Medical Policy

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Title: Hyperbaric Oxygen Therapy (HBOT)

Professional
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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

Populations	Interventions	Comparators	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
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:	Comparators of interest are: • Medication • Surgical therapy	Relevant outcomes include: • Overall survival • Symptoms

Populations	Interventions	Comparators	Outcomes
	• Systemic hyperbaric oxygen therapy	• Rehabilitation	• 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
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 effects	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 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

DESCRIPTION

Hyperbaric oxygen therapy (HBOT) involves breathing 100% oxygen at pressures between 1.5 and 3.0 atmospheres (atm). Hyperbaric oxygen therapy is generally applied systemically with the patient inside a hyperbaric chamber. It can also be applied topically; that is, the body part to be treated is isolated, eg, 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 the tissues.

OBJECTIVE

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

BACKGROUND

Hyperbaric Oxygen Therapy

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

Systemic HBOT

In systemic or large chamber hyperbaric oxygen, 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 hyperbaric oxygen therapy 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.

Topical HBOT

Topical hyperbaric oxygen 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. Topical hyperbaric oxygen 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 oxygen 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.

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 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 policy does not address topical oxygen therapy in the absence of pressurization.

REGULATORY STATUS

Since 1979, the Food and Drug Administration (FDA) has cleared multiple topical and systemic hyperbaric oxygen administration devices through the 510(k) pathway. In 2013, 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 FDA, they may delay or forgo proven medical therapies.

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; **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. 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;
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 Item A4 above);
45. Acute arterial peripheral insufficiency;
46. Mental illness (ie, posttraumatic stress disorder, generalized anxiety disorder, or depression);
47. Bell's palsy; and
48. Central retinal artery occlusion.

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

Policy Guidelines

Topical Hyperbaric Oxygen

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.

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.

Below are suggestions from the Undersea and Hyperbaric Medical Society's (UHMS) 2014 Hyperbaric Oxygen Therapy Committee report on utilization of hyperbaric oxygen therapy (HBOT) (13th edition):

1. Crush injury, compartment syndrome, and other acute traumatic ischemias.
2. Decompression sickness.
3. Air or Gas embolism.
4. Carbon monoxide poisoning and carbon monoxide poisoning complicated by cyanide poisoning.
5. Gas gangrene (ie, clostridial myonecrosis and myonecrosis).
6. Severe anemia.
7. Refractory osteomyelitis.
8. Arterial insufficiencies.
9. Intracranial abscess.
10. Necrotizing soft tissue infections.
11. Delayed radiation injury (soft tissue and bony necrosis).
12. Compromised grafts and flaps.
13. Acute thermal burn injury.
14. Idiopathic sudden sensorineural hearing loss.

RATIONALE

Updated literature reviews were conducted most recently through October 29, 2018.

Evidence reviews assess the clinical evidence to determine whether the use of a technology improves the net health outcome. Broadly defined, health outcomes are length of life, quality of life, and ability to function¾including benefits and harms. Every clinical condition has specific outcomes that are important to patients and to 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 a technology, 2 domains are examined: the relevance and the 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.

The original evidence review on systemic hyperbaric oxygen therapy [HBOT] was based entirely on the 1996 guidelines published by the Undersea and Hyperbaric Medical Society; it was subsequently revised in 1999 based on 3 TEC Assessments.[3,4,5,]The TEC Assessments had

conclusions similar to the Undersea and Hyperbaric Medical Society, except, in contrast to the Society guidelines, TEC stated that there was insufficient evidence to conclude that HBOT improved the net health outcome for compromised skin grafts, acute thermal burns, chronic refractory osteomyelitis, necrotizing soft tissue infections, and brown recluse spider bites.

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

The purpose of topical HBOT is to provide a treatment option that is an alternative 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 PICOTS were used to select literature to inform this review.

Patients

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, débridement, 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.

Outcomes

The general outcomes of interest are overall survival, symptoms, change in disease status, and functional outcomes.

Timing

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.

Setting

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.

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.

Studies with duplicative or overlapping populations were excluded.

de Smet (2017) et al conducted a systematic review of various oxygen therapies (oxygen dressing therapy, topical oxygen therapy, HBOT, inspired oxygen therapy).[6,] Three RCTs 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 ($p<0.001$). 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.

A small RCT reported by Leslie (1988) not included in the systematic review evaluated 28 patients with diabetic foot ulcers who were assigned to topical HBOT plus standard wound care or standard wound care alone.[7,] Changes in ulcer size and depth did not differ between the 2 groups following 2 weeks of treatment.

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)[6,]	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 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 or an improvement on existing therapies in patients with chronic diabetic ulcers.

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 PICOTS were used to select literature to inform this review.

Patients
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 heterogeneic 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.

Timing
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 one outcome of interest, longer follow-up was necessary to fully observe outcomes. Therefore, at least one year of follow-up is considered necessary to demonstrate efficacy.

Setting
Patients with chronic diabetic ulcers are managed by surgeons, wound care specialists, podiatrists and primary care providers in a clinical setting.

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.

Studies with duplicative or overlapping populations were excluded.

Systematic Reviews
A Cochrane review of RCTs on HBOT for chronic wounds was published by Kranke et al in 2015 (see Table 2).[8,] Reviewers identified 12 RCTs (total 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 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 (ie, 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 2016 systematic review by Elraiyah et al evaluated adjunctive therapies (HBOT, arterial pumps, and pharmacologic agents) used to treat diabetic foot ulcers (see Table 2).[9,] 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 (odds ratio, 0.30; 95% confidence interval, 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)[8,]	Feb 2015	12	Patients with chronic wounds associated with venous or arterial disease, diabetes, or external pressure	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% 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)[9,]	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)

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

Section Summary: Chronic Diabetic Ulcers
Multiple RCTs and 2 systematic reviews have been published. Seven RCTs were common in the 2 systematic reviews. 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 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?

The following PICOTS were used to select literature to inform this review.

Patients
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 overall survival and symptoms.

Timing
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 one outcome of interest, but longer follow-up was necessary to fully observe outcomes. Therefore, at least one year of follow-up is considered necessary to demonstrate efficacy.

Setting
Patients with carbon monoxide poisoning are managed in the emergency care setting by emergency medicine physicians.

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.

Studies with duplicative or overlapping populations were excluded.

A 2011 Cochrane review by Buckley et al included 6 RCTs evaluating HBOT for carbon monoxide poisoning (see Table 3).[10,] 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.

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

Study (Year)	Literature Search	Studies	Participants	N	Design	Results
Buckleyet al (2011)[10,]	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.

Section Summary: 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.

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 or an improvement on existing therapies in patients with radionecrosis, osteoradionecrosis, and treatment of irradiated jaw.

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 PICOTS were used to select literature to inform this review.

Patients
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 débridement 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.

Timing
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 one outcome of interest, but longer follow-up was necessary to fully observe outcomes. Therefore, at least one year of follow-up is considered necessary to demonstrate efficacy.

Setting

Patients with radionecrosis, osteoradionecrosis, and treatment of irradiated jaw are managed by radiation oncologists, orthopedic surgeons and oral maxillofacial surgeons potentially in both inpatient and outpatient clinical settings.

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.

Studies with duplicative or overlapping populations were excluded.

Bennett (2016) et al published a Cochrane review on HBOT for late radiation tissue injury (see Table 4).[11,] 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 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=0.02). There were insufficient data to conduct meta-analyses on other outcomes.

Borab (2017) et al 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).[12,] 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 (2017) et al published a systematic review on the use of HBOT to treat patients who had received radiotherapy for head and neck cancer.[13,] 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)[11,]	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)
Borab et al (2017)[12,]	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)[13,]	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 anotherfinding no difference in survival

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

Section Summary: 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 or an improvement on existing therapies in patients with chronic refractory osteomyelitis.

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 PICOTS were used to select literature to inform this review.

Patients
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 débridement. Systemic HBOT may be used as an adjunct to these comparators.

Outcomes
The general outcomes of interest are symptoms and change in disease status.

Timing
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 five years is considered necessary to demonstrate efficacy.

Setting
Patients with chronic refractory osteomyelitis are managed by orthopedic surgeons, wound specialists, and primary care providers.

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.

Studies with duplicative or overlapping populations were excluded.

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.[14,] Follow-up data were available on 34 patients who had received a mean of 35 adjunctive HBOT sessions (range, 6-99 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.

Davis et al (1986) reviewed outcomes for 38 patients with chronic refractory osteomyelitis treated at another U.S. institution.[15,] Patients received HBOT until the bone was fully recovered with healthy vascular tissue; this resulted in a mean of 48 daily treatments (range, 8-

103 treatments). After a mean posttreatment follow-up of 34 months, 34 (89%) of 38 patients remained clinically free of infection (ie, drainage-free and no tenderness, pain, or cellulitis). Success rates from several smaller case series (N range, 13-15 patients), all conducted in Taiwan (1998-2000), ranged from 79% to 92%.[16,17,18,] A high percentage of refractory patients in these series had successful outcomes.

Section Summary: 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 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 PICOTS were used to select literature to inform this review.

Patients
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 overall survival, symptoms, and change in disease status.

Timing
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 therapy based on the site and severity of the acute thermal burn, at least one year of follow-up is considered necessary to demonstrate efficacy.

Setting
Patients with acute thermal burns are managed by burn specialists and surgeons in an inpatient clinical setting.

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.

Studies with duplicative or overlapping populations were excluded.

In 2004, a Cochrane review assessed HBOT for thermal burns (see Table 5).[19,] 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 were identified when an updated literature search was conducted in 2009 (the 2004 publication date continues to be used).

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)[19,]	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<0.001) 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: 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.

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 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 PICOTS were used to select literature to inform this review.

Patients
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, débridement, 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 overall survival, symptoms, and change in disease status.

Timing
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 one year of follow-up is considered necessary to demonstrate efficacy.

Setting
Patients with acute surgical and traumatic wounds are actively managed by emergency care providers and surgeons in an inpatient clinical setting.

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.

Studies with duplicative or overlapping populations were excluded.

In 2013, a Cochrane review of RCTs on HBOT for acute surgical and traumatic wounds was published by Eskes et al (see Table 6).[20,] HBOT was administered at pressures above 1 atmosphere (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 mean time to wound healing.

A 2014 systematic review of studies on HBOT for acute wounds, published by Dauwe et al, included RCTs and controlled nonrandomized studies (see Table 6).[21,] Reviewers included 8 studies, with sample sizes ranging from 5 to 125 patients. Four studies were randomized, three were prospective observational studies, and one was a retrospective observational study. As in the Eskes systematic review, data were not pooled. Reviewers noted that 7 of the 8 studies reported statistically significant findings for their primary end points, but the end points differed among studies (eg, graft survival, hospital length of stay, wound size). Moreover, the studies were heterogeneous regarding treatment regimens, patient indications (eg, 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)[20,]	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)[21,]	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.

Section Summary: Acute Surgical and Traumatic Wounds
Two systematic reviews identified 4 RCTs; one of the reviews also included nonrandomized studies. Heterogeneity among studies (eg, 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 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 PICOTS were used to select literature to inform this review.

Patients
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.

Timing
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 one year of follow-up is considered necessary to demonstrate efficacy and superiority to comparators.

Setting
Patients with bisphosphonate-related osteonecrosis of the jaw are managed by surgeons, dentists, and oral maxillofacial surgeons in both inpatient and outpatient clinical settings.

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.

Studies with duplicative or overlapping populations were excluded.

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).[22,] The investigators did a per-protocol analysis (actual treatment received) because of the relatively large amount of crossover. 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 (eg, 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)[22,]	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; RCT: randomized controlled trial.
[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)			
Study (Year)	**3 Months**	**Between-Group P Value**	**18 Months**	**Between-Group P Value**	**3 Months**	**Between-Group P Value**	**18 Months**	**Between-Group P Value**
Freiberger et al (2012)[22,]	46		46		46		46	
HBOT	68.0 (25)	0.03	58.3 (12)	0.31	36.0 (25)	0.04	33.3 (12)	1.0
Control	35.0 (20)		33.3 (6)		10.0 (20)		33.3 (6)	

HBOT: hyperbaric oxygen.

Section Summary: 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 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 PICOTS were used to select literature to inform this review.

Patients
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.

Outcomes
The general outcomes of interest are overall survival, symptoms, and change in disease status.

Timing
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 one year of follow-up is considered necessary to demonstrate efficacy.

Setting
Patients with necrotizing soft tissue infections are managed by surgeons, wound care specialists, and infectious disease specialists in an inpatient clinical setting.

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.

Studies with duplicative or overlapping populations were excluded.

A Cochrane review by Levett et al (2015) evaluated the literature on HBOT as adjunctive therapy for necrotizing fasciitis.[23,] No RCTs were identified. Previously, a systematic review by Jallali et al (2005) identified only a few retrospective studies with small sample sizes.[24,] Findings from these studies were inconsistent. A retrospective cohort study (2009) compared outcomes in 48 patients at 1 center who received adjunctive HBOT for necrotizing soft tissue infections with those in 30 patients at a different center who did not receive HBOT.[25,] There were no significant differences in the mortality rates between the HBOT group (8% [4/48]) and the non-HBOT group (13% [4/30]; p=0.48). The median number of days in the intensive care unit and the median number of days in the hospital also did not differ significantly between groups. There was a higher median number of débridement procedures per person in the HBOT group (3.0) than in the non-HBOT group (2.0; p=0.03).

Section Summary: Necrotizing Soft Tissue Infections
No RCTs have evaluated HBOT for necrotizing soft tissue infection. A retrospective cohort study did not find a difference in outcomes after HBOT or standard care.

Systemic Hyperbaric Oxygen Therapy for Acute Coronary Syndrome
Clinical Context and Therapy Purpose
The purpose of systemic HBOT is to provide a treatment option that is an alternative 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 PICOTS were used to select literature to inform this review.

Patients
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 overall survival, symptoms, change in disease status, and functional outcomes.

Timing
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 one year of follow-up is considered necessary to demonstrate efficacy.

Setting
Patients with acute coronary syndrome are managed by emergency physicians, cardiologists, and intensivists in an inpatient clinical setting.

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.

Studies with duplicative or overlapping populations were excluded.

A 2015 Cochrane review by Bennett et al identified 6 trials (total N=665 patients) evaluating HBOT for acute coronary syndrome (see Table 9).[26,] Included studies were published between 1973 and 2007. All studies included patients with acute myocardial infarction; a study also included individuals with unstable angina. Additionally, all trials used HBOT, administered between 2 and 3 ATA, for 30 to 120 minute sessions, as an adjunct to standard care. Control

interventions varied; only a trial described using a sham therapy to blind participants to treatment group allocation. In a pooled analysis of data from 5 trials, there was a significantly lower rate of death 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)[26,]	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: Acute Coronary Syndrome

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

Systemic Hyperbaric Oxygen Therapy for Acute Ischemic Stroke

Clinical Context and Therapy Purpose

The purpose of systemic HBOT is to provide a treatment option that is an alternative 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 PICOTS were used to select literature to inform this review.

Patients

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 overall survival, symptoms, change in disease status, and functional outcomes.

Timing
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 one outcome of interest, but longer follow-up was necessary to fully observe outcomes. Therefore, six months to one year or more of follow-up is considered necessary to demonstrate efficacy.

Setting
Patients with acute ischemic stroke are managed by emergency physicians, cardiologists, and intensivists in an inpatient clinical setting.

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.

Studies with duplicative or overlapping populations were excluded.

In a 2014 Cochrane systematic review of RCTs, Bennett et al evaluated HBOT for acute ischemic stroke (see Table 10).[27,] Reviewers identified 11 RCTs (total N=705 participants) that compared HBOT with sham HBOT or no treatment. Reviewers could pool study findings for only 1 outcome (mortality at 3-6 months), and no difference was detected between the treatment groups for that outcome. There was heterogeneity in the participants enrolled and in the clinical and functional outcomes measured across the studies.

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

Study (Year)	Literature Search	Studies	Participants	N	Design	Results
Bennett et al (2014)[27,]	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: 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 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 PICOTS were used to select literature to inform this review.

Patients
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.

Timing
The existing literature evaluating systemic HBOT as a treatment for motor dysfunction associated with stroke had a treatment-group follow-up time of two months. In the RCT described below, longer follow-up was recommended to fully observe outcomes. Therefore, three months to one year or more of follow-up is considered necessary to demonstrate efficacy.

Setting
Patients with motor dysfunction associated with stroke are actively managed by physical therapists, physiatrists, and primary care providers in an outpatient clinical setting.

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.

Studies with duplicative or overlapping populations were excluded.

Efrati (2013) et al published an RCT evaluating HBOT for treatment of neurologic deficiencies associated with a history of stroke (see Tables 11 and 12).[28,] 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 poststroke patients with motor deficits. However, the results are not definitive, as the RCT was small and enrolled a heterogeneous group of poststroke 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)[28,]	Israel	1	2008-2010	Patients ≥18 y with ischemic or hemorrhagic stroke 6 to 36 mo prior to inclusion with ≥1 motor dysfunction	· Hyperbaric oxygen · 100% oxygen at 2 ATA · 40 times over 2 mo	Same as active, delayed after 2 mo

ATA: atmospheres absolute; HBOT: hyperbaric oxygen therapy.

Table 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)[28,]	50	50		50	50	
Mean HBOT (SD)	8.5 (3.6)	5.5 (3.6)	0.004	16.1 (6.5)	12.8 (7.3)	0.02
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: 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 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 PICOTS were used to select literature to inform this review.

Patients

The relevant population of interest is individuals with Bell palsy.

Interventions

The therapy being considered is systemic HBOT.

Comparators

Comparators of interest include self-care (eg, 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.

Timing

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 one year or more is considered necessary to demonstrate efficacy.

Setting

Patients with Bell palsy are actively managed by neurologists and primary care providers in an outpatient clinical setting.

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.

Studies with duplicative or overlapping populations were excluded.

Holland (2012) et al published a Cochrane review evaluating HBOT in adults with moderate-to-severe Bell palsy.[29,] 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: 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 or an improvement on existing therapies in patients with traumatic brain injury.

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

The following PICOTS were used to select literature to inform this review.

Patients
The relevant population of interest is individuals with traumatic brain injury.

Interventions
The therapy being considered is systemic HBOT.

Comparators
Comparators of interest include medication, surgical therapy, and rehabilitation protocols. Medications prescribed for traumatic brain injury 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 overall survival, symptoms, change in disease status, and functional outcomes.

Timing
The existing literature evaluating systemic HBOT as a treatment for traumatic brain injury has varying lengths of follow-up. In the systematic reviews described below, all studies reported at least one outcome of interest, but longer follow-up was necessary to fully observe outcomes. Therefore, at least one year of follow-up is considered necessary to demonstrate efficacy.

Setting
Patients with traumatic brain injury are actively managed by neurosurgeons in an inpatient clinical setting. After immediate emergency care, neurologists, physiatrists, physical therapists and primary care providers manage patients in an outpatient clinical setting.

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.

Studies with duplicative or overlapping populations were excluded.

A 2016 meta-analysis by Wang et al assessed HBOT for treatment of traumatic brain injury (TBI see Table 14).[30,] Eight studies (total 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 2016 systematic review, by Crawford et al, did not conduct pooled analyses (see Table 13).[31,] Reviewers identified 12 RCTs evaluating HBOT for patients with TBI. Using 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 (ie, postconcussive symptom severity, psychological outcomes). Seven trials evaluated HBOT for the acute treatment of patients with moderate-to-severe TBI. Four were rated as acceptable quality and three 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 two of them, outcomes were better with HBOT than with standard care; in the third study, outcomes did not differ significantly.

In 2012, a Cochrane review by Bennett et al evaluated HBOT as adjunctive therapy for acute TBI (see Table 13).[32,] 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; eg, 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 one 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.

Also, several trials on mild TBI in military populations have been published; they did not find significant benefits of HBOT compared with sham treatment.[33,34,35,] In 2015, Miller et al evaluated HBOT in 72 military service members with symptoms continuing at least 4 months after mild TBI.[35,] 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=0.24). 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).[36,] 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 post-concussive syndrome.

Table 13. Systematic Reviews of Trials Assessing HBOT for Traumatic Brain Injury

Study (Year)	Literature Search	Studies	Participants	N	Design	Results
Wang et al (2016)[30,]	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)[31,]	Aug 2014	12	Military and civilian patients with traumatic brain injury		RCTs	· Pooled analyses not performed · Among 3 trials with GCS outcomes, 2 reported improvements with HBOT and 1 found no difference · 4 trials assessed as acceptable quality did not find significant differences in symptom severity or psychological outcomes
Bennett et al (2012)[32,]	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; GCS: Glasgow Coma Scale; HBOT: hyperbaric oxygen therapy; OR: odds ratio; PTSD: post-traumatic stress disorder; RCT: randomized controlled trial; RR: relative risk.

Section Summary: Traumatic Brain Injury
A number of RCTs and systematic reviews have been published. RCTs were heterogeneous regarding intervention protocols, patient populations, and outcomes reported. 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 or an improvement on existing therapies in patients with inflammatory bowel disease.

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

The following PICOTS were used to select literature to inform this review.

Patients
The relevant population of interest is individuals with inflammatory bowel disease.

Interventions
The therapy being considered is systemic HBOT.

Comparators
Comparators of interest include medication and surgical therapy. Medications prescribed for inflammatory bowel disease 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.

Timing
The existing literature evaluating systemic HBOT as a treatment for inflammatory bowel disease 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 one outcome of interest, but longer follow-up was necessary to fully observe outcomes. Therefore, at least one year of follow-up is considered necessary to demonstrate efficacy.

Setting
Patients with inflammatory bowel disease are managed by gastroenterologists and primary care providers in a clinical setting.

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.

Studies with duplicative or overlapping populations were excluded.

A 2014 systematic review by Dulai et al examined the evidence on HBOT for inflammatory bowel disease (Crohn disease, ulcerative colitis; see Table 14).[37,] 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.[38,] 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.[39] 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 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 14. Systematic Reviews of Studies Assessing HBOT for Inflammatory Bowel Disease

Study (Year)	Literature Search	Studies	Participants	N	Design	Results
Dulai et al (2014)[37,]	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: 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 (eg, 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 or an improvement on existing therapies for individuals with idiopathic sudden sensorineural hearing loss.

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

The following PICOTS were used to select literature to inform this review.

Patients
The relevant population of interest is individuals with idiopathic sudden sensorineural hearing loss.

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 idiopathic sudden sensorineural hearing loss 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.

Timing
Follow-up for the evaluation of systemic HBOT as a treatment for idiopathic sudden sensorineural hearing loss would be weeks to months after early intervention. Longer follow-up of at least one year is necessary to demonstrate efficacy.

Setting
Patients with idiopathic sudden sensorineural hearing loss are managed by otolaryngologists and primary care providers in an outpatient clinical setting.

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.

Studies with duplicative or overlapping populations were excluded.

Systematic Reviews
A 2012 Cochrane review by Bennett et al on HBOT for idiopathic sudden sensorineural hearing loss (ISSNHL) and/or tinnitus identified 7 RCTs (N=392; see Table 15).[40,] 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/ortinnitus (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 (eg, the total number of treatment sessions ranged from 10-25).

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 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 15). 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 SSNHL treatment.[41,]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, 1.05-2.44) and any hearing recovery (OR, 1.43; 95% CI, 1.20-1.67). 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.

Table 15. Systematic Reviews and Meta-Analyses of Trials Assessing HBOT for Idiopathic Sudden Sensorineural Hearing Loss

Study (Year)	Literature Search	Studies	Participants	N	Design	Results
Bennett (2012)[40,]	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

Study (Year)	Literature Search	Studies	Participants	N	Design	Results
						HBOT vs control (mean difference, 15.6 dB; 95% CI, 1.5 to 29.8 dB)
Rhee (2018)[41,]	Feb 2018	19	Patients with with SSNHL	2401	3 RCTs, 16 nonRCTs	· 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)

CI: confidence interval; HBOT: hyperbaric oxygen therapy; RCT: randomized controlled trial; RR: relative risk; SSNHL: sudden senosorineural hearing loss.

Randomized Controlled Trials

Cvorovic et al (2013) conducted an RCT that included 50 patients with ISSNHL who had failed primary therapy with intravenous steroids.[42,] This study was included in the 2018 systematic review. Patients were randomized to HBOT (20 sessions, 5 daily sessions per week) or intratympanic steroid injection (4 injections in 13 days). The HBOT sessions consisted of 10 minutes of compression on air, 60 minutes of 100% oxygen at 2 atm, and 10 minutes of decompression on air. Outcomes were change in the mean hearing thresholds at each of 5 frequencies (0.25, 0.5, 1, 2, and 4 kHz). After treatment, there were no statistically significant differences in mean hearing thresholds at 4 of the 5 frequencies. The exception was 2 kHz, and at that frequency, the improvement was significantly greater in the HBOT group.

Nonrandomized Observational Studies: Sun et al (2018) compared the efficacy of intratympanic dexamethasone therapy and hyperbaric oxygen therapy for salvage treatment of 104 patients with refractory high-frequency SSNHL.[43,] Patient charts were retrospectively allocated into three groups: ITD alone group (n=31), HBO alone group (n=32), and a control group in which patients received no salvage therapy (n=41). No significant difference was found between the groups for total effective rate of hearing recovery (p=0.213); also, no significant differences were found between ITD and HBO (p=0.368) or between ITD and the control group (p=0.197). At 2 and 4 KHz, no significant differences were found between any groups; however, at 8 KHz, there was a significant difference for ITD vs HBO (p=0.049) and for ITD vs control (p=0.025), but not for HBO vs control (p=0.873).

Almosnino et al (2018) conducted a matched control retrospective case series evaluating hyperbaric oxygen (HBO2) as salvage therapy for sudden sensorineural hearing loss (SSNHL).[44,] In total, 36 (18 received IT steroids and HBO2 and 18 received IT steroids alone) SSNHL patients >18 years were included in the study. The post-treatment pure tone average (PTA) did not vary significantly between the HBO2 (60.3 dB) and non-HBO2 (53.2 dB) groups; the mean post-treatment word recognition scores (WRSs) also did not differ significantly (HBO2 42%, WRS 51%). In the HBO2 group, 33% of patients improved from nonserviceable hearing (WRS of <50%) to serviceable hearing (WRS of ≥50%) after treatment, while 42% of non-HBO2 patients went from nonserviceable hearing to serviceable hearing (p>0.05). The study was limited by its retrospective nature, small sample size, lack of randomization, and differences in dosing and duration of treatment between patients.

In a retrospective chart review of 178 idiopathic SSNHL patients, Xie et al (2018) evaluated potential prognostic factors of idiopathic SSNHL treated with HBOT.[45,] Overall recovery rate was

37.1%; complete recovery was 19.7% and partial recovery was 17.4%. Higher initial hearing threshold and later onset of HBOT were associated with a poor prognosis in idiopathic SSNHL patients treated with HBOT. The study was limited by its retrospective chart review design.

Section Summary: Idiopathic Sudden Sensorineural Hearing Loss
A Cochrane review of RCTs had mixed findings from studies that included individuals with tinnitus. Some outcomes (ie, 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. One RCT included in this review included patients with ISSNHL and found no differences in HBOT treatment compared with steroid injections in mean hearing thresholds at 0.25, 0.5, 1, and 4 kHz; however, a significant difference was detected at the 2-kHz level. Nonrandomized studies of HBOT used as adjunctive therapy did not support incremental value.

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 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 PICOTS were used to select literature to inform this review.

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

Interventions
The therapy being considered is systemic HBOT.

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

Outcomes
The general outcomes of interest are symptoms and functional outcomes.

Timing
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 one outcome of interest, but longer follow-up was necessary to fully observe outcomes. Therefore, at least one month of follow-up is considered necessary to demonstrate efficacy.

Setting
Patients with delayed-onset muscle soreness are managed by physical therapists, physiatrists, and primary care providers in an outpatient clinical setting.

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.

Studies with duplicative or overlapping populations were excluded.

In a 2005 Cochrane review updated in 2010, Bennett et al identified 9 small RCTs on HBOT for delayed-onset muscle soreness and closed soft tissue injury (see Table 16).[46,] 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 (eg, swelling, muscle strength).

Table 16. Systematic Reviews of Trials Assessing HBOT for DOMS

Study (Year)	Literature Search	Studies	Participants	N	Design	Results
Bennett et al (2010)[46,]	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.

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

Systemic Hyperbaric Oxygen Therapy for Autism Spectrum Disorder
Clinical Context and Therapy Purpose
The purpose of systemic HBOT is to provide a treatment option that is an alternative 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?

The following PICOTS were used to select literature to inform this review.

Patients
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.

Timing
The existing literature evaluating systemic HBOT as a treatment for autism spectrum disorder had a follow-up of ten weeks. However, longer term follow-up may show difference between the intervention and comparators. Therefore, at least six months of follow-up is considered necessary to demonstrate efficacy.

Setting
Patients with autism spectrum disorder are actively managed by behavioral therapists and psychologists in an outpatient clinical setting.

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.

Studies with duplicative or overlapping populations were excluded.

A 2016 Cochrane review by Xiong et al identified 1 RCT evaluating systemic HBOT for people with autism spectrum disorder that met eligibility criteria (see Table 17).[47,] 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 one-hour sessions with HBOT or sham air (n=30 per group).[48,]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. Posttreatment 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 17. Systematic Reviews of Trials Assessing HBOT for Autism Spectrum Disorder

Study (Year)	Literature Search	Studies	Participants	N	Design	Results Mean Difference
Xiong et al (2016)[47,]	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.

Section Summary: 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 vs sham.

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 or an improvement on existing therapies in patients with cerebral palsy.

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

The following PICOTS were used to select literature to inform this review.

Patients
The relevant population of interest is individuals with cerebral palsy.

Interventions
The therapy being considered is systemic HBOT.

Comparators
Comparators of interest include physical therapy and medication. Medications directed at isolated (eg, onabotulinumtoxinA) and generalized spasticity (eg, diazepam, dantrolene, and baclofen) may be prescribed for cerebral palsy. Systemic HBOT may be used as an adjunct to these comparators.

Outcomes
The general outcomes of interest are symptoms and functional outcomes.

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

Setting
Patients with cerebral palsy are managed by physical therapists, physiatrists and primary care providers in an outpatient clinical setting.

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.

Studies with duplicative or overlapping populations were excluded.

Two published RCTs were identified on use of HBOT for cerebral palsy (see Tables 18 and 19). In 2012, Lacey et al published a double-blind RCT that included 49 children ages 3 to 8 years with spastic cerebral palsy.[49,] 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 cerebral palsy to 40 treatments over a 2-month period of HBOT or slightly pressurized room air.[50,] Investigators found similar improvements in outcomes such as gross motor function and activities of daily living in both treatment groups.

In 2017, an observational study by Long et al evaluated the effects of HBOT as a treatment for sleep disorders in children with cerebral palsy (N=71).[51,] 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 18. Characteristics of Trials Assessing HBOT for Cerebral Palsy

					Treatment	
Study (Year)	Countries	Sites	Dates	Participants	Active	Comparator
Lacey et al (2012)[49,]	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)[50,]	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 19. 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)[49],	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)[50],			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; HBOT: hyperbaric oxygen; PEDI: Pediatric Evaluation of Disability Inventory.
[a] Positive score represents improvement in function from baseline.

Section Summary: Cerebral Palsy
Two RCTs and an observational study were identified. One RCT was stopped early due to futility and the other did not find significantly better outcomes with HBOT than with a sham intervention. The observational study, which focused on improving sleep in patients with cerebral palsy, 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 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 chronic diabetic ulcers improve net health outcomes?

The following PICOTS were used to select literature to inform this review.

Patients
The relevant population of interest is individuals with vascular dementia.

Interventions
The therapy being considered is systemic HBOT.

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

Outcomes
The general outcomes of interest are symptoms and functional outcomes.

Timing
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 one year of follow-up is considered necessary to demonstrate efficacy.

Setting
Patients with vascular dementia are managed by neurologists and primary care providers in an outpatient clinical setting.

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.

Studies with duplicative or overlapping populations were excluded.

A 2012 Cochrane review identified a small RCT evaluating HBOT for vascular dementia (see Table 20).[52,] 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 20. Systematic Reviews of Trials Assessing HBOT for Vascular Dementia

Study (Year)	Literature Search	Studies	Participants	N	Design	Results
Xiao et al (2012)[52,]	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; WMD: weighted mean difference.

Section Summary: 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 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 PICOTS were used to select literature to inform this review.

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

Interventions
The therapy being considered is systemic HBOT.

Comparators
Comparators of interest include medication. Medications to treat cardiovascular and pulmonary adverse events (eg, pentoxifylline), gastrointestinal toxicity (eg, amifostine, antidiarrheals), radiation-induced emesis (5-HT3), radiation cystitis (eg, phenazopyridine, oxybutynin, and flavoxate), and sexual dysfunction (eg, 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.

Timing
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 one outcome of interest, but longer follow-up was necessary to fully observe outcomes. Therefore, at least one year of follow-up is considered necessary to demonstrate efficacy.

Setting
Patients with radiotherapy adverse events are actively managed by oncologists and primary care providers in an outpatient clinical setting.

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.

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.

Spiegelberg (2010) et al 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 21).[53,] 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 four 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 (2017) et al conducted a systematic review assessing the effect of HBOT on patients with head and neck cancer who had received radiotherapy (see Table 21).[13,] Pooled analyses were not performed; however, summary results were discussed for the following outcomes: salivary gland 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).

Table 21. Systematic Reviews of Studies Assessing HBOT for Radiotherapy Adverse Events

Study (Year)	Literature Search	Studies	Participants	N	Design	Results
Spiegelberg et al (2010)[53,]	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 4concluded that HBOT was not
Ravi et al (2017)[13,]	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 (eg, SF-36, EORTC, HADS), reporting that many subsets of the questionnaires (eg, swallowing, pain, salivary quantity) showed significant improvements with HBOT

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

Several RCTs were identified in literature searches. A 2009 trial by Teguh et al, included in the reviews, evaluated 17 patients with oropharyngeal or nasopharyngeal cancer who were treated with radiotherapy; the trial was conducted in The Netherlands.[54,]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, ($p<0.001$). 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.[55,] 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=*NS*). Other outcomes (eg, QOL scores on the 36-Item Short-Form Health Survey [SF-36]) also did not differ significantly between groups.

Section Summary: Radiotherapy Adverse Events
Two systematic reviews have noted a lack of RCTs 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.

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 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 PICOTS were used to select literature to inform this review.

Patients
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.

Timing
The existing literature evaluating systemic HBOT as a treatment for idiopathic femoral neck necrosis analyzed HBOT therapy at six weeks of follow-up. Longer follow-up is necessary to fully observe outcomes. Therefore, at least one year of follow-up is considered necessary to demonstrate efficacy.

Setting
Patients with idiopathic femoral neck necrosis are actively managed by orthopedic surgeons in an inpatient clinical setting.

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.

Studies with duplicative or overlapping populations were excluded.

A double-blind RCT evaluating HBOT for treatment of femoral head necrosis was published in 2010 by Camporesi et al (see Tables 22 and 23).[56,] 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 ($p<0.001$) 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 22. 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)[56,]	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 23. 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
Camporesi et al (2010)[56,]				
HBOT	7.5 (4.0-20.0)	*NS*	20.0 (15.0-20.0)	<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: Idiopathic Femoral Neck Necrosis
One small RCT (N=20) was identified. Six-week outcomes and results were mixed, with improvements reported in extension, abduction, and adduction, but not flexion. Significant

improvements in pain were reported after 30 sessions, though no differences were detected after 10 or 20 sessions. This RCT does not provide sufficient data to permit conclusions about the efficacy of HBOT for femoral head necrosis.

Systemic Hyperbaric Oxygen Therapy for Migraine Headache

Clinical Context and Therapy Purpose

The purpose of systemic HBOT is to provide a treatment option that is an alternative 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 PICOTS were used to select literature to inform this review.

Patients

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.

Timing

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 one outcome of interest, but longer follow-up was necessary to fully observe outcomes. Therefore, at least one month of follow-up is considered necessary to demonstrate efficacy.

Setting

Patients with migraine are managed by neurologists and primary care providers in an outpatient clinical setting.

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.

Studies with duplicative or overlapping populations were excluded.

A 2015 Cochrane review by Bennett et al identified 11 RCTs (total 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 24).[57,]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 posttreatment period, and the methodologic quality of selected trials was moderate to low (eg, randomization was not well-described in any trial).

Table 24. Systematic Reviews of Trials Assessing HBOT for Migraine or Cluster Headaches

Study (Year)	Literature Search	Studies	Participants	N	Design	Results
Bennett et al (2015)[57,]	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: 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 posttreatment 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 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?

The following PICOTS were used to select literature to inform this review.

Patients
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.

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

Setting
Patients with herpes zoster are managed by infectious disease specialists and primary care providers in an outpatient clinical setting.

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.

Studies with duplicative or overlapping populations were excluded.

Peng (2012) et al in China published an RCT evaluating HBOT for herpes zoster (see Tables 25 and 26).[58,] 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 25. Characteristics of Trials Assessing HBOT for Herpes Zoster

Study (Year)	Countries	Sites	Dates	Participants	Treatment Active (n=36)	Comparator (n=32)
Peng et al (2012)[58,]	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	Medication alone, including: antiviral, nerve nutritive, pain relief, and antidepressives

Study (Year)	Countries	Sites	Dates	Participants	Treatment Active (n=36)	Comparator (n=32)
					that control group received	

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

Table 26. 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)[58,]	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.
[a] Calculation: (number cases with healing + number cases with improvement)/(total number cases × 100).
[b] Between-group difference p<0.05.

Section Summary: 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 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 PICOTS were used to select literature to inform this review.

Patients
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.

Timing
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 one outcome of interest, but longer follow-up was necessary to fully observe outcomes. Therefore, at least one year of follow-up is considered necessary to demonstrate efficacy.

Setting
Patients with fibromyalgia are managed by neurologists, physiatrists, physical therapists, and primary care providers in an outpatient clinical setting.

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.

Studies with duplicative or overlapping populations were excluded.

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

Efrati (2015) et al published an RCT that included 60 symptomatic women who had fibromyalgia for at least 2 years (see Tables 27 and 28).[59,] 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.

Yildiz (2004) et al assessed 50 patients with fibromyalgia (see Tables 27 and 28).[60,] 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 (ie, 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 27. Characteristics of Trials Assessing HBOT for Fibromyalgia

					Treatment	
Study (Year)	**Countries**	**Sites**	**Dates**	**Participants**	**Active**	**Comparator**
Efrati et al (2015)[59,]	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)[60,]	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 28. 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)[59,]	50			50		
Mean HBOT (SD)	17.3 (1.4)	8.9 (6.0)	<0.001	0.5 (1.2)	1.7 (0.8)	<0.001
Mean control (SD)	17.7 (0.7)	17.2 (1.1)		0.7 (0.5)	0.6 (0.5)	
Yildiz et al (2004)[60,]	50			50		
Mean HBOT (SD)	15.0 (1.5)	6.0 (1.2)	<0.001	0.7 (0.1)	1.3 (0.1)	<0.001
Mean air (SD)	15.3 (1.2)	12.5 (1.1)		0.7 (0.1)	0.8 (0.1)	

HBOT: hyperbaric oxygen therapy.

Section Summary: Fibromyalgia

Two RCTs assessing HBOT for fibromyalgia were identified. Both had relatively small sample sizes and methodologic limitations (eg, 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 or an improvement on existing therapies in patients with multiple sclerosis.

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

The following PICOTS were used to select literature to inform this review.

Patients
The relevant population of interest is individuals with multiple sclerosis.

Interventions
The therapy being considered is systemic HBOT.

Comparators
Comparators of interest include medication. Medications prescribed to treat multiple sclerosis 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.

Timing
The existing literature evaluating systemic HBOT as a treatment for multiple sclerosis has varying lengths of follow-up, ranging from four weeks to six months. In the systematic review described below, nearly all studies reported at least one outcome of interest, but longer follow-up was necessary to fully observe outcomes. Therefore, at least one year of follow-up is considered necessary to demonstrate efficacy.

Setting
Patients with multiple sclerosis are managed by neurologists and primary care providers in an outpatient clinical setting.

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.

Studies with duplicative or overlapping populations were excluded.

Bennett (2010) et al published a systematic review on the use of HBOT for treatment of multiple sclerosis (see Table 29).[61] Nine RCTs (total 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 vs control or after 6 months of follow-up.

Table 29. Systematic Reviews of Trials Assessing HBOT for Multiple Sclerosis

Study (Year)	Literature Search	Studies	Participants	N	Design	Results
Bennett et al (2010)[61,]	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: Multiple Sclerosis
A Cochrane review of RCTs did not find a significant difference in outcomes when patients with multiple sclerosis were treated with HBOT vs a comparison intervention.

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

Clinical Context and Therapy Purpose
The purpose of systemic HBOT is to provide a treatment option that is an alternative 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 PICOTS were used to select literature to inform this review.

Patients
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 overall survival and change in disease status.

Timing
The existing literature evaluating systemic HBOT as a treatment for cancer who are undergoing radiotherapy or chemotherapy has varying lengths of follow-up, six months to five years. In the

systematic review and RCT described below, nearly all studies reported at least one outcome of interest, but longer follow-up was necessary to fully observe outcomes. Therefore, at least one year of follow-up is considered necessary to demonstrate efficacy.

Setting
Patients with cancer who are undergoing radiotherapy or chemotherapy are managed by oncologists in an outpatient clinical setting.

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.

Studies with duplicative or overlapping populations were excluded.

In a 2005 Cochrane review,[62,] which was updated in 2012,[63,] and in 2018, Bennett et al identified 19 randomized and quasi-randomized trials (total N=2286 patients) comparing outcomes following radiotherapy with and without HBOT in patients with solid tumors (see Table 30). The latest trial identified in the Cochrane search was published in 1999. Reviewers did not find any ongoing RCTs in this area. Results from the review reported that HBOT given with radiotherapy might be useful in tumor control in head and neck cancer. However, reviewers expressed caution because significant adverse events, such as severe radiation tissue injury (relative risk, 2.3; p<0.001) and seizures (relative risk, 6.8; p=0.03) occurred more frequently in patients treated with HBOT.

Table 30. 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)[63,]	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=0.03) · 5-year mortality: RR=0.8 (p=0.03) · 5-y recurrence: RR=0.8 (p=0.01) 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.[64,]

Section Summary: Tumor Sensitization During Cancer Treatment: Radiotherapy or Chemotherapy
A Cochrane review on the use of HBOT with radiotherapy and an RCT on the use of HBOT with chemotherapy were identified. While the Cochrane review found improvements in tumor control in patients with head and neck cancer, the adverse events accompanying HBOT treatment (eg,

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

Other Indications

For the indications listed below, literature searches did could not identify sufficient evidence to support the use of HBOT. Since 2000, there have been no published controlled trials or large case series (ie, ³25 patients) assessing:

- bone grafts;
- carbon tetrachloride poisoning, acute;
- 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;
- amyotrophic lateral sclerosis; 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 overall survival, 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 single small RCT (N=28) was not included in the review and the uncontrolled studies do not provide sufficient data that topical HBOT is efficacious. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals with wounds, burns or infections who receive topical HBOT, the evidence includes a systematic review, case series, and a randomized controlled trial (RCT). Relevant outcomes are overall survival, 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 single small RCT (N=28) was not included in the review and the uncontrolled studies do not provide sufficient data that topical HBOT is efficacious. The evidence is insufficient to determine the effects of the technology on health outcomes.

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. One of the 2 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 a meaningful 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 overall survival 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 insufficient to determine the effects of the technology on health outcomes.

However, clinical input obtained in 2010 and guidelines from the Undersea and Hyperbaric Medical Society and the 10th European Consensus Conference on Hyperbaric Medicine support HBOT for the treatment of acute carbon monoxide poisoning. Thus, based on clinical input and guideline support, this indication may be considered medically necessary.

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 a meaningful 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 the effects of the technology on health outcomes.

However, clinical input obtained in 2010 and Undersea and Hyperbaric Medical Society guidelines support HBOT for the treatment of chronic refractory osteomyelitis. Thus, based on clinical input and guideline support, this indication may be considered medically necessary.

For individuals with acute thermal burns who receive systemic HBOT, the evidence includes a systematic review of 2 RCTs. Relevant outcomes are overall survival, symptoms, and change in disease status. Only 2 RCTs were identified, and both were judged to have poor methodologic quality. Evidence from well-conducted controlled trials is needed. The evidence is insufficient to determine the effects of the technology on health outcomes.

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 overall survival, symptoms, change in disease status, and functional outcomes. There was considerable heterogeneity across the 4 RCTs identified (eg, 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 the effects of the technology on health outcomes.

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 the effects of the technology on health outcomes.

For individuals with necrotizing soft tissue infections who receive systemic HBOT, the evidence includes systematic reviews and a retrospective cohort study. Relevant outcomes are overall survival, symptoms, and change in disease status. A Cochrane review did not identify any RCTs. Another systematic review identified a retrospective cohort study, which did not find better outcomes after HBOT than after standard care without HBOT in patients with necrotizing soft tissue infections. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals with acute coronary syndrome who receive systemic HBOT, the evidence includes RCTs and a systematic review. Relevant outcomes are overall survival, symptoms, change in disease status, and functional outcomes. A Cochrane review identified 6 RCTs. There were 2 pooled analyses, one 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 the effects of the technology on health outcomes.

For individuals with acute ischemic stroke who receive systemic HBOT, the evidence includes RCTs and a systematic review. Relevant outcomes are overall survival, symptoms, change in disease status, and functional outcomes. Cochrane reviewers could only pool data for a single outcome (mortality at 3-6 months), and for that outcome, there was no significant difference between active and sham HBOT treatments. The evidence is insufficient to determine the effects of the technology on health outcomes.

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 (eg, 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 the effects of the technology on health outcomes.

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 the effects of the technology on health outcomes.

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

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 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 the effects of the technology on health outcomes.

A Cochrane review of RCTs had mixed findings from studies that included individuals with tinnitus. Some outcomes (ie, 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. One RCT included in this review included patients with ISSNHL and found no differences in HBOT treatment compared with steroid injections in mean hearing thresholds at 0.25, 0.5, 1, and 4 kHz; however, a significant difference was detected at the 2-kHz level. Nonrandomized studies of HBOT used as adjunctive therapy did not support incremental value. The evidence is insufficient to determine the effects of the technology on health outcomes.

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 (eg, swelling). The evidence is insufficient to determine the effects of the technology on health outcomes.

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. The evidence is insufficient to determine the effects of the technology on health outcomes.

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 the effects of the technology on health outcomes.

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

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. Two systematic reviews were identified, but pooled analyses were not possible due to heterogeneity in treatment regimens and outcomes measured. One systematic review concluded that more RCTs would be needed. The 2 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. The evidence is insufficient to determine the effects of the technology on health outcomes.

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 (ie, 6-week) outcomes. Larger well-conducted RCTs reporting longer term outcomes are needed. The evidence is insufficient to determine the effects of the technology on health outcomes.

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 the effects of the technology on health outcomes.

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 (ie, 6-week) outcomes. Additional well-conducted RCTs with longer follow-up are needed. The evidence is insufficient to determine the effects of the technology on health outcomes.

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 (eg, 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 the effects of the technology on health outcomes.

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 vs a comparator intervention. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals with cancer and are undergoing chemotherapy who receive systemic HBOT, the evidence includes an RCT and a systematic review. Relevant outcomes are overall survival 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 (eg, 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 the effects of the technology on health outcomes.

CLINICAL INPUT FROM PHYSICIAN MEDICAL 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.

In response to requests, input was received through 6 physician specialty societies and 5 academic medical centers while this policy was under review in 2010. The clinical input varied depending on the condition. There was universal agreement that topical HBOT and systemic HBOT for autism spectrum disorder and headache/migraine are investigational. There was also wide support for changing 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

Diabetic Foot Conditions

Undersea and Hyperbaric Medical Society

In 2015, the Undersea and Hyperbaric Medical Society (UHMS) published guidelines on use of hyperbaric oxygen therapy (HBOT) for treating diabetic foot ulcers.[65] Recommendations included:

- 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.

Infectious Disease Society of America
In 2012, the Infectious Disease Society of America published guidelines on the diagnosis and treatment of diabetic foot infections.[66] The guidelines stated that "for selected diabetic foot wounds that are slow to heal, clinicians might consider using hyperbaric oxygen therapy (strength of evidence: strong; quality of evidence: moderate)."

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.[67] 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).

Other Conditions
Underseas and Hyperbaric Medical Society
UHMS published indications that the society considered appropriate for HBOT; the latest update was published in 2014 (13th edition).[68] These indications are as follows:

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. Arterial Insufficiencies
7. Severe Anemia
8. Intracranial Abscess
9. Necrotizing Soft Tissue Infections
10. Osteomyelitis (Refractory)
11. Delayed Radiation Injury (Soft Tissue and Bony Necrosis)
12. Compromised Grafts and Flaps
13. Acute Thermal Burn Injury
14. Idiopathic Sudden Sensorineural Hearing Loss.

UHMS has also published position statements that concluded there was insufficient evidence to recommend topical HBOT for chronic wounds (2005),[69] multiple sclerosis,[70] and autism spectrum disorder (2009).[71]

American Academy of Otolaryngology – Head and Neck Surgery
In 2012, the American Academy of Otolaryngology-Head and Neck Surgery published a clinical guideline on treatment of sudden hearing loss.[72] The guideline includes a statement that HBOT may be considered a treatment option for patients who present within 3 months of a diagnosis of idiopathic sudden sensorineural hearing loss (ISSNHL). The document states, "Although HBOT is not widely available in the United States and is not recognized by many U.S. clinicians as an intervention for ISSNHL, the panel felt that the level of evidence for hearing improvement, albeit modest and imprecise, was sufficient to promote greater awareness of HBOT as an intervention for ISSNHL." (Grade B recommendation, based on systematic review of RCTs with methodological limitations.)

Tenth European Consensus Conference on Hyperbaric Medicine

The 10th European Consensus Conference on Hyperbaric Medicine (ECHM) convened in April 2016 to update HBOT indication recommendations.[73] Evidence was assessed using a modified GRADE system with the DELPHI system for consensus evaluation. Table 31 presents the updated recommendations:

Table 31. Recommendations on Hyperbaric Medicine

Condition	SOR	LOE
Carbon monoxide poisoning	Strong	Moderate
Open fractures with crush injury	Strong	Moderate
Prevention of osteoradionecrosis	Strong	Moderate
Osteoradionecrosis (mandible)	Strong	Moderate
Soft tissue radionecrosis (cystitis, proctitis)	Strong	Moderate
Decompression illness	Strong	Low
Gas embolism	Strong	Low
Anaerobic or mixed bacterial infection	Strong	Low
Sudden deafness	Strong	Moderate
Diabetic foot lesions	Weak	Moderate
Femoral head necrosis	Weak	Moderate
Compromised skin grafts and musculocutaneous flaps	Weak	Low
Central retinal artery occlusion	Weak	Low
Crush injury without fracture	Weak	Low
Osteoradionecrosis (other than mandible)	Weak	Low
Radio-induced lesions of soft tissues	Weak	Low
Radio-induced lesions of soft tissues (preventive)	Weak	Low
Ischemic ulcers	Weak	Low
Refractory chronic osteomyelitis	Weak	Low
Burns, second degree, >20% body surface area	Weak	Low
Pneumatosis cystoides intestinalis	Weak	Low
Neuroblastoma, stage IV	Weak	Low
Brain injury in highly selected patients	Neutral	Low
Radio-induced lesions of larynx	Neutral	Low
Radio-induced lesions of central nervous system	Neutral	Low
Post-vascular procedure reperfusion syndrome	Neutral	Low
Limb replantation	Neutral	Low
Selected non-healing wounds, secondary to systemic process	Neutral	Low
Sickle cell disease	Neutral	Low
Interstitial cystitis	Neutral	Low

Adapted from Mathieu et al (2017).[69]
LOE: level of evidence; SOR: strength of recommendation.

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			
NCT01659723	Radiation Induced Cystitis Treated With Hyperbaric Oxygen - A Randomized Controlled Trial (RICH-ART)	80	Dec 2017

NCT No.	Trial Name	Planned Enrollment	Completion Date
NCT03147352	Pro-Treat – Prognosis and Treatment of Necrotizing Soft Tissue Infections: a Prospective Cohort Study	310	Jan 2018
NCT02089594	Hyperbaric Oxygen Therapy Treatment of Chronic Mild Traumatic Brain Injury (mTBI)/Persistent Post-Concussion Syndrome (PCCS)	59	Mar 2019
NCT02714465	Treatment of Adverse Radiation Effects after Gamma Knife Radiosurgery (GKS) by Hyperbaric Oxygen Therapy (HBO)	65	May 2019
NCT03325959	Hyperbaric Oxygen versus Standard Pharmaceutical Therapies for Fibromyalgia Syndrome – Prospective, Randomized, Crossover Clinical Trial	70	Nov 2019
NCT00596180	Hyperbaric Oxygen Therapy and SPECT Brain Imaging in Carbon Monoxide Poisoning	40	Dec 2019
NCT01002209	Postoperative Hyperbaric Oxygen Treatments to Reduce Complications in Diabetic Patients Undergoing Vascular Surgery (HODiVA)	112	Oct 2020
NCT01847755	Phase 1-2 Study of Hyperbaric Treatment of Traumatic Brain Injury	100	Dec 2020
Unpublished			
NCT02085330	Hyperbaric Oxygen Therapy for Mild Cognitive Impairment	60	Feb 2017 (unknown)

NCT: national clinical trial.

CODING

The following codes for treatment and procedures applicable to this policy are included below for informational purposes. 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.

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

- Topical Hyperbaric Oxygen
  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.

ICD-10 Diagnoses

A42.2	B36.2	B37.49	B46.9	E08.59	E09.628
A42.89	B36.3	B37.83	B47.1	E08.620	E10.52
A42.9	B36.8	B46.0	B47.9	E08.621	E10.59
A43.1	B36.9	B46.1	B48.3	E08.622	E10.620
A43.8	B37.0	B46.2	B48.8	E08.628	E10.621
A43.9	B37.2	B46.3	B49	E09.59	E10.622
A48.0	B37.3	B46.4	B78.1	E09.620	E10.628
B36.0	B37.41	B46.5	D62	E09.621	E11.52
B36.1	B37.42	B46.8	E08.52	E09.622	E11.59

E11.620
E11.621
E11.622
E11.628
E13.52
E13.59
E13.620
E13.621
E13.622
E13.628
G06.0
H34.11
H34.12
H34.13
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T58.93XA	T65.0X4D	T79.0XXS	T79.A21A	T81.89XD	

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). 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, 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; 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;" ▪ 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, 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".

	▪ 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.
	Updated Rationale section.
	Updated References section.

REFERENCES

1. Sadri RA, Cooper JS. Hyperbaric, complications. NCBI Bookshelf 2017; https://www.ncbi.nlm.nih.gov/books/NBK459191/. Accessed November 21, 2017.
2. Federal Food and Drug Administration. Hyperbaric Oxygen Therapy: Don't Be Misled. 2013; http://www.fda.gov/forconsumers/consumerupdates/ucm364687.htm. Accessed November 21, 2017.
3. Blue Cross and Blue Shield Association Technology Evaluation Center (TEC). Hyperbaric oxygen therapy for wound healing. Part I. TEC Assessments. 1999;Volume 14:Tab 13. PMID
4. Blue Cross and Blue Shield Association Technology Evaluation Center (TEC). Hyperbaric oxygen therapy for wound healing. Part II. TEC Assessments. 1999;Volume 14:Tab 15. PMID
5. Blue Cross and Blue Shield Association Technology Evaluation Center (TEC). Hyperbaric oxygen therapy for wound healing. Part III. TEC Assessments. 1999;Volume 14:Tab 16. PMID
6. de Smet GHJ, Kroese LF, Menon AG, et al. Oxygen therapies and their effects on wound healing. Wound Repair Regen. Aug 2017;25(4):591-608. PMID 28783878
7. Leslie CA, Sapico FL, Ginunas VJ, et al. Randomized controlled trial of topical hyperbaric oxygen for treatment of diabetic foot ulcers. Diabetes Care. Feb 1988;11(2):111-115. PMID 3289861
8. Kranke P, Bennett MH, Martyn-St James M, et al. Hyperbaric oxygen therapy for chronic wounds. Cochrane Database Syst Rev. Jun 24 2015(6):CD004123. PMID 26106870
9. Elraiyah T, Tsapas A, Prutsky G, et al. A systematic review and meta-analysis of adjunctive therapies in diabetic foot ulcers. J Vasc Surg. Feb 2016;63(2 Suppl):46S-58S e41-42. PMID 26804368
10. Buckley NA, Juurlink DN, Isbister G, et al. Hyperbaric oxygen for carbon monoxide poisoning. Cochrane Database Syst Rev. Apr 13 2011(4):CD002041. PMID 21491385
11. Bennett MH, Feldmeier J, Hampson NB, et al. Hyperbaric oxygen therapy for late radiation tissue injury. Cochrane Database Syst Rev. Apr 28 2016;4:CD005005. PMID 27123955
12. Borab Z, Mirmanesh MD, Gantz M, et al. Systematic review of hyperbaric oxygen therapy for the treatment of radiation-induced skin necrosis. J Plast Reconstr Aesthet Surg. Apr 2017;70(4):529-538. PMID 28081957
13. Ravi P, Vaishnavi D, Gnanam A, et al. The role of hyperbaric oxygen therapy in the prevention and management of radiation-induced complications of the head and neck - a systematic review of literature. J Stomatol Oral Maxillofac Surg. Dec 2017;118(6):359-362. PMID 28838774
14. Maynor ML, Moon RE, Camporesi EM, et al. Chronic osteomyelitis of the tibia: treatment with hyperbaric oxygen and autogenous microsurgical muscle transplantation. J South Orthop Assoc. Spring 1998;7(1):43-57. PMID 9570731
15. Davis JC, Heckman JD, DeLee JC, et al. Chronic non-hematogenous osteomyelitis treated with adjuvant hyperbaric oxygen. J Bone Joint Surg Am. Oct 1986;68(8):1210-1217. PMID 3771602

16. Chen CE, Ko JY, Fu TH, et al. Results of chronic osteomyelitis of the femur treated with hyperbaric oxygen: a preliminary report. Chang Gung Med J. Feb 2004;27(2):91-97. PMID 15095953
17. Chen CE, Shih ST, Fu TH, et al. Hyperbaric oxygen therapy in the treatment of chronic refractory osteomyelitis: a preliminary report. Chang Gung Med J. Feb 2003;26(2):114-121. PMID 12718388
18. Chen CY, Lee SS, Chan YS, et al. Chronic refractory tibia osteomyelitis treated with adjuvent hyperbaric oxygen: a preliminary report. Changgeng Yi Xue Za Zhi. Jun 1998;21(2):165-171. PMID 9729650
19. Villanueva E, Bennett MH, Wasiak J, et al. Hyperbaric oxygen therapy for thermal burns. Cochrane Database Syst Rev. Jul 2004(3):CD004727. PMID 15266540
20. Eskes A, Vermeulen H, Lucas C, et al. Hyperbaric oxygen therapy for treating acute surgical and traumatic wounds. Cochrane Database Syst Rev. Dec 16 2013;12(12):CD008059. PMID 24343585
21. Dauwe PB, Pulikkottil BJ, Lavery L, et al. Does hyperbaric oxygen therapy work in facilitating acute wound healing: a systematic review. Plast Reconstr Surg. Feb 2014;133(2):208e-215e. PMID 24469192
22. Freiberger JJ, Padilla-Burgos R, McGraw T, et al. What is the role of hyperbaric oxygen in the management of bisphosphonate-related osteonecrosis of the jaw: a randomized controlled trial of hyperbaric oxygen as an adjunct to surgery and antibiotics. J Oral Maxillofac Surg. Jul 2012;70(7):1573-1583. PMID 22698292
23. Levett D, Bennett MH, Millar I. Adjunctive hyperbaric oxygen for necrotizing fasciitis. Cochrane Database Syst Rev. Jan 15 2015;1:CD007937. PMID 25879088
24. Jallali N, Withey S, Butler PE. Hyperbaric oxygen as adjuvant therapy in the management of necrotizing fasciitis. Am J Surg. Apr 2005;189(4):462-466. PMID 15820462
25. George ME, Rueth NM, Skarda DE, et al. Hyperbaric oxygen does not improve outcome in patients with necrotizing soft tissue infection. Surg Infect (Larchmt). Feb 2009;10(1):21-28. PMID 18991520
26. Bennett MH, Lehm JP, Jepson N. Hyperbaric oxygen therapy for acute coronary syndrome. Cochrane Database Syst Rev. Jul 23 2015(7):CD004818. PMID 26202854
27. Bennett MH, Weibel S, Wasiak J, et al. Hyperbaric oxygen therapy for acute ischaemic stroke. Cochrane Database Syst Rev. Nov 12 2014;11(11):CD004954. PMID 25387992
28. Efrati S, Fishlev G, Bechor Y, et al. Hyperbaric oxygen induces late neuroplasticity in post stroke patients--randomized, prospective trial. PLoS One. Jan 2013;8(1):e53716. PMID 23335971
29. Holland NJ, Bernstein JM, Hamilton JW. Hyperbaric oxygen therapy for Bell's palsy. Cochrane Database Syst Rev. Feb 15 2012;2(2):CD007288. PMID 22336830
30. Wang F, Wang Y, Sun T, et al. Hyperbaric oxygen therapy for the treatment of traumatic brain injury: a meta-analysis. Neurol Sci. May 2016;37(5):693-701. PMID 26746238
31. Crawford C, Teo L, Yang E, et al. Is hyperbaric oxygen therapy effective for traumatic brain injury? a rapid evidence assessment of the literature and recommendations for the field. J Head Trauma Rehabil. May/Jun 2017;32(3):E27-E37. PMID 27603765
32. Bennett MH, Trytko B, Jonker B. Hyperbaric oxygen therapy for the adjunctive treatment of traumatic brain injury. Cochrane Database Syst Rev. Dec 12 2012;12:CD004609. PMID 23235612
33. Wolf G, Cifu D, Baugh L, et al. The effect of hyperbaric oxygen on symptoms after mild traumatic brain injury. J Neurotrauma. Nov 20 2012;29(17):2606-2612. PMID 23031217
34. Cifu DX, Walker WC, West SL, et al. Hyperbaric oxygen for blast-related postconcussion syndrome: three-month outcomes. Ann Neurol. Feb 2014;75(2):277-286. PMID 24255008
35. Miller RS, Weaver LK, Bahraini N, et al. Effects of hyperbaric oxygen on symptoms and quality of life among service members with persistent postconcussion symptoms: a randomized clinical trial. JAMA Intern Med. Jan 2015;175(1):43-52. PMID 25401463
36. Marois P, Mukherjee A, Ballaz L. Hyperbaric oxygen treatment for persistent postconcussion symptoms-a placebo effect? JAMA Intern Med. Jul 1 2015;175(7):1239-1240. PMID 26146912
37. Dulai PS, Gleeson MW, Taylor D, et al. Systematic review: The safety and efficacy of hyperbaric oxygen therapy for inflammatory bowel disease. Aliment Pharmacol Ther. Jun 2014;39(11):1266-1275. PMID 24738651

38. Pagoldh M, Hultgren E, Arnell P, et al. Hyperbaric oxygen therapy does not improve the effects of standardized treatment in a severe attack of ulcerative colitis: a prospective randomized study. Scand J Gastroenterol. Sep 2013;48(9):1033-1040. PMID 23879825
39. Lewis JD, Chuai S, Nessel L, et al. Use of the noninvasive components of the Mayo score to assess clinical response in ulcerative colitis. Inflamm Bowel Dis. Dec 2008;14(12):1660-1666. PMID 18623174
40. Bennett MH, Kertesz T, Perleth M, et al. Hyperbaric oxygen for idiopathic sudden sensorineural hearing loss and tinnitus. Cochrane Database Syst Rev. Oct 17 2012;10:CD004739. PMID 23076907
41. Rhee TM, Hwang D, Lee JS, et al. Addition of Hyperbaric Oxygen Therapy vs Medical Therapy Alone for Idiopathic Sudden Sensorineural Hearing Loss: A Systematic Review and Meta-analysis. JAMA Otolaryngol Head Neck Surg. Sep 27 2018. PMID 30267033
42. Cvorovic L, Jovanovic MB, Milutinovic Z, et al. Randomized prospective trial of hyperbaric oxygen therapy and intratympanic steroid injection as salvage treatment of sudden sensorineural hearing loss. Otol Neurotol. Aug 2013;34(6):1021-1026. PMID 23820795
43. Sun H, Qiu X, Hu J, et al. Comparison of intratympanic dexamethasone therapy and hyperbaric oxygen therapy for the salvage treatment of refractory high-frequency sudden sensorineural hearing loss. Am J Otolaryngol. Sep - Oct 2018;39(5):531-535. PMID 29891394
44. Almosnino G, Holm JR, Schwartz SR, et al. The Role of Hyperbaric Oxygen as Salvage Therapy for Sudden Sensorineural Hearing Loss. Ann Otol Rhinol Laryngol. Oct 2018;127(10):672-676. PMID 30009614
45. Xie S, Qiang Q, Mei L, et al. Multivariate analysis of prognostic factors for idiopathic sudden sensorineural hearing loss treated with adjuvant hyperbaric oxygen therapy. Eur Arch Otorhinolaryngol. Jan 2018;275(1):47-51. PMID 29071444
46. Bennett M, Best TM, Babul S, et al. Hyperbaric oxygen therapy for delayed onset muscle soreness and closed soft tissue injury. Cochrane Database Syst Rev. Oct 19 2005(4):CD004713. PMID 16235376
47. Xiong T, Chen H, Luo R, et al. Hyperbaric oxygen therapy for people with autism spectrum disorder (ASD). Cochrane Database Syst Rev. Oct 13 2016;10:CD010922. PMID 27737490
48. Sampanthavivat M, Singkhwa W, Chaiyakul T, et al. Hyperbaric oxygen in the treatment of childhood autism: a randomised controlled trial. Diving Hyperb Med. Sep 2012;42(3):128-133. PMID 22987458
49. Lacey DJ, Stolfi A, Pilati LE. Effects of hyperbaric oxygen on motor function in children with cerebral palsy. Ann Neurol. Nov 2012;72(5):695-703. PMID 23071074
50. Collet JP, Vanasse M, Marois P, et al. Hyperbaric oxygen for children with cerebral palsy: a randomised multicentre trial. HBO-CP Research Group. Lancet. Feb 24 2001;357(9256):582-586. PMID 11558483
51. Long Y, Tan J, Nie Y, et al. Hyperbaric oxygen therapy is safe and effective for the treatment of sleep disorders in children with cerebral palsy. Neurol Res. Mar 2017;39(3):239-247. PMID 28079475
52. Xiao Y, Wang J, Jiang S, et al. Hyperbaric oxygen therapy for vascular dementia. Cochrane Database Syst Rev. Jul 11 2012;7(7):CD009425. PMID 22786527
53. Spiegelberg L, Djasim UM, van Neck HW, et al. Hyperbaric oxygen therapy in the management of radiation-induced injury in the head and neck region: a review of the literature. J Oral Maxillofac Surg. Aug 2010;68(8):1732-1739. PMID 20493616
54. Teguh DN, Levendag PC, Noever I, et al. Early hyperbaric oxygen therapy for reducing radiotherapy side effects: early results of a randomized trial in oropharyngeal and nasopharyngeal cancer. Int J Radiat Oncol Biol Phys. Nov 1 2009;75(3):711-716. PMID 19386439
55. Gothard L, Haviland J, Bryson P, et al. Randomised phase II trial of hyperbaric oxygen therapy in patients with chronic arm lymphoedema after radiotherapy for cancer. Radiother Oncol. Oct 2010;97(1):101-107. PMID 20605648
56. Camporesi EM, Vezzani G, Bosco G, et al. Hyperbaric oxygen therapy in femoral head necrosis. J Arthroplasty. Sep 2010;25(6 Suppl):118-123. PMID 20637561
57. Bennett MH, French C, Schnabel A, et al. Normobaric and hyperbaric oxygen therapy for the treatment and prevention of migraine and cluster headache. Cochrane Database Syst Rev. Dec 28 2015(12):CD005219. PMID 26709672

58. Peng Z, Wang S, Huang X, et al. Effect of hyperbaric oxygen therapy on patients with herpes zoster. Undersea Hyperb Med. Nov-Dec 2012;39(6):1083-1087. PMID 23342765
59. Efrati S, Golan H, Bechor Y, et al. Hyperbaric oxygen therapy can diminish fibromyalgia syndrome--prospective clinical trial. PLoS One. May 2015;10(5):e0127012. PMID 26010952
60. Yildiz S, Kiralp MZ, Akin A, et al. A new treatment modality for fibromyalgia syndrome: hyperbaric oxygen therapy. J Int Med Res. May-Jun 2004;32(3):263-267. PMID 15174219
61. Bennett M, Heard R. Hyperbaric oxygen therapy for multiple sclerosis. CNS Neurosci Ther. Apr 2010;16(2):115-124. PMID 20415839
62. Bennett M, Feldmeier J, Smee R, et al. Hyperbaric oxygenation for tumour sensitisation to radiotherapy. Cochrane Database Syst Rev. Oct 19 2005(4):CD005007. PMID 16235387
63. Bennett MH, Feldmeier J, Smee R, et al. Hyperbaric oxygenation for tumour sensitisation to radiotherapy. Cochrane Database Syst Rev. Apr 18 2012(4):CD005007. PMID 22513926
64. Heys SD, Smith IC, Ross JA, et al. A pilot study with long term follow up of hyperbaric oxygen pretreatment in patients with locally advanced breast cancer undergoing neo-adjuvant chemotherapy. Undersea Hyperb Med. Jan-Feb 2006;33(1):33-43. PMID 16602255
65. Huang ET, Mansouri J, Murad MH, et al. A clinical practice guideline for the use of hyperbaric oxygen therapy in the treatment of diabetic foot ulcers. Undersea Hyperb Med. May-Jun 2015;42(3):205-247. PMID 26152105
66. Lipsky BA, Berendt AR, Cornia PB, et al. 2012 infectious diseases society of america clinical practice guideline for the diagnosis and treatment of diabetic foot infections. J Am Podiatr Med Assoc. Jan-Feb 2013;103(1):2-7. PMID 23328846
67. Hingorani A, LaMuraglia GM, Henke P, et al. The management of diabetic foot: A clinical practice guideline by the Society for Vascular Surgery in collaboration with the American Podiatric Medical Association and the Society for Vascular Medicine. J Vasc Surg. Feb 2016;63(2 Suppl):3S-21S. PMID 26804367
68. Weaver LK, editor. Hyperbaric Oxygen Therapy Indications. 13th ed. North Palm Beach, FL: Undersea and Hyperbaric Medical Society; 2014.
69. Feldmeier JJ, Hopf HW, Warriner RA, 3rd, et al. UHMS position statement: topical oxygen for chronic wounds. Undersea Hyperb Med. May-Jun 2005;32(3):157-168. PMID 16119307
70. Bennett M., Heard R. UHMS Position Paper: the treatment of multiple sclerosis with hyperbaric oxygen therapy. North Palm Beach, FL: Undersea & Hyperbaric Medical Society (UHMS); n.d.
71. Bennett M., B. H. UHMS Position Paper: the treatment of autism spectrum disorder with hyperbaric oxygen therapy. North Palm Beach, FL: Undersea & Hyperbaric Medical Society (UHMS); 2009.
72. American Academy of Otolaryngology-Head and Neck Surgery. Clinical practice guideline: sudden hearing loss. 2012; https://www.entnet.org/sites/default/files/SHL-talking-points-physicians.pdf. Accessed November 21, 2017.
73. Mathieu D, Marroni A, Kot J. Tenth European Consensus Conference on Hyperbaric Medicine: recommendations for accepted and non-accepted clinical indications and practice of hyperbaric oxygen treatment. Diving Hyperb Med. Mar 2017;47(1):24-32. PMID 28357821
74. Sultan A, Hanna GJ, Margalit DN, et al. The use of hyperbaric oxygen for the prevention and management of osteoradionecrosis of the jaw: a Dana-Farber/Brigham and Women's Cancer Center Multidisciplinary Guideline. Oncologist. Mar 2017;22(3):343-350. PMID 28209748
75. Centers for Medicare and Medicaid Services (CMS). National Coverage Determination (NCD) for Hyperbaric Oxygen Therapy (20.29). 2006; https://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=12&ncdver=3&bc=AAAAgAAAAAAAAA%3d%3d&. Accessed November 21, 2017.

Other References

1. Blue Cross and Blue Shield of Kansas, Board of Directors meeting, May 17, 1990 (see Blue Cross and Blue Shield of Kansas Newsletter, Blue Shield Report BS-3-90).
2. Blue Cross and Blue Shield of Kansas, Surgery Liaison Committee meeting, November 2, 1989 (see Blue Cross and Blue Shield of Kansas Newsletter, Blue Shield Report BS-3-90).
3. Blue Cross and Blue Shield of Kansas Podiatry Liaison Committee Consent Ballot, March 2019.

4. Blue Cross and Blue Shield of Kansas Surgery Liaison Committee Consent Ballot, March 2019.
5. Blue Cross and Blue Shield of Kansas Podiatry Liaison Committee, January 2015; January 2018.