S45.011S	S45.301S	S45.912S	S55.109S	S55.892S
S07.9XXA	S45.012A	S45.302A	S45.919A	S55.111A	S55.899A
S07.9XXD	S45.012D	S45.302D	S45.919D	S55.111D	S55.899D
S07.9XXS	S45.012S	S45.302S	S45.919S	S55.111S	S55.899S
S17.0XXA	S45.091A	S45.311A	S45.991A	S55.112A	S55.901A
S17.0XXD	S45.091D	S45.311D	S45.991D	S55.112D	S55.901D
S17.0XXS	S45.091S	S45.311S	S45.991S	S55.112S	S55.901S
S17.8XXA	S45.092A	S45.312A	S45.992A	S55.191A	S55.902A
S17.8XXD	S45.092D	S45.312D	S45.992D	S55.191D	S55.902D
S17.8XXS	S45.092S	S45.312S	S45.992S	S55.191S	S55.902S
S17.9XXA	S45.101A	S45.391A	S47.1XXA	S55.192A	S55.911A
S17.9XXD	S45.101D	S45.391D	S47.1XXD	S55.192D	S55.911D
S17.9XXS	S45.101S	S45.391S	S47.1XXS	S55.192S	S55.911S
S55.912A	S65.112A	S65.401A	S65.510A	S65.597A	S67.02XA
S55.912D	S65.112D	S65.401D	S65.510D	S65.597D	S67.02XD
S55.912S	S65.112S	S65.401S	S65.510S	S65.597S	S67.02XS
S55.991A	S65.191A	S65.402A	S65.511A	S65.598A	S67.190A
S55.991D	S65.191D	S65.402D	S65.511D	S65.598D	S67.190D
S55.991S	S65.191S	S65.402S	S65.511S	S65.598S	S67.190S
S55.992A	S65.192A	S65.411A	S65.512A	S65.801A	S67.191A
S55.992D	S65.192D	S65.411D	S65.512D	S65.801D	S67.191D
S55.992S	S65.192S	S65.411S	S65.512S	S65.801S	S67.191S
S57.01XA	S65.201A	S65.412A	S65.513A	S65.802A	S67.192A
S57.01XD	S65.201D	S65.412D	S65.513D	S65.802D	S67.192D
S57.01XS	S65.201S	S65.412S	S65.513S	S65.802S	S67.192S
S57.02XA	S65.202A	S65.419A	S65.514A	S65.811A	S67.193A
S57.02XD	S65.202D	S65.419D	S65.514D	S65.811D	S67.193D
S57.02XS	S65.202S	S65.419S	S65.514S	S65.811S	S67.193S
S57.81XA	S65.211A	S65.491A	S65.515A	S65.812A	S67.194A
S57.81XD	S65.211D	S65.491D	S65.515D	S65.812D	S67.194D
S57.81XS	S65.211S	S65.491S	S65.515S	S65.812S	S67.194S
S57.82XA	S65.212A	S65.492A	S65.516A	S65.891A	S67.195A
S57.82XD	S65.212D	S65.492D	S65.516D	S65.891D	S67.195D
S57.82XS	S65.212S	S65.492S	S65.516S	S65.891S	S67.195S
S65.001A	S65.219A	S65.500A	S65.517A	S65.892A	S67.196A
S65.001D	S65.219D	S65.500D	S65.517D	S65.892D	S67.196D
S65.001S	S65.219S	S65.500S	S65.517S	S65.892S	S67.196S
S65.002A	S65.291A	S65.501A	S65.518A	S65.901A	S67.197A
S65.002D	S65.291D	S65.501D	S65.518D	S65.901D	S67.197D
S65.002S	S65.291S	S65.501S	S65.518S	S65.901S	S67.197S
S65.011A	S65.292A	S65.502A	S65.590A	S65.902A	S67.198A
S65.011D	S65.292D	S65.502D	S65.590D	S65.902D	S67.198D

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REVISIONS						
	S65.011S	S65.292S	S65.502S	S65.590S	S65.902S	S67.198S
	S65.012A	S65.301A	S65.503A	S65.591A	S65.911A	S67.21XA
	S65.012D	S65.301D	S65.503D	S65.591D	S65.911D	S67.21XD
	S65.012S	S65.301S	S65.503S	S65.591S	S65.911S	S67.21XS
	S65.091A	S65.302A	S65.504A	S65.592A	S65.912A	S67.22XA
	S65.091D	S65.302D	S65.504D	S65.592D	S65.912D	S67.22XD
	S65.091S	S65.302S	S65.504S	S65.592S	S65.912S	S67.22XS
	S65.092A	S65.311A	S65.505A	S65.593A	S65.991A	S67.31XA
	S65.092D	S65.311D	S65.505D	S65.593D	S65.991D	S67.31XD
	S65.092S	S65.311S	S65.505S	S65.593S	S65.991S	S67.31XS
	S65.101A	S65.312A	S65.506A	S65.594A	S65.992A	S67.32XA
	S65.101D	S65.312D	S65.506D	S65.594D	S65.992D	S67.32XD
	S65.101S	S65.312S	S65.506S	S65.594S	S65.992S	S67.32XS
	S65.102A	S65.391A	S65.507A	S65.595A	S65.999A	S67.41XA
	S65.102D	S65.391D	S65.507D	S65.595D	S65.999D	S67.41XD
	S65.102S	S65.391S	S65.507S	S65.595S	S65.999S	S67.41XS
	S65.111A	S65.392A	S65.508A	S65.596A	S67.01XA	S67.42XA
	S65.111D	S65.392D	S65.508D	S65.596D	S67.01XD	S67.42XD
	S65.111	S65.392S	S65.508S	S65.596S	S67.01XS	S67.42XS
	S67.91XA	S75.892A	S85.091A	S85.211A	S87.82XA	S95.212A
	S67.91XD	S75.892D	S85.091D	S85.211D	S87.82XD	S95.212D
	S67.91XS	S75.892S	S85.091S	S85.211S	S87.82XS	S95.212S
	S67.92XA	S75.901A	S85.092A	S85.291A	S95.001A	S95.291A
	S67.92XD	S75.901D	S85.092D	S85.291D	S95.001D	S95.291D
	S67.92XS	S75.901S	S85.092S	S85.291S	S95.001S	S95.291S
	S75.001A	S75.902A	S85.131A	S85.292A	S95.002A	S95.292A
	S75.001D	S75.902D	S85.131D	S85.292D	S95.002D	S95.292D
	S75.001S	S75.902S	S85.131S	S85.292S	S95.002S	S95.292S
	S75.002A	S75.911A	S85.132A	S85.802A	S95.011A	S95.801A
	S75.002D	S75.911D	S85.132D	S85.802D	S95.011D	S95.801D
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	S75.011D	S75.912D	S85.141D	S85.811D	S95.012D	S95.802D
	S75.011S	S75.912S	S85.141S	S85.811S	S95.012S	S95.802S
	S75.012A	S75.991A	S85.142A	S85.891A	S95.091A	S95.809A
	S75.012D	S75.991D	S85.142D	S85.891D	S95.091D	S95.809D
	S75.012S	S75.991S	S85.142S	S85.891S	S95.091S	S95.809S
	S75.021A	S75.992A	S85.151A	S85.892A	S95.092A	S95.811A
	S75.021D	S75.992D	S85.151D	S85.892D	S95.092D	S95.811D
	S75.021S	S75.992S	S85.151S	S85.892S	S95.092S	S95.811S
	S75.022A	S77.01XA	S85.152A	S85.901A	S95.101A	S95.812A
	S75.022D	S77.01XD	S85.152D	S85.901D	S95.101D	S95.812D
	S75.022S	S77.01XS	S85.152S	S85.901S	S95.101S	S95.812S
	S75.091A	S77.02XA	S85.161A	S85.902A	S95.102A	S95.891A
	S75.091D	S77.02XD	S85.161D	S85.902D	S95.102D	S95.891D
	S75.091S	S77.02XS	S85.161S	S85.902S	S95.102S	S95.891S
	S75.092A	S77.11XA	S85.162A	S85.911A	S95.111A	S95.892A
	S75.092D	S77.11XD	S85.162D	S85.911D	S95.111D	S95.892D
	S75.092S	S77.11XS	S85.162S	S85.911S	S95.111S	S95.892S
	S75.801A	S77.12XA	S85.171A	S85.912A	S95.112A	S95.901A
	S75.801D	S77.12XD	S85.171D	S85.912D	S95.112D	S95.901D
	S75.801S	S77.12XS	S85.171S	S85.912S	S95.112S	S95.901S

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REVISIONS	
	S75.802A, S75.802D, S75.802S, S75.811A, S75.811D, S75.811S, S75.812A, S75.812D, S75.812S, S75.819A, S75.819D, S75.819S, S75.891A, S75.891D, S75.891S, S85.001A, S85.001D, S85.001S, S85.002A, S85.002D, S85.002S, S85.011A, S85.011D, S85.011S, S85.012A, S85.012D, S85.012S, S85.019A, S85.019D, S85.019S, S85.172A, S85.172D, S85.172S, S85.179A, S85.179D, S85.179S, S85.181A, S85.181D, S85.181S, S85.182A, S85.182D, S85.182S, S85.202A, S85.202D, S85.202S, S85.991A, S85.991D, S85.991S, S85.992A, S85.992D, S85.992S, S87.01XA, S87.01XD, S87.01XS, S87.02XA, S87.02XD, S87.02XS, S87.81XA, S87.81XD, S87.81XS, S95.191A, S95.191D, S95.191S, S95.192A, S95.192D, S95.192S, S95.201A, S95.201D, S95.201S, S95.202A, S95.202D, S95.202S, S95.211A, S95.211D, S95.211S, S95.902A, S95.902D, S95.902S, S95.911A, S95.911D, S95.911S, S95.912A, S95.912D, S95.912S, S95.991A, S95.991D, S95.991S, S95.992A, S95.992D, S95.992S
02-02-2022	Updated Description Section
	Updated Policy Section ▪ Section B: Added word "systemic" before Hyperbaric oxygen pressurization
	Updated Policy Guidelines section ▪ Updated Systemic Hypobaric Oxygen section
	Updated Rationale Section
	Updated Coding Section ▪ Added ICD-10 Diagnosis Codes: K52.0, M46.20-M46.28, N30.40-N30.41 ▪ Converted ICD-10 codes to code ranges
	Updated Rationale Section
08-23-2022	Archived

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No review or update is scheduled on this Medical Policy as it is unlikely that further published literature would change the policy position. If there are questions about coverage of this service, please contact Blue Cross and Blue Shield of Kansas customer service, your professional or institutional relations representative, or submit a predetermination request.

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