Washington State Health Care Authority

Hyperbaric Oxygen Therapy for Sudden Sensorineural Hearing Loss

Draft Evidence Report

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Health Technology Assessment Program (HTA)

Washington State Health Care Authority

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This evidence report is based on research conducted by the RTI–University of North Carolina Evidence-based Practice Center through a contract between RTI International and the State of Washington Health Care Authority (HCA). The findings and conclusions in this document are those of the authors, who are responsible for its contents. The findings and conclusions do not represent the views of the Washington HCA, and no statement in this report should be construed as an official position of Washington HCA.

The information in this report is intended to help the State of Washington's independent Health Technology Clinical Committee make well-informed coverage determinations. This report is not intended to be a substitute for the application of clinical judgment. Anyone who makes decisions concerning the provision of clinical care should consider this report in the same way as any medical reference and in conjunction with all other pertinent information (i.e., in the context of available resources and circumstances presented by individual patients).

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List of Abbreviations

AGREE II	Appraisal of Guidelines for Research & Evaluation II
AI	artificial intelligence
AAO-HNSF	American Academy of Otolaryngology - Head and Neck Surgery Foundation
AAT	acute acoustic trauma
AE	adverse event
AMD	absolute mean deviation
ATA	atmosphere absolute
COE	certainty of evidence
CQ	cost question
dB HL	decibels in hearing level
ECHM	European Committee for Hyperbaric Medicine
EQ	efficacy question
FDA	Food and Drug Administration
GRADE	Grading of Recommendations, Assessment, Development, and Evaluation
HBOT	hyperbaric oxygen therapy
HCA	Health Care Authority
HPTA	high pure-tone average
HTA	health technology assessment
ITS	intratympanic steroid
ITSI	intratympanic steroid injection
ITT	intent to treat
IV	intravenous
IQR	interquartile range
MD	mean difference
MeSH	Medical Subject Headings
NA	not available
NBOT	normobaric oxygen therapy
NLR	neutrophil-lymphocyte ratio
NICE	National Institute for Health and Care Excellence
NR	not reported
NRSI	nonrandomized studies of interventions
NS	not significant
OS	oral steroid
PICOTS	population, intervention, comparator, outcome, timing, setting, study design
PLR	platelet-lymphocyte ratio
PP	per protocol
PTA	pure-tone average
RCT	randomized controlled trial

RoB	risk of bias
SE	standard error
SQ	safety question
SS	systemic steroids
SSNHL	sudden sensorineural hearing loss
TT5	Treatment Table 5
TT9	Treatment Table 9
UHMS	Underseas and Hyperbaric Medical Society
UN	United Nations
U.S.	United States
WDS	word discrimination scores

Executive Summary

Structured Abstract

Purpose: To conduct a health technology assessment (HTA) on the efficacy, safety, and cost-effectiveness of hyperbaric oxygen therapy (HBOT) among adults or children with acute or chronic sudden idiopathic sensorineural hearing loss (SSNHL) or acute acoustic trauma (AAT).

Data Sources: PubMed and Cochrane Library from inception through July 2024; clinical trial registry; government, payor, and clinical specialty organization websites; hand searches of systematic reviews.

Study Selection: We selected English-language studies conducted in very highly developed countries that reported effectiveness, differential effectiveness in select subpopulations, safety, or cost-effectiveness for HBOT treatment, with or without steroid therapy or other medical management, in patients with idiopathic SSNHL or AAT. We included randomized controlled trials (RCTs) for idiopathic SSNHL and included RCTs or nonrandomized studies of interventions (NRSIs) for AAT. Eligible outcomes included patient-centered outcomes (e.g., hearing improvement or recovery); differential effectiveness by age, sex, or severity of hearing loss at baseline; adverse events; and cost-effectiveness from studies that used U.S.-based cost data.

Data Abstraction and Analysis: One reviewer abstracted data and a second checked for accuracy. Two reviewers independently assessed risk of bias (RoB) of included studies. We rated the certainty of the evidence using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) approach.

Data Synthesis: From 652 unique citations screened, we included a total of 17 studies. For idiopathic SSNHL, we included 10 RCTs conducted in Europe, Asia, or Turkey. Sample sizes ranged from 50 to 171. We assessed 3 RCTs as low RoB, 6 as some concerns, and 1 as high RoB. Most studies required participants to begin treatment within 15 days of symptom onset and to have hearing loss of at least 30 dB.

Seven of 10 RCTs compared the effectiveness of HBOT with steroids to steroid use. Five of these RCTs reported hearing recovery categorically as complete, partial or no recovery; definitions varied but were similar enough to combine in a meta-analysis. There was moderate certainty of evidence (COE) that participants treated with HBOT plus steroids within 14 days of symptom onset were 39% more likely to achieve complete or partial hearing recovery compared with those treated with steroids alone (pooled RR, 1.39; 95% CI, 1.03 to 1.86; 5 RCTs; 294 participants; I^2=44.9%). Most studies defined complete or partial hearing recovery as treatment success. There was moderate COE that participants treated with HBOT plus steroids within 14 days of symptom onset were 41% less likely to experience no recovery compared with those treated with steroids alone (pooled RR 0.59; 95% CI, 0.42 to 0.83; 5 RCTs; 294 participants; I^2=0%). For mean or median hearing improvement, there was very low COE for greater hearing improvement in participants treated with HBOT with steroids compared with those treated with

steroids alone based on mixed findings from 4 RCTs, with 2 RCTs reporting hearing improvement favoring HBOT plus steroid use over steroid use alone and 2 reporting no significant difference. There was moderate COE from 1 RCT that improvement in word discrimination scores (WDS), a measure of the proportion of words a person understands correctly, was significantly greater in the HBOT plus steroid group (mean: 65.9% correct, SD: 14.1) compared with the steroid only group (mean: 56.7% correct, SD: 19.1, P=0.035; calculated absolute mean deviation [AMD], 9.2%; 95% CI, 0.52% to 17.9%). There was very limited evidence for differential efficacy by subpopulations. One RCT suggested better hearing recovery among participants who began treatment with HBOT plus steroids within 7 days of symptom onset, findings from 2 RCTs regarding differences by hearing loss at baseline were mixed, 1 RCT found no differences by age, and 1 RCT suggested women, compared to men, had better hearing improvement. Four of the 7 RCTs comparing HBOT with steroids to steroids alone reported safety outcomes. There were no major complications reported. There were 4 adverse events (AEs) (all-minor ear pain) reported in HBOT plus steroid use groups and 0 AEs reported in the steroid use alone groups. There was low COE that there was no difference between groups (pooled RR 0.36, 95% 0.07 to 1.94, 4 RCTs; N=281; I^2=0.0%).

Evidence for other comparisons was limited. There was low COE from a single RCT that hearing improvement as measured by change in pure-tone average (PTA) was significantly greater in participants treated with HBOT alone compared with those treated with steroids alone. One RCT of salvage therapy compared HBOT to intratympanic steroids among participants who failed an initial course of intravenous steroids; there was low COE for no difference in hearing improvement between the groups, which was only significant at 1 of 5 frequencies, 2000 Hz (HBOT: 16.4 dB; steroids: 11.4 dB; P<0.05; calculated mean difference: 5.0 dB); hearing improvements at other frequencies ranged from -3.0 to 4.8 dB. There was very low COE for no difference in AEs between HBOT use and steroid use (RR: 1.67, 95% CI, 0.45 to 6.24). Two RCTs comparing different HBOT treatment protocols suggests higher pressure (2.5 atmosphere absolute [ATA]) may be more effective than lower pressure (1.5 ATA) and 2 sessions per day for 5 days is comparable to 1 session per day for 10 days.

We did not identify any studies reporting differential safety outcomes by subpopulations or any studies reporting cost or cost-effectiveness outcomes.

For AAT, we identified 7 studies predominantly conducted in Europe among male military participants. Sample sizes ranged from 35 to 108. We assessed 1 RCT as high RoB, 3 NRSIs as serious RoB, and 3 NRSIs as critical RoB. Substantial heterogeneity in baseline hearing loss, measured outcomes, and definitions of recovery prevented quantitative analysis. The largest body of evidence included 3 studies and favored HBOT plus steroids versus steroids only for the treatment of AAT across a range of hearing recovery outcomes. The COE for this treatment comparison ranged from low to very low, suggesting that the true effect may be substantially different from that reported. Similarly, 2 studies favored HBOT versus control or usual care for hearing recovery and improvement in tinnitus symptoms. Very low COE from single bodies of evidence provide little insight into the optimal timing (early vs. late), frequency, dose, and duration of HBOT to treat AAT. Additionally, we did not identify any studies reporting on the differential effectiveness of HBOT for treating AAT by age, sex, race or ethnicity, disability,

comorbidities, or severity of hearing loss, and we did not identify any studies for the cost question (CQ).

Limitations: There are several important limitations of the evidence base. Studies were generally small, limiting precision of effect estimates. No studies were conducted in the United States, limiting generalizability. Definitions of hearing recovery varied, introducing heterogeneity into analysis of this outcome. Follow-up times were limited, reducing understanding of long-term outcomes. Safety outcome reporting was limited and inconsistent across studies. In addition, we identified no studies that examined cost-effectiveness. Furthermore, for AAT, all identified studies were assessed as high, critical, or serious RoB.

Conclusions: HBOT may provide meaningful additional benefit when combined with steroid therapy for idiopathic SSNHL. Evidence for HBOT as salvage therapy after failed steroid treatment or as a stand-alone therapy is very limited; and no cost-effectiveness data were identified. Although the overall evidence supports HBOT for idiopathic SSNHL as an adjunctive therapy to steroid treatment, there was limited evidence by factors like severity of hearing loss and time to treatment, which may be important for optimal outcomes. Low to very low COE across all reported outcomes limits our ability to draw meaningful conclusions regarding the effectiveness of HBOT to treat SSNHL resulting from AAT. It is unclear whether the body of evidence for the effectiveness of HBOT to treat idiopathic SSNHL is relevant to the treatment of AAT.

ES 1. Background

This health technology assessment (HTA) reviews the efficacy, safety, and cost-effectiveness of hyperbaric oxygen treatment (HBOT) for sudden hearing loss, including idiopathic sudden sensorineural hearing loss (SSNHL) and sudden hearing loss due to acute acoustic trauma (AAT), to assist the State of Washington's Health Technology Clinical Committee in determining coverage of HBOT for sudden hearing loss.

ES 1.1 Condition Description

SSNHL or sudden deafness is rapid loss of hearing with onset over a period of less than 72 hours. It involves a decrease in hearing of ≥30 dB affecting at least 3 consecutive frequencies.[1] More than 90% of cases are idiopathic. Notably, 32% to 62% of cases of SSNHL recover spontaneously, which complicates the evaluation of treatments for this condition.[1]

AAT is a less common cause of SSNHL. In AAT, exposure to a short-impact, acoustic impulse with an intensity of 90 to 130 dB for a duration of 1 millisecond causes the inner ear to become mechanically damaged with resulting microcirculation vasospasm and hypoxia of cochlear sensory cells occur.[2] Symptoms include sensorineural hearing loss mostly occurring at high frequencies (4 kHz and higher) with accompanying tinnitus. AAT is primarily seen in military or law enforcement personnel, who are exposed to impulse noises from firearms.[2-4]

Pure-tone average (PTA) is the measurement of an individual's hearing sensitivity for calibrated pure tones. PTA is calculated based on averaging thresholds at various frequencies typical for

normal conversation, most often 500 Hz, 1,000 Hz, 2,000 Hz, and 4,000 Hz.[5,6] ***Table ES-1*** shows a commonly used classification system for hearing loss. For example, an individual with a PTA of 30 dB will have difficulty understanding whispering; some words involving "p," "h," and "g"; and the sound of birds chirping. An individual with a PTA of 80 dB will find it difficult to hear a dog barking or a baby crying and will find normal conversation very challenging without hearing assistance.[7]

Table ES-1. American Speech-Language-Hearing Association Hearing Loss Categories[8]

Degree of Hearing Loss	PTA Range (in dB HL)
Normal	–10 to 15
Slight	16 to 25
Mild	26 to 40
Moderate	41 to 55
Moderately severe	56 to 70
Severe	71 to 90
Profound	91+

Abbreviations: dB HL = decibels in hearing level.

ES 1.2 Technology Description

HBOT involves the therapeutic administration of 100% oxygen at environmental pressures >1 atmosphere absolute (ATA), the atmospheric pressure at sea level. Administering oxygen at pressures greater than 1 ATA requires compression. This is achieved by placing the patient in an airtight chamber and slowly increasing pressure while administering 100% oxygen. This results in increased oxygen delivery to the lungs, blood, and other body tissues.[9]

ES 1.3 Rationale for Use of HBOT for SSNHL

Vascular compromise, and associated cochlear ischemia, is a potential etiology of idiopathic SSNHL and SSNHL resulting from AAT. The cochlea and the structures within it require a high oxygen supply, but the direct vascular supply is minimal. The increased partial pressure of oxygen from HBOT allows for delivery of more oxygen to the cochlea, which is exquisitely sensitive to ischemia. HBOT may reverse the oxygen deficit, increase oxygen pressures in the cochlea, and improve microcirculation, which may result in hearing improvement.[1,10]

ES 1.4 Regulatory Status

The U.S. Food and Drug Administration (FDA) regulates both the oxygen used in HBOT and the hyperbaric chambers. As of July 2021, the FDA has cleared hyperbaric chambers for hearing loss (complete hearing loss that occurs suddenly and without any known cause).[9]

ES 1.5 Policy Context

An HTA of HBOT that included SSNHL, along with several other indications, was published in 2013.[11] This HTA found low certainty evidence (COE) due to mixed results from 8 randomized controlled trials (RCTs). Findings were inconclusive as to whether there is a benefit of HBOT in the acute phase and there was moderate COE from 2 RCTs, suggesting no benefit of HBOT.[11]

The Healthcare Technology Clinical Committee voted to not cover HBOT for SSNHL in the acute or chronic phase.[12]

The State of Washington Health Care Authority (HCA) selected HBOT for idiopathic SSNHL or AAT for a HTA because of medium concerns for safety and high concerns for efficacy and cost. The HCA also cited new evidence for SSNHL that could change the previous determination.[13]

ES 2. Methods

This section describes the methods we used to conduct this HTA.

ES 2.1 Research Questions and Analytic Framework

We developed the following research questions to guide this HTA (***Figure ES-1***):

Efficacy Question 1 (EQ1). Is HBOT effective in improving patient-centered outcomes for individuals with SSNHL?

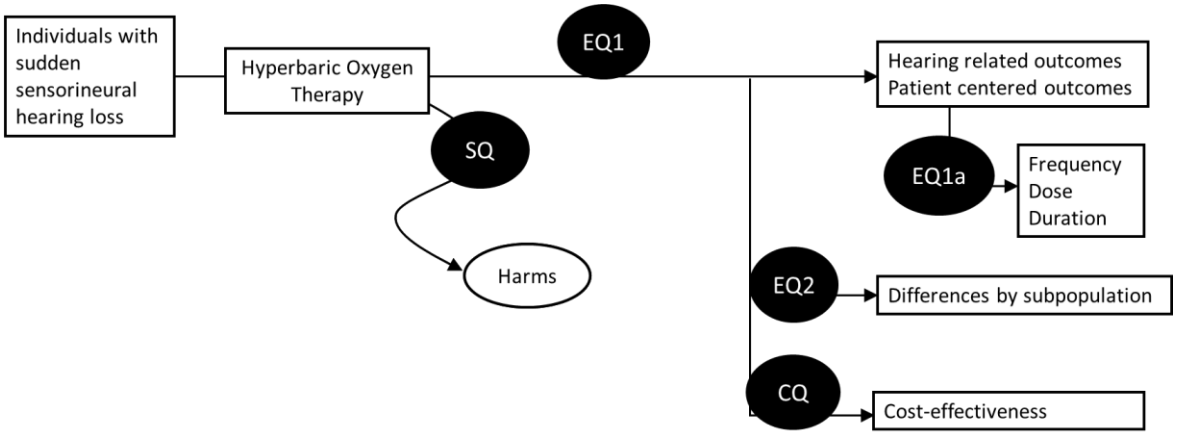
Efficacy Question 1a (EQ1a). What is the optimal frequency, dose, and duration of HBOT treatment for SSNHL?

Efficacy Question 2 (EQ2). What is the differential effectiveness of HBOT according to factors such as age, sex, race or ethnicity, disability, comorbidities, treatment setting, hearing loss duration, severity, or type of hearing loss (e.g., idiopathic vs. noise-induced or acute vs. chronic)?

Safety Question (SQ). What are the harms associated with HBOT for SSNHL?

Cost Question (CQ). What is the cost-effectiveness of HBOT for SSNHL?

Figure ES-1. Analytic Framework Depicting Scope of This Health Technology Assessment



Abbreviations: CQ = cost question; EQ = efficacy question; SQ = safety question.

The State of Washington HTA Program posted a draft of these research questions and proposed scope for public comment from August 29 to September 12, 2024. The key questions were revised in response to a public comment requesting distinct analyses of idiopathic SSNHL and ATA. The final key questions were published on the Program's website on January 5, 2024.[13]

ES 2.2 Data Sources and Search

We searched PubMed and the Cochrane Database of Systematic Reviews on July 17, 2024, and July 12, 2024, respectively, using Medical Subject Headings (MeSH) and text words in the title and abstract for terms related to HBOT. We limited the search to English-language studies in humans. The detailed search strategy is presented in ***Appendix A***. In addition, we searched the ClinicalTrials.gov registry on July 12, 2024, for completed or ongoing studies of HBOT for hearing loss.

ES 2.3 Study Selection

Two reviewers independently screened titles and abstracts and full-text articles based on the following study inclusion criteria. (Complete details are in ***Table 2*** of the Full Technical Report.)

- **Population:** Individuals of any age diagnosed with sudden idiopathic or noise-induced acute or chronic SSNHL or AAT with SSNHL.

- **Interventions:** We selected studies that reported on HBOT delivered via a hyperbaric oxygen chamber, either with or without steroid therapy or other medical management.

- **Comparators:** Eligible comparators included no treatment, other treatments, or sham HBOT treatments. This could include steroid treatments, control or usual care other than steroids, and different HBOT treatments.

- **Outcomes:** For EQ1, we selected studies that reported patient-centered outcomes such as hearing improvement, hearing recovery, return of hearing, improvement in pure-tone average (PTA), tinnitus, speech discrimination score, depression, functional status, quality of life, and return to school or work. For EQ2, we included studies that reported differential effectiveness or safety by factors such as age, sex, race or ethnicity, disability, comorbidities, severity of hearing loss, and treatment setting. For the SQ, we included studies that reported any clinical utility or health outcome or other findings that suggest harm. For the CQ, we included studies that reported measures of cost-effectiveness or cost-utility.

- **Setting**: Studies in any care setting conducted in countries with a development rating designated as *very high* by the United Nations Human Development Index.

- **Study design**: For idiopathic SSNHL, we included RCTs; for AAT indication specifically, we also included nonrandomized studies of interventions (NSRIs) where a clear comparison between 2 or more treatment strategies could be identified. For the CQ, we included cost-utility analysis and cost-effectiveness analysis performed from a societal or payor perspective.

- **Other:** English-language only; no restrictions on publication date.

ES 2.4 Data Abstraction, Risk-of-Bias Assessment, and Synthesis

One team member extracted relevant study data into a structured abstraction form in DistillerSR, and another investigator checked those data for accuracy for all included studies. Two team members conducted independent RoB assessments; discrepancies were resolved by discussion or a third reviewer. We used the Cochrane Risk of Bias 2 tool for randomized trials[14] and the ROBINS-I instrument for NSRI.[15] We assessed the most relevant clinical practice guidelines using Appraisal of Guidelines for Research & Evaluation II (AGREE II) instrument.[16] We qualitatively synthesized study characteristics and results for each research question in tabular and narrative formats. If 3 or more studies reported similar outcomes, we conducted meta-analyses. We used the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach for assessing the COE for select outcomes.[17]

ES 3. Results

ES 3.1 Literature Search

We identified and screened 652 unique citations. We excluded 546 citations after title and abstract review. We reviewed the full text of 106 articles and included 17 studies published between 1985 and 2023. Among the included studies, 10 assessed HBOT for the treatment of idiopathic SSNHL.[18-27] and 7 studies assessed HBOT for the treatment of AAT.[3,4,28-32]

ES 3.2 Idiopathic SSNHL

ES 3.2.1 Idiopathic SSNHL Study and Population Characteristics

Among the 10 RCTs on idiopathic SSNHL, 8 were included for EQ1,[19-24,26,27] 2 studies for EQ1a,[18,25] 5 studies for EQ2,[19,20,23,24,27] and 6 for SQ.[19,21-25] Studies were predominantly conducted in Europe, Asia, or Turkey in adults with unilateral hearing loss of at least 30 dB that began in the last 15 days. We assessed 3 RCTs as low RoB, 6 as some concerns, and 1 as high RoB. Mean baseline PTA ranged from 40.7 dB (mild to moderate hearing loss)[26] to 98.9 dB (profound hearing loss).[25] Most studies defined complete or partial hearing recovery as treatment success.

We did not identify any studies that reported differential safety outcomes by subpopulation or any studies that reported cost or cost-effectiveness outcomes.

ES 3.2.2 HBOT with Steroids vs. Steroids Only

We identified 7 RCTs that compared the effectiveness of HBOT with steroids to steroid use alone.[19-22,24,26,27]

ES 3.2.2.1 HBOT with Steroids vs. Steroids Only: EQ1

- Participants treated with HBOT plus steroids within 14 days of symptom onset were 39% more likely to achieve complete or partial hearing recovery compared with those treated with

steroids (pooled RR, 1.39; 95% CI, 1.03 to 1.86; 5 RCTs; 294 participants; I^2=44.9%). (*Moderate* COE)

- Participants treated with HBOT plus steroids within 14 days of symptom onset were 41% less likely to experience no recovery compared with those treated with steroids (pooled RR 0.59; 95% CI, 0.42 to 0.83; 5 RCTs; 294 participants; I^2=0%). (*Moderate* COE)

- There were mixed findings among 4 RCTs reporting mean or median hearing improvement as measured by PTA; 2 RCTs found no significant difference and 2 RCTs found a statistical difference between groups favoring HBOT with steroids. (*Very low* COE for greater effect with HBOT)

- One RCT found improvement in word discrimination scores (WDS), a measure of the proportion of words a person understand correctly, was significantly greater in the HBOT plus steroid group (mean [SD] % correct, 65.9 [14.1]) compared with the steroid only group (mean [SD] % correct, 56.7 [19.1]; *P*=0.035). (*Moderate* COE)

ES 3.2.2.2 HBOT with Steroids vs. Steroids Only: EQ2

Among the 7 RCTs that compared HBOT with steroids with steroids alone, 4 RCTs reported differential effectiveness outcomes.[19,20,24,27]

- One RCT found participants treated with HBOT plus steroids within 7 days of symptom onset had statistically significant hearing recovery; however, those treated after 7 days did not have statistically significant hearing recovery.

- One RCT found mean hearing improvements were significantly better among those with greater hearing loss at baseline; however, a second RCT found no difference by hearing loss at baseline, though this was based on very small sample sizes.

- One RCT found no difference in hearing recovery by age and another RCT found women, compared with men, had better hearing improvement with treatment.

ES 3.2.2.3 HBOT with Steroids vs. Steroids Only: SQ

Four of 7 studies comparing HBOT plus steroids with steroid use alone group reported adverse events (AEs).[19,21,22,24]

- There were no major complications reported in 4 RCTs that included 281 participants, and AEs were rare. A pooled analysis found no significant difference between treatment groups (pooled RR 0.36; 95% CI, 0.07 to 1.94; I^2=0.0%) based on 4 AEs (all cases of mild ear pain) in HBOT plus steroid use groups and 0 AEs in steroid alone groups. (*Low* COE)

ES 3.2.3 HBOT Only vs. Steroids Only

We identified 1 RCT that compared HBOT alone to steroid use alone.[19] This study also included a third study arm (HBOT with steroids) that was discussed in the previous section.

ES 3.2.3.1 HBOT Only vs. Steroids Only: EQ1

- Significant improvement in hearing as measured by PTA from baseline to 20 days posttreatment in both the HBOT only group and steroid only group ($p<0.05$ for each within group difference); HBOT only group obtained a greater improvement in hearing as measured by PTA compared with the steroid only group ($p<0.05$). (*Low* COE)

ES 3.2.3.2 HBOT Only vs. Steroids Only: EQ2

- Among participants treated within 7 days of symptom onset, HBOT treatment was associated with significant hearing improvement in the HBOT only group ($p<0.05$ compared to baseline PTA) but not the oral steroid only group ($P=0.08$ compared to baseline and the *P* reported was not significant for within 8 to 14 days of onset). Treatment after 14 days of symptom onset was not associated with a statistically significant recovery in either group.

ES 3.2.3.3 HBOT Only vs. Steroids Only: SQ

- The authors observed no short- or long-term posttreatment complications. This RCT did not report outcomes related to differential safety.

ES 3.2.4 Salvage Therapy

We identified 1 RCT that investigated HBOT as salvage therapy compared to intratympanic steroids as salvage therapy among participants who failed initial treatment with intravenous steroids. Treatment failure was defined as a hearing improvement of less than 10 dB at the end of 6 days of intravenous steroid treatment.

ES 3.2.4.1 Salvage Therapy: EQ1

- Hearing improvement was significantly better in the HBOT salvage therapy group compared with the steroid group at 2,000 Hz (HBOT: 16.4 dB; steroids: 11.4 dB; $p<0.05$, calculated mean difference 5.0 dB); the difference between groups was not significant at 250 Hz, 500 Hz, 1,000 Hz, or 4,000 Hz. (*Low* COE for no difference)

ES 3.2.4.2 Salvage Therapy: EQ2

- Patients with pretreatment PTA≥81 dB who received HBOT after failing intravenous steroids had significantly worse hearing improvement compared with those with the same degree of hearing loss who received intratympanic steroid treatment after failing intravenous steroids (improvement of 13.5 dB vs. 40.8, $P<0.05$).

- There were no statistically significant differences between the HBOT group and the intratympanic steroid group for those with baseline hearing of ≤60 dB (improvement of 23.3 dB vs. 25.5 dB; *P*=NS) and those with baseline hearing between 61 dB to 80 dB (improvement of 25.2 dB vs. 28.7 dB; *P*=NS).

ES 3.2.4.3 Salvage Therapy: SQ

- There was no significant difference in AEs between HBOT use and steroid use (RR: 1.67; 95% CI, 0.45 to 6.24) with 3 of 25 (12%) participants in the HBOT group with fluid in the

ear and 5 of 25 (20%) participants in the intratympanic steroid group experiencing mild ear pain after injections. (*Very Low* COE)

ES 3.2.5 Optimal Frequency, Dose, and Duration of HBOT

We identified 2 RCTs that compared different HBOT protocols plus steroids to steroid use alone.[18,25]

ES 3.2.6 Optimal Frequency, Dose, and Duration of HBOT: EQ1A

- One RCT comparing 2 HBOT sessions per day for 5 days with 1 HBOT session per day over 10 days found no significant differences in hearing outcomes between HBOT regimens. (PTA increase within each group ~29 dB; calculated mean difference 0.1 dB; 95% CI, −12.6 to 12.8), suggesting each protocol is a reasonable option.[18]

- One RCT found that higher pressure (2.5 ATA vs. 1.5 ATA) provided significantly better hearing and WDS improvement; however, increasing the duration of treatment (2 hours vs. 1 hour) under 2.5 ATA did not result in a significant difference.[25]

ES 3.3 Acute Acoustic Trauma

ES 3.3.1 AAT Study and Population Characteristics

We identified 7 studies reporting on the use of HBOT for the treatment of SSNHL resulting from AAT. Studies were predominantly conducted in Europe among male military participants and sample sizes ranged from 35 to 108. One study was an RCT[30] and 6 were NRSIs.[3,4,28,29,31,32] We assessed the RCT as high RoB due to lack of information about baseline differences and allocation concealment, as well as concerns regarding outcome selection and lack of blinding for outcome assessors.[30] We assessed 2 NRSIs as serious RoB,[3,28] and 3 NRSIs as critical RoB.[29,31,32] The critical and serious RoB assessments were predominantly because the authors made no attempt or made poor attempts to control for confounding. We assessed 1 NRSI as serious RoB for the outcome of tinnitus due to poor control for important confounding variables, and rated as critical RoB for the outcome of hearing improvement due to poor control for confounding and the exclusion of some participants from analysis.[4]

We did not identify any studies that reported differential safety outcomes by subpopulation or any studies that reported cost or cost-effectiveness outcomes.

ES 3.3.2 HBOT with Steroids vs. Steroids Only

ES 3.3.2.1 HBOT with Steroids vs. Steroids Only: EQ1

We identified 3 studies comparing the effectiveness of HBOT plus steroids to steroid use alone.[3,28,32]

- All 3 NRSIs found statistically significant hearing improvement favoring HBOT with steroids compared with steroids alone. The mean hearing improvement in PTA ranged from 15.2 to 23.5 dB among participants who received HBOT with steroids versus 5.6 to 12.5 dB among those who received steroids alone. (*Low* COE)

- One NRSI found statistically significant greater mean residual hearing loss at 10 days posttreatment among patients who received steroids only (mean 14.7 dB; SD 8.3) versus those who received either early HBOT plus steroids (mean 2.4 dB; SD 10.7) or those who received delayed HBOT plus steroids (mean 5.0 dB; SD 8.0) (p<0.05 for any HBOT with steroids vs. steroids only). (*Low* COE)

- One NRSI reported no statistically significant difference in tinnitus between the HBOT plus steroids versus steroids alone. (*Very Low* COE)

ES 3.3.2.2 HBOT with Steroids vs. Steroids Only: EQ2

- Among 23 patients (29 affected ears) receiving HBOT, 1 NRSI reported statistically significant greater relative mean hearing improvement at 1-year follow-up among military personnel who received HBOT within 2 days of symptoms onset versus those who received HBOT after 2 days of symptoms onset (% relative improvement, 71.4%; SD, 27.5 vs. 47.9%; SD 31.6; p<0.05).

ES 3.3.2.3 HBOT with Steroids vs. Steroids Only: SQ

- One NRSI reported no AEs from either steroids or HBOT and 1 NRSI reported no serious AEs associated with HBOT and did not report AEs in the steroid group. (*Very Low* COE)

ES 3.3.3 HBOT vs. Control or Usual Care (other than steroids)

ES 3.3.3.1 HBOT vs. Control or Usual Care (other than steroids): EQ1

We identified 2 studies comparing the effectiveness of HBOT to usual care or a control.[4,30]

- One RCT found a greater proportion of participants who received HBOT with infusions achieved hearing recovery compared with those who received infusion only. (*Very Low* COE)

- One NRSI found a greater proportion of participants who received HBOT had PTA recovery (74.1%; SD 19.9) compared with those who received normobaric oxygen therapy (NBOT) (60.2%; SD 28.9; p=0.024). (*Very Low* COE)

- One NRSI found fewer participants who received HBOT reported tinnitus compared with those who received NBOT (5% vs. 18%; p<0.05). (*Very Low* COE)

ES 3.3.3.2 HBOT vs. Control or Usual Care (other than steroids): SQ

- One RCT reported no side effects in either group receiving infusions alone: 3 AEs in the group receiving HBOT plus infusions and 1 AE in the group receiving HBOT plus HBOT plus infusions with oral anti-vertigo medication. (*Very Low* COE for no effect)

ES 3.3.4 Early vs. Late Treatment with HBOT: EQ2

One study compared early HBOT treatment (within 10 days of symptom onset) versus late HBOT treatment (11 to 30 days after symptom onset).[31]

- At 6 weeks follow-up, there was no statistically significant difference in complete, partial, and no hearing recovery between early and late HBOT treatment groups.

ES 3.3.5 Alternative HBOT Protocols EQ1a

We identified 1 NRSI comparing the effectiveness of HBOT treatment protocols in 35 patients treated at an undersea medical center in Japan.[29]

- At 3 weeks posttreatment, there was no significant difference in mean PTA recovery between groups receiving alternative protocols (37.9% vs. 41.7%; p=0.738).

ES 4. Discussion

ES 4.1 Summary of the Evidence

ES 4.1.1 Idiopathic SSNHL

We identified 10 RCTs evaluating HBOT for idiopathic SSNHL.[18-27] The strongest evidence comes from studies comparing HBOT plus steroids to steroids alone. Moderate COE indicates that participants who received HBOT with steroids were 39% more likely to achieve complete or partial hearing recovery (pooled RR, 1.39; 95% CI, 1.03 to 1.86; 5 RCTs; 294 participants; I^2=44.9%) and 41% less likely to experience no recovery compared with those treated with steroids (pooled RR: 0.59; 95% CI, 0.42 to 0.83; 5 RCTs; 294 participants; I^2=0%).[20-22,24,26] Moderate COE from 1 RCT indicated WDS, which reflects functional hearing ability, showed greater improvement with HBOT plus steroids.[22] Safety data from 4 RCTs including 281 participants found no major complications and rare minor adverse events (primarily mild ear pain), with no significant differences in AEs between HBOT plus steroids versus steroids alone (pooled RR 0.36; 95% CI, 0.07 to 1.94; I^2=0.0%).[19,21,22,24] Evidence that HBOT with steroids favors hearing recovery and mean improvement is consistent with recent systematic reviews.[33] Evidence was limited for other comparisons. Findings from a single RCTs comparing HBOT without steroids to steroids alone favored HBOT. Findings from a single RCT comparing HBOT and intratympanic salvage therapy found no difference between groups for hearing improvement. Evidence on differential effectiveness was also very limited. Due to a limited number of studies, small sample sizes for subgroup analyses, a lack of reporting regarding whether these analyses were preplanned, and RoB concerns, it is not possible to reach meaningful conclusions about the differential effectiveness of HBOT based on this evidence. Across RCTs, AEs were rare and minor. This is consistent with systematic reviews on HBOT for other indications that have also found few AEs associated with HBOT.[34-36] These findings are summarized in ***Table ES-2.***

Table ES-2. Summary of Findings and COE for HBOT for Idiopathic SSNHL

Outcome	Studies (N)	Effect	Certainty of Evidence	Direction of Effect
HBOT with steroids vs. steroids only				
Complete/partial hearing recovery	5 RCTs.[20-22,24,26] (294)	Pooled RR 1.39 (95% CI, 1.03 to 1.86)	●●●○	Favors HBOT
No hearing recovery	5 RCTs[20-22,24,26] (294)	Pooled RR 0.59 (95% CI, 0.42 to 0.83)	●●●○	Favors HBOT
Hearing improvement	4 RCTs[19,22,24,27] (332)	Mixed findings	●○○○	Favors HBOT
Word discrimination (% correct)	1 RCT[22] (60)	9.2% point larger improvement with HBOT (95% CI, 0.52% to 17.9%)	●●●○	Favors HBOT
Safety (AEs)	4 RCTs.[19,21,22,24] (281)	Pooled RR 0.36 (95% CI, 0.07 to 1.94)	●●○○	No effect
HBOT alone vs. steroids alone				
Hearing improvement	1 RCT[19] (115)	Favors HBOT (p<0.05)	●●○○	Favors HBOT
Salvage HBOT vs. intratympanic steroids, both after failed intravenous steroids				
Hearing improvement	1 RCT[23] (50)	Difference of 5 dB at 2,000 Hz (P<0.05), difference of −3.0 to 4.8 at other frequencies (P=NS)	●●○○	No effect
Safety (AEs)	1 RCT[23] (50)	12% vs. 20%; P=NS	●○○○	No effect

COE ratings: ●●●● High, ●●●○ Moderate, ●●○○ Low, ●○○○ Very Low

Abbreviations: AE = adverse event; COE = certainty of evidence; HBOT = hyperbaric oxygen therapy; NS = not significant; RCT = randomized controlled trial.

ES 4.1.2 AAT

We identified 7 studies reporting on the use of HBOT for the treatment of SSNHL resulting from AAT.[3,4,28-32] Low to very low COE across all reported outcomes limits our ability to draw meaningful conclusions. The largest body of evidence included 3 studies, all of which favored HBOT plus steroids versus steroids only for hearing improvement outcomes.[3,28,32] Low COE for this body of research found a statistically significant greater improvement in absolute mean hearing improvement as measured by PTA in dB from pretreatment to posttreatment, ranging from 15.2 to 23.5 dB among participants receiving HBOT plus steroids versus 5.6 to 12.5 dB among those receiving steroids alone.[3,28,32] We have little confidence in a body of evidence consisting of two studies, graded mostly as very low COE, which favored HBOT versus control or usual care for hearing recovery and improvement in tinnitus symptoms.[4,30] In addition, very low COE from single bodies of evidence provide little insight into the optimal timing (early vs. late), frequency, dose, and duration of HBOT to treat AAT.[3,29,31] Additionally, we did not identify any studies reporting on the differential effectiveness of HBOT for treating AAT by age, sex, race or ethnicity, disability, comorbidities, or severity of hearing loss, and we did not identify any studies for the CQ. Low RoB RCTs and larger well-controlled prospective cohort studies with clearly defined clinical hearing recovery outcomes are needed. It is unclear whether the body of evidence for the effectiveness of HBOT to treat idiopathic SSNHL is relevant to the treatment of AAT. Findings and COE are summarized in ***Table ES-3***.

Table ES-3. Summary of Findings and COE for HBOT for AAT

Outcome	Studies (N)	Effect	Certainty of Evidence	Direction of Effect
HBOT + steroids vs. steroids alone				
Mean hearing improvement	3 NRSIs[3,28,32] /224	Significant improvement favoring HBOT plus steroids in all 3 NRSIs	●●○○	Favors HBOT
Mean residual hearing loss	1 NRSI[28] /68	HBOT with steroids (early: 2.4 dB; SD 10.7 and late: 5.0 dB; SD 8.0) significantly better than steroids (14.7 dB; SD 8.3) (p<0.05 for any HBOT vs. steroids only)	●●○○	Favors HBOT
Tinnitus	1 NRSI[32] /78	No significant difference between groups	●○○○	No effect
Safety (AEs)	2 NRSIs[3,32] /119	1 NRSI reported no AEs and 1 NRSI reported no serious AEs from HBOT[32]	●○○○	No effect
HBOT vs. control/usual care				
Proportion with hearing recovery vs. usual care	1 RCT[30] /120	HBOT + infusion vs. infusion only: 83% vs. 87% HBOT + infusion +anti-vertigo medication vs. infusion + anti-vertigo medication: 92% vs. 62% p=0.001 across the 4 study groups; no between-group values reported	●○○○	Favors HBOT
Proportion with hearing recovery vs. NBOT	1 NRSI[4] /118	HBOT vs. NBOT: 74.1% (19.9) vs. 60.2% (28.9); p=0.024	●○○○	Favors HBOT
Tinnitus	1 NRSI[4] /118	Less self-reported tinnitus among patients receiving HBOT vs. NBOT (5% vs. 18%); p<0.05	●○○○	Favors HBOT

Outcome	Studies (N)	Effect	Certainty of Evidence	Direction of Effect
Safety (AEs)	1 RCT[30] /120	N (%) AEs HBOT + infusion vs. infusion only: 1 (3.0) vs. 0 (0) HBOT + infusion +anti-vertigo medication vs. infusion + anti-vertigo medication: 1 (3) vs. 0 (0)	●○○○	No effect

COE ratings: ●●●● High, ●●●○ Moderate, ●●○○ Low, ●○○○ Very Low

Abbreviations: AAT = acute acoustic trauma; AE = adverse event; COE = certainty of evidence; HBOT = hyperbaric oxygen therapy; NBOT = normobaric oxygen therapy; NR = not reported; NRSI = nonrandomized study of intervention; RCT = randomized controlled trial.

ES 4.2 Limitations of the Evidence Base

The evidence base for HBOT in treating idiopathic SSNHL has several important limitations. Studies were generally small, with sample sizes ranging from 50[23] to 171[19] participants, limiting statistical power and precision of effect estimates. None of the identified trials were conducted in the United States, potentially affecting generalizability to U.S. health care settings. The specific steroid treatments used as cointerventions or comparators varied, as did the timing of HBOT treatment after onset of symptoms. Definitions of hearing recovery varied across studies, making it difficult to directly compare outcomes, some studies defined recovery based on PTA, while others used different frequency combinations or categorical definitions of hearing improvement. Importantly, studies did not define what degree of hearing recovery was clinically meaningful. Several studies had methodological limitations leading to RoB concerns, with only 3[21,22,24] of 10 trials assessed as low RoB. The reporting of safety outcomes was limited and inconsistent across studies, with 4[18,20,26,27] of 10 trials not reporting any safety information. Follow-up periods varied widely, from 10 days[26] to 180 days posttreatment,[21] limiting understanding of long-term outcomes. Additionally, no studies examined cost-effectiveness, leaving a critical evidence gap. These limitations create some uncertainty about the optimal use of HBOT in SSNHL and its economic impact in clinical practice.

All of the limitations described above for idiopathic SSNHL hold true for the evidence base for AAT. In addition, the body of evidence for AAT is further limited by a paucity of methodologically rigorous studies. The evidence base for SSNHL resulting from AAT is limited to 1 high RoB RCT and 7 retrospectively conducted NRSIs assessed as serious or critical RoB, with sample sizes ranging from 35 to 118, follow-up ranging from 6.5 days to 1-year, and time to HBOT treatment ranging from 15 hours to 28 days.

ES 4.3 Clinical Practice Guidelines

We identified 4 organizations with treatment guidelines. The National Institute for Health and Care Excellence (NICE) made no mention of HBOT.[37] Both the American Academy of Otolaryngology - Head and Neck Surgery Foundation (AAO-HNSF) [1] and the European Committee for Hyperbaric Medicine (ECHM) [38] recommend HBOT as an option for the treatment of SSNHL when combined with medical therapy (e.g., steroid therapy) in patients who

present within 2 weeks of hearing loss and no later than 1 month of SSNHL onset. The Underseas and Hyperbaric Medical Society (UHMS) suggests HBOT should be considered for patients with moderate to profound idiopathic SSNHL (≥41 dB) who present within 14 days of symptom onset.[10] Additional details are reported in ***Table 23*** of the Full Report.

ES 4.4 Selected Payer Coverage Policies

Aetna, Cigna, Humana, Kaiser Permanente, Premera Blue Cross, Regence Blue Shield, and United Healthcare consider HBOT medically necessary for SSNHL and cover it under specified conditions (***Table ES-4***).[39-45] We did not identify a Centers for Medicare & Medicaid National Coverage Determination for HBOT that was specific to the SSNHL indication. TRICARE does not include SSNHL in the list indications that are covered or not covered for HBOT.[46,47]

Table ES-4. Overview of Payer Coverage Policies for HBOT for SSNHL

Medicare [46]	Aetna [39]	Cigna[40]	Humana [41]	Kaiser Permanente [42]	Premera Blue Cross[43]	Regence Blue Shield [44]	TRICARE [47]	United-Healthcare[45]
—	✓[a]	✓[a]	✓[a]	✓[a]	✓[a]	✓[a]	—	✓[a]

Notes: ✓ = covered; ✗ = not covered; — = no policy identified.
[a] Covered with conditions (see Table 8 in the Full Report).

Abbreviations: HBOT = hyperbaric oxygen therapy; SSNHL = sudden sensorineural hearing loss.

ES 4.5 Limitations of This HTA

This HTA was limited to peer-reviewed articles published in English. Studies conducted in countries other than *very high* on the United Nations Human Development Index were also excluded from this review as those settings may have health care infrastructure and standards of medical practice that are not applicable to U.S. settings. For idiopathic SSNHL, we did not include NRSIs, which increases the quality of evidence and our ability to draw causal inferences but may present a less comprehensive summary of all evidence.

ES 4.6 Ongoing and Future Research

We searched ClinicalTrials.gov on November 12, 2024, with terms related to hearing and HBOT and retrieved 14 trials. We identified 2 studies that are potentially relevant to this HTA. One is a prospective cohort study in South Korea that is actively recruiting participants with any SSNHL who receive HBOT in conjunction with other treatments including steroids, vasodilators, or antiviral agents.[48] The other potentially relevant study is specific to AAT in a military population. Despite a target completion date of December 2020, the status of this trial is listed as unknown in ClinicalTrials.gov, and we did not identify any results or publications associated with this trial registry.[49]

ES 5. Conclusion

There is moderate COE that HBOT plus steroid treatment within 14 days of symptom onset increased likelihood of complete or partial hearing recovery and reduced the risk of no hearing recovery compared with steroid treatment alone for idiopathic SSNHL. Evidence for HBOT

alone, salvage therapy, and optimal HBOT protocols was very limited. Adverse events were rare in included RCTs and the broader literature supports the general safety of HBOT. We identified no studies that examined cost-effectiveness, leaving a meaningful evidence gap. These findings suggest HBOT may provide meaningful additional benefit when combined with steroid therapy for idiopathic SSNHL, particularly for those who can begin treatment promptly. Low to very low COE across all reported outcomes limits our ability to draw meaningful conclusions regarding the effectiveness of HBOT to treat SSNHL resulting from AAT. It is unclear whether the body of evidence for the effectiveness of HBOT to treat idiopathic SSNHL is relevant to the treatment of AAT.

Full Technical Report

1. Background

1.1 Condition Description

Sudden sensorineural hearing loss (SSNHL) is the rapid loss of hearing with onset over a period of less than 72 hours.[1] It involves a decrease in hearing of ≥ 30 decibels (dB) affecting at least 3 consecutive frequencies.[1] More than 90% of cases are idiopathic.[1] SSNHL is accompanied by tinnitus in nearly all cases and vertigo in 30% to 60% of cases.[1] The rationale for the treatment of SSNHL with hyperbaric oxygen therapy (HBOT) is that the hearing loss may be caused by a hypoxic event; therefore, HBOT may reverse the oxygen deficit.[1] Notably, 32% to 62% of cases of SSNHL recover spontaneously, which complicates treatment evaluation for this condition.[1]

Acute acoustic trauma (AAT) is a less common cause of SSNHL. In AAT, exposure to a short-impact, acoustic impulse with an intensity of 90 to 130 dB for a duration of 1 millisecond or longer causes the cochlea to become mechanically damaged with resulting microcirculation vasospasm and hypoxia to the cochlear sensory cells.[2] Symptoms include high-frequency sensorineural hearing loss (4,000 Hz and higher) and tinnitus. Exposure to HBOT after AAT could provide increased oxygen to the cochlear apparatus, promoting healing. Thus, the rationale for HBOT for AAT is similar to the rational for idiopathic SSNHL.[2-4] AAT is primarily seen in military or law enforcement personnel, who are exposed to impulse noises from firearms.[2-4]

Pure-tone average (PTA) is the measurement of an individual's hearing sensitivity for calibrated pure tones calculated from a pure-tone audiometry test. PTA results are plotted on a graph called an audiogram, with sound frequency appearing on the horizontal axis and sound intensity appearing on the vertical axis. Data from the right and left ears are plotted separately. PTA is calculated based on averaging thresholds at various frequencies typical for normal conversation, most often 500 Hz, 1,000 Hz, 2,000 Hz, and 4,000 Hz.[5,6] ***Table 1*** shows commonly used classification system for hearing loss, which includes the degree of hearing loss based on PTA. For example, an individual with a PTA of 30 dB will have difficulty understanding whispering; some words involving "p", "h", and "g"; and the sound of birds chirping. An individual with a PTA of 80 dB will find it difficult to hear a dog barking or a baby crying and will find normal conversation very challenging without hearing assistance.[7]

Table 1. American Speech-Language-Hearing Association Hearing Loss Categories[8]

Degree of Hearing Loss	PTA Range (in dB)
Normal	–10 to 15
Slight	16 to 25
Mild	26 to 40
Moderate	41 to 55
Moderately severe	56 to 70
Severe	71 to 90
Profound	91+

Abbreviations: dB = decibels in hearing level.

1.2 Technology Description

HBOT involves the therapeutic administration of 100% oxygen at environmental pressures >1 atmosphere absolute (ATA), which corresponds to the atmospheric pressure at sea level. Administering oxygen at pressures greater than 1 ATA requires environmental compression. This is achieved by placing the patient in an airtight chamber and slowly increasing the environmental pressure while administering 100% oxygen. This results in increased oxygen delivery to the lungs, blood, and other body tissues. There are 2 types of chambers used for administering HBOT: a monoplace chamber for a single patient and a multiplace chamber used for multiple patients and medical personnel. A standard protocol for administering HBOT for SSNHL does not exist.[9]

1.3 Rationale for Use of HBOT for SSNHL

Vascular compromise, and associated cochlear ischemia, is a potential etiology of idiopathic SSNHL and sudden hearing loss resulting from AAT. The cochlea and the structures within it require a high oxygen supply, but the direct vascular supply is minimal. The increased partial pressure of oxygen from HBOT allows for delivery of more oxygen to the cochlea, which is exquisitely sensitive to ischemia. HBOT may reverse the oxygen deficit, increase oxygen pressures in the cochlea, and improve microcirculation, which may result in hearing improvement.[1,10]

1.4 Regulatory Status

The U.S. Food and Drug Administration (FDA) regulates both the oxygen used in HBOT and the hyperbaric chambers. As of July 2021, the FDA cleared hyperbaric chambers for use in treating hearing loss (complete hearing loss that occurs suddenly and without any known cause).[9]

1.5 Policy Context

A health technology assessment (HTA) of HBOT that included SSNHL, along with several other indications, was published in 2013 for the State of Washington's Health Technology Assessment Program.[11] This HTA found low certainty evidence (COE) that was inconclusive as to whether there is a benefit of HBOT based on mixed results from 8 RCTs of treatment in the acute phase, defined as treatment starting within 2 weeks of onset of hearing loss. With respect to treatment after 2 weeks of symptom onset (also known as the chronic phase), there was moderate COE from 2 randomized controlled trials (RCTs) suggesting no benefit of HBOT.[11] The State of Washington's Health Technology Clinical Committee voted not to cover HBOT for SSNHL in the acute or chronic phase.[12] The State of Washington Health Care Authority (HCA) selected HBOT for idiopathic SSNHL or AAT for an HTA because of medium concerns for safety and high concerns for efficacy and cost. The HCA also cited new evidence for sensorineural hearing loss that could change the previous determination.[13]

2. Methods

This section describes the methods we used to conduct this HTA, in accordance with the PRISMA 2020 statement on reporting systematic reviews.[50]

2.1 Research Questions and Analytic Framework

Efficacy Question 1 (EQ1). Is HBOT effective in improving patient-centered outcomes for individuals with SSNHL?

Efficacy Question 1a (EQ1a). What is the optimal frequency, dose, and duration of HBOT treatment for SSNHL?

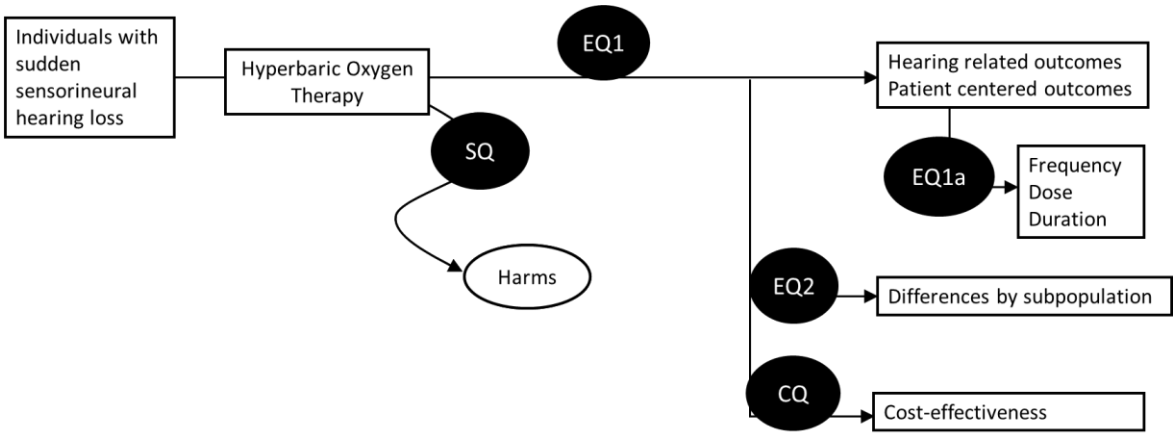
Efficacy Question 2 (EQ2). What is the differential effectiveness of HBOT according to factors such as age, sex, race or ethnicity, disability, comorbidities, treatment setting, hearing loss duration, severity, or type of hearing loss (e.g., idiopathic vs. noise-induced or acute vs. chronic)?

Safety Question (SQ). What are the harms associated with HBOT for SSNHL?

Cost Question (CQ). What is the cost-effectiveness of HBOT for SSNHL?

Figure 1 depicts the analytic framework of the proposed HTA.

Figure 1. Analytic Framework Depicting Scope of This Health Technology Assessment



Abbreviations: CQ = cost question; EQ = efficacy question; SQ = safety question.

Studies investigating idiopathic SSNHL and AAT were analyzed separately. The State of Washington HTA Program posted a draft of these research questions and proposed scope for public comment from August 29 to September 12, 2024. The final research questions and response to public comments on the draft research questions were published on the Program's website on September 25, 2024.[51,52]

2.2 Data Sources and Searches

We searched PubMed and the Cochrane Database of Systematic Reviews on July 17, 2024, and July 12, 2024, respectively, using Medical Subject Headings (MeSH) and text words in the title and abstract for terms related to HBOT. We limited the search to English-language studies in humans. The detailed search strategy is presented in ***Appendix A***. In addition, we searched the ClinicalTrials.gov registry on July 12, 2024, for completed or ongoing studies of HBOT for hearing loss.

2.3 Study Selection

Table 2 provides the study selection criteria we used for this HTA, which is organized by population, intervention, comparator, outcomes, timing, setting, and study design (PICOTS). Two review team members independently screened titles, abstracts, and full-text articles based on these study selection criteria using DistillerSR version 2.35 (DistillerSR, Inc.). Discrepancies in study selection at the full-text level were adjudicated by a senior investigator or, in some cases, by consensus among the team. We used DistillerSR's Artificial Intelligence (AI) rank feature to prioritize citations for review.

Table 2. Population, Intervention, Comparator, Outcome, Timing, and Setting for Review

Domain	Included	Excluded
Population	• Adults or children with sudden idiopathic or noise-induced acute or chronic SSNHL • Acute acoustic trauma with SSNHL	Adults or children with other forms of hearing loss
Intervention	Hyperbaric oxygen treatment, delivered via a hyperbaric oxygen chamber, with or without steroid therapy or other medical management	Other interventions
Comparator	No treatment, other treatments, or sham HBOT treatments **EQ1a.** Varying HBOT protocols	No comparator group
Outcomes	**EQ1 and EQ1a**. Patient-centered outcomes: • Hearing recovery (categorical measures) • Hearing improvement (continuous measured based on PTA) • Return of hearing (>25%, >50%, complete) • Tinnitus • Speech discrimination score • Depression • Functional status • Quality of life • Return to school or work **EQ2**. Differential effectiveness or safety by factors such as: • Age • Sex • Race or ethnicity • Disability • Comorbidities	• Inflammatory markers, such as neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) • Oxidative stress markers • Cost-effectiveness or cost-utility measures based on non-U.S.-based costs

Domain	Included	Excluded
	• Severity of hearing loss • Etiology (idiopathic vs. acute trauma) • Treatment setting **SQ.** Harms: • Barotrauma • Temporary visual disturbances • Oxygen toxicity • Other adverse events **CQ** • Cost-effectiveness; cost-utility	
Setting	Any clinical setting in countries categorized as *very high*[a] on the 2022 UN Human Development Index[53]	Countries categorized as other than *very high*[a] on the 2022 UN Human Development Index[53]
Study design	**EQ1, EQ1a, EQ2, SQ** Idiopathic SSNHL • RCT AAT • RCT; controlled clinical trial; comparative cohort studies **CQ** • Cost-utility analysis or cost-effectiveness analysis performed from societal or payor perspective	• Editorials, commentaries, narrative reviews, letters, conference abstracts, case reports or case series • Pre-post studies, case-control studies, noncomparative observational study designs, nonrandomized studies of interventions • Qualitative studies • Relevant systematic reviews and meta-analyses will be excluded but may be manually searched to identify potentially eligible studies
Language and time period	• English • No restrictions on publication date	• Any language other than English

[a] Countries identified as *very high* on the 2022 UN Human Development Index: Andorra, Antigua and Barbuda, Argentina, Australia , Austria, Bahamas, Bahrain, Barbados, Belarus, Belgium, Brunei Darussalam, Canada, Chile, Costa Rica, Croatia, Cyprus, Czechia, Denmark, Estonia, Finland, France, Georgia, Germany, Greece, Hong Kong, China (SAR), Hungary, Iceland, Ireland, Israel, Italy, Japan, Kazakhstan, Korea (Republic of), Kuwait, Latvia, Liechtenstein, Lithuania, Luxembourg, Malaysia, Malta, Montenegro, Netherlands, New Zealand, Norway, Oman, Panama, Poland, Portugal, Qatar, Romania, Russian Federation, Saint Kitts and Nevis, San Marino, Saudi Arabia, Serbia, Seychelles, Singapore, Slovakia, Slovenia, Spain, Sweden, Switzerland, Thailand, Trinidad and Tobago, Türkiye, United Arab Emirates, United Kingdom, United States, Uruguay.[53]

Abbreviations: AAT = acute acoustic trauma; CQ = cost question; EQ = efficacy question, HBOT = hyperbaric oxygen therapy; SQ = safety question; SSNHL = sudden sensorineural hearing loss; PTA = pure-tone average; RCT = randomized controlled trial; UN=United Nations; U.S. = United States.

2.3.1 Population

We selected studies that analyzed children, adults, or both who were diagnosed with sudden idiopathic or noise-induced acute or chronic SSNHL or AAT with SSNHL.

2.3.2 Intervention and Comparator

We selected studies that reported on HBOT delivered via a hyperbaric oxygen chamber, either with or without steroid therapy or other medical management. Eligible comparators included no treatment, other treatments, or sham HBOT treatments. This could include steroid treatments, control or usual care other than steroids, and for EQ1a, different HBOT treatments.

2.3.3 Outcomes

For EQ1 and EQ1a, we selected studies that reported patient-centered outcomes such as categorical hearing improvement, hearing recovery based on continuous measures of hearing like PTA, tinnitus, speech discrimination score, depression, functional status, quality of life, and return to school or work. For EQ2, we included studies that reported differential effectiveness or safety by factors such as age, sex, race or ethnicity, disability, comorbidities, severity of hearing loss, etiology (idiopathic vs. acute trauma), and treatment setting. For the SQ, we included studies that reported any clinical utility or health outcome or other findings that suggest harm. This included but was not limited to barotrauma, temporary visual disturbances, oxygen toxicity, and other adverse events. For the CQ, we included studies that reported measures of cost-effectiveness or cost-utility.

2.3.4 Settings

We included studies conducted in any clinical setting in countries designated as *very high* on the 2022 United Nations Human Development Index.[54] The rationale for this limit was to focus on evidence from countries with the most similar standards of medical practice as the United States.

2.3.5 Study Design

For idiopathic SSNHL, we included RCTs; for AAT indication specifically, we also included nonrandomized studies of interventions (NSRIs) where a clear comparison between 2 or more treatment strategies could be identified. For the CQ, we included cost-utility analysis and cost-effectiveness analysis performed from a societal or payor perspective.

2.3.6 Language and Time Period

We selected studies published in English. There were no restrictions on publication date.

2.3.7 What Is Excluded from This HTA

This HTA did not include studies conducted among healthy individuals or individuals with conductive hearing loss, or any kind of hearing loss other than idiopathic SSNHL or AAT. We excluded studies that did not include a comparator or studies in which we could not isolate the impact of HBOT (e.g., HBOT with steroid treatment compared with HBOT alone was not included). We did not include intermediate outcomes such as inflammatory markers or oxidative stress markers. For idiopathic SSNHL, we excluded comparative cohort studies for EQ1, EQ1a, EQ2, and SQ. We excluded pre-post studies, case-control studies, noncomparative observational study designs, and qualitative studies since we believed a sufficient volume of trials for idiopathic SSNHL and comparative cohorts for AAT were available, which provided a more methodologically rigorous evidence base for informing coverage decisions. Relevant systematic reviews and meta-analyses were excluded but were manually searched to identify potentially eligible studies. For the CQ, we excluded any non-U.S.-based cost studies.

2.4 Data Abstraction and Risk-of-Bias Assessment

One team member extracted relevant study data into a structured abstraction form in DistillerSR, and another investigator checked those data for accuracy. Two team members conducted independent risk-of-bias assessments on all included studies; discrepancies were resolved by

discussion or a third reviewer. To assess risk of bias (RoB), we used the Cochrane Risk of Bias 2 tool for randomized trials[14] and the ROBINS-I instrument for NRSIs.[15] We did not exclude studies based on their RoB rating. We assessed the most relevant clinical practice guidelines using Appraisal of Guidelines for Research & Evaluation II (AGREE II) instrument.[16]

2.5 Data Synthesis and Strength-of-Evidence Rating

We qualitatively synthesized study characteristics and results for each research question in tabular and narrative formats. We used R Studio (version 2023.06.0, Build 421) to calculate absolute mean differences and 95% CIs between groups when not explicitly reported by study authors.[55] If 3 or more studies reported similar outcomes, we conducted meta-analyses. For meta-analyses, we used random effects models using the inverse variance method of DerSimonian and Laird to generate pooled effects.[56] We used a manual continuity correction for outcomes with few or rare events. Statistical significance was assumed when 95% CIs of pooled results did not include the null effect (i.e., 1.0 for RRs) and all testing was two-sided. For all quantitative syntheses, the I^2 statistic was calculated to assess statistical heterogeneity in effects between studies.[57,58] An I^2 from 0% to 40% might not be important, 30% to 60% may represent moderate heterogeneity, 50% to 90% may represent substantial heterogeneity, and 75% or greater represents considerable heterogeneity.[57,58] Stata version (release 17, StataCorp) was used to conduct all pooled analyses.[59]

We used the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach for assessing the certainty of evidence.[17] COE can be graded as *very low*, *low*, *moderate*, or *high* and reflects our confidence in the findings based on concerns related to study limitations (i.e., RoB), consistency, precision, directness, and reporting bias. When CIs were either not provided or we could not exclude a meaningful difference within the range of the CI, we downgraded for imprecision.

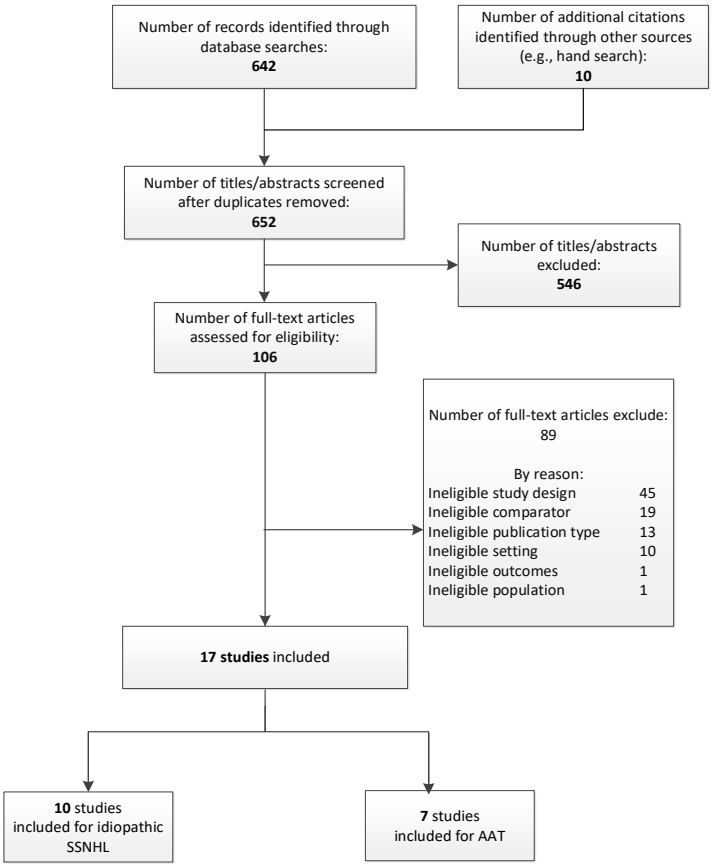
3. Results

3.1 Literature Search Yield

Figure 2 depicts the study flow diagram. We identified and screened 652 unique citations and included 17 studies published between 1985 and 2023. Among the included studies, 10 assessed HBOT for the treatment of idiopathic SSNHL[18-27] and 7 studies assessed HBOT for the treatment of AAT.[3,4,28-32] Individual study-level design, population, and intervention characteristics and findings for all included studies are summarized in ***Appendix B***. The list of articles we screened at the full-text stage, but which we excluded, is provided in ***Appendix C***. Note that articles may have been excluded for more than 1 reason, but we report only 1 reason. Among 11 RCTs, we assessed 3 studies as low RoB;[21,22,24] 6 studies as some RoB,[18-20,23,25,26] and the rest as high RoB.[27,30] Among NRSIs, we assessed 2 studies as serious RoB[3,28] and 3 studies as having critical RoB.[29,31,32] We assessed 1 NRSI as serious RoB for the outcome of tinnitus due to poor control for important confounding variables, and rated as critical RoB for the outcome of hearing improvement due to poor control for confounding and the exclusion of some participants from analysis.[4]

We report our individual study RoB assessments in ***Appendix D***.

Figure 2. Study Flow Diagram for HTA on HBOT for Hearing Loss



Abbreviations: AAT = acute acoustic trauma; HBOT = hyperbaric oxygen therapy; HTA, health technology assessment; SSNHL = sudden sensorineural hearing loss.

3.2 Idiopathic SSNHL

3.2.1 Study and Population Characteristics for Idiopathic SSNHL

We identified 10 RCTs published between 2004 and 2023 reporting on the use of HBOT for the treatment of idiopathic SSNHL.[18-27] Eight studies were included for EQ1,[21-25] 2 studies for EQ1a,[18-20,23,25,26,32] 5 studies for EQ2,[19,20,23,24,27] 6 studies for SQ,[19-24,26,27] and no studies for CQ. Key overall study and population characteristics are described in ***Table 3.***

Table 3. Study and Population Characteristics of Included Studies on Idiopathic SSNHL

Characteristic	Number of Studies
Country setting	European countries: 5[18,19,23,24,26] South Korea: 2[22,25] Turkey: 2[20,27] Taiwan: 1[21]
Study funding	Government: 1 [26]. None: 4[19,22,24,25] Not reported: 5[18,20,21,23,27]
Unilateral or bilateral hearing loss	Unilateral hearing loss only: 6[18,21,22,24-26] Unilateral or bilateral hearing loss permitted:3[19,20,27] NR: 1[23]
Comparisons	HBOT + steroids vs. steroids only: 6[21,22,24,26,27] HBOT protocol vs. alternative HBOT protocol: 2[18,25] HBOT + steroid vs. HBOT only vs. steroids only: 1[19] Salvage therapy after initial intravenous steroid treatment, HBOT vs. intratympanic steroids: 1[23]
Age of participants	Adults:8[18-22,24-26] Children and adults:2[23,27] (age range in these studies: 13 to 75 years)
Number analyzed	Median: 58.5; range: 50 to 171
Sex	% Female: Range 10 to 55 NR: 2[18,23]
Race or ethnicity	Not reported by any study
Required duration of hearing loss at baseline for study inclusion	<7 days: 2[24,26] <10 to 15 days: 4 [18,22,25,27] <28 or 30 days: 2 [19,23] No inclusion criteria specified: 2[20,21][a]
Mean baseline hearing loss	Range: 40.7 dB (mild to moderate hearing loss)[26] to 98.9 dB (profound hearing loss)[25]
Required severity of hearing loss at baseline for study inclusion	At least 30 dB (at least mild hearing loss or more): 3 [20,24,27] 41 to 60 dB (moderate to moderately severe): 1 RCT[26] >70 dB (severe to profound): 2 RCTs[22,25] Salvage therapy (<10 dB improvement after initial steroid treatment): 1 RCT[23] No related inclusion criteria: 3 RCTs[18,19,21][b]
RoB	Low: 3[21,22,24] Some concerns: 6[18-20,23,25,26] High: 1[27]

[a] In 1 RCT, 96% (53 of 55) participants began treatment within 3 days and the remaining 4% (2 of 56) within 10 days.[20] In the other RCT, mean symptom duration before treatment was 4.2 days in the HBOT + steroid group and 3.5 days in the steroid group.[21]

[b] Two RCTs reported baseline hearing of enrolled participants by study arm; this ranged from 55.9 dB to 92.0 dB,[18,19] and the third RCT did not report baseline hearing of enrolled participants.[21]

Abbreviations: HBOT = hyperbaric oxygen therapy; NR = not reported; RCT = randomized controlled trial; SSNHL = sudden sensorineural hearing loss.

3.2.2 HBOT with Steroids vs. Steroids Only

We identified 7 RCTs that compared the effectiveness of HBOT with steroid to steroid use.[19-22,24,26,27] We assessed 3 as low RoB,[21,22,24] 3 as some concerns,[19,20,26] and 1 as high RoB.[27]

3.2.2.1 HBOT with Steroids vs. Steroids Only: EQ1

Key findings include:

- Participants treated with HBOT plus steroids within 14 days of symptom onset were 39% more likely to achieve complete or partial hearing recovery compared with those treated with steroids (pooled RR: 1.39; 95% CI, 1.03 to 1.86; 5 RCTs; 294 participants; I^2=44.9%). (*Moderate* COE)

- Participants treated with HBOT plus steroids within 14 days of symptom onset were 41% less likely to experience no recovery compared with those treated with steroids (pooled RR: 0.59; 95% CI, 0.42 to 0.83; 5 RCTs; 294 participants; I^2=0%). (*Moderate* COE)

- There were mixed findings among 4 RCTs reporting mean or median hearing improvement as measured by PTA; 2 RCTs found no significant difference and 2 RCTs found a statistical difference between groups favoring HBOT with steroids. (*Very low* COE for greater effect with HBOT)

- One RCT found improvement in word discrimination scores (WDS), a measure of the proportion of words a person understand correctly, was significantly greater in the HBOT plus steroid group (mean [SD] % correct, 65.9 [14.1]) compared with the steroid only group (mean [SD] % correct, 56.7 [19.1]; *P*=0.035). (*Moderate* COE)

Study and Population Characteristics

Two studies were conducted in Turkey,[20,27] and 1 each in Italy,[19] Greece,[24] Slovakia,[26] South Korea,[22], and Taiwan.[21] Three did not report study funding,[20,21,27] 3 reported that they received no funding,[19,22,24] and 1 study reported government funding.[26] Sample sizes ranged from 50[24] to 111.[19] HBOT treatment occurred within 14 days of hearing loss onset in 6 of 7 studies. Mean symptom duration to HBOT treatment was not reported in 3 studies[19,26,27] and ranged from 3.5 [21] to 4.8 days[22] in 3 studies. In the remaining study, 96% (55 of 57) of participants started treatment within 3 days and the remaining 2 participants started treatment within 10 days.[20] Outcome measurement ranged from immediately after 10 days of treatment [26] to 180 days after treatment.[21]

HBOT regimens varied across studies but most often included 10, 90-minute sessions once a day for 10 days. Specifically, 5 studies included 10 HBOT sessions,[19-22,26] 1 included 15 sessions,[24] and 1 included 25 sessions.[27] Duration of each session ranged from 60 minutes[22] to 90 minutes.[19-21,26,27] Duration of HBOT treatment ranged from 5 days[21] to 20 days,[27] with 10 days being the most frequently reported duration.[20,22,26] All HBOT sessions were administered at 2.5 ATA, except for 2 studies that used 2.2 ATA[24] and 2.0 ATA.[26]

Steroid regimens varied across studies. Modes of steroid administration included oral, IV, and intratympanic (i.e., injected directly into the middle ear). Four studies included only steroids.[19,20,22,24] In the other studies, steroids were combined with hemorheological agents (drugs to reduce viscosity), plasma expanders, or anti-vertigo and anti-anxiety medication.

A summary of study characteristics is presented in ***Table 4***; detailed study characteristics are in ***Appendix B, Tables B-1 to B-3***.

Table 4. Summary of Study Characteristics Comparing HBOT with Steroids vs. Steroids Only

Author, Year Country RoB	Sample Size (N)	Mean Age (SD) N (%) Female Baseline Hearing Loss	Symptom duration prior to treatment Number and length HBOT sessions Steroid dose, administration, and duration
Cavaliere et al, 2022[19] Italy Some concerns	Total sample size: 111[a] HBOT + steroids: 56 Steroids: 55	Mean age (SD): HBOT + steroids: 44.1 (13.8) Steroids: 67.7 (9.4) N (%) Female: HBOT + steroids: 25 (45) Steroids: 26 (47) Mean (SD) initial PTA (dB) HBOT + steroids: 55.9 (23.9) Steroids: 66.3 (19.7)	Time to HBOT treatment: all <30 days HBOT sessions: 10 sessions, 1 per day, 90 minutes per session Steroids: 1 mg/kg prednisone per day (for a maximum dose of 60 mg per day), oral, 12-14 consecutive days
Cekin et al, 2009[20] Turkey Some concerns	Total sample size: 57 HBOT + steroids: 36 (38 ears) Steroids: 21 (21 ears)	Mean age (SD): HBOT + steroids: 46.8 (range: 18 to 82 years) Steroids: 44.5 (range: 20 to 75 years) N (%) Female: HBOT + steroids: 12 (33) Steroids: 8 (38) Mean (SD) initial PTA (dB) HBOT + steroids: 81.5 (NR) Steroids: 95.9 (NR)	Time to HBOT treatment, N (%) Within 3 days: 34 (94) 7 days: 1 (3) 10 days: 1 (3) HBOT sessions: 10 sessions, 1 per day for 90 minutes Steroids: 1 mg/kg prednisolone, oral, tapering over 3 weeks
Chi et al., 2018[21] Taiwan Low	Total sample size: 60 HBOT + steroids + other: 30 Steroids + other: 30	Mean age (SD): HBOT + steroids + other: 31.1 (12.6) Steroids + other: 29.5 (14.7) N (%) Female: HBOT + steroids + other: 3 (10) Steroids + other: 4 (13) Mean (SD) initial PTA (dB): NR	Mean (SD) time to HBOT treatment: 4.2 (2.2) days HBOT sessions: 10 sessions, 2 per day for 90 minutes Steroids and other drugs: 1 mg/kg per prednisolone, oral, tapering over 3 weeks with 400 mg pentoxifylline for 2 weeks and 500 mL IV dextran for 1 week
Cho et al., 2018[22] South Korea Low	Total sample size: 60 HBOT + steroids: 30 Steroids: 30	Mean age (SD): HBOT + steroids: 53.8 (13.1) Steroids: 56.1 (13.6) N (%) Female: HBOT + steroids: 13 (43) Steroids: 19 (63) Mean (SD) initial PTA (dB) HBOT + steroids: 89.3 (10.9) Steroids: 92.4 (14.8)	Mean (SD) time to HBOT treatment: 4.1 (3.7) days HBOT sessions: 10 sessions, 1 per day for 60 minutes Steroids: 0.8 mg/kg/day methylprednisolone, oral, tapering over 5 days; 4 mg/mL per day, dexamethasone, intratympanic, 7 days
Dova et al., 2022[24] Greece Low	Total sample size: 50 HBOT + steroids + other: 25 Steroids + other: 25	Median (IQR) HBOT + steroids: 48.0 (37.5 to 57.5) Steroids: 55.0 (49.5 to 60.0) N (%) Female: HBOT + steroids: 13 (52) Steroids: 9 (36)	Median (IQR) time to HBOT treatment: 4.0 (1.0 to 5.5) days HBOT sessions: 15 sessions, 2 periods of 40 minutes per session Steroids: 8 mg dexamethasone, IV, 9 days

Author, Year Country RoB	Sample Size (N)	Mean Age (SD) N (%) Female Baseline Hearing Loss	Symptom duration prior to treatment Number and length HBOT sessions Steroid dose, administration, and duration
		Median (IQR) initial PTA1 (dB) (average of threshold values at 0, 5, 1, 2, 4 kHz) HBOT + steroids: 75.0 (60.6 to 91.2) Steroids: 63.7 (51.9 to 79.4) Median (IQR) initial PTA2 (dB) (average of threshold values at 0, 5, 1, 2, 4 kHz) HBOT + steroids: 76.7 (60.8 to 91.7) Steroids: 69.2 (50.0 to 78.7)	
Krajcovicova et al., 2018 [26] Slovakia Some concerns	Total sample size: 67 HBOT + steroids + other: 47 Steroids + other: 20	Mean age (SD): Total: 50 (14) N (calculated %) Female: Total: 35 (51.5) Baseline hearing loss reported by frequency only	Time to HBOT treatment: all <7 days HBOT sessions: 10 sessions per day, for 90 minutes per session Steroids and other drugs: 250 mg Solu-Medrol, IV, tapering over 5 days; 500 mg prednisone, oral, tapering days 6 to 15; 100 mg x2 per day, Agapurin; 16 mg x3 per day, Betahistin
Topuz et al, 2004 [27] Turkey High	Total sample size: 51 HBOT + steroids +other: 30 (34 ears) Steroids +other: 21 (21 ears)	HBOT + steroids + other: 42.1 (13.4) Steroids + other: 40.4 (11.2) Age range: 13 to 75 years N (%) Female: HBOT + steroids + other: 16 (53) Steroids + other: 9 (43) Mean (SD) initial PTA (dB) HBOT + steroids + other: 70.4 (NR) Steroids + other: 70.5 (NR)	Time to HBOT treatment: all <14 days HBOT sessions: 25 sessions, 2 per day, 90 minutes per session Steroids and other drugs: 1 mg/kg per day, prednisone, oral, 2 weeks; 500 ml/d Rheomacrodex, infusion, 5 days; 200 mg x2 per day, pentoxiphyllin, IV, duration: NR

[a] This RCT also included a third arm, HBOT only (N=60), so the total sample size was 171 participants.

Abbreviations: IQR = interquartile range; HBOT = hyperbaric oxygen therapy; IV = intravenous; NR = not reported; PTA = pure-tone average.

Findings

Outcome measures included hearing recovery reported categorically as the proportions of participants with complete, partial, slight or no hearing recovery; hearing improvement reported as mean or median change in PTA; and WDS. RCTs varied in how categorical hearing recovery was reported and these definitions are summarized in ***Table 5.***

Table 5. Summary of Hearing Recovery Outcome Definitions

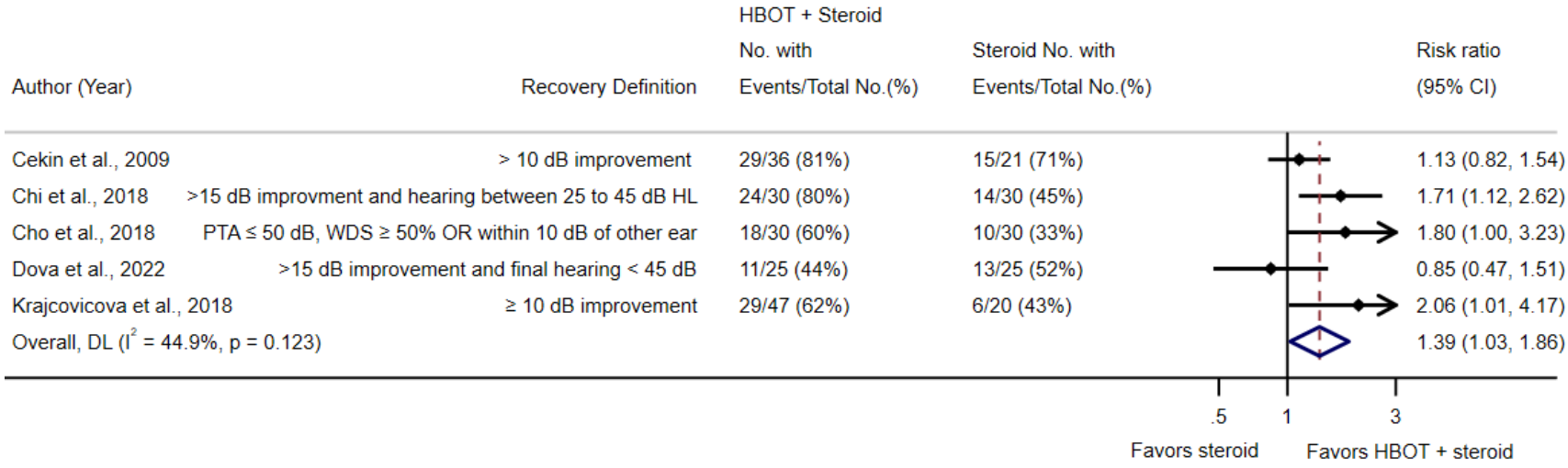
Complete Recovery	
1 RCT[20] (N=57)	>50 dB PTA improvement
2 RCTs[21,24] (total N=110)	>25 dB PTA improvement
1 RCT[22] (N=60)	Final PTA within 10 dB and WDS 5 to 10% of unaffected ear
Partial Recovery	
2 RCTs[20,26] (total N=124)	≥10 dB PTA improvement
2 RCTs[21,24] (total N=110)	>15 dB PTA improvement and final PTA <45 dB
1 RCT[22] (N=60)	Final PTA ≤50 dB and WDS ≥50%
No Recovery	
3 RCTs[20,22,26] (total N=184)	<10 dB PTA improvement
2 RCTs[21,24] (total N=110)	<15 dB PTA improvement and hearing poorer than 75 dB

Abbreviations: PTA = pure-tone average; RCT = randomized controlled trial; WDS = word discrimination scores.

Complete or partial hearing recovery: Five studies reported complete or partial hearing recovery categorically.[20,21,22,24,26] Most studies considered complete or partial recovery an indication of treatment success. Based on a pooled analysis, participants treated within 14 days of symptom onset with HBOT with steroids (plus or minus other drugs) were 39% more likely to achieve complete or partial recovery compared with those treated with steroids alone (pooled RR: 1.39; 95% CI, 1.03 to 1.86; 5 RCTs; 294 participants; I^2=44.9%; ***Figure 3*)**. This translates to an absolute risk difference of 180 more people per 1,000 (ranging from 14 more to 396 more) achieving complete or partial hearing recovery with HBOT compared with steroids alone (plus or minus other drugs). There was moderate heterogeneity in the meta-analysis. Sources of heterogeneity include differences in definitions of complete and partial recovery, hearing loss at baseline, and differences in treatment regimens. We also report results for complete recovery and partial recovery separately in ***Appendix E***.

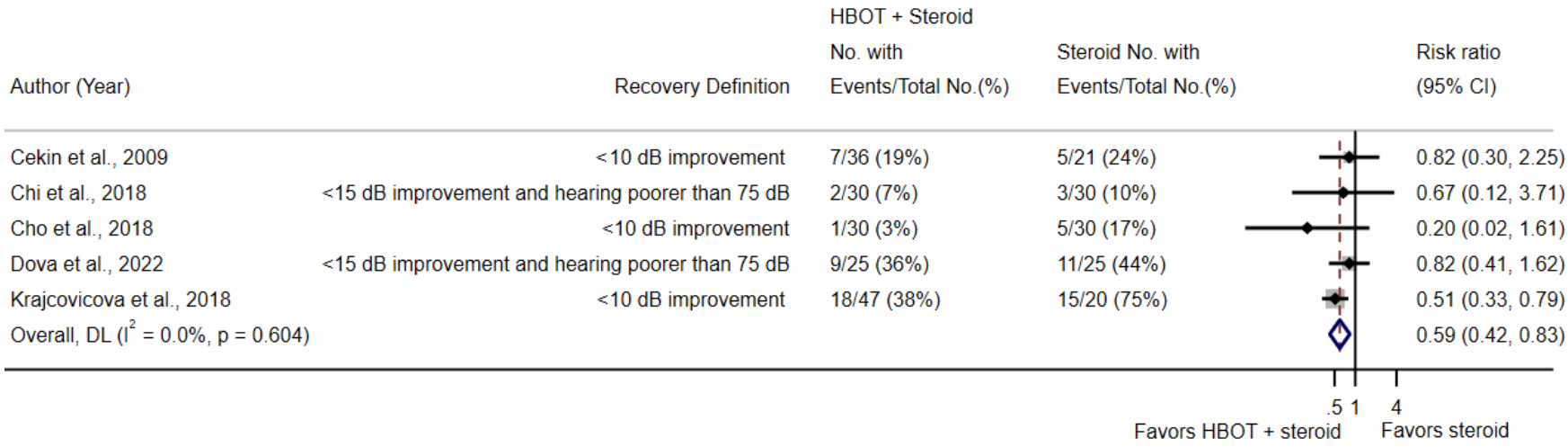
No hearing recovery: These 5 studies also reported the proportion of participants who experienced no recovery, defined in 3 studies as a hearing improvement of <10 dB[20,22,26] and in 2 studies as improvement of <15 dB with final hearing level poorer than 75 dB.[21,24] Participants treated within 14 days of symptom onset with HBOT plus steroids had a 41% lower likelihood of experiencing no recovery compared with those treated with steroids alone (pooled RR: 0.59; 95% CI, 0.42 to 0.83; 5 RCTs; 294 participants; I^2=0%, ***Figure 4***). This translates to an absolute risk difference of 127 fewer per 1,000 experiencing no recovery (ranging from 180 fewer to 53 fewer).

Figure 3. Effect of HBOT and Steroids vs. Steroids Only on Complete or Partial Recovery



Abbreviations: HBOT = hyperbaric oxygen therapy; PTA = pure-tone average.

Figure 4. Effect of HBOT and Steroids vs. Steroids Only on No Recovery



Abbreviation: HBOT = hyperbaric oxygen therapy.

Hearing improvement: Four studies reported hearing improvement.[19,22,24,27] as mean or median change in PTA from baseline. Findings were mixed with 2 RCTs[19,27] reporting statistically significant hearing improvement from HBOT with steroid use and 2 RCTs[22,24] reporting no significant difference between HBOT with steroid use compared with steroid use alone.

Of the 2 RCTs favoring HBOT with steroid use, Topuz et al. (high RoB) reported a significant difference favoring HBOT with steroids at 4 of 5 frequencies measured.[27] Statistical significance or information to calculate statistical significance was not reported for overall hearing levels, but mean hearing improvement was 33.3 dB in the HBOT with steroid group (mean PTA improved from 70.4 dB to 37.1 dB) and 17.4 in the steroid group (mean PTA improved from 70.5 dB to 53.1 dB) for a calculated mean difference of 15.9 dB favoring HBOT with steroids.[27] These data suggest hearing improved from a range considered as severe hearing loss to a range considered as mild hearing loss in the HBOT with steroid group and to a range considered as moderate hearing loss in the steroid use alone group. In the second RCT, Cavaliere et al. did not report baseline or follow-up hearing levels and only reported significant larger hearing improvement for HBOT plus steroid use compared with steroid use alone ($p<0.05$).[19]

In the 2 RCTs that reported no significant difference in hearing improvement between groups, there were significant improvements from baseline to follow-up within each group.[22,24] Cho et al. reported mean PTA with HBOT plus steroid use improved from 89.3 dB to 42.8 dB and from 92.4 dB to 54.7 dB in the steroid use alone group, resulting in a calculated mean difference of 8.8 dB, favoring HBOT plus steroids.[22] These mean PTA levels suggest that, on average, hearing improved from severe/profound hearing loss to moderate hearing loss in both groups. Dova et al. found no significant difference in median hearing improvement between HBOT plus steroid use (median improvement,17.5; interquartile range [IQR],7.5 to 33.7) compared with steroid use alone (median improvement, 22.5; IQR, 0.0 to 45.6).[24]

Word discrimination scores: WDS reflects the proportion of words a person understands correctly. Cho et al. found mean WDS at 3 months posttreatment were significantly greater in the HBOT with steroid group (mean [SD] % correct, 65.9 [14.1]) compared with the steroid only group (mean [SD] % correct, 56.7 [19.1]; $P=0.035$).[22]

A summary of findings and COE are provided in ***Table 6***.

Table 6. Summary of Findings and COE for HBOT with Steroids vs. Steroids Only

No. Studies/No. Participants	Summary of Effect	RoB	Consistency	Precision	Directness	Overall COE/ Direction
Complete or partial hearing recovery; follow-up time 10 days to 180 days						
5 RCTs[20-22,24,26]/ 294	Participants treated with HBOT plus steroids were 39% more likely to achieve complete or partial recovery compared with those treated with steroids (pooled RR: 1.39, 95% CI, 1.03 to 1.86; 294 participants; I^2=44.9%).	Not serious	Not serious[a]	Serious[b]	Not serious	Moderate for greater effect with HBOT plus steroids[a, b] ●●●○
No hearing recovery; follow-up time 10 days to 180 days						
5 RCTs[20-22,24,26]/ 294	Participants treated with HBOT plus steroids were 41% less likely to experience no recovery compared with those treated with steroids (pooled RR: 0.59; 95% CI, 0.42 to 0.83; 5 RCTs; 294 participants; I^2=0%).	Not serious	Not serious	Serious[c]	Not serious	Moderate for greater effect with HBOT plus steroids[c] ●●●○
Hearing Improvement (mean or median change in PTA); follow-up time 20 days to 3 months						
4 RCTs [19,22,24,27] /332	2 low RoB studies found improvements within both groups but no statistical difference in mean or median hearing improvement between groups, 2 studies (1 high RoB and 1 some concerns) found a statistical difference between groups favoring HBOT plus steroid use.	Serious[d]	Serious[e]	Serious[f]	Not serious	Very low for greater effect with HBOT plus steroids[d, e, f] ●○○○
Word discrimination scores (% correct); follow-up time 3 months						
1 RCT[22]/ 60	Improvement in WDS was significantly greater in the HBOT with steroid group (mean: 65.9% correct; SD: 14.1) compared with the steroid only group (mean: 56.7% correct; SD: 19.1; *P*=0.035; calculated AMD: 9.2%; 95% CI, 0.52% to 17.88%).	Not serious	Not applicable—single study	Serious[g]	Not serious	Moderate for greater effect with HBOT plus steroids ●●●○

COE ratings: ●●●● High, ●●●○ Moderate, ●●○○ Low, ●○○○ Very Low

[a] Moderate heterogeneity (I^2 = 49%), partially explainable because of variations in definitions of complete/partial recovery, baseline hearing levels, and treatment regimens.

[b] We are uncertain if the lower end of the pooled CI represents a clinically meaningful effect, downgraded for imprecision.

[c] We are uncertain if the upper end of the pooled CI represents a clinically meaningful effect; downgraded for imprecision.

[d] One RCT reported limited data to assess this outcome and 1 RCT rated as high RoB; downgraded 1 step for RoB.

[e] Differences in hearing improvement (as measured by change in PTA) among participants treated with HBOT with steroids compared with steroids alone ranged from −5.0 to 15.9 in the 3 studies providing data to assess the difference in magnitude among groups; the difference in the fourth study is presumed to be >0 based on data presented; downgraded 1 step for inconsistency.

[f] Three of 4 RCTs provided limited data to evaluate the precision of their estimates, 1 RCT reported an IQR for HBOT that ranged from a hearing improvement associated with little benefit (improvement of 7.5 dB), while the upper limited of 33.7 dB would be potentially meaningful improvement.[24]

[g] The calculated AMD is 9.2 (95% CI, 0.52 to 17.88). We did not identify estimates for a minimal clinically important difference for WDS, so assumed a 20% relative difference would be meaningful. The lower end of the CI represents no improvement, while the upper limit represents potentially meaningful improvement.[22]

Abbreviations: AMD = absolute mean deviation; COE = certainty of evidence; HBOT = hyperbaric oxygen therapy; IQR = interquartile range; PTA = pure-tone average; RCT = randomized controlled trial; WDS = word discrimination score.

3.2.2.2 HBOT with Steroids vs. Steroids Only: EQ2

Study and Population Characteristics

Among the 7 RCTs that compared HBOT with steroids with steroids alone, 3 RCTs reported differential effectiveness by severity of hearing loss at baseline,[19,24,27] 2 RCTs reported differential effectiveness of HBOT by age group,[20] and 1 RCT reported differential effectiveness of HBOT by sex.[19] Detailed information about the characteristics of these studies are described previously in ***Section 3.2.2*** and ***Table 4***.

Key findings include:

- One RCT found participants treated with HBOT plus steroids within 7 days of symptom onset had statistically significant hearing recovery; however, those treated after 7 days did not have statistically significant hearing recovery.
- One RCT found mean hearing improvements were significantly better among those with greater hearing loss at baseline; however, a second RCT found no difference by hearing loss at baseline, though this was based on very small sample sizes.
- One RCT found no difference in hearing recovery by age and another RCT found women, compared with men, had better hearing improvement with treatment.

Findings

Time to treatment: In a subgroup analysis from a single RCT, the authors reported that participants who received treatment within 7 days of symptom onset had statistically significant hearing recovery from HBOT with steroid use ($P<0.05$) but not with steroid use alone ($P=0.08$). Hearing recovery was not statistically significant for participants in either group who started treatment at 8 to 14 days after symptom onset or more than 14 days after symptom onset.[19]

Hearing loss severity at baseline: Dova et al., which reported no significant differences between HBOT plus steroids compared with steroids alone for hearing outcomes among a sample of 50 participants, also reported no significant differences in hearing recovery in any subpopulations defined by 5 categories of hearing loss at baseline.[24] However, the number of participants in each subgroup ranged from only 3 to 13, limiting our ability to draw definitive conclusions based on baseline hearing loss. Topuz et al. found that mean hearing improvement with HBOT plus steroids compared with steroids was larger for participants with more severe hearing loss at baseline compared with participants with less severe hearing loss.[27] In this study, which we assessed as high RoB, mean hearing improvements were significantly better in the HBOT plus steroid group compared with the steroid use alone group among those with greater hearing loss at baseline (initial hearing PTA 61 to 80 dB; calculated mean difference in improvement, 19.3; 95% CI, 3.8 to 34.8; P=0.014; initial PTA greater than or equal to 81 dB; calculated mean difference in improvement, 37.7; 95% CI, 21.2 to 54.2; $P=0.005$). The difference between HBOT plus steroid use and steroid use alone was not significantly different among those with less severe hearing loss at baseline (initial PTA less than 60 dB; calculated mean difference in improvement, 0.2; 95% CI, −11.0 to 11.4).[27]

Age: Cekin et al., 2009 found no significant differences in hearing recovery between participants aged younger than 50 years compared with those aged 50 years or older (P>0.05).[20]

Sex: Although hearing improvements were higher in both men and women with HBOT plus steroids compared with steroids alone, women had larger hearing improvements compared with men (P<0.05).[19]

3.2.2.3 HBOT with Steroids vs. Steroids Only: SQ

Study and Population Characteristics

Four studies comparing HBOT plus steroids with steroid use alone group reported on harms.[19,21,22,24] A summary of study characteristics is presented previously in ***Table 4***; a summary of findings and COE is presented in ***Table 7;*** detailed study characteristics are in ***Appendix B, Table B-6.***

Key findings include:

- There were no major complications reported in 4 RCTs that included 281 participants, and adverse events (AEs) were rare. A pooled analysis found no significant difference between treatment groups (pooled RR: 0.36, 95% CI, 0.07 to 1.94; I^2=0.0%) based on 4 AEs (all cases of mild ear pain) in HBOT plus steroid use groups and 0 AEs in steroid alone groups. (*Low* COE)

Findings

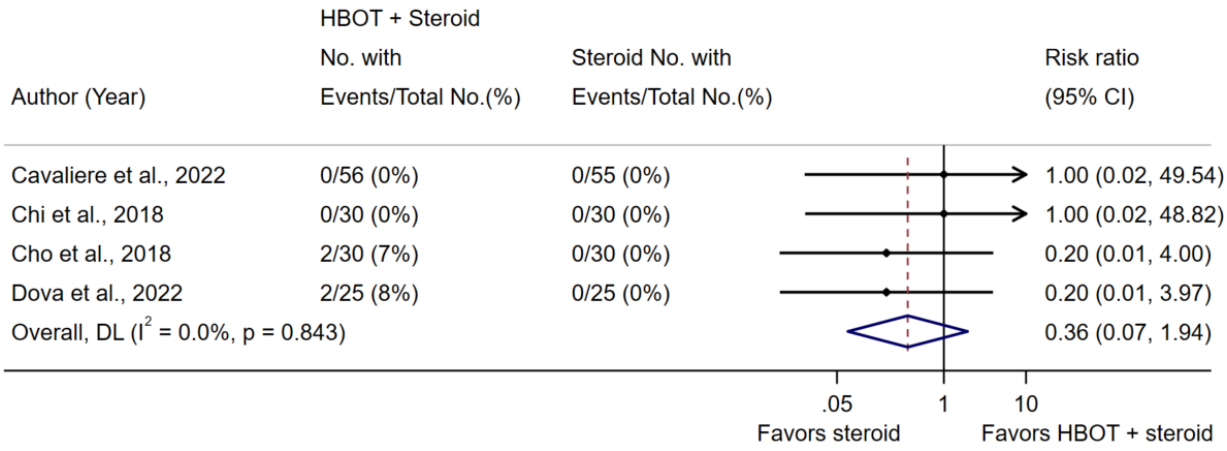
Four studies comparing HBOT plus steroids with steroids reported on harms.[19,21,22,24] Two studies reported no complications in either group.[19,21] Two studies reported a small number of AEs in the HBOT plus steroid groups and no AEs in the steroid alone groups. Specifically, Cho et al., 2018[22] reported that 2 participants had mild otalgia or mild ear pain during the beginning of HBOT. Dova et al., 2022 reported that 2 participants experienced transient ear pain, which was successfully treated with topical nasal decongestants and did not result in a barotrauma.[24] Based on a pooled analysis, there was no significant difference in the probability of experiencing an AE between those who received HBOT plus steroids compared with those who received steroids alone (pooled RR: 0.36; 95% CI, 0.07 to 1.94; 4 RCTs; 281 participants; I^2=0.0, **Figure 5**).

No studies reported outcomes related to differential safety.

3.2.2.4 HBOT with Steroids vs. Steroids Only: CQ

We found no studies reporting cost or cost-effectiveness of HBOT for idiopathic SSNHL.

Figure 5. Effect of HBOT and Steroids vs. Steroids Only on Any Adverse Event



Abbreviation: HBOT = hyperbaric oxygen therapy.

Table 7. Summary of Findings and COE for HBOT with Steroids vs Steroids Only for Any Adverse Events

No. Studies/No. Participants	Summary of Effect	RoB	Consistency	Precision	Directness	Overall COE/ Direction
HBOT + steroids vs steroids alone; follow-up time 20 days to 180 days						
4 RCTs[19,21,22,24] / 281	A pooled analysis found no significant difference between groups (RR: 0.36, 95% CI, 0.07 to 1.94). There were 4 AEs reported in HBOT plus steroid use groups (all mild ear pain) and 0 AEs reported in the steroid use alone groups.	Not serious	Not serious	Serious[a]	Serious[b]	Low for no effect [a, b] ●●○○

COE ratings: ●●●● High, ●●●○ Moderate, ●●○○ Low, ●○○○ Very Low

[a] Wide confidence intervals, the upper end of the pooled CI represents a large number of AEs, due to rare events and small sample sizes, downgraded 1 step for imprecision.

[b] Limited information reported regarding how adverse events were defined and monitored, downgraded 1 step for indirectness.

Abbreviations: AE = adverse event; COE = certainty of evidence; HBOT = hyperbaric oxygen therapy; RCT = randomized controlled trial.

3.2.3 HBOT Only vs. Steroids Only

We identified 1 RCT that compared HBOT alone with steroid use alone.[19] This study also included a third study arm (HBOT with steroids) that was discussed in the previous section. We assessed the RoB as some concerns.

3.2.3.1 HBOT Only vs. Steroids Only: EQ1

Key findings include:

- Significant improvement in hearing as measured by PTA from baseline to 20 days posttreatment in both the HBOT only group and steroid only group ($p<0.05$ for each within group difference); the HBOT only group obtained a greater improvement in hearing as measured by PTA compared with the steroid only group ($p<0.05$). (*Low* COE)

Study and Population Characteristics

This study was conducted in Italy and did not involve external funding. Mean symptom duration before treatment was not reported, but the study only included participants with onset of hearing loss in the past 30 days. HBOT treatment included 10, 90-minute sessions over a 15-day period, with sessions occurring Monday through Friday. Steroid treatment was oral prednisone at 1 mg/kg per day (for a maximum dose of 60 mg per day) over 12 to 14 consecutive days. Follow-up was 20 days posttreatment.[19] A summary of study characteristics is presented in ***Table 8;*** detailed study characteristics are in ***Appendix B, Tables B-1 to B-3***.

Table 8. Summary of Study Characteristics Comparing HBOT Only vs. Steroids Only

Author, Year Country RoB	Sample Size (N)	Mean Age (SD) N (%) Female Baseline Hearing Loss	Symptom duration prior to treatment Number and length HBOT sessions Steroid dose, administration, and duration
Cavaliere et al., 2022[19] Italy Some concerns	Total sample size: 115 HBOT: 60 OS: 55	Mean age (SD): HBOT: 55.7 (14.2) OS: 67.7 (9.4) N (%) Female: HBOT: 29 (48) OS: 26 (47) Mean (SD) initial PTA (dB) HBOT: 57.8 (25.5) OS: 66.3 (19.7)	Time to HBOT treatment: <30 days HBOT sessions: 10 sessions, 1 per day, 90 minutes per session Steroids: 1 mg/kg prednisone per day (for a maximum dose of 60 mg per day), oral, 12-14 consecutive days

Abbreviations: HBOT = hyperbaric oxygen therapy; OS = oral steroids; PTA = pure-tone average; RoB = risk of bias.

Findings

Hearing improvement: The study did not report the actual baseline or follow-up PTA measures. However, the authors reported significant improvement in PTAs from baseline to 20 days posttreatment in both the HBOT only group and in the steroid only group ($p<0.05$ for each within group difference). The HBOT only group obtained a greater improvement in PTA compared with the steroid only group ($p<0.05$, actual values not reported).[19]

3.2.3.2 HBOT Only vs. Steroids Only: EQ2

Time to treatment: Treatment within 7 days or within 8 to 14 days of symptom onset was associated with significant hearing improvement in the HBOT only group ($p<0.05$ compared with baseline PTA) but not the oral steroid only group ($P=0.08$ compared with baseline PTA for

within 7 days of onset and *P* reported as not significant for within 8 to 14 days of onset). Treatment after 14 days of symptom onset was not associated with a statistically significant recovery in either group.[19]

Sex: Although larger improvements in hearing were observed for both men and women for HBOT alone versus steroids alone; improvements were greater for women, compared with men ($P<0.05$).[19]

3.2.3.3 HBOT Only vs. Steroids Only: SQ

Authors observed no short- or long-term posttreatment complications. This RCT did not report outcomes related to differential safety.[19]

3.2.3.4 HBOT Only vs. Steroids Only: CQ

We found no studies reporting cost or cost-effectiveness of HBOT for idiopathic SSNHL.

3.2.4 Salvage Therapy

We identified 1 RCT that investigated HBOT as salvage therapy compared with intratympanic steroids among participants who failed initial treatment with intravenous steroids. Treatment failure was defined as a hearing improvement of less than 10 dB at the end of 6 days of intravenous steroid treatment.[23] We assessed the RoB of this study as some concerns.

3.2.4.1 Salvage Therapy: EQ1

Key findings include:

- Hearing improvement was significantly better in the HBOT salvage therapy group compared with the steroid group at 2,000 Hz (HBOT: 16.4 dB, steroids: 11.4 dB; $p<0.05$); the difference between groups was not significant at 250 Hz, 500 Hz, 1,000 Hz, or 4,000 Hz. (*Low* COE for no difference)

Study Characteristics

The study was conducted in Serbia among 50 participants, and no information about funding was reported. Mean symptom duration before treatment was not reported, but the study excluded participants who began treatment more than 4 weeks after symptom onset. Last follow-up was at the conclusion of 20 days of treatment. HBOT treatment included 20, 60-minute sessions over 20 days, with sessions Monday to Friday. Steroid treatment in the comparator group consisted of 4 intratympanic injections of dexamethasone over a 13-day period.[23] A summary of study characteristics is presented in ***Table 9***; detailed study characteristics are in ***Appendix B, Tables B-1 to B-3***.

Table 9. Study Characteristics for HBOT Salvage Therapy

Author, Year Country RoB	Sample Size (N)	Mean Age (SD) N (%) Female Baseline Hearing Loss	Symptom duration prior to treatment Number and length HBOT sessions Steroid dose, administration, and duration
Cvorovic et al., 2013[23] Serbia Some concerns	Total sample size: 50 HBOT: 25 ITS: 25	Mean age (SD):[a] HBOT: 53.6 (15.5) ITS: 47.3 (10.8) N (%) Female: NR Reported by frequency only	**HBOT group** Time to HBOT treatment: < 4 weeks HBOT sessions: 20 sessions, 1 per day, 60 min per session **ITS group** Time to treatment: < 4 weeks Steroids: dexamethasone (0.3-0.5 ml (4 mg/ml)), 4 intratympanic injections, over 13 days

[a] Age ranged from 14 to 72 years.

Abbreviations: ITS = intratympanic steroid; HBOT = hyperbaric oxygen therapy; NR = not reported; RoB = risk of bias.

Findings

Hearing improvement: Hearing improvement was only reported at individual frequencies (250 Hz, 500 Hz, 1,000 Hz, 2,000 Hz, and 4,000 Hz).[23] The difference in hearing improvement between the HBOT group and the steroid group was only significant at 2,000 Hz (HBOT: 16.4 dB; steroids: 11.4 dB; $p<0.05$).[23]

3.2.4.2 Salvage Therapy: EQ2

Severity of hearing loss at baseline: Patients with pretreatment PTA ≥81 dB who received HBOT after failing intravenous steroids had significantly worse hearing improvement compared with those with the same degree of hearing loss who received intratympanic steroid treatment after failing intravenous steroids (improvement of 13.5 dB vs. 40.7; $P<0.05$).[23] There were no statistically significant differences between the HBOT group and the steroid group for those with baseline hearing of ≤60 dB (improvement of 23.3 dB vs. 25.5 dB; P=NS) and those with baseline hearing between 61 dB to 80 dB (improvement of 25.2 dB vs. 28.7 dB; P=NS).[23]

3.2.4.3 Salvage Therapy: SQ

Adverse events: One RCT of salvage therapy, which compared HBOT after failed intravenous steroid treatment to intratympanic steroids, reported 3 of 25 (12%) participants in the HBOT group had serous otitis media or fluid in the ear without infection, which were successfully treated. This study also reported that 5 of 25 (20%) of participants in the intratympanic steroid group experienced mild ear pain immediately after injections, all of which were successfully treated with analgesics.[23] There was no significant difference in AEs between HBOT use and steroid use (RR: 1.67; 95% CI, 0.45 to 6.24). This study did not report outcomes related to differential safety.

A summary of findings and COE is provided in **Table 10 and Table 11.**

3.2.4.4 Salvage Therapy: CQ

We found no studies reporting cost or cost-effectiveness of HBOT for idiopathic SSNHL.

Table 10. Summary of Findings and COE for HBOT Therapy Compared with Intratympanic Steroids as Salvage Therapy

No. Studies/No. Participants	Summary of Effect	RoB	Consistency	Precision	Directness	Overall COE/ Direction
Hearing improvement; follow-up time 13 days to 20 days						
1 RCT/ 50 [23]	Salvage therapy refers to treatment after failed course of intravenous steroids; difference in hearing improvement between the HBOT group and the steroid group was only significant at 1 of 5 frequencies, 2,000 Hz (HBOT: 16.4 dB; steroids: 11.4 dB; *P*<0.05; calculated mean difference 5.0 dB); hearing improvement at other frequencies ranged from −3.0 to 4.8 dB.	Not serious	Not Applicable - single study	Serious[a]	Serious[b]	Low for no effect [a, b] ●●○○

COE ratings: ●●●● High, ●●●○ Moderate, ●●○○ Low, ●○○○ Very Low
[a] A significant difference favoring HBOT was only reported for 1 of 5 frequencies; data for estimating CIs around mean differences NR; downgraded 1 step for imprecision.
[b] Clinical significance of reporting changes for multiple single frequencies is unclear; downgraded 1 step for indirectness.

Abbreviations: COE = certainty of evidence; HBOT = hyperbaric oxygen therapy; NR = not reported; RCT = randomized controlled trial.

Table 11. Summary of Findings and COE for Any Adverse Events

No. Studies/No. Participants	Summary of Effect	RoB	Consistency	Precision	Directness	Overall COE/ Direction
Salvage therapy; follow-up time 13 days to 20 days						
1 RCT[23]/ 50	No significant difference in AEs between HBOT use and steroid use (RR: 1.67; 95% CI, 0.45 to 6.24); 3 of 25 (12%) participants in the HBOT group with fluid in the ear and 5 of 25 (20%) participants in the intratympanic steroid group experienced mild ear pain after injections.	Not serious	Not applicable—single study	Serious[a]	Very serious[b]	Very low for no effect[a,b] ●○○○

COE ratings: ●●●● High, ●●●○ Moderate, ●●○○ Low, ●○○○ Very Low
[a] Wide confidence intervals; the upper end of the pooled CI represents a large number of AEs due to rare events and small sample sizes; downgraded 1 step for imprecision.
[b] Limited information reported regarding how AEs were defined and monitored; downgraded 1 step for indirectness.

Abbreviations: AE = adverse event; COE = certainty of evidence; HBOT = hyperbaric oxygen therapy; RCT = randomized controlled trial.

3.2.5 Optimal Frequency, Dose, and Duration of HBOT: EQ1A

We identified 2 RCTs that compared different HBOT protocols plus steroids with steroid use alone.[18,25] We assessed the RoB as some concerns in both studies.

Key findings include:

- One RCT comparing 2 HBOT sessions per day for 5 days with 1 HBOT session per day over 10 days found no significant differences in hearing outcomes between HBOT regimens (PTA increase within each group ~29 dB; calculated mean difference, 0.1 dB; 95% CI, −12.6 to 12.8), suggesting each protocol is a reasonable option.[18]

- One RCT found that higher pressure (2.5 ATA vs. 1.5 ATA) provided significantly better hearing and WDS improvement; however, increasing the duration of treatment (2 hours vs. 1 hour) under 2.5 ATA did not result in a significant difference.[25]

Study Characteristics

One RCT was conducted in Italy[18] and the other was conducted in South Korea.[25] One RCT did not report any information on funding[18] and the other reported that no additional funding was needed.[25] The sample sizes were 55[18] and 105.[25] Attanasio et al., 2015[18] did not report mean time from symptom onset to treatment but only enrolled participants with symptom onset in the last 15 days. Kim et al.[25] only enrolled participants with symptom onset in the last 14 days and reported that the mean number of days from symptom onset to treatment ranged from 3.5 days to 5.4 days across study groups. Baseline mean PTA levels were 85.5 dB[18] and 98.8 dB,[25] indicating severe to profound hearing loss at baseline. Follow-up was at the end of treatment in 1 RCT[18] and after 3 months in the other RCT.[25]

Attanasio et al.[18] included 2 HBOT treatment protocols that varied in the numbers of sessions per day and the duration of treatment. One group received 2 HBOT sessions per day for 5 days and the other group received 1 session per day for 10 days. Both groups also received intratympanic prednisolone over the first 3 days. All sessions were at 2.4 ATA.[18]

Kim et al., 2023[25] included 3 HBOT treatment regimens that varied by pressure and session length. Group 1 received 1-hour sessions at 2.5 ATA, group 2 received 2-hour sessions at 2.5 ATA, and group 3 received 1-hour sessions at 1.5 ATA. All groups received 10 HBOT sessions, oral steroids, and intratympanic dexamethasone.[25]

A summary of study characteristics is presented in ***Table 12***; detailed study characteristics are in ***Appendix B, Tables B-1 to B-3***.

Table 12. Study Characteristics Comparing Optimal Frequency, Dose, and Duration of HBOT

Author, Year Country RoB	Sample Size (N)	Mean Age (SD) N (%) Female Baseline Hearing Loss	Symptom Duration to Treatment Number and Length HBOT Sessions Steroid Dose, Administration, and Duration
Attanasio et al., 2015[18] Italy Some concerns	Total sample size: 55 HBOT 1 + steroids: 27 HBOT 2 + steroids: 28	Mean age (SD): NR N (%) Female: NR Mean (SD) initial PTA (dB) HBOT 1+ steroids: 92.0 (18.6) HBOT 2 + steroids 2: 85.5 (16.3)	Time to HBOT treatment: <15 days HBOT1: 10 sessions, 1 per day, 90 minutes per session HBOT 2: 10 sessions, 2 per day, 90 minutes per session Steroids: 0.4 ml of 62.5 mg/ml prednisolone, intratympanic, before the HBOT session during the first 3 days of the protocol
Kim et al., 2023[25] South Korea Low	Total sample size: 105 HBOT 1 + SS + ITS: 35 HBOT 2 + SS + ITS: 35 HBOT 3 + SS + ITS: 35	Mean age (SD): HBOT 1 + SS + ITS: 54.1 (15.0) HBOT 2 + SS + ITS: 52.9 (13.0) HBOT 3 + SS + ITS: 55.1 (13.4) N (%) Female: HBOT 1 + SS + ITS: 18 (54.5) HBOT 2 + SS + ITS: 17 (50.0) HBOT 3 + SS + ITS: 15 (46.9) Mean (SD) intial PTA (dB) HBOT 1 + SS + ITS: 98.8 (15.3) HBOT 2 + SS + ITS: 93.3 (15.3) HBOT 3 + SS + ITS: 95.6 (18.6)	**HBOT 1 + OS + ITS group** Time to HBOT treatment, mean (SD): 3.5 (2.0) days HBOT sessions: 10 sessions, 1 per day, 60 minutes per session, delivered at 2.5 ATA Steroids: 0.8 mg/kg/day methylprednisolone, oral, 12 days (7 days and then tapered for 5 days); 0.4-0.8 ml at a dose of 4 mg/ml once a day dexamethasone, intratympanic, 8 days **HBOT 2 + OS + ITS group** Time to HBOT treatment, mean (SD): 4.7 (3.7) days HBOT sessions: 10 sessions, 1 per day, 120 minutes per session, deliverated at 2.5 ATA Steroids: 0.8 mg/kg/day methylprednisolone, oral, 12 days (7 days and then tapered for 5 days); 0.4-0.8 ml at a dose of 4 mg/ml once per day dexamethasone, intratympanic, 8 days **HBOT 3 + OS + ITS group** Time to HBOT treatment, mean (SD): 5.4 (4.2) days HBOT sessions: 10 sessions, 1 per day, 60 minutes per session, delivered at 1.5 ATA Steroids: 0.8 mg/kg/day methylprednisolone, oral, 12 days (7 days and then tapered for 5 days); 0.4-0.8 ml at a dose of 4 mg/ml once a day dexamethasone, intratympanic, 8 days

Abbreviations: ATA = atmospheric absolute (measure of atmospheric pressure); ITS = intratympanic steroid; HBOT = hyperbaric oxygen therapy; NR = not reported; PTA = pure-tone average; SS = systemic steroids; OS = oral steroids.

Findings

Hearing improvement: In the study that compared 2 HBOT sessions per day for 5 days with 1 HBOT session per day for 10 days, there were no significant differences in hearing outcomes between groups. The authors observed similar improvements in PTA (absolute difference pre-post treatment within each group ~ 29 dB; calculated mean difference between groups, 0.1; 95% CI, -12.6 to 12.8; *P*=0.98).[18]

In the study that compared 3 HBOT protocols,[25] mean hearing improvement was 53.8 dB (SD, 16.0) in the group that received 1-hour HBOT sessions at 2.5 ATA, 52.5 dB (SD, 18.0) in the group that received 2-hour sessions at 2.5 ATA, and 36.5 dB (SD, 24.8) in the group that received 1-hour sessions at 1.5 ATA. The first and second groups were each associated with significantly better improvement when compared with the third group (Group 1 vs. Group 3, calculated AMD, 17.6; 95% CI, 6.6 to 28.6; *P*<0.002; Group 2 vs. Group 3, calculated AMD, 16.3; 95% CI, 5.2 to 27.4; *P*<0.004), suggesting that 2.5 ATA is associated with better hearing outcomes than 1.5 ATA. There were no significant differences between the first group and the second group, suggesting no benefit to 2-hour HBOT sessions compared with 1-hour HBOT sessions at 2.5 ATA.[25]

Word discrimination score: In the study that compared 3 HBOT protocols,[25] WDS as measured by percentage correct improved from pretreatment scores of 10.5% or less to 73% and 76% in the groups that received 1 and 2 hours of HBOT at 2.5 ATA, respectively, and to 54% for the group that received HBOT at 1.5 ATA. The first and second groups were each associated with significantly more improvement compared with the third group (Group 1 vs. Group 3; *P*=0.041; Group 2 vs. Group 3, *P*=0.017).

Hearing loss at baseline: No significant differences were found between those with severe versus profound hearing loss at baseline between the 2 treatment protocols (*P*=0.27).[18]

Comorbidities: No significant differences were found in response to treatment for participants with diabetes or vertigo.[25]

Adverse events: In the RCT that compared 3 HBOT protocols,[25] there were no significant differences in the number of AEs between groups. There were 4 (12%) AEs in the group that received 1-hour HBOT sessions at 2.5 ATA, 2 (6%) in the group that received 2-hour sessions at 2.5 ATA, and 2 (6.3%) in the group that received 1-hour sessions at 1.5 ATA. All AEs were mild, mostly middle ear effusion or ear pain, and improved with treatment.[25]

Cost-effectiveness: We found no studies reporting cost or cost-effectiveness of HBOT for idiopathic SSNHL.

3.3 Acute Acoustic Trauma

3.3.1 Study and Population Characteristics for AAT

We identified 7 studies published between 1985 and 2020 reporting on the use of HBOT for the treatment of SSNHL resulting from AAT. One study was an RCT[30] and 6 were NRSIs.[3,4,28,29,31,32] We assessed the RCT as high RoB due to lack of information about baseline differences and

allocation concealment, and concerns regarding outcome selection and lack of blinding for outcome assessors.[30] We assessed 2 NRSIs as serious RoB[3,28] and 3 NRSIs as critical RoB.[29,31,32] The critical and serious RoB assessments were predominantly because the authors made no attempt or poor attempts to control for confounding. We assessed 1 NRSI as serious RoB for the outcome of tinnitus due to poor control for important confounding variables and rated it as critical RoB for the outcome of hearing improvement due to poor control for confounding and the exclusion of some participants from analysis.[4]

We present the findings in this section by treatment comparison. We did not identify any studies reporting on the differential effectiveness of HBOT for treating AAT by age, sex, race or ethnicity, disability, comorbidities, or severity of hearing loss, and we did not identify any studies for the CQ. Key overall study and population characteristics are described in ***Table 13.*** Studies were predominantly conducted in Europe, and generally enrolled adult military men who suffered AAT as a result of firearms exposure.

Table 13. Study and Population Characteristics of Included Studies on AAT

Characteristic	Number of Studies
Country setting	Europe: 5[3,4,28,30,32] Japan: 1[29] Turkey: 1[31]
Funding	None: 1[3] Not reported: 6[4,28-32]
Recruitment setting	Military hospital/medical center: 5[3,4,28-30] Hospital: 2[31,32]
Enrolled unilateral or bilateral hearing loss	Unilateral or bilateral hearing loss permitted: 4[3,30-32] Unilateral hearing loss only: 1[28] NR: 2[4,29]
Comparisons	HBOT + steroids vs. steroids only: 3[3,28,32] HBOT vs. control or usual care (other than steroids): 2[4,30] HBOT protocol vs. alternative HBOT protocol: 1[29] HBOT + steroid early treatment vs. HBOT + steroid late treatment: 1[31]
Age of participants	Adults: 6[3,4,28,30-32] Children and adults: 1[29] (age ranged from 16 to 48 years)
Number analyzed	Median: 73; Range 35 to 108
Sex	% Female: Range 0% to 9% NR: 3[3,28,32]
Race or ethnicity	NR by any study

Abbreviations: AAT = acute acoustic trauma; HBOT = hyperbaric oxygen therapy; NR = not reported.

3.3.2 HBOT with Steroids vs. Steroids Only

3.3.2.1 HBOT with Steroids vs. Steroids Only: EQ1

We identified 3 studies comparing the effectiveness of HBOT plus steroids to steroid use alone to treat SSHNL resulting from AAT.[3,28,32] All were NRSIs; 2 studies were assessed as RoB[3,28] and 1 study was assessed as critical RoB.[32]

Study and Population Characteristics

All 3 studies were conducted in Europe. Two studies did not report a funding source[28,32] and 1 study reported no funding.[3] The cause of AAT was explicitly reported as firearm shots in 2 studies.[3,28] Sample sizes ranged from 41 to 78 participants and mean age ranged from 21 to 26. Mean symptom duration prior to HBOT treatment ranged from 15 hours to 4.4 days. The number of HBOT sessions across studies ranged from 5 to13 sessions for 1 to 2 hours per session. Follow-up ranged from 6.5 days to 1 year posttreatment. Steroid dose, route, and duration varied. Initial hearing loss following AAT varied across studies and was more severe at higher frequencies. Bayoumy et al. reported initial hearing loss as the difference (measured as PTA in dB) between the affected ear and the contralateral ear.[3] Lafère et al. calculated initial hearing loss as the difference between PTA in dB at entry into the military and PTA in dB following the AAT incident.[28] Vavrina and Miiller did not report initial hearing loss other than to state that there was no difference in initial hearing loss between study groups.[32] Participants in the Bayoumy et al. study appeared to self-select into treatment groups, with the most severely affected patients selecting HBOT.[3] Participants in the Lafère et al. study were selected into the HBOT group based on ability to be evacuated to a military hospital,[28] and treatment group selection was unclear in the Vavrina and Miiller study.[32] A summary of study characteristics is presented in ***Table 14***; detailed study characteristics are in ***Appendix B***, ***Tables B-7 to B-9***.

Table 14. Summary of Study Characteristics of Studies Comparing HBOT + Steroids vs. Steroids Only

Author, Year Country RoB	Study Design	Sample Size (N)	Mean Age (SD) N (%) Female Baseline Hearing Loss	Symptom Duration Prior to Treatment Number and Length HBOT Sessions Steroid Dose, Administration, and Duration
Bayoumy et al., 2020[3] Netherlands Serious	NRSI	Total sample size: 41 HBOT + steroids: 23 (29 ears) Steroids: 18 (24 ears)	Mean age (SD): NR HBOT + steroids: 26.1 (4.8) Steroids: 24.9 (4.0) N (%) Female: NR Mean (SD) initial hearing loss (relative to the contralateral ear) across all frequencies as PTA in dB: HBOT + steroids: 26.7 (16.8) Steroids: 26.6 (15.0) *P*=NS Mean initial hearing loss (relative to the contralateral ear) at affected frequencies as PTA in dB, HBOT + steroids: 46.1 (14.4) Steroids: 38.6 (11.3) *p*<0.05	Time to treatment HBOT + steroids: HBOT treatment: 4.4 (2.7) days Steroid treatment: 2.7 (2.9) days Steroids : 5.9 (2.7) days HBOT sessions: 10 for 90 minutes Steroids: 60 mg prednisone, oral, 7 days
Lafere et al., 2010 [28] Belgium Serious	NRSI	Total sample size: 68 Early HBOT + steroids: 32 Delayed HBOT + steroids: 19 Steroids: 17	Mean age (SD): 20.9 (4.6) HBOT + steroids: NR Steroids: NR N (%) Female: NR Mean (SD) initial hearing loss (calculated from baseline PTA at entry to the military) at affected frequencies as PTA in dB HBOT + steroids: 31.4 (19.0) Delayed HBOT + steroids: 29.7 (15.7) Steroids: 25.8 (11.7) *p*=NS	Time to treatment Early HBOT + steroids: <36 hours HBOT sessions: 13 for 70 minutes Steroid 1:125 mg decreasing to 40 mg IV methylprednisolone for 5 days, 12 g IV piracetam for 5 days, 32 mg decreasing to 40 mg, 3 times per day, oral Methylprednisolone for 5 days Delayed HBOT treatment: 36 to 43 hours Time to steroid treatment: NR HBOT sessions: 10 for 70 minutes Steroid: Methylprednisolone 32 mg decreasing to 40 mg 3 times per day, oral, for 5 days Steroid only: Immediate Methylprednisolone 64 mg reducing to 8 mg over 10 days and 2,400 mg piracetam 3 times per day for 10 days

Author, Year Country RoB	Study Design	Sample Size (N)	Mean Age (SD) N (%) Female Baseline Hearing Loss	Symptom Duration Prior to Treatment Number and Length HBOT Sessions Steroid Dose, Administration, and Duration
Vavrina et al., 1995 [32] Switzerland Critical	NRSI	Total sample size: 78 HBOT + steroids: 36 Steroids only: 42	Mean age (SD):NR HBOT + steroids: 24.9 (6.3) Steroids: 22.7 (7.6) N (%) Female: NR Mean (SD) initial hearing loss: NR	Time to treatment: 15-72 hours HBOT sessions: 5-10 for 60 minutes Steroids: Cortisone 150 mg IV on day 1 followed by 80 mg oral cortisone, duration NR

Abbreviations: HBOT = hyperbaric oxygen therapy; IV = intravenous; NR = not reported; NRSI = nonrandomized study of interventions; NS = not significant; PTA = pure-tone average; RoB = risk of bias.

Findings

Reported outcomes for this treatment comparison include absolute hearing improvement from pretreatment, residual hearing loss, tinnitus, timing of treatment, and harms.

Absolute mean hearing improvement from pretreatment. Three studies found a statistically significant greater improvement in absolute mean hearing improvement as measured by PTA in dB from pretreatment to posttreatment among patients receiving HBOT with steroids versus those receiving steroids alone.[3,28,32] Bayoumy et al. reported mean (SD) hearing improvement (measured as PTA in dB) as 23.5 dB (12.1) for the HBOT with steroid group versus 12.5 dB (12.5) for the steroid alone group ($p<0.05$). Lafère et al. reported somewhat similar findings with mean (SD) hearing improvement of 20.6 dB (17.7) and 17.0 dB (14.0) for the HBOT with steroids and delayed HBOT plus steroid groups, respectively, versus 5.6 dB (3.6) for the steroid alone group ($p<0.05$ any HBOT vs. steroids). An older study by Vavrina et al., 1995 reported mean hearing improvement of 15.2 dB in the HBOT plus steroid group and 9.3 dB in the steroid alone group ($p<0.004$) (variance not reported).[32]

Residual hearing loss: Lafere et al. reported statistically significant greater mean (SD) residual hearing loss at 10 days posttreatment among patients receiving steroids only (mean 14.7 dB; SD 8.3) versus those who received either early HBOT plus steroids (mean 2.4 dB; SD 10.7) or those who received delayed HBOT plus steroids (mean 5.0 dB; SD 8.0) ($p<0.05$ for any HBOT with steroids vs. steroids only).[28] Residual hearing loss was calculated based on PTA at enlistment into the military.

Tinnitus: Vavrina et al. reported no statistically significant difference in tinnitus from baseline to posttreatment between the HBOT plus steroids versus steroid alone groups.[32]

3.3.2.2 HBOT with Steroids vs. Steroids Only: EQ2

Timing of treatment: Among 23 patients (29 affected ears) receiving HBOT, Bayoumy et al. reported statistically significant greater relative mean hearing improvement at 1-year follow-up among military personnel who received HBOT within 2 days of symptom onset versus those who received HBOT after 2 days of symptom onset (% relative improvement, 71.4%; SD, 27.5 vs. 47.9%, SD 31.6; $p<0.05$).[3]

3.3.2.3 HBOT with Steroids vs. Steroids Only: SQ

Harms: Among 2 studies reporting on harms, 1 reported no side effects from either HBOT with steroids or steroids only, and the other reported no serious side effects associated with HBOT with steroids.[32] Vavrina et al. did not report harms from steroid treatment.

A summary of findings and COE are provided in ***Table 15***.

Table 15. Summary of Findings and COE for HBOT with Steroids vs. Steroids

No. Studies/No. Participants	Summary of Effect	RoB	Consistency	Precision	Directness	Overall COE/ Direction
Mean hearing improvement from pretreatment (measured as PTA in dB); follow-up time 6.5 days to 1 year						
3 NRSIs[3,28,32] /224	3 studies found statistically significant greater hearing improvement with HBOT plus steroids vs. steroids alone. Mean (SD) hearing improvement from pretreatment: 23.5 dB (12.1) vs. 12.5 dB (12.5) (p<0.05);[3] 20.6 dB (17.7) and 17.0 dB (14.0) vs. 5.6 dB (3.6) (p<0.05);[28] 15.2 (NR) vs. 9.3 (NR) (p<0.004)[32]	Very serious[a]	Not serious	Not serious	Not serious	Low for greater effect with HBOT plus steroids[a] ●●○○
Mean residual hearing loss measured as PTA (dB); follow-up time 10 days						
1 NRSI[28]/68	Greater mean (SD) residual hearing loss at 10 days posttreatment with steroids only (mean 14.7 dB; SD 8.3) vs. early HBOT plus steroids (mean 2.4 dB; SD 10.7) and vs. delayed HBOT plus steroids (mean 5.0 dB; SD 8.0) (p<0.05 for any HBOT vs. steroids only).	Serious[b]	NA—single study body of evidence	Serious[c]	Not serious	Low for greater effect with HBOT plus steroids[b, c] ●●○○
Mean posttreatment tinnitus; follow-up time 6.5 days to 47 days						
1 NRSI[32] /78	1 study reported no statistically significant difference in tinnitus between the HBOT plus steroids vs. steroid alone groups.	Very serious[d]	NA—single study body of evidence	Very serious[e]	Not serious	Very low for no effect[d, e] ●○○○
Harms						
2 NRSIs[3,32] /119	1 study reported no AEs from either steroids or HBOT.	Very serious[a]	Not serious	Very serious[e]	Serious[f]	Very low for no effect[a, f] ●○○○

COE ratings: ●●●● High, ●●●○ Moderate, ●●○○ Low, ●○○○ Very Low

[a] Serious to critical RoB in selection of participants into the studies and serious to critical RoB for confounding; downgraded 2 levels for RoB.

[b] Serious RoB in selection of participants into the study and serious RoB for confounding; downgraded 1 level for RoB.

[c] Despite statistical significance, it is unclear whether the mean % difference in residual hearing loss between the groups represents a meaningful clinical difference; downgraded 1 level for imprecision.

[d] Critical RoB in selection of participants into the study and serious RoB for confounding; downgraded 2 levels for RoB.

[e] No point estimates, confidence intervals, or measures of variance provided for tinnitus and no information on validation of the measure; downgraded 2 levels for imprecision.

[f] Limited information reported regarding how AEs were defined and monitored; downgraded 1 step for indirectness.

Abbreviations: AE = adverse event; COE = certainty of evidence; HBOT = hyperbaric oxygen therapy; NA = not available; NR = not reported; NRSI = nonrandomized study of interventions; PTA = pure-tone average; RoB = risk of bias.

3.3.3 HBOT vs. Control or Usual Care (other than steroids)

3.3.3.1 HBOT vs. Control or Usual Care (other than steroids): EQ1

We identified 2 studies comparing the effectiveness of HBOT to usual care or a control to treat SSHNL resulting from AAT.[4,30] One was an RCT assessed as high RoB due to lack of information about baseline differences and allocation concealment and concerns regarding outcome selection and lack of blinding for outcome assessors,[30] and 1 was an NRSI assessed as serious RoB for the outcome of tinnitus due to poor control for important confounding variables, and rated as critical RoB for the outcome of hearing improvement due to poor control for confounding and the exclusion of some participants from analysis.[4]

Study and Population Characteristics

Both studies were conducted in Europe, neither reported a funding source, and participants were 100% men in both studies. The cause of AAT was exposure to firearm shots in both studies. Sample size was 120 in the RCT[30] and 118 in the NRSI.[4] Mean symptom duration to HBOT treatment ranged from 17 to 72 hours. The RCT compared 10, 60-minute HBOT sessions and 14 days of infusions of dextran and sorbitol (plasma expanders) with and without betahisine (an anti-vertigo medication) to infusions alone.[30] The NRSI compared HBOT sessions with a control group of normobaric oxygen therapy (NBOT) sessions.[4] The RCT randomly allocated soldiers to treatment groups, whereas the NRSI retrospectively selected a subgroup of patients into the HBOT and control groups from a cohort of all patients who had suffered AAT over a selected time period.[4] The RCT reported initial hearing loss as PTA in dB at pretreatment in figure format only,[30] while the NRSI calculated initial hearing loss as the difference between PTA in dB at entry into the military and PTA in dB following the AAT incident.[4] A summary of study characteristics is presented in ***Table 16***; detailed study characteristics are in ***Appendix B***, ***Tables B-7 to B-9***.

Table 16. Summary of Study Characteristics Comparing HBOT vs. Control or Usual Care (not including steroids)

Author, Year Country RoB	Study Design	Sample Size (N)	Mean Age (SD) N (%) Female Baseline Hearing Loss	Symptom duration prior to treatment Number and length HBOT sessions Control intervention
Pilgramm et al.,1985[30] Germany High	RCT	Total sample size: 120 HBOT + infusion 1 (29) HBOT + infusion 2 (32) Infusion 1 (33) Infusion 2 (26)	Mean age (SD): 21.2 (4.6) N (%) Female: 0 Mean (SD) initial PTA dB Reported in figure only	Time to treatment: 24 to 72 hours HBOT sessions: 10 for 60 minutes Infusion 1: IV 10% dextran-40 with 5% sorbitol for 14 days Infusion 2: IV 10% dextran-40 with 5% sorbitol, 24 mg oral betahistine for 14 days
Ylikoski et al., 2008[4] Finland Critical for hearing recovery; serious for tinnitus	NRSI	Total sample size: 118 HBOT (58) NBOT (60)	Mean age (SD): NR HBOT: 19.9 (1.5) Control: 20.3 (2.4) N (%) Female: 0 Mean (SD) initial lower frequency hearing loss (measured as PTA in dB at 0.5, 1, 2 kHz) HBOT: 13.2 (9.2) Control: 13.7 (9.2) *p*=NS Mean initial high-frequency hearing loss (measured as HPTA in dB at 4, 6, 8 kHz) HBOT: 37.1(14.4) NBOT: 37.3 (15.2) *p*=NS Mean (SD) initial maximal hearing loss (measured at PTA in dB typically at 6 kHz) HBOT: 53.5 (12.1) NBOT: 51.8 (15.7) *p*=NS	Time to HBOT treatment: Mean (SD): 16.8 (10.2) hours HBOT sessions: Mean (SD): 3.2 (1.4) for 90 minutes once per day Time to NBOT treatment: Mean (SD): 16.5 (11.7) hours NBOT sessions: Mean (SD): 6.2 (1.9) for 90 minutes twice per day

Abbreviations: HBOT = hyperbaric oxygen therapy; HPTA = high pure-tone average; IV = intravenous; NBOT = normobaric oxygen therapy; NR = not reported; NRSI = nonrandomized study of interventions; NS = not significant; PTA = pure-tone average; RCT = randomized controlled trial; RoB = risk of bias.

Findings

Both the RCT and the NRSI reported hearing recovery and tinnitus. The RCT did not define hearing recovery and reported percentage recovery change from pretreatment for both groups.[30] The NRSI defined hearing recovery as absolute hearing improvement in dB divided by initial hearing loss.[4] The RCT reported changes in tinnitus by comparing the number of participants reporting tinnitus in the affected ear on day 1 with the number reporting tinnitus at the end of treatment.[30] The NRSI reported on the presence of tinnitus at the end of treatment among participants who had reported tinnitus at the first visit.[4] A summary of findings and the COE are provided in ***Table 17***. Detailed findings are provided in ***Appendix B***, ***Tables B-7 to B-9***.

Hearing recovery: At 42 days posttreatment, the RCT reported 83% recovery of hearing loss as measured by PTA in dB among participants receiving HBOT plus an infusion of dextran and sorbitol versus 87% recovery among participants receiving infusions only (p=NR).[30] This study also reported 92% recovery among participants receiving HBOT, infusions of dextran and sorbitol plus oral betahistine compared with 62% recovery among patients receiving infusions and betahistine only. A statistically significant difference (p=0.001) was reported across the 4 study groups, but the study did not provide pairwise p values between groups.[30] At 7 days posttreatment, the NRSI reported statistically significant greater hearing recovery at frequencies of 0.5, 1, and 2 kHz as measured by percentage recovery in PTA among patients receiving HBOT versus a control group receiving NBOT (% PTA recovery, 74.1% vs. 60.2%; p=0.024).[4] This study also reported statistically significant greater hearing recovery among patients receiving HBOT versus NBOT at high frequencies of 4, 6, and 8 kHz (% PTA recovery 69.3% vs. 56.2%; p<0.001).[4] Notably, particpants without any abnormal threshold level in PTA range were excluded from the statistical analysis when calculating the hearing recovery percentage PTA. The NRSI reported a statistically significant greater number of patients with normal hearing posttreatment among those receiving HBOT versus NBOT (70% vs 40%, p<0.01).[4]

Tinnitus: The NRSI reported tinnitus among all patients immediately following AAT, but reported statistically lower tinnitus at the time of discharge from military service (1-4 months after AAT) among patients who had received HBOT versus those who had received NBOT (5% versus 18%, p<0.05).[4] The RCT reported statistically significant less development of tinnitus in the affected ear among the HBOT groups versus the infusions groups posttreatment (p<0.001), but the presentation of tinnitus findings in the article were not interpretable.[30]

3.3.3.2 HBOT vs. Control or Usual Care (other than steroids): SQ

Harms: The RCT reported no side effects in ether group receiving infusions alone, 3 instances of maxillary barosinusitis in the group receiving HBOT plus infusions of dextran and sorbitol, and 1 instance of oxygen intoxication in the group receiving HBOT plus HBOT plus infusions of dextran and sorbitol plus oral betahistine.[30]

Table 17. Summary of Findings and COE for HBOT vs. Control or Usual Care

No. Studies/No. Participants	Summary of Effect	RoB	Consistency	Precision	Directness	Overall COE/ Direction
Hearing recovery for HBOT plus infusion vs. infusions only as measured by % PTA Recovery, follow-up time 42 days						
1 RCT[30] /120	Greater % PTA recovery with HBOT plus infusions vs. infusions only (HBOT plus an infusion of dextran and sorbitol vs. infusion of dextran and sorbitol only, 83% vs; 87%, and HBOT plus infusions of dextran and sorbitol plus oral betahistine vs. infusion of dextran and sorbitol plus oral betahistine only, 92% vs. 62%; *p*=0.001 across the 4 study groups); no between-group values reported	Serious[a]	NA—single study body of evidence	Very serious[b]	Not serious	Very low for greater effect with HBOT[a, b] ●○○○
Hearing recovery for HBOT vs. NBOT as measured by % PTA recovery; follow-up time 7-days posttreatment, if treatment lasted 7 days, or at the end of military service if some degree of damage was present on day 7						
1 NRSI[4] /118	Greater % (SD) PTA recovery at frequencies of 0.5, 1, and 2 kHz among patients receiving HBOT vs. NBOT, 74.1% (19.9) vs. 60.2% (28.9); *p*=0.024 Greater % HPTA recovery at 4, 6, and 8 kHz among patients receiving HBOT vs. NBOT, 69.3% (17.1) vs. 56.2% (20.3); *p*<0.001	Very serious[c]	NA—single study body of evidence	Serious[d]	Not serious	Very low for greater effect with HBOT[c, d] ●○○○
Tinnitus posttreatment for HBOT vs. NBOT; follow-up time 1-4 months after AAT						
1 NRSI[4] /118	Lower reported tinnitus among patients receiving HBOT vs. NBOT (5% vs. 18%; *p*<0.05)	Serious[e]	NA—single study body of evidence	Very serious[f]	Not serious	Very low for greater effect with HBOT[e, f] ●○○○
Harms						
1 RCT[30] /120	Reported AEs: HBOT plus infusions of dextran and sorbitol vs. infusion only; N (%) 1 (3.0) vs. 0 (0) HBOT plus dextran and sorbitol plus oral betahistine vs. infusions only; N (%) 1 (3) vs. 0 (0)	Serious[a]	NA—single study body of evidence	Very serious[g]	Serious[h]	Very low for no effect[a, g, h] ●○○○

COE ratings: ●●●● High, ●●●○ Moderate, ●●○○ Low, ●○○○ Very Low

[a] High RoB due to lack of information about baseline differences and allocation concealment and concerns regarding outcome selection and lack of blinding for outcome assessors; downgraded 1 level for RoB.

[b] No measures of variance provided and no between-group *p* values to determine where the statistical difference lies; downgraded 2 levels for imprecision.

[c] Critical RoB due to confounding related to measurement of hearing recovery; downgraded 2 levels for RoB.

[d] Despite statistical significance, it is unclear whether the mean % difference in hearing recovery between the groups represents a meaningful clinical difference; downgraded 1 level for imprecision.

[e] Serious RoB in selection of participants into the study and serious RoB for confounding; downgraded 1 level for RoB.

[f] No confidence intervals or measures of variance provided for tinnitus and no information on validation of the measure; downgraded 2 levels for imprecision.

[g] No confidence intervals or measures of variance provided for harms; downgraded 2 levels for imprecision.

[h] Limited information reported regarding how AEs were defined and monitored; downgraded 1 level for indirectness.

Abbreviations: AAT = acute acoustic trauma; AE = adverse event; COE = certainty of evidence; HBOT = hyperbaric oxygen therapy; HPTA = high pure-tone average; NA = not available; NBOT = normobaric oxygen therapy; NRSI = nonrandomized study of interventions; PTA = pure-tone average; RCT = randomized controlled trial; RoB = risk of bias.

3.3.4 Early vs. Late Treatment with HBOT: EQ2

One study compared early (defined as initiated within the first 10 days of symptom onset) versus late HBOT treatment (defined as initiated between 11 to 30 days after symptom onset) as the primary outcome of the study.[31] The study was an NRSI conducted in Turkey and did not report a funding source.[31] We assessed the study as critical RoB[31] due to no control for confounding variables.

Study and Population Characteristics

The cause of AAT was firearm shots. Patients self-selected into treatment groups mainly due to patients' conceptions that their hearing would spontaneously improve over time. The study reported baseline pretreatment PTA at each frequency. A summary of study characteristics is presented in ***Table 18***; detailed study characteristics are in ***Appendix B***, ***Tables B-7 to B-9***.

Table 18. Summary of Study Characteristics for Early vs. Late Treatment with HBOT

Author, Year Country RoB	Study Design	Total Sample Size Intervention and Comparator (N)	Mean Age (SD) N (%) Female Baseline hearing loss	Timing of HBOT Number and length HBOT sessions
Salihoglu et al. (2015)[31] Turkey Critical	NRSI	Total sample size: 73 Early HBOT (37 ears) Late HBOT (36 ears)	Mean age (SD): 25.8 (3.9) N (%) Female: 0 Mean (SD) Pretreatment PTA dB: Calculated early HBOT: 41.1 (18.1) Calculated late HBOT: 45.9 (18.1)	Early HBOT Time to HBOT treatment, mean (SD) days: 7.4 (2.0) # HBOT sessions: 10-20 for 90 minutes Steroids: 90 mg oral Deflaszakort tapered to 15 mg in 3-day intervals Late HBOT Time to HBOT treatment, mean (SD) days: 18.9 (7.0) # HBOT sessions: 10-20 for 90 minutes Steroids: 90 mg oral Deflaszakort tapered to 15 mg in 3-day intervals

Abbreviations: HBOT = hyperbaric oxygen therapy; NRSI = nonrandomized study of interventions; PTA = pure-tone average; RoB = risk of bias.

Findings

Hearing recovery: The NRSI reported no statistically significant difference in complete, partial, and unchanged hearing recovery at 6-week follow-up among military personnel receiving early (<10 days of symptom onset) versus late (between 11-30 days of symptom onset) HBOT.[31] Complete recovery was defined as hearing restored to within 20 dB of hearing level; partial recovery as hearing loss improvement of 10 dB or more, and unchanged as hearing loss improvement of less than 10 dB or deteriorated after treatment.

Harms: Among 73 patients receiving HBOT, 1 patient underwent bilateral myringotomy because of Eustachian tube dysfunction on the seventh day of HBOT therapy, and 1 patient underwent bilateral myringotomy and ventilation tube insertion because of middle ear effusion, which developed after barotrauma in the HBOT chamber on the third day of HBOT therapy.[31] In this study, all patients' tympanic membranes were intact in the control examination 6 weeks after admission.

3.3.5 Alternative HBOT Protocols: EQ1A

We identified 1 NRSI comparing the effectiveness of U.S. Navy HBOT Treatment Table 5 (TT5) protocol to U.S. Navy HBOT Treatment Table 9 protocol (TT9) in 35 patients treated at an undersea medical center in Japan between April 1997 and August 2017 for SSHNL resulting from AAT.[29] We assessed the study as critical RoB due to no control for confounding variables. The TT5 protocol involves the consumption of 3,000 L of oxygen with unit pulmonary toxic doses of 334. The TT9 protocol involves 2,500 L of oxygen with unit pulmonary toxic doses of 270.

Study and Population Characteristics

Thirty of the 35 participants included in this study suffered AAT as a result of firearm shots. Selection of participants for HBOT protocol TT5 versus TT9 was not explicitly reported; however, TT9 was introduced by the U.S. Navy in 1999 as an alternative dosing protocol to TT5, and because the TT5 group included just 7 participants, it's likely that selection into treatment protocol was based on the date of introduction of TT9. The TT5 protocol group included 7 male patients ranging in age from 16 to 48 years who received 2-hour, 15-minute HBOT sessions at 180 kPa decreasing to 90 kPa, for a mean (SD) of 6.5 (1.1) days.[29] The TT9 protocol group included 28 patients (3 females) ranging in age from 17 to 45 years who received 1-hour ,45-minute HBOT sessions at 135 kPa, for a mean (SD) of 8.5 (2.4) days.[29] Notably, the mean (SD) number of days from symptom onset to treatment was 10.3 (7.6) days for the TT5 group and 27.8 (53.7) days for the TT9 group. A summary of study characteristics is presented in ***Table 19***; detailed study characteristics are in ***Appendix B***, ***Tables B-7 to B-9***.

Table 19. Summary of Study Characteristics of Alternative HBOT Protocols

Author, Year Country RoB	Study Design	Total Sample Size Intervention and Comparator (N)	Mean Age (SD) N (%) Female Baseline hearing loss	Timing of HBOT Number and length HBOT sessions
Oya et al. (2019)[29] Japan Critical	NRSI	Total sample size: 35 TT5: 7 TT9: 28	Mean age TT5 (SD): 23.9 (10.7) Mean age TT9 (SD): 27.7 (8.4) N (%) Female: 10 Mean (SD) pretreatment hearing loss measured as PTA in dB at 0.5, 1, 2 kHz HBOT TT5: 19.6 (11.7) HBOT TT9: 29.7 (18.8) Mean (SD) pretreatment hearing loss measured as PTA in dB at 4 and 8 kHz HBOT TT5: 35.4 (19.1) HBOT TT9: 51.4 (21.2)	TT5 Time to HBOT tx, mean days (SD): 10.3 (7.6) # HBOT sessions: NR Mean (SD) # days of HBOT tx: 6.5 (1.1) TT9 Time to HBOT treatment, mean days (SD): 27.8 (53.7) # HBOT sessions: NR Mean (SD) # days of HBOT tx.: 8.5 (2.4)

Abbreviations: HBOT = hyperbaric oxygen therapy; NR = not reported; NRSI = nonrandomized study of interventions; PTA = pure-tone average; TT5 = Treatment Table 5; TT9 = Treatment Table 9; Tx = treatment

Findings

The study reported mean PTA and high pure-tone average (HPTA) recovery percentage at 3 weeks posttreatment, and the number and percentage of ears with complete (Grade 1), partial

(Grade 2), and unchanged (Grade 3) recovery at 3 weeks posttreatment.[29] Complete recovery was defined as hearing restored to within less than 20 dB of preinjury hearing, partial recovery was defined as mean hearing loss improved by 10 dB, and unchanged recovery as observed improvement less than10 dB or the patient's hearing had deteriorated.[29] Detailed findings are provided in ***Appendix B***, ***Tables B-7 to B-9***.

Hearing recovery: At 3 weeks posttreatment, there was no significant difference in mean PTA (measured at 0.5, 1, and 2 kHz) recovery between groups receiving TT5 and TT9 HBOT protocols (37.9% vs. 41.7%; *p*=0.738).[29] Patients receiving the TT9 HBOT protocol had statistically greater HPTA (measured at 4 and 8 kHz) recovery (43.6% vs. 17.1%; *p*=0.028) and were more likely to achieve complete (13.3% vs. 0%) or partial (66.7% vs. 28.6%) recovery compared with patients receiving the TT5 HBOT protocol (*p*=0.016).[29]

4. Discussion

4.1 Summary of the Evidence

4.1.1 Idiopathic SSNHL

We identified 10 RCTs published between 2004 and 2023 reporting on the use of HBOT for the treatment of idiopathic SSNHL.[18-27] A summary of findings and COE are provided in ***Table 20***.

For EQ1, there was moderate COE that HBOT with steroids compared to steroids alone increased the likelihood of complete/partial recovery, decreased likelihood of no recovery, [21,22,24,26] decreased the likelihood of no recovery,[20] and improved a participant's ability to understand speech based on WDS.[22] There was very low COE that HBOT with steroids compared with steroids alone had no effect on mean or median hearing improvement as measured by changes in PTA.[19,22,24,27] There was low COE from a single RCT that HBOT alone significantly improved hearing compared with steroids alone[19] and low COE from a single RCT evaluating salvage therapy after initial failed intravenous steroid therapy that HBOT had no effect on hearing improvement compared to intratympanic steroids.[23]

For EQ1a, on optimal HBOT regimens, we identified 2 RCTs that provided evidence that higher pressure (2.5 ATA vs. 1.5 ATA) resulted in better outcomes,[25] while increasing duration from 1 to 2 hours and shortening total duration of treatment to 10 sessions over 5 days from 10 sessions over 10 days showed no difference.[18] Notably, all RCTs included for idiopathic SSNHL conducted HBOT sessions at between 2.0 and 2.5 ATA. Shorter treatment durations, with more concentrated HBOT sessions, which may be more feasible for patients, may have comparable effectiveness to longer treatment durations. We did not grade the certainty of this evidence base.

For EQ2, we identified very limited evidence on the differential effectiveness of HBOT according to hearing loss at baseline, age, or sex. We identified no evidence of differential effectiveness according to other factors and no evidence of differential safety. Among RCTs that compared HBOT with steroids to steroids alone, 1 high RoB RCT[27] found mean hearing improvements were significantly better among those with greater hearing loss at baseline; however, a second RCT found no difference by hearing loss at baseline, though this was based

on very small sample sizes.[24] One RCT found no difference in hearing recovery by age[20] and another found women, compared with men, had better hearing improvement with treatment (either HBOT with steroids or HBOT alone).[19] One RCT of salvage therapy comparing HBOT to intratympanic steroid injections after failed treatment with intravenous steroids found worse outcomes among participants with severe hearing loss at baseline (PTA ≥81 dB) who received HBOT and no difference between HBOT and intratympanic steroids among participants with less severe hearing loss. Due to a limited number of studies, small sample sizes for subgroup analyses, a lack of reporting regarding whether these analyses were preplanned, and RoB concerns, it is not possible to reach meaningful conclusions about the differential effectiveness of HBOT based on this evidence.

For the SQ, we identified 4 RCTs comparing HBOT with steroids to steroids alone that reported harms. None of these RCTs reported major complications and AEs were rare (ranging from 0 to 2).[19,21,22,24] There was low COE for no differences in AEs between treatment groups (pooled RR: 0.36; 95% CI, 0.07 to 1.94; 4 RCTs; 281 participants; I^2=0.0). We downgraded this body of evidence for imprecision due to small sample sizes and for indirectness due to lack of information on reporting and monitoring of harms. In 1 RCT of salvage therapy, which compared HBOT after failed intravenous steroid treatment to intratympanic steroids, there was very low COE for no difference in AEs between HBOT use and steroid use (RR: 1.67; 95% CI, 0.45 to 6.24).[23] All reported AEs were minor, (i.e., ear pain and fluid in the ear) and all were resolved. It is important to note that HBOT has been used therapeutically for multiple conditions over many decades. Several systematic reviews on HBOT for other indications have also found few AEs associated with HBOT confirming that it is generally safe.[34-36]

Our findings align with recent systematic reviews. Joshua et al.[33] also found evidence that HBOT plus steroid treatment was more effective than steroid treatment alone for hearing improvement and recovery. Joshua et al. included 3 RCTs[22,26,60] with a combined total of 88 participants and reported pooled mean improvement in PTA following HBOT was 10.3 dB (95% CI, 6.5 to 14.1; I^2=0.0%). Based on 2 of the 3 RCTs, Joshua et al. reported that the odds of hearing recovery, defined as PTA improvement of 10 dB or more, were 4.3 times greater (95% CI, 1.6 to 11.7; I^2=0%) in participants who received HBOT compared with those who receive steroids alone. Note that 1 of the RCTs[60] included in the systematic review by Joshua et al. was excluded from the current HTA because it was conducted in a country not categorized as very high on the 2022 UN Human Development Index.[53]

Table 20. Summary of Findings and COE for HBOT for Idiopathic SSNHL

Outcome	Studies (N)	Effect	Certainty of Evidence	Direction of Effect
HBOT with steroids vs. steroids only				
Complete/partial hearing recovery	5 RCTs.[20-22,24,26] (294)	Pooled RR 1.39 (95% CI, 1.03 to 1.86)	●●●○	Favors HBOT
No hearing recovery	5 RCTs[20-22,24,26] (294)	Pooled RR 0.59 (95% CI, 0.42 to 0.83)	●●●○	Favors HBOT
Hearing improvement	4 RCTs[19,22,24,27] (332)	Mixed findings	●○○○	Favors HBOT
Word discrimination (% correct)	1 RCT[22] (60)	9.2% point larger improvement with HBOT (95% CI, 0.52% to 17.9%)	●●●○	Favors HBOT
Safety (AEs)	4 RCTs.[19,21,22,24] (281)	Pooled RR 0.36 (95% CI, 0.07 to 1.94)	●●○○	No effect
HBOT alone vs. steroids alone				
Hearing improvement	1 RCT[19] (115)	Favors HBOT (p<0.05)	●●○○	Favors HBOT
Salvage HBOT vs. intratympanic steroids, both after failed intravenous steroids				
Hearing improvement	1 RCT[23] (50)	Difference of 5 dB at 2,000 Hz (P<0.05), difference of −3.0 to 4.8 at other frequencies (P=NS)	●●○○	No effect
Safety (AEs)	1 RCT[23] (50)	12% vs. 20%; P=NS	●○○○	No effect

COE ratings: ●●●● High, ●●●○ Moderate, ●●○○ Low, ●○○○ Very Low

Abbreviations: AE = adverse event; COE = certainty of evidence; HBOT = hyperbaric oxygen therapy; NS = not significant; RCT = randomized controlled trial; SSNHL = sudden sensorineural hearing loss.

4.1.2 AAT

We identified 7 studies reporting on the use of HBOT for the treatment of SSNHL resulting from AAT.[3,4,28-32] A summary of findings and COE are provided in ***Table 21***. Low to very low COE across all reported outcomes limits our ability to draw meaningful conclusions. The largest body of evidence included 3 studies, all of which favored HBOT plus steroids versus steroids only for hearing improvement outcomes.[3,28,32] Low COE for this body of research found a statistically significant greater improvement in absolute mean hearing improvement as measured by PTA in dB from pretreatment to posttreatment, ranging from 15.2 to 23.5 dB among participants receiving HBOT plus steroids versus 5.6 to 12.5 dB among those receiving steroids alone.[3,28,32] We have little confidence in a body of evidence consisting of two studies, graded mostly as very low COE, which favored HBOT versus control or usual care for hearing recovery and improvement in tinnitus symptoms.[4,30] In addition, very low COE from single bodies of evidence provide little insight into the optimal timing (early vs. late), frequency, dose, and duration of HBOT to treat AAT.[3,29,31] Additionally, we did not identify any studies reporting on the differential effectiveness of HBOT for treating AAT by age, sex, race or ethnicity, disability, comorbidities, or severity of hearing loss, and we did not identify any studies for the CQ. Low RoB RCTs and larger well-controlled prospective cohort studies with clearly defined clinical hearing recovery outcomes are needed. It is unclear whether the body of evidence for the effectiveness of HBOT to treat idiopathic SSNHL is relevant to the treatment of AAT.

Table 21. Summary of Findings and COE for HBOT for AAT

Outcome	Studies (N)	Effect	Certainty of Evidence	Direction of Effect
HBOT + steroids vs. steroids only				
Mean hearing improvement	3 NRSIs[3,28,32] /224	Significant improvement favoring HBOT plus steroids in all 3 NRSIs	●●○○	Favors HBOT
Mean residual hearing loss	1 NRSI[28] /68	HBOT with steroids (early: 2.4 dB; SD 10.7 and late: 5.0 dB; SD 8.0) significantly better than steroids (14.7 dB, SD 8.3) (p<0.05 for any HBOT vs. steroids only).	●●○○	Favors HBOT
Tinnitus	1 NRSI[32] /78	No significant difference between groups	●○○○	No effect
Safety (AEs)	2 NRSIs[3,32] /119	1 NRSI reported no AEs and 1 NRSI reported no serious AEs from HBOT[32]	●○○○	No effect
HBOT vs. control/usual care				
Proportion with hearing recovery vs. usual care	1 RCT[30] /120	HBOT + infusion vs. infusion only: 83% vs. 87% HBOT + infusion + anti-vertigo medication vs. infusion + anti-vertigo medication: 92% vs. 62% p=0.001 across the 4 study groups; no between-group values reported	●○○○	Favors HBOT
Proportion with hearing recovery vs. NBOT	1 NRSI[4] /118	HBOT vs. NBOT: 74.1% (19.9) vs. 60.2% (28.9); p=0.024	●○○○	Favors HBOT
Tinnitus	1 NRSI[4] /118	Less self-reported tinnitus among patients receiving HBOT vs. NBOT (5% versus 18%; p<0.05)	●○○○	Favors HBOT
Safety (AEs)	1 RCT[30] /120	N (%) AEs HBOT + infusion vs. infusion only: 1 (3.0) vs. 0 (0) HBOT + infusion +anti-vertigo medication vs. infusion + anti-vertigo medication: 1 (3) vs. 0 (0)	●○○○	No effect

COE ratings: ●●●● High, ●●●○ Moderate, ●●○○ Low, ●○○○ Very Low

Abbreviations: AE = adverse event; COE = certainty of evidence; HBOT = hyperbaric oxygen therapy; NBOT = normobaric oxygen therapy; NR = not reported; NRSI = nonrandomized study of intervention; RCT = randomized controlled trial.

4.2 Limitations of the Evidence Base

4.2.1 Idiopathic

The evidence base for HBOT in treating idiopathic SSNHL has several important limitations. Studies were generally small, with sample sizes ranging from 50[23] to 171[19] participants, limiting statistical power and precision of effect estimates. None of the identified trials were conducted in the United States, potentially affecting generalizability to U.S. health care settings. The specific steroid treatments used as cointerventions or comparators varied, as did the timing of HBOT treatment after onset of symptoms. Definitions of hearing recovery varied across studies, making it difficult to directly compare outcomes—some studies defined recovery based on PTA, while others used different frequency combinations or categorical definitions of hearing improvement. Importantly, studies did not define what degree of hearing recovery was clinically meaningful. Several studies had methodological limitations leading to RoB concerns, with only 3[21,22,24] of 10 trials assessed as low RoB. The reporting of safety outcomes was limited and inconsistent across studies, with 4[18,20,26,27] of 10 trials not reporting any safety information. Follow-up periods varied

widely, from 10 days[26] to 180 days posttreatment,[21] limiting understanding of long-term outcomes. Additionally, no studies examined cost-effectiveness, leaving a critical evidence gap. These limitations create some uncertainty about the optimal use of HBOT in SSNHL and its economic impact in clinical practice.

4.2.2 AAT

All of the limitations described above for idiopathic SSNHL hold true for the evidence base for AAT. In addition, the body of evidence for AAT is further limited by a paucity of methodologically rigorous studies. The evidence base for SSNHL resulting from AAT is limited to one high RoB RCT and 7 retrospectively conducted NRSIs assessed as serious or critical RoB, with sample sizes ranging from 35 to 118, follow-up ranging from 6.5 days to 1 year, and time to HBOT treatment ranging from 15 hours to 28 days.

4.3 Clinical Practice Guidelines

We searched the ECRI Guidelines Trust, the National Institute for Health and Care Excellence (NICE), the International Network of Agencies for Health Technology Assessment database, and the websites of relevant medical specialty societies to identify HTAs or practice guidelines relevant to HBOT for SSNHL. We describe relevant items in ***Table 22***.

Table 22. Clinical Practice Guidelines on the Use of HBOT for SSNHL

Title	Year	AGREE II Rating[a]	Summary of Recommendation(s)
American Academy of Otolaryngology - Head and Neck Surgery Foundation (AAO-HNSF): Clinical practice guideline: sudden hearing loss (update)[1]	2019	5	HBOT is treatment option but only when combined with steroid therapy for either initial treatment (within 2 weeks of onset) or salvage therapy (between 2 weeks and 1 month of onset).
European Committee for Hyperbaric Medicine (ECHM): The Tenth European Conference on Hyperbaric Medicine: recommendations for accepted and non-accepted clinical indications and practice of hyperbaric oxygen treatment[38]	2017	4	Recommends HBOT combined with medical therapy in patients with acute idiopathic SSNHL who present within 2 weeks of disease onset (Type 1 recommendation, Level B evidence). Do not recommend the use of HBOT alone or combined with medical therapy in patients with idiopathic SSNHL who present after 6 months of disease onset (Type 1 recommendation, Level C evidence). It would be reasonable to use HBOT as an adjunct to corticosteroids in patients presenting after the first 2 weeks but not later than 1 month, particularly in patients with severe and profound hearing loss (Type 3 recommendation, Level C evidence).
National Institute of Health and Care Excellence (NICE): Hearing loss in adults: assessment and management[37]	2018 (updated 2023)	5	Consider a steroid to treat idiopathic SSNHL in adults; no mention of HBOT.

Title	Year	AGREE II Rating[a]	Summary of Recommendation(s)
The Underseas and Hyperbaric Medical Society (UHMS): Idiopathic SSNHL[10]	2011	3	Patients with moderate to profound idiopathic SSNHL (≥ 41 dB) who present within 14 days of symptom onset should be considered for HBOT. While patients presenting after this time may experience improvement when treated with HBOT, the medical literature suggests that early intervention is associated with improved outcomes. The best evidence supports the use of HBOT within 2 weeks of symptom onset.

[a] Rating scale goes from 1 (worse score possible) to 7 (best score possible).

Abbreviations: AAO-HNSF = American Academy of Otolaryngology - Head and Neck Surgery Foundation; AGREE = Appraisal of Guidelines for Research & Evaluation II instrument; ECHM = European Committee for Hyperbaric Medicine; HBOT = hyperbaric oxygen therapy; NICE = National Institute of Health and Care Excellence; SSNHL = sudden sensorineural hearing loss; UHMS = Underseas and Hyperbaric Medical Society.

Among recent guidelines related to SSNHL, NICE makes no mention of HBOT.[37] Both the American Academy of Otolaryngology - Head and Neck Surgery Foundation (AAO-HNSF) [1] and the European Committee for Hyperbaric Medicine (ECHM)[38] recommend HBOT as an option for the treatment of SSNHL when combined with medical therapy (e.g., steroid therapy) in patients who present within 2 weeks of hearing loss and no later than 1 month of SSNHL onset. The Underseas and Hyperbaric Medical Society (UHMS) suggests HBOT should be considered for patients with moderate to profound idiopathic SSNHL (≥41 dB) who present within 14 days of symptom onset.[10]

4.4 Selected Payer Coverage Policies

We conducted a scan of payor coverage documents on HBOT for SSNHL, and a summary is shown in ***Table 23***. We did not identify a Centers for Medicare & Medicaid National Coverage Determination for HBOT specific to the SSNHL indication. TRICARE does not include SSNHL in the list of indications that are covered or not covered for HBOT.[46,47] Aetna, Cigna, Humana, Kaiser Permanente, Premera Blue Cross, Regence Blue Shield, and United Healthcare consider HBOT medically necessary for SSNHL and cover it under specified conditions (***Table 24***).[39-45]

Table 23. Overview of Payer Coverage Policies for HBOT for SSNHL

Medicare [46]	Aetna [39]	Cigna[40]	Humana [41]	Kaiser Permanente [42]	Premera Blue Cross[43]	Regence Blue Shield [44]	TRICARE [47]	United Healthcare[45]
—	✓[a]	✓[a]	✓[a]	✓[a]	✓[a]	✓[a]	—	✓[a]

Notes: ✓ = covered; ✗ = not covered; — = no policy identified.
[a] Covered with conditions (see Table 24).

Abbreviations: HBOT = hyperbaric oxygen therapy; SSNHL = sudden sensorineural hearing loss.

Table 24. Details of Payor Coverage Policies for HBOT for SSNHL

Payer (Date of Policy)	Coverage policy
Medicare[46]	SSNHL is not listed in the national coverage determination on HBOT in the Medicare Coverage Database.
Aetna [39]	Aetna considers systemic HBOT medically necessary for any of the following conditions (with usual medically necessary number of sessions (dives) in parentheses):

Payer (Date of Policy)	Coverage policy
	Idiopathic SSNHL greater than 30 dB affecting greater than 3 consecutive frequencies of pure-tone thresholds when member has failed oral and intratympanic steroids and HBOT is initiated within 3 months after symptom onset (up to 20 sessions). Aetna considers the use of systemic HBOT experimental, investigational, or unproven for the following conditions (not an all-inclusive list) because there is insufficient evidence in the medical literature establishing that systemic HBOT is more effective than conventional therapies: noise-induced sensorineural hearing loss.
Cigna[40]	Systemic HBOT in single or multiplace chambers is considered medically necessary adjunctive treatment for idiopathic SSNHL within 4 weeks of symptom onset.
Humana[41]	HBOT treatments are required 5 times per week to optimize treatment response. Humana members may be eligible under the plan for HBOT as primary treatment for the following indications: idiopathic SSNHL as an adjunctive treatment to systemic or intratympanic steroid therapy with documentation of diagnosis from a specialist (e.g., otolaryngologist) when the following criteria are met: • At least 3 consecutive frequencies are affected with no identifiable cause AND • Decrease in hearing of greater than or equal to 30 dB
Kaiser Permanente[42]	For non-Medicare members, HBOT may be indicated with a confirmed diagnosis of 1 or more of the following: Idiopathic SSNHL (will need 20 visits maximum) Patients presenting with mild to moderate HL: • Oral and IT steroid should be discussed with all patients. • Treatment should be initiated, if possible, within 2 weeks of onset. • Oral steroid alone should be recommended as initial therapy for mild to moderate HL within 2 weeks of onset but can be offered up to 6 weeks after onset. • IT steroid should be strongly recommended for salvage for oral steroid failure within 6 weeks of onset. • Combo therapy (oral and IT steroid) should be recommended for those presenting more than 2 weeks after onset and within 6 weeks of onset. • HBOT should not be offered unless there are medical contraindications to oral or IT steroid therapy or special situations (i.e., only hearing ear). • Patients with >25% drop in discrimination regardless of the severity of their pure-tone loss should be treated as presenting with severe to profound HL patients. Patients presenting with severe to profound HL: • HBOT combined with steroid treatment should be initiated within 2 weeks of onset if possible. • Combo therapy (oral and IT steroid) should be "strongly" considered within 6 weeks of onset. • IT steroid should be strongly recommended for salvage for oral steroid failure within 6 weeks of onset. • HBOT should not be considered routinely as isolated adjuvant initial or salvage therapy without steroid therapy unless there are medical contraindications to oral or IT steroid therapy or special situations (i.e., only has 1 hearing ear and that is the ear that is affected by sudden hearing loss). Treatment: • Oral prednisone should be 60 mg for at least 7 days. • IT steroids should be dexamethasone 10 mg/ml up to 3 injections as needed. Treatment intervals—"weekly." • HBOT: 100% at 2 to 2.5 ATA 10-20 dives lasting 90 or 60 minutes. A. Audiogram: Initial, after treatment start; consider audiograms prior to additional interventions or if patient reports significant improvement, 6 months after last intervention. B. Ruling out retrocochlear lesion: MRI (or CT with contrast if MRI contraindicated) required to rule out retrocochlear lesion

Payer (Date of Policy)	Coverage policy
	C. Routine laboratory testing: Not recommended
Premera Blue Cross[43]	Systemic HBOT may be considered medically necessary in the treatment of idiopathic SSNHL.
Regence Blue Shield[44]	Systemic HBOT may be considered medically necessary when both of the following criteria (A. and B.) are met: A. Systemic HBOT must comply with the following guidelines that are consistent with the Undersea and Hyperbaric Medical Society criteria: 1. Patient must breathe 100% oxygen intermittently or continuously while the pressure of the treatment chamber is increased above 1 atmosphere absolute; and 2. Systemic HBOT pressurization should be at least 1.4 atmospheres absolute (ATM ABS) (20.5 psi); and 3. Treatment is provided in a hospital or clinic setting; and B. Treatment meets one or more of the following conditions: • Idiopathic SSNHL of greater than or equal to 41 decibels and an onset of treatment within 14 days (recommended treatment review threshold: 20 treatments)
TRICARE[47]	Hearing loss of any kind is not listed in the coverage policy for HBOT.
UnitedHealthcare[45]	HBOT is medically necessary for the following condition: idiopathic SSNHL.

Abbreviations: ATA = atmosphere absolute; HBOT = hyperbaric oxygen therapy; HL = hearing loss; IT = intratympanic; SSNHL = sudden sensorineural hearing loss.

4.5 Limitations of This HTA

This HTA was limited to peer-reviewed articles published in English. Studies conducted in countries other than *very high* on the United Nations Human Development Index were excluded from this review as those settings may have health care infrastructure and standards of medical practice that are not applicable to U.S. settings. For idiopathic SSNHL, we excluded NRSIs, which increases the methodological quality of evidence and our ability to draw causal inferences but may present a less comprehensive summary of all evidence.

4.6 Ongoing and Future Research

We searched ClinicalTrials.gov on November 12, 2024, with terms related to hearing and HBOT and retrieved 14 trials. We identified 2 studies that are potentially relevant to this HTA. One is a prospective cohort study in South Korea that is actively recruiting participants with SSNHL who receive HBOT in conjunction with other treatments including steroids, vasodilators, or antiviral agents.[48] The other potentially relevant study is specific to sensorineural hearing loss caused by AAT in a military population.[49] The status of this trial is unknown in ClinicalTrials.gov; however, the target completion date was December 2020. We did not identify any results or publications associated with this trial registration.[49]

5. Conclusion

There is moderate COE that HBOT plus steroid treatment within 14 days of symptom onset increased likelihood of complete or partial hearing recovery and reduced the risk of no hearing recovery compared with steroid treatment alone for idiopathic SSNHL. Evidence for HBOT alone, salvage therapy, and optimal HBOT protocols was very limited. AEs were rare in included RCTs, and the broader literature supports the general safety of HBOT. We identified no studies that examined cost-effectiveness, leaving a meaningful evidence gap. These findings suggest

HBOT may provide meaningful additional benefit when combined with standard steroid therapy for idiopathic SSNHL, particularly for those who can begin treatment promptly. Very low COE across all reported outcomes seriously limits our ability to draw meaningful conclusions regarding the effectiveness of HBOT to treat SSNHL resulting from AAT. It is unclear whether the body of evidence for the effectiveness of HBOT to treat idiopathic SSNHL is relevant to the treatment of AAT.

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Appendix A. Search Strategy

Databases: PubMed, Cochrane Database of Systematic Reviews

PubMed

Search date: July 17, 2024

Search Number	Search Details	Results
1	("Hyperbaric Oxygenation"[Mesh] OR "hyperbaric"[All Fields] OR "hyperbarics"[All Fields])	21,429
2	AND ("Ear"[Mesh] OR "ear"[All Fields] OR "Hearing"[Mesh] OR "hearing"[All Fields] OR "hearings"[All Fields] OR "sensorineur*"[All Fields] OR "Deafness"[Mesh] OR "deafness"[All Fields] OR "deafnesses"[All Fields] OR "Persons With Hearing Impairments"[Mesh] OR ("persons"[All Fields] AND "hearing"[All Fields] AND "impairments"[All Fields]) OR "persons with hearing impairments"[All Fields] OR "deaf"[All Fields])	855
3	AND "english"[Language]) NOT ("Animals"[Mesh] NOT "Humans"[Mesh])	637

Cochrane Library

Search date: July 12, 2024

Search Number	Search Details	Results
1	([mh "Hyperbaric Oxygenation"] OR ("hyperbaric" OR "hyperbarics"):ti,ab,kw) AND ([mh "Ear"] OR [mh "Hearing"] OR [mh "Deafness"] OR [mh "Persons With Hearing Impairments"] OR ("ear" OR "hearing" OR "hearings" OR sensorineur* OR "deafness" OR "deafnesses" OR ("persons" AND "hearing" AND "impairments") OR "persons with hearing impairments" OR "deaf"):ti,ab,kw)	7

Clinicaltrials.gov

Search date: July 12, 2024

Search Number	Search Details	Results
1	(ear OR hearing OR deafness OR hearings OR sensorineur OR sensorineural OR deafnesses OR deaf) in Condition/Disease AND (hyperbaric OR hyperbarics) in Other Terms OR Intervention/Treatment	14

Appendix B. Evidence Tables

Table B-1. Study Characteristics for Idiopathic SSNHL

Authors (Year) Study Design Risk of Bias	Setting Country Study Period	Study Population Inclusion Criteria Exclusion Criteria	Eligible Study Arms (sample size)
Attanasio et al.,2015[18] RCT Some concerns	Sensory organs department of a university hospital Italy January 2012 to December 2013	Adults aged 19 to 85 years with unilateral severe and profound idiopathic SSNHL with onset in the last 15 days Aged 19 to 85 years, onset of ISSNHL in the last 15 days, no previous therapy for ISSNHL, no surgery affecting the ipsilateral ear and no retrocochlear disease, no acoustic trauma and no autoimmune or fluctuating hearing loss Chronic bronco-pulmonary obstructive syndrome, emphysema, sinusitis, seizure syndrome, pregnancy, and claustrophobia in a hyperbaric environment	HBOT 1+ steroids; n=27 1 session per day (6 days per week) at 2.4 ATA with 90 minutes per session for treatment (14 minutes compression in air, followed by a 90-minute treatment, and then a decompression period of 15 minutes in oxygen), for 10 days (10 sessions total), plus intratympanic prednisolone (0.4 ml of 62.5 mg/ml) before the HBOT session during the first 3 days of the protocol HBOT 2 + steroids; n=28 2 sessions per day at 2.4 ATA with 90 minutes per session for treatment, for 5 days (10 sessions total), plus intratympanic prednisolone (0.4 ml of 62.5 mg/ml) between the 2 sessions of HBOT during the first 3 days of the protocol
Cavaliere et al., 2022[19] RCT Some concerns	Otolaryngology department of tertiary referral center Italy February 2016 to December 2019	Adults with unilateral or bilateral idiopathic SSNHL with onset in the last 30 days Aged older than 18 years, onset of SSNHL in the last 30 days, unilateral and/or bilateral symptom(s), unknown cause of hearing loss, no fluctuations in hearing loss, no previous otologic surgery in the ear affected from SSNHL, no previous cancer treatment, normal function of Eustachian tube Aged younger than18 years, known cause of hearing loss, persistent SSNHL >31 days, previous history of cancer, hypertension not under control, untreated diabetes, history of stroke, current or history of neurologic and/or psychiatric disorders	HBOT + Oral Steroid, n = 56 1 session per day from Monday to Friday at 2.5 ATA with 90 minutes per session (time of the whole HBOT session), for a variable total number of sessions for 15 days (10 sessions total), plus oral prednisone 1 mg/kg per day (for a maximum dose of 60 mg per day) for 12-14 consecutive days HBOT only; n=60 1 session per day from Monday to Friday at 2.5 ATA with 90 minutes per session (time of the whole HBOT session), for a variable total number of sessions for 15 days (10 sessions total) Oral steroids only; n=55 Oral prednisone 1 mg/kg per day (for a maximum dose of 60 mg per day) for 12-14 consecutive days

Authors (Year) Study Design Risk of Bias	Setting Country Study Period	Study Population Inclusion Criteria Exclusion Criteria	Eligible Study Arms (sample size)
Cekin et al., 2009[20] RCT Some concerns	Otolaryngology department of a training hospital and military medical academy Turkey 1994 and 2006	Adults with unilateral or bilateral SSNHL, 55 of 59 participants admitted within 3 days of symptom onset (all those admitted after 3 days in HBOT + OS group) Aged 18 years or older, diagnosed with SSNHL defined as sensorineural hearing loss of a minimum of 30 dB in at least 3 frequencies occurring within a period of 3 days Aged younger than 18 years, history of fluctuant hearing loss, intracranial malignancy and presentation with acute neurological symptoms.	HBOT + OS, n = 36 (38 ears) 1 session per day at 2.5 ATA with 90 min per session, 10 sessions total, plus prednisolone (5 mg, 1 mg/kg starting dose, reducing thereafter and ceasing in 3 weeks) and famotidine (40 mg once daily) OS; n=21 (21 ears) Prednisolone (5 mg, 1 mg/kg starting dose, reducing thereafter and ceasing in 3 weeks) and famotidine (40 mg once daily)
Chi et al., 2018[21] RCT Low	Otolaryngology department of a regional hospital Taiwan January 2007 to December 2016	Adult soldiers with unilateral idiopathic SSNHL Aged 18 years or older, unilateral ISSNHL, no previous diagnosis of ISSNHL, no underlying systemic diseases Previous diagnosis of ISSNHL, bilateral ISSNHL or underlying systemic diseases such as hypertension, diabetes mellitus or hyperlipidaemia	HBOT + OS; n=30 2 sessions per day at 2.5 ATA with 90 minutes per session, for a total of 5 days (10 sessions total), plus oral prednisolone (1mg/kg per day for 1 week and then gradually tapered to 20 mg every 3 days for the next week) for 2 weeks, oral pentoxifylline (400 mg twice per day) for 2 weeks, and intravenous dextran (500mL once per day) for 1 week OS; n=30 Oral prednisolone (1 mg/kg per day for 1 week and then gradually tapered to 20 mg every 3 days for the next week) for 2 weeks, oral pentoxifylline (400 mg twice per day) for 2 weeks, and intravenous dextran (500 mL once per day) for 1 week

Authors (Year) Study Design Risk of Bias	Setting Country Study Period	Study Population Inclusion Criteria Exclusion Criteria	Eligible Study Arms (sample size)
Cho et al., 2018[22] RCT Low	Otorhinolaryngology department of a university hospital South Korea July 2014 to September 2016	Adults with severe to profound unilateral ISSNHL with onset in the last 9 days Aged 18 to 65 years, unilateral severe to profound idiopathic SSNHL with an average PTA (4 tone averages of 500 Hz and 1, 2, and 4 kHz) hearing loss of 70 dB (1) potential reasons for ISSNHL, such as trauma (head, noise, or barotrauma), ototoxic treatment drugs (e.g., minoglycosides, cisplatin, loop diuretics, or quinine), radiation, infections (herpes, HIV, hepatitis B or C, otitis media, or meningitis), retrocochlear disease, and congenital or autoimmune hearing loss; (2) conductive or mixed hearing loss, such as structural abnormalities (tympanic membrane or perilymphatic fistula), Ménière's disease, and otosclerosis; (3) potential to prevent the patient from following the study visits, including drug and alcohol abuse, and concomitant severe disease (psychological, respiratory, or cardiovascular); (4) any pretreatment or ongoing treatment for ISSNHL-related hearing loss or tinnitus; (5) younger than 18 years or older than 65 years; and (6) presentation 10 days after onset	HBOT + OS + ITSI; n=30 1 session per day at 2.5 ATA with 60 minutes per session, for a total number of 10 days (10 sessions), plus oral methylprednisolone 0.8 mg/kg/day (maximum dose of 48 mg/day for 7 days) tapered over the subsequent 5 days (to 40, 32, 24, 16, and 8 mg) and dexamethasone injections 4 mg/mL per day for 7 days administered 2 to 3 hours before HBOT OS + ITSI; n=30 Oral methylprednisolone 0.8 mg/kg/day (maximum dose of 48 mg/day for 7 days) tapered over the subsequent 5 days (to 40, 32, 24, 16, and 8 mg) and dexamethasone injections 4 mg/mL per day for 7 days
Cvorovic et al., 2013[23] RCT Some concerns	Tertiary referral center Serbia January 2005 to December 2011	Children and adults with idiopathic SSNHL with onset in the last 4 weeks who did not recover after primary treatment with steroid (IV dexamethasone) Age older than 14 years, onset of idiopathic SSNHL in the last 4 weeks, failure of primary therapy with steroid (intravenous dexamethasone 40 mg once daily for 3 days, followed by 10 mg once daily for 3 days) with failure defined as hearing improvement less than 10 dB at the end of steroid treatment Patients who were treated longer than 4 weeks after onset of sudden deafness	HBOT; n=25 1 session per day from Monday to Friday at 2 ATA with 60 minutes per session (10 minutes of compression on air, 60 minutes of oxygen breathing, and 10 min of decompression of air) for 20 days (20 sessions total) ITS; n=25 4 intratympanic injections of dexamethasone (0.3-0.5 ml (4 mg/ml)) over 13 days

Authors (Year) Study Design Risk of Bias	Setting Country Study Period	Study Population Inclusion Criteria Exclusion Criteria	Eligible Study Arms (sample size)
Dova et al., 2022[24] RCT Low	Otolaryngology department in a university hospital Greece October 2016 to September 2019	Adults with idiopathic SSNHL with onset within 7 days of symptoms Aged 18 years or older, loss >30 dB in 3 continuous frequencies, treatment delay no longer than 7 days Exclusion criteria for the participants were: (1) patients with bilateral sudden sensorineural hearing loss; (2) patients who sought assistance after >7 days from the presence of symptoms; (3) cases who had already received another treatment for SSNHL; (4) cases with other causes of sudden sensorineural hearing loss such as autoimmune disease, Meniere's disease, use of ototoxic agents, syphilis, trauma; (5) presence of acoustic neuroma or demyelinating disease in MRI or other lesion in the cerebellopontine angle; (6) patients younger than 18 years; (7) pregnancy; (8) contraindication (absolute or relative) of HBOT such as tension or untreated or recent pneumothorax, administration of certain drugs (Bleomycin, Cisplatin, Disulfiram, Doxorubicin), untreated epilepsy or seizures, congenital spherocytosis, upper respiratory infection, heart failure, presence of pacemaker, severe ocular problems (macula degeneration, keratoconus, cataract), chronic obstructive pulmonary disease, claustrophobia; (9) glaucoma; (10) mental disorder; (11) middle ear disease; (12) diabetes mellitus; (13) difficult to treat hypertension; (14) contraindication of steroids administration (peptic ulcer disease, osteoporosis, immunosupression)	HBOT + steroids; n=25 (25 ears) 1 session per day (Monday-Friday) at 2.2 ATA with 2 periods of 40 minutes per session for 15 days (15 sessions total), plus dexamethasone IV (8 mg 3 times for 3 days, 8 mg 2 times for 3 days, 8 mg 1 time for 3 days) Steroids; n=25 (25 ears) Dexamethasone IV (8 mg 3 times for 3 days, 8 mg 2 times for 3 days, 8 mg 1 time for 3 days)

Authors (Year) Study Design Risk of Bias	Setting Country Study Period	Study Population Inclusion Criteria Exclusion Criteria	Eligible Study Arms (sample size)
Kim et al., 2023[25] RCT Low	Otorhinolaryngology department of a university hospital South Korea January 2017 to December 2020	Adults with unilateral severe to profound SSNHL with onset in the last 13 days Adults aged 18 to 65 years, unilateral SSNHL, onset in the last 13 days, PTA of >70 dB HL Trauma (head trauma, noise trauma, or barotrauma), ototoxic drugs (e.g., aminoglycosides, cisplatin, loop diuretics, or quinine), radiation exposure, infection (herpes, human immune deficiency virus, hepatitis, otitis media, or meningitis), retrocochlear disease, and autoimmune HL as potential causes of SSNHL; severe disease (renal, hepatic, or respiratory), emphysema, severe heart failure, history of myocardial infarction within the previous 4 weeks, and pregnancy or childbearing potential; any pretreatment or ongoing treatment for SSNHL; aged younger than 18 years or older than 65 years; and delayed presentation (14 days after onset)	HBOT 1 + SS + ITS; n=35 1 session per day at 2.5 ATA with 60 minutes per session for 10 consecutive days (10 sessions total), plus oral methylprednisolone for 12 days (0.8 mg/kg/day for 7 days, tapered for 5 days), and intratympanic dexamethasone for 8 days (0.4-0.8 ml at a dose of 4 mg/ml once per day) HBOT 2 + SS + ITS; n=35 1 session per day at 2.5 ATA with 120 minutes per session for 10 consecutive days (10 sessions total), plus oral methylprednisolone for 12 days (0.8 mg/kg/day for 7 days, tapered for 5 days), and intratympanic dexamethasone for 8 days (0.4-0.8 ml at a dose of 4 mg/ml once per day) HBOT 3 + SS + ITS; n=35 1 session per day at 1.5 ATA with 60 minutes per session for 10 consecutive days (10 sessions total), plus oral methylprednisolone for 12 days (0.8 mg/kg/day for 7 days, tapered for 5 days), and intratympanic dexamethasone for 8 days (0.4-0.8 ml at a dose of 4
Krajcovicova et al., 2018[26] RCT Some concerns	Otolaryngology department of an university hospital Slovakia July 2015 to June 2017	Adults with unilateral SSNHL with onset in the last 7 days Unilateral SSNHL, onset of SSNHL in the last 7 days, moderate degree of hearing impairment (41-60 dB) Pediatric patients, patients with preexisting Menière's disease, tumors, acoustic trauma, barotrauma, retrocochlear disease, bilateral hearing loss, those with a history of chronic otitis in the same ear, and those with a history of surgery of the same ear	HBOT + steroids; n=47 1 session per day at 2.0 ATA with 90 minutes per session for a total of 10 days (10 sessions total), plus IV Solu-Medrol for the first 5 days (250 mg for days 1-2, 125 mg for days 3-4, 80 mg for day 5), oral prednisone for the following 10 days (400 mg for days 6-10, 20 mg for days 11-15), and oral Agapurin (100 mg twice per day) and Betahistin (16 mg three times daily) Steroids; n = 20 IV Solu-Medrol for the first 5 days (250 mg for days 1-2, 125 mg for days 3-4, 80 mg for day 5), oral prednisone for the following 10 days (400 mg for days 6-10, 20 mg for days 11-15), and oral Agapurin (100 mg twice daily) and Betahistin (16 mg three times per day)

Authors (Year) Study Design Risk of Bias	Setting Country Study Period	Study Population Inclusion Criteria Exclusion Criteria	Eligible Study Arms (sample size)
Topuz et al., 2004[27] RCT High	Otolaryngology department of a university hospital Turkey 1998 to 2002	Children and adults with idiopathic SSNHL with onset in the last 2 weeks Hearing loss of 30 dB or greater in at least 3 contiguous frequencies NR	HBOT + drugs; n=30 (34 ears) 2 sessions per day for the first 5 days and then 1 session per day for 15 days at 2.5 ATA with 90 minutes per session for a total of 20 days (25 sessions total), plus oral prednisone (1 mg/kg per day) for 2 weeks, IV rheomacrodex (500 ml/d (infusion in 6 h)) for 5 days, oral diazepam (5 mg) twice per day, IV pentoxiphyllin (200 mg) twice per day, and salt restriction Drugs; n=21 (21 ears) Oral prednisone (1 mg/kg per day) for 2 weeks, IV rheomacrodex (500 ml/d [infusion in 6 hours]) for 5 days, oral diazepam (5 mg) twice per day, IV pentoxiphyllin (200 mg) twice per day, and salt restriction

Abbreviations: ATA = atmosphere absolute; HBOT = hyperbaric oxygen therapy; ISSNHL = idiopathic sudden sensorineural hearing loss; ITS/ITSI = intratympanic steroid injection; IV = intravenous; OS = oral steroids; PTA = pure-tone average; RCT = randomized controlled trial; SS = systemic steroids; SSNHL = sudden sensorineural hearing loss.

Table B-2. Population Characteristics for Idiopathic SSNHL

Authors (Year) Study Design Risk of Bias	Mean Age (SD)	N (%) Female	N (%) Race/Ethnicity	Hearing Loss at Baseline PTA Hearing Loss
Attanasio et al., 2015[18] RCT Some concerns	Age mean (SD): NR	NR	NR	Mean (SD) pretreatment PTA (dB) HBOT 1+ steroids: 92.0 (18.6) HBOT 2 + steroids 2: 85.5 (16.3) N (calculated %) with profound hearing loss (PTA >90 dB) HBOT 1+ steroids: 13 (48.1) HBOT 2 + steroids: 10 (35.7) N (%) with severe hearing loss (PTA=70-90 dB) HBOT 1+ steroids: 14 (51.9) HBOT 2+ steroids: 18 (64.3)
Cavaliere et al., 2022[19] RCT Some concerns	HBOT + OS: 44.1 (13.8) HBOT: 55.7 (14.2) OS: 67.7 ((9.4)	HBOT + OS: 25 (45) HBOT: 29 (48) OS: 26 (47)	NR	Mean (SD) pretreatment PTA (dB) HBOT + OS: 55.9 (23.9) HBOT: 57.79 (25.5) OS: 66.25 (19.7) Proportion with profound hearing loss HBOT + OS: 13.9 HBOT: 9.3 OS: 8.3 Proportion with upsloping (greater loss of hearing at low frequencies) HBOT + OS: 13.9 HBOT: 14.8 OS: 0 Proportion flat (similar loss of hearing across frequencies) HBOT + OS: 38.9 HBOT: 44.4 OS: 50.0 Proportion with downsloping (greater loss of hearing at high frequencies) HBOT + OS: 33.3 HBOT: 31.5 OS: 41.7

Authors (Year) Study Design Risk of Bias	Mean Age (SD)	N (%) Female	N (%) Race/Ethnicity	Hearing Loss at Baseline PTA Hearing Loss
Cekin et al., 2009[20] RCT Some concerns	HBOT + OS: 46.8 (age range: 18 to 82 years) OS: 44.5 (age range: 20 to 75 years)	HBOT + OS: 12 (calculated 33) OS: 8 calculated (38)	NR	Mean (SD) initial PTA (dB) HBOT + OS: 81.5 (NR) OS: 95.9 (NR) NR
Chi et al., 2018[21] RCT Low	HBOT + steroids: 31.1 (12.6) Steroids: 29.5 (14.7)	HBOT + steroids: 3 (10.0) Steroids: 4 (13.3)	NR	NR N (%) with mild hearing loss (26-40 dB HL) HBOT + steroids: 1 (3.3) Steroids: 3 (10.0) N (%) with moderate hearing loss (41-55 dB HL) HBOT + steroids: 9 (30.0) Steroids: 8 (26.7) N (%) with moderate-severe hearing loss (56-70 dB HL) HBOT + steroids: 9 (30.0) Steroids: 10 (33.3) N (%) with severe hearing loss (71-90 dB HL) HBOT + steroids: 8 (26.7) Steroids: 6 (20.0) N (%) with profound hearing loss (91 dB HL and above) HBOT + steroids: 3 (10.0) Steroids: 3 (10.0) N (%) with tinnitus HBOT + steroids: 19 (63.3) Steroids: 20 (66.7) N (%) with vertigo HBOT + steroids: 2 (6.7) Steroids: 3 (10.0)
Cho et al., 2018[22] RCT Low	HBOT + OS + ITSI: 53.8 (13.1) OS + ITSI: 56.1 (13.6)	HBOT + OS + ITSI: 13 (calculated 43.3) OS + ITSI: 19 (calculated 63.3)	NR	Mean (SD) pretreatment PTA (dB) HBOT + OS + ITSI: 89.3 (11.1) OS + ITSI: 92.4 (14.8) Pretreatment WDS; n (%) HBOT + OS + ITSI: 6.4 (4.6) OS + ITSI: 5.3 (5.1) Tinnitus; n (%) HBOT + OS + ITSI: 13 (43.3) OS + ITSI: 10 (33.3)

Authors (Year) Study Design Risk of Bias	Mean Age (SD)	N (%) Female	N (%) Race/Ethnicity	Hearing Loss at Baseline PTA Hearing Loss
Cvorovic et al., 2013[23] RCT Some concerns	HBOT: 53.6 (15.5) ITS: 47.3 (10.8) Age range: 14 to 72 years All patients enrolled had failed 6 days of IV steroids, with failure defined as <10 dB improvement in PTA	NR	NR	Baseline PTA values: NR (only frequency specific reported) Frequencies 250 Hz HBOT: 52.6 ITS: 59.6 500 Hz HBOT: 70.3 ITS: 68.3 1,000 Hz HBOT: 72.7 ITS: 72.7 2,000 Hz HBOT: 72.6 ITS: 70.6 4,000 Hz HBOT: 78.0 ITS: 73.0 There were significant differences between hearing thresholds at all frequencies before treatment for both groups. NR

Authors (Year) Study Design Risk of Bias	Mean Age (SD)	N (%) Female	N (%) Race/Ethnicity	Hearing Loss at Baseline PTA Hearing Loss
Dova et al., 2022[24] RCT Low	Median (IQR) HBOT + Steroids: 48.0 (37.5-57.5) Steroids: 55.0 (49.5-60.0)	HBOT + steroids: 13 (52) Steroids: 9 (36)	NR	Median (IQR) pretreatment PTA1 (average of threshold values at 0.5, 1, 2, 4 kHz) HBOT + steroids: 75.0 (60.6-91.2) Steroids: 63.7 (51.9-79.4) Median (IQR) pretreatment PTA 2 (average of threshold values at 0.25, 0.5, 1, 2, 4, 8 kHz) HBOT + steroids: 76.7 (60.8-91.7) Steroids: 69.2 (50.0-78.7) N (calculated %) with mild SSNHL HBOT + steroids: 2 (8) Steroids: 1 (4) N (calculated %) with moderate SSNHL HBOT + steroids: 1 (4) Steroids: 7 (28) N (calculated %) with moderately severe SSNHL HBOT + steroids: 8 (32) Steroids: 6 (24) N (calculated %) with severe SSNHL HBOT + steroids: 4 (16) Steroids: 9 (36) N (calculated %) with deafness/profound SSNHL HBOT + steroids: 10 (40) Steroids: 2 (8) N (%) with tinnitus HBOT + steroids: 18 (72) Steroids: 15 (60) N (%) with vertigo HBOT + steroids: 5 (20) Steroids: 5 (20)

Authors (Year) Study Design Risk of Bias	Mean Age (SD)	N (%) Female	N (%) Race/Ethnicity	Hearing Loss at Baseline PTA Hearing Loss
Kim et al., 2023[25] RCT Low	HBOT 1 + SS + ITS: 54.1 (15.0) HBOT 2 + SS + ITS: 52.9 (13.0) HBOT 3 + SS + ITS: 55.1 (13.4)	HBOT 1 + SS + ITS: 18 (calculated 54.5) HBOT 2 + SS + ITS: 17 (calculated 50.0) HBOT 3 + SS + ITS: 15 (calculated 46.9)	NR	Mean (SD) pretreatment PTA (dB) HBOT 1 + SS + ITS: 98.8 (15.3) HBOT 2 + SS + ITS: 93.3 (15.3) HBOT 3 + SS + ITS: 95.6 (18.6) Mean (SD) initial WDS (%) HBOT 1 + SS + ITS: 6.1 (14.7) HBOT 2 + SS + ITS: 7.8 (19.0) HBOT 3 + SS + ITS: 10.5 (21.9) Mean (SD) with tinnitus HBOT 1 + SS + ITS: 26 (78.8) HBOT 2 + SS + ITS: 27 (79.4) HBOT 3 + SS + ITS: 22 (68.8) Mean (SD) with vertigo HBOT 1 + SS + ITS: 12 (36.4) HBOT 2 + SS + ITS: 10 (29.4) HBOT 3 + SS + ITS: 15 (46.9)
Krajcovicova et al., 2018[26] RCT Some concerns	Total: 50 (14)	Total: 35 (calculated 51.5)	NR	Mean (SD) pretreatment PTA 250 to 500 Hz HBOT + steroids: 45.4 (23.8) Steroids: 35.0 (23.0) 1,000 to 2,000 Hz HBOT + steroids: 45.2 (24.9) Steroids: 40.7 (22.0) 4,000 to 8,000 Hz HBOT + steroids: 48.8 (27.4) Steroids: 45.1 (21.6) No significant differences in hearing impairment between the HBOT group and the control group at baseline (low frequencies: *P*=0.15; spoken speech frequencies: *P*=0.75; high frequencies: *P*=0.66) NR

Authors (Year) Study Design Risk of Bias	Mean Age (SD)	N (%) Female	N (%) Race/Ethnicity	Hearing Loss at Baseline PTA Hearing Loss
Topuz et al., 2004[27] RCT High	HBOT + drugs: 42.1 (13.4) Drugs: 40.4 (11.2)	HBOT + steroids and other drugs: 16 (calculated 53.3 Steroids and other drugs: 9 (calculated 42.9)	NR	Mean (SD) pretreatment hearing levels (dB) HBOT + steroids and other drugs: 70.4 (NR) Steroids and other drugs: 70.5 (NR) N (calculated %) with initial hearing levels of ≤60 dB HBOT + steroids and other drugs: 13 (38.2) Steroids and other drugs: 6 (28.6) N (calculated %) with initial hearing levels of 61 to 80 dB HBOT + steroids and other drugs: 11 (32.4) Steroid and other drugs: 11 (52.4) N (calculated %) with initial hearing levels of ≥81 dB HBOT + steroids and other drugs: 10 (29.4) Steroids and other drugs: 4 (19.0)

Abbreviations: HBOT = hyperbaric oxygen therapy; IQR = interquartile range; ITS/ITSI = intratympanic steroid injection; IV = intravenous; NR = not reported; OS = oral steroids; PTA = pure-tone average; RCT = randomized controlled trial; SS = systemic steroids; WDS = word discrimination scores.

Table B-3. Intervention Characteristics for Idiopathic SSNHL

Authors (Year) Study Design Risk of Bias	Time to Treatment Duration of Follow-up	HBOT Regiment Number of HBOT Sessions Length of Session Total Duration of Treatment Pressure	Steroid Regiment Steroid Mode of Administration Dosage Duration of Treatment	Adherence to Intervention
Attanasio et al., 2015[18] RCT Some concerns	Time to HBOT treatment: < 15 days HBOT 1+ Steroid: 11 days HBOT 2+ Steroid: 6 days	10 sessions 90 minutes per session 10 days (1 session per day, 6 days per week) 2.4 ATA 10 sessions 90 minutes per session 5 days (twice per day) 2.4 ATA	Prednisolone Intratympanic 0.4 ml of 62.5 mg/ml per day 3 days	NR
Cavaliere et al., 2022[19] RCT Some concerns	Time to HBOT treatment: all < 30 days 20 days after treatment	10 sessions 90 minutes per session 15 days (sessions Monday to Friday) 2.5 ATA	Prednisone Oral 1 mg/kg per day (for a maximum dose of 60 mg per day) 12 to 14 consecutive days	NR
Cekin et al., 2009[20] RCT Some concerns	N (%) Within 3 days: 34 (94) 7 days: 1 (3) 10 days: 1 (3) NR	10 sessions 90 minutes per session 10 days 2.5 ATA	Prednisolone Oral 5 mg (1 mg/kg starting dose, reducing thereafter) 3 weeks Famotidine Oral 40 mg once per day NR	NR

Authors (Year) Study Design Risk of Bias	Time to Treatment Duration of Follow-up	HBOT Regiment Number of HBOT Sessions Length of Session Total Duration of Treatment Pressure	Steroid Regiment Steroid Mode of Administration Dosage Duration of Treatment	Adherence to Intervention
Chi et al., 2018[21] RCT Low	Mean (SD) time to HBOT treatment: 4.2 (2.2) days Duration of follow-up: 180 days	10 sessions 90 minutes per session 5 days (twice per day, started on day 8 after 1 week of conventional treatment) 2.5 ATA	Prednisolone Oral 1 mg/kg per day for 1 week and then gradually tapered to 20 mg every 3 days for the next week 2 weeks Pentoxifylline Oral 400 mg twice per day 2 weeks Dextran IV 500 mL once per day 1 week	NR
Cho et al., 2018[22] RCT Low	Mean (SD) time to HBOT treatment: 4.1 (3.7) days Duration of follow-up: 3 months after treatment	10 sessions 60 minutes per session 10 days (1 session per day) 2.5 ATA	Methylprednisolone Oral 0.8 mg/kg/day (maximum dose of 48 mg/day for 7 days), tapered over the subsequent 5 days (to 40, 32, 24, 16, and 8 mg) 12 days Dexamethasone Intratympanic 4 mg/mL per day 7 days	NR
Cvorovic et al., 2013[23] RCT Some concerns	Time to HBOT treatment: < 4 weeks Mean (SD) time to HBOT treatment: 4.1 (3.7) days Time to Steroids treatment: < 4 weeks Duration of follow-up: At the end of salvage therapy treatment	20 sessions 60 minutes per session 20 days (sessions Monday to Friday) 2 ATA	Dexamethasone Intratympanic 4 injections of 0.3-0.5 ml (4 mg/ml) 13 days	NR

Authors (Year) Study Design Risk of Bias	Time to Treatment Duration of Follow-up	HBOT Regiment Number of HBOT Sessions Length of Session Total Duration of Treatment Pressure	Steroid Regiment Steroid Mode of Administration Dosage Duration of Treatment	Adherence to Intervention
Dova et al., 2022[24] RCT Low	Median (IQR) time to HBOT treatment: 4.0 (1.0 to 5.5) days Duration of follow-up: 3 months	15 sessions 2 periods of 40 minutes per session 15 days (Monday to Friday) 2.2 ATA	Dexamethasone IV 8 mg x 3 for 3 days, 8 mg x 2 for 3 days, 8 mg x 1 for 3 days 9 days	NR
Kim et al., 2023[25] RCT Low	Time to HBOT treatment, mean (SD): 3.5 (2.0) days Time to HBOT treatment, mean (SD): 4.7 (3.7) days Time to HBOT treatment, mean (SD): 5.4 (4.2) days Duration of follow-up: 3 months after onset	10 sessions 60 minutes per session 10 consecutive days 2.5 ATA 10 sessions 120 minutes per session 10 consecutive days 2.5 ATA 10 sessions 60 minutes per session 10 consecutive days 1.5 ATA	Methylprednisolone Oral 0.8 mg/kg/day for 7 days, tapered for 5 days 12 days Dexamethasone Intratympanic 0.4-0.8 ml at a dose of 4 mg/ml once per day 8 days	NR
Krajcovicova et al., 2018[26] RCT Some concerns	Time to HBOT treatment: all < 7 days Duration of follow-up: After treatment	10 sessions 90 minutes per session 10 days (once per day) 2.0 ATA	Solu-Medrol IV 250 mg for days 1 to 2, 125 mg for days 3 to 4, 80 mg on day 5 5 days Prednisone Oral 400 mg for days 6 to 10, 20 mg for days 11 to 15 10 days Agapurin Oral 100 mg twice per day NR Betahistin Oral 16 mg three times per day NR	NR

Authors (Year) Study Design Risk of Bias	Time to Treatment Duration of Follow-up	HBOT Regiment Number of HBOT Sessions Length of Session Total Duration of Treatment Pressure	Steroid Regiment Steroid Mode of Administration Dosage Duration of Treatment	Adherence to Intervention
Topuz et al., 2004[27] RCT High	Time to HBOT treatment: all < 14 days Duration of follow-up: 4 weeks	25 sessions 90 minutes per session 20 days (twice daily for the 1st 5 days and then once per day for 15 days) 2.5 ATA	Prednisone Oral 1 mg/kg per day 2 weeks Rheomacrodex IV 500 ml/d (infusion in 6 hours) 5 days Diazepam Oral 5 mg twice per day NR Pentoxiphyllin IV 200 mg twice per day NR	NR

Abbreviations: ATA = atmosphere absolute; IV = intravenous; HBOT = hyperbaric oxygen therapy; OS = oral steroids; RCT = randomized controlled trial; SD = standard deviation.

Table B-4. Efficacy Outcomes for Idiopathic SSNHL

Authors (Year) Study Design Risk of Bias Comparison	Outcomes Definitions	Efficacy Outcomes
Attanasio et al., 2015[18] RCT Some concerns HBOT Treatment Protocol 1 vs. HBOT Treatment Protocol 2	Complete recovery: PTA ≤25 dB or identical to the contralateral, nonaffected ear Marked improvement: PTA improvement >30 dB Slight improvement: PTA improvement 10 to 30 dB No recovery: PTA improvement <10 dB Successful treatment includes complete recovery and marked recovery	Mean (SD) pretreatment PTA (dB) HBOT 1 + steroids: 92.0 (18.6) HBOT 2 + steroids: 85.5 (16.3) Mean (SD) posttreatment PTA (dB) HBOT 1 + steroids: 62.7 (29.1); *P*<0.001 compared to baseline HBOT 2 + steroids: 56.1 (29.2); *P*<0.001 compared to baseline Calculated mean hearing improvement from baseline to posttreatment PTA (dB) HBOT 1 + steroids: 29.4 HBOT 2 + steroids: 29.5 Calculated AMD, 0.1; 95% CI, −12.6 to 12.8; *P*=0.98
Cavaliere et al., 2022[19] RCT Some concerns HBOT only vs. steroids only vs. HBOT + steroids	NR	Hearing Improvement (PTA) All patients improved significantly from baseline independent of treatment used (ANOVA: *p*<0.05) HBOT + OS vs. OS: HBOT + OS significantly better improvement (*p*<0.05) HBOT vs. OS: HBOT significantly better improvement than OS (*p*<0.05) Note: No additional data reported; the authors queried for additional information. Time to treatment Within 7 days HBOT + OS: significant recovery from baseline (*p*<0.05) HBOT: significant recovery from baseline (*p*<0.05) OS: no significant recovery from baseline (*p*=0.08) Across groups, patients who started the therapy within 7 days from SSNHL onset presented a statistically significant recovery of their PTA after treatment (ANOVA: *p*<0.05) 8 to 14 days: HBOT + OS: no significant recovery (*p*=NR) HBOT: significant recovery from baseline (*p*<0.05) OS: no significant recovery (*p*=NR) When the treatment started 8 to 14 days from symptom onset, the recovery was not statistically significant (ANOVA: *p*=0.07), except in case of patients treated by HBOT (*p*<0.05). More than 14 days HBOT + OS: no significant recovery (*p*=NR) HBOT: no significant recovery (*p*=NR)

Authors (Year) Study Design Risk of Bias Comparison	Outcomes Definitions	Efficacy Outcomes
		OS: no significant recovery (*p*=NR) Across groups, the improvement of PTA was never statistically significant (ANOVA: p=0.08). The authors noted the recovery of PTA was better in group HBOT + OS than in groups with HBOT and OS but did not report if the difference was statistically significant.
Cekin et al., 2009[20] RCT Some concerns Steroids only vs. HBOT + steroids	Complete recovery: >50 dB improvement Moderate recovery: 10 to 50 dB improvement No improvement: <10 dB improvement	Mean (SD) posttreatment PTA (dB) for those with complete hearing recovery after treatment HBOT + OS: 23.5 (NR) OS: 28.5 (NR) Mean (SD) posttreatment PTA (dB) for those with moderate hearing recovery after treatment HBOT + OS: 52.2 (NR) OS: 53.0 (NR) Mean (SD) posttreatment PTA (dB) for those with no hearing recovery after treatment HBOT + OS: 82.7 (NR) OS: 92.5 (NR) N (calculated %) patients with complete hearing recovery after treatment HBOT + OS: 21 (58) OS: 11 (52) N (calculated %) patients with moderate hearing recovery after treatment HBOT + OS: 8 (22) OS: 4 (19) N (calculated %) patients with no hearing recovery after treatment HBOT + OS: 7 (19) OS: 5 (24) The success rate of the study group (78.95%) was greater than that of the control group (71.30%), but this difference was not statistically significant (*p*>0.05).
Chi et al., 2018[21] RCT Low Steroids only vs. HBOT + steroids	Complete recovery: hearing threshold better than 25 dB HL Partial recovery: hearing improvement of >15 dB HL and a hearing threshold between 25 to 45 dB HL Slight recovery: hearing improvement of >15 dB HL and hearing threshold poorer than 45 dB HL	N (%) with complete recovery on day 13 HBOT + steroids: 4 (13.3) Steroids: 2 (6.7) N (%) with partial recovery on day 13 HBOT + steroids: 14 (46.7) Steroids: 15 (50.0) N (%) with slight recovery on day 13

Authors (Year) Study Design Risk of Bias Comparison	Outcomes Definitions	Efficacy Outcomes
	No recovery: hearing improvement of <15 dB HL and hearing poorer than 75 dB HL	HBOT + steroids: 10 (33.3) Steroids:9 (30.0) N (%) with no recovery on day 13 HBOT + steroids: 2 (6.7) Steroids: 4 (13.3) *p*=0.701 N (%) with complete recovery on day 180 HBOT + OS: 8 (26.7) OS: 3 (10.0) N (%) with partial recovery on day 180 HBOT + OS: 16 (53.3) OS: 11 (36.7) N (%) with slight recovery on day 180 HBOT + OS: 4 (13.3) OS: 13 (43.3) N (%) with no recovery on day 180 HBOT + OS: 2 (6.7) OS: 3 (10.0) *p*=0.043
Cho et al., 2018)[22] RCT Low Steroids only vs. HBOT + steroids	Complete recovery: PTA within 10 dB of the unaffected ear and word discrimination score within 5%-10% of the unaffected ear Partial recovery: PTA ≤50 dB HL and word discrimination score ≥50% Slight improvement: ≥10 dB improvement in PTA or ≥10% improvement in WDS No improvement: PTA <10 dB improvement in PTA WDS, % correct	Mean (SD) PTA hearing thresholds after treatment (dB), 3 months, ITT HBOT + OS + ITSI: 42.8 (20.6) OS + ITSI: 54.7 (25.6) Calculated mean PTA improvement from baseline, 3 months, ITT HBOT + OS + ITSI: 46.8 OS + ITSI: 37.7 Calculated mean difference: 8.8 Mean (SD) hearing thresholds after treatment (dB), 3 months, per protocol (PP) HBOT + OS + ITSI: 42.5 (21.3) OS + ITSI: 54.7 (25.6) N (%) complete recovery after treatment, 3 months, ITT HBOT + OS + ITSI: 11 (36.7) OS + ITSI: 5 (16.7) *p*=0.080 N (%) complete recovery after treatment, 3 months, PP HBOT + OS + ITSI: 10 (35.7) OS + ITSI: 5 (16.7)

Authors (Year) Study Design Risk of Bias Comparison	Outcomes Definitions	Efficacy Outcomes
		p=0.098 N (%) partial recovery after treatment, 3 months, ITT HBOT + OS + ITSI: 7 (23.3) OS + ITSI: 5 (16.7) *p*=0.519 N (%) partial recovery after treatment, 3 months, PP HBOT + OS + ITSI: 7 (25.0) OS + ITSI: 5 (16.7) *p*=0.434 N (%) slight improvement after treatment, 3 months, ITT HBOT + OS + ITSI: 11 (36.7) OS + ITSI: 15 (50.0) *p*=0.217 N (%) slight improvement after treatment, 3 months, PP HBOT + OS + ITSI: 10 (35.7) OS + ITSI: 15 (50.0) *p*=0.272 N (%) no improvement after treatment, 3 months, ITT HBOT + OS + ITSI: 1 (3.3) OS + ITSI: 5 (16.7) *p*=0.097 N (%) no improvement after treatment, 3 months, PP HBOT + OS + ITSI: 1 (3.6) OS + ITSI: 5 (16.7) *p*=0.102 WDS % (SD), 3 months, ITT HBOT + OS + ITSI: 65.9 (14.1) OS + ITSI: 56.7 (19.1) *p*<0.05 WDS % (95% CI) AMD (calculated) 9.2 (0.52 to 17.88) WDS % (SD), 3 months, PP HBOT + OS + ITSI: 66.4 (13.3) OS + ITSI: 56.7 (19.1) *p*<0.05

Authors (Year) Study Design Risk of Bias Comparison	Outcomes Definitions	Efficacy Outcomes
		**p<0.05 compared to the control group; average means calculated PTA as the mean of thresholds at 4 frequencies (500 Hz; 1, 2, and 4 kHz)
Cvorovic et al., 2013[23] RCT Some concerns Salvage therapy: HBOT vs. steroids	NR	Final value of thresholds at 5 frequencies at the end of salvage therapy 250 Hz HBOT: 35.5 ITS: 39.45 500 Hz HBOT: 45.3 ITS: 43.2 1,000 Hz HBOT: 47.6 ITS: 45.6 2,000 Hz HBOT: 56.2 ITS: 59.2 4,000 Hz HBOT: 60.5 ITS: 60.3 Hearing improvement in 5 frequencies at the end of salvage therapy Frequencies 250 Hz HBOT: 17.2 ITS: 20.2 *P*=NS Calculated mean difference: −3.0 500 Hz HBOT: 25.0 ITS: 26.1 *P*=NS Calculated mean difference: −1.1 1,000 Hz HBOT: 25.2 ITS: 27.1 *P*=NS Calculated mean difference: −1.9

Authors (Year) Study Design Risk of Bias Comparison	Outcomes Definitions	Efficacy Outcomes
		2,000 Hz HBOT: 16.4 ITS: 11.4 *P*<0.05 Calculated mean difference: 5.0 4,000 Hz HBOT: 17.5 ITS: 12.7 *P*=NS Calculated mean difference: 4.8
Dova et al., 2022[24] RCT Low Steroids only vs. HBOT + steroids	Success: improvement in PTA of ≥10 dB Complete recovery: final hearing better than 25 dB Partial recovery: >15 dB improvement and final hearing 25 to 45 dB Slight improvement: >15 dB improvement and final hearing poorer than 45 dB No improvement: <15 dB improvement and final hearing poorer than 75 dB	Median (IQR) improvement from pretreatment PTA1 to posttreatment PTA1 HBOT + steroids: 17.5 (7.5 to 33.7) Steroids: 22.5 (0.0 to 45.6) *p*=0.771 N (%) with successful treatment based on PTA1 HBOT + steroids: 17 (68) Steroids: 14 (56) *p*=0.382 Median (IQR) improvement from pretreatment PTA2 to posttreatment PTA2 HBOT + steroids: 19.2 (6.7 to 32.5) Steroids: 21.7 (1.7 to 42.9) *p*=0.915 N (%) with successful treatment based on PTA2 HBOT + steroids: 18 (72) Steroids: 16 (64) *p*=0.544 N (%) hearing recovery based on Siegel's criteria PTA1 Complete HBOT + steroids: 6 (24) Steroids: 8 (32) Partial recovery HBOT + steroids: 5 (20) Steroids: 5 (20) Slight improvement HBOT + steroids: 5 (20) Steroids: 1 (4)

Authors (Year) Study Design Risk of Bias Comparison	Outcomes Definitions	Efficacy Outcomes
		No improvement HBOT + steroids: 9 (36) Steroids: 11 (44) N (%) hearing recovery based on Siegel's criteria PTA2 Complete HBOT + steroids: 5 (20) Steroids: 9 (36) Partial recovery HBOT + steroids: 5 (20) Steroids: 5 (20) Slight improvement HBOT + steroids: 7 (28) Steroids: 2 (8) No improvement HBOT + steroids: 8 (32) Steroids: 9 (36)
Kim et al. (2023)[25] RCT Low HBOT Treatment Protocol 1 vs HBOT Treatment Protocol 2 vs. HBOT Treatment Protocol 3	Complete recovery: return of the PTA to within 10 dB HL of that of the unaffected ear and recovery of WDS to within 5%-10% of that of the unaffected ear Partial recovery: final hearing threshold of <50 dB HL and a WDS of >50% Slight improvement: improvement of >10 dB No improvement: <10 dB improvement in PTA	Mean (SD) pretreatment PTA (dB) HBOT 1 + SS + ITS: 98.8 (15.3) HBOT 2 + SS + ITS: 93.3 (15.3) HBOT 3 + SS + ITS: 95.6 (18.6) *P*=0.401 (between-group ANOVA) Mean (SD) posttreatment PTA (dB) HBOT 1 + SS + ITS: 45.0 (26.1) HBOT 2 + SS + ITS: 40.8 (27.4) HBOT 3 + SS + ITS: 59.4 (26.4) *P*=0.048 (between-group ANOVA) HBOT 1 vs. HBOT 3: *P*=0.079HBOT + 2 vs. HBOT 3: *p*=0.015 HBOT 1 vs. HBOT 2: *P*=0.797 Mean (SD) improvement in PTA (dB) HBOT 1 + SS + ITS: 53.8 (16.0) HBOT 2 + SS + ITS: 52.5 (18.0) HBOT 3 + SS + ITS: 36.5 (24.8) *P*=0.002 (between-group ANOVA) Post-hoc pairwise comparisons: HBOT 1 vs. HBOT 3: *P*=0.002; calculated AMD, 17.6; 95% CI, 6.6 to 28.6 HBOT 2 vs. HBOT 3: *P*=0.004; calculated AMD, 16.3; 95% CI, 5.2 to 27.4

Authors (Year) Study Design Risk of Bias Comparison	Outcomes Definitions	Efficacy Outcomes
		HBOT 1 vs. HBOT 2: *P*=0.964; calculated AMD, 1.3; 95% CI, −9.3 to 11.9 N (%) with complete recovery after treatment HBOT 1 + SS + ITS: 12 (36.4) HBOT 2 + SS + ITS: 15 (44.1) HBOT 3 + SS + ITS: 4 (12.5) *P*=0.016 (between-group ANOVA) N (%) with partial recovery after treatment HBOT 1 + SS + ITS: 7 (21.2) HBOT 2 + SS + ITS: 5 (14.7) HBOT 3 + SS + ITS: 6 (18.8) *P*=0.784 (between-group ANOVA) N (%) with slight improvement after treatment HBOT 1 + SS + ITS: 12 (36.4) HBOT 2 + SS + ITS: 12 (35.3) HBOT 3 + SS + ITS: 15 (46.9) *P*=0.572 (between-group ANOVA) N (%) with no improvement after treatment HBOT 1 + SS + ITS: 2 (6.1) HBOT 2 + SS + ITS: 2 (5.9) HBOT 3 + SS + ITS: 7 (21.9) *P*=0.083 (between-group ANOVA) Mean (SD) posttreatment WDS (%) HBOT 1 + SS + ITS: 72.7 (24.5) HBOT 2 + SS + ITS: 76.0 (27.9) HBOT 3 + SS + ITS: 53.9 (34.3) *P*=0.034 (between-group ANOVA) Post-hoc pairwise comparisons: HBOT 1 + SS + ITS vs. HBOT 3 + SS + ITS: *P*=0.041 HBOT 2 + SS + ITS vs. HBOT 3 + SS + ITS: *P*=0.017 HBOT 1 + SS + ITS vs. HBOT 2 + SS + ITS: *P*=0.964 Calculated change in WDS (change in % correct) HBOT 1 + SS + ITS: 66.6 HBOT 2 + SS + ITS: 68.2 HBOT 3 + SS + ITS: 43.4

Authors (Year) Study Design Risk of Bias Comparison	Outcomes Definitions	Efficacy Outcomes
Krajcovicova et al., 2018[26] RCT Some concerns Steroids only vs. HBOT + steroids	Complete recovery: recovering to within 10 dB of the hearing level of the unaffected ear Improvement: hearing gain (change in PTA) of ≥10 dB No improvement: hearing gain <10 dB	Mean (SD) hearing after treatment 250 to 500 Hz HBOT + steroids: 24.8 (17.0) Steroids: 27.2 (18.6) 1,000 to 2,000 Hz HBOT + steroids: 26.5 (23.5) Steroids: 28.9 (18.8) 4,000 to 8,000 Hz HBOT + steroids: 37.5 (29.6) Steroids: 45.1 (21.6) Calculated mean hearing improvements 250 to 500 Hz HBOT + steroids: 20.6 Steroids: 7.8 1,000 to 2,000 Hz HBOT + steroids: 20.4 Steroids: 11.8 4,000 to 8,000 Hz HBOT + steroids: 11.3 Steroids: 4.3 Calculated difference-in-differences between HBOT + steroids vs. control 250 to 500 Hz: 12.8 1,000 to 2,000 Hz: 8.6 4,000 to 8,000 Hz: 7.0 Calculated N (%) with no improvement HBOT + steroids: 18 (38.3) Steroids: 15 (71.4) Calculated N (%) with improvement HBOT + steroids: 29 (61.7) Steroids: 6 (28.6) Calculated N (%) complete recovery after treatment by frequency 250 to 500 Hz HBOT + steroids: 9 (19.2) Steroids: 3 (14.3) 1,000 to 2,000 Hz HBOT + steroids: 10 (21.3)

Authors (Year) Study Design Risk of Bias Comparison	Outcomes Definitions	Efficacy Outcomes
		Steroids: 1 (4.8) 4,000 to 8,000 Hz HBOT + steroids: 3 (6.4) Steroids: 0 (0.0) 250 to 8,000 Hz HBOT + steroids: 3 (6.4) Steroids: 0 (0.0)
Topuz et al., 2004[27] RCT High Steroids only vs. HBOT + steroids	NR	Mean (SD) posttreatment hearing levels (dB) HBOT + steroids and other drugs: 37.1 (NR) Steroids and other drugs: 53.1 (NR) Mean (SD) hearing improvement (dB) HBOT + steroids and other drugs: 33.3 Steroids and other drugs: 17.4 Calculated mean difference: 15.9

Abbreviations: AMD = absolute mean deviation; ITS/ITSI = intratympanic steroid injection; ITT = intent-to-treat analysis; IQR = interquartile range; HBOT = hyperbaric oxygen therapy; HL = hearing loss; NR = not reported; OS = oral steroids; PP = per protocol; PTA = pure-tone average; RCT = randomized controlled trial; SD = standard deviation; SS = systemic steroids; SSNHL = sudden sensorineural hearing loss; WDS = word discrimination scores.

Table B-5. Subgroup Outcomes for Idiopathic SSNHL

Authors (Year) Study Design Risk of Bias Comparisons	Subgroups Reported	Subgroup Outcomes
Attanasio et al., 2015[18] RCT Some concerns HBOT Treatment Protocol 1 vs. HBOT Treatment Protocol 2	Severity of hearing loss at baseline	Comparing the PTA results within the severe and profound hearing loss group, no significant difference between the two protocols was seen (*p*=0.27). N (%) with successful treatment (complete recovery and marked recovery) among severe hearing loss group HBOT 1 + steroids: 10 (71.4) HBOT 2 + steroids: 14 (77.8) N (%) with unsuccessful treatment among severe hearing loss group HBOT 1+ steroids: 4 (28.6) HBOT 2+ steroids: 4 (22.2) N (%) with successful treatment (complete recovery and marked recovery) among profound hearing loss group HBOT 1+ steroids: 6 (46.2) HBOT 2+ steroids: 5 (50.0) N (%) with unsuccessful treatment among profound hearing loss group HBOT 1 + steroids: 7 (53.9) HBOT 2 + steroids: 5 (50.0) For clinical evaluation of hearing outcomes (successful or unsuccessful treatment), no significant difference between the 2 protocols among those with profound and severe hearing loss were found (*p*=0.58).
Cavaliere et al., 2022[19] RCT Some concerns HBOT only vs. steroids only vs. HBOT + steroids	Severity of hearing loss at baseline Other	Profound hearing loss (>90 dB in each frequency): Greater propotion of HBOT + OS participants had hearing recovery vs. OS (data reported in figure only; point estimates NR) Greater proportion of HBOT participants had hearing recovery vs. OS (Data reported in figure only, point estimates NR) Upsloping hearing loss (hearing loss affecting 250 and 500 Hz): Greater propotion of HBOT + OS participants had hearing recovery vs. OS (data reported in figure only; point estimates NR) Greater proportion of HBOT participants had hearing recovery vs. OS (data reported in figure only; point estimates NR) Downsloping hearing loss (hearing loss affecting 4,000 and 8,000 Hz more) Greater propotion of HBOT + OS participants had hearing recovery vs. OS (data reported in figure only; point estimates NR) Greater proportion of HBOT participants had hearing recovery vs. OS (data reported in figure only; point estimates NR) No difference across age groups for OS only patients Women vs. men Larger improvements in PTA for women compared with men (*P*<0.05).

Authors (Year) Study Design Risk of Bias Comparisons	Subgroups Reported	Subgroup Outcomes
Cekin et al., 2009[20] RCT Some concerns Steroids only vs. HBOT + steroids	Age	Patients younger than 50 years N (%) patients with complete hearing recovery after treatment HBOT + OS: 11 (52.40) OS: 7 (58.34) N (%) patients with moderate hearing recovery after treatment HBOT + OS: 5 (23.80) OS: 2 (16.66) N (%) patients with no hearing recovery after treatment HBOT + OS: 5 (23.80) OS: 3 (25) Patients older than 50 years N (%) patients with complete hearing recovery after treatment HBOT + OS: 10 (58.83) OS: 2 (22.23) N (%) patients with moderate hearing recovery after treatment HBOT + OS: 5 (29.41) OS: 3 (33.33) N (%) patients with no hearing recovery after treatment HBOT + OS: 2 (11.76) OS: 4 (44.44) The differences in treatment outcome between those younger than 50 years and older than 50 years were not statistically significant ($p>0.05$).

Authors (Year) Study Design Risk of Bias Comparisons	Subgroups Reported	Subgroup Outcomes
Cvorovic et al., 2013[23] RCT Some concerns Salvage therapy: HBOT vs. steroids	Age Severity of hearing loss at baseline	Severity of hearing loss at baseline Mean (SD) recovery of hearing (dB) for those with baseline PTA ≤60 dB HBOT: 23.3 (NR) ITS: 25.5 (NR) Mean (SD) recovery of hearing (dB) for those with baseline PTA 61 to 80 dB HBOT: 25.2 (NR) ITS: 28.7 (NR) Mean (SD) recovery of hearing (dB) for those with baseline PTA ≥81 dB HBOT: 13.5 (NR) ITS: 40.7 (NR) Patients with PTA >81 dB had significantly higher hearing improvement on IT steroid than on HBO treatment. Age Mean (SD) hearing improvement Patients younger than 60 years HBOT: 40.22 (12.44) ITS: NR Patients aged 60 years or older HBOT: 21.2 (10.4) ITS: NR In the HBOT group, hearing improvement was significantly better in patients younger than 60 years.

Authors (Year) Study Design Risk of Bias Comparisons	Subgroups Reported	Subgroup Outcomes
Dova et al., 2022[24] RCT Low (for overall study not subgroup results) Steroids only vs. HBOT + steroids	Severity of hearing loss at baseline	N (%) with successful treatment among those with mild SSNHL HBOT + steroids: 2 (100) Steroids: 1 (100) *P*=NR N (%) with successful treatment among those with moderate SSNHL HBOT + steroids: 1 (100) Steroids: 3 (43) *P*<0.999 N (%) with successful treatment among those with moderately severe SSNHL HBOT + steroids: 4 (50) Steroids: 3 (50) *P*<0.999 N (%) with successful treatment among those with severe SSNHL HBOT + steroids: 3 (75) Steroids: 1 (25) *P*<0.999 N (%) with successful treatment among those with deafness/profound SSNHL HBOT + steroids: 6 (60) Steroids: 0 (0) *P*=0.455
Kim et al., 2023[25] RCT Low HBOT Treatment Protocol 1 vs. HBOT Treatment Protocol 2 vs. HBOT Treatment Protocol 3	Comorbidities	Response to treatment (>10 dB improvement in PTA) rates for diabetes subgroup HBOT 1 + SS + ITS: 71.4 HBOT 2 + SS + ITS: 83.3 HBOT 3 + SS + ITS: 80.0 Response to treatment (>10 dB improvement in PTA) rates for vertigo subgroup HBOT 1 + SS + ITS: 83.3 HBOT 2 + SS + ITS: 80.0 HBOT 3 + SS + ITS: 73.3

Authors (Year) Study Design Risk of Bias Comparisons	Subgroups Reported	Subgroup Outcomes
Topuz et al., 2004[27] RCT High Steroids only vs. HBOT + steroids	Severity of hearing loss at baseline Other	Mean (SD) posttreatment hearing improvements (dB) among those with initial hearing levels of≤60 dB HBOT + steroids and other drugs: 22.5 (12.7) Steroids and other drugs: 22.3 (9.3) *p*=0.758 Calculated AMD, 0.2, 95% CI, -11.0 to 11.4 Mean (SD) posttreatment hearing improvements (dB) among those with initial hearing levels of 61-80 dB HBOT + steroids and other drugs: 35.5 (22.1) Steroids and other drugs: 16.2 (9.0) *p*=0.014 Calculated AMD, 19.3; 95% CI, 3.8 to 34.8 Mean (SD) posttreatment hearing improvements (dB) among those with initial hearing levels of ≥81 dB HBOT + steroids and other drugs: 50.7 (21.5) Steroid and other drugs: 13.0 (6.6) *p*=0.005 Calculated AMD, 37.7; 95% CI, 21.2 to 54.2

Abbreviations: AMD = absolute mean deviation; ITS/ITSI = intratympanic steroid injection; HBOT = hyperbaric oxygen therapy; NR = not reported; OS = oral steroids; PTA = pure-tone average; RCT = randomized controlled trial; SD = standard deviation; SS = systemic steroids; SSNHL = sudden sensorineural hearing loss.

Table B-6. Safety Outcomes for Idiopathic SSNHL

Authors (Year) Study Design Risk of Bias Comparisons	Safety Outcomes
Cavaliere et al., 2022[19] RCT Some concerns HBOT only vs. steroids only vs. HBOT + steroids	No short- or long-term posttreatment complications were observed.
Chi et al., 2018[21] RCT Low Steroids only vs. HBOT + steroids	No complications of treatment were seen in either group.
Cho et al., 2018[22] RCT Low Steroids only vs. HBOT + steroids	A complication of HBOT (i.e., mild otalgia during HBOT at the beginning of the therapy) was reported in 2 patients in the study group, but they were soon addressed and could terminate the treatment. Otherwise, no adverse effects were noted in either of the 2 groups.
Cvorovic et al., 2013[23] RCT Some concerns Salvage therapy: HBOT vs. steroids	During the HBOT treatment, 3 patients had serous otitis media, which were treated conservatively. There were no unexpected side effects or complications because of ITS application in the follow-up period. Five patients had mild pain in the ear during application, and this successfully resolved with analgesics.
Dova et al., 2022[24] RCT Low Steroids only vs. HBOT + steroids	No significant complications occurred during hyperbaric oxygen therapy sessions. Two patients of 25 in the study (8%) experienced a transient ear pain due to slight Eustachian tube dysfunction, which was successfully treated with topical nasal anticongestants, and did not result in a barotrauma.

Authors (Year) Study Design Risk of Bias Comparisons	Safety Outcomes
Kim et al., 2023[25] RCT Low HBOT Treatment Protocol 1 vs. HBOT Treatment Protocol 2 vs. HBOT Treatment Protocol 3	N (calculated %) with adverse events after HBOT HBOT 1 + SS + ITS: 4 (12.1) HBOT 2 + SS + ITS: 2 (5.9) HBOT 3 + SS + ITS: 2 (6.3) *p*=NS Middle ear effusion was the most common adverse event (3 patients) among the 8 patients, followed by otalgia (2 patients), claustrophobia (2 patients), and hemotympanum (1 patient). Patients with claustrophobia were excluded from the study; however, the others had mild symptoms and improved.

Abbreviations: HBOT = hyperbaric oxygen therapy; ITS/ITSI = intratympanic steroid injection; NS = not significant; RCT = randomized controlled trial; SS = systemic steroids; SSNHL = sudden sensorineural hearing loss.

Table B-7. Study Characteristics for AAT

Authors (Year) Study Design Risk of Bias	Setting Country Study Period	Study Population Inclusion Criteria Exclusion Criteria	Eligible Study Arms (sample size)
Bayoumy et al., 2020[3] NRSI Serious	Otolaryngology department in a Military Hospital The Netherlands November 2012 and December 2017	Military personnel with AAT who were able to start treatment within 2 weeks following AAT. Included individuals with hearing loss after AAT who were eligible for HBO (Defined for Dutch military personnel as a hearing loss of 30 dB or greater on at least 1, 25 dB or more on at least 2, or 20 dB or more on 3 or more frequencies as compared with the contralateral ear or a previous audiogram not older than 2 years.); treatment with corticosteroid monotherapy or HBO combination therapy, possibility to start within 2 weeks following AAT. Excluded those with a history of SSNHL before firearms use, vestibular schwannoma, idiopathic sudden sensorineural hearing loss, presentation at the Department of Otolaryngology more than 2 weeks after trauma, or absence of pretreatment and/or posttreatment audiograms	HBOT + OS; n=23 (29 ears) 60 mg prednisolone for 7 days plus 10 sessions of HBOT (usually on weekdays) in a multiperson recompression chamber, where subjects breathed 100% oxygen via a built-in breathing mask at a pressure of 253 kPa for 90 minuntes, with 3, 5 minute “air breaks.” OS; n=18 (24 ears) 60 mg prednisolone for 7 days plus 10 sessions
Lafere et al., 2010[28] NRSI Serious	Military hospital Belgium January 2006 to December 2008	Soldiers with unilateral AAT Hearing loss of at least 25 dB in at least 1 frequency (as compared with their baseline PTA) Less severe hearing loss or improvement in hearing of more than 20 dB in any frequency in the first 24 hours after AAT (temporary threshold shift); history of previous AAT	HBOT + IV + OS; n=32 2 sessions per day for 3 consecutive days followed by 1 session per day for 7 days at 253 kPa with 70 minutes per session, plus IV methylprednisolone (125 mg decreasing to 40 mg) and IV piracetam (12 g over 15 minutes) daily for 5 days, followed by oral methylprednisolone (32 mg decreasing to 40 mg) and oral piracetam (2400 mg 3 times a day) for 5 days HBOT + OS; n=19 1 session per day at 253 kPa with 70 minutes per session for 10 days total, plus oral methylprednisolone (decreasing daily dosage 64 mg reducing to 8 mg) over 10 days and piracetam (2400 mg 3 times a day) for 10 days OS; n=17 Oral methylprednisolone (decreasing daily dosage 64 mg reducing to 8 mg) over 10 days and piracetam (2400 mg 3 times a day) for 10 days

Authors (Year) Study Design Risk of Bias	Setting Country Study Period	Study Population Inclusion Criteria Exclusion Criteria	Eligible Study Arms (sample size)
Oya et al., 2019[29] NRSI Critical	Military undersea medical center Japan April 1997 to August 2017	Military personnel with AAT Patients treated with HBOT for acute acoustic trauma at the Japan Maritime Self-Defense Force Undersea Medical Center NR	HBOT TT5; n=7 (7 ears) 2-hours, 15 minutes per session at 180 kPa and then decreasing to 90 kPa, for a mean (SD) of 6.5 (1.1) days In a subgroup of those treated with steroids: methylprednisolone 500 mg for patients whose subjective symptoms were ameliorated; prednisolone gradual dose reduction starting at maximum of 200 mg; prednisolone Gradual dose reduction starting at a maximum of 70 mg for patients who showed no improvements in their subjective symptoms after steroid treatment HBOT TT9; n=28 (30 ears) 1 hour, 45 minutes per session at 135 kPa, for a mean (SD) of 8.5 (2.4) days In a subgroup of those treated with steroids: methylprednisolone 500 mg for patients whose subjective symptoms were ameliorated; prednisolone gradual dose reduction starting at maximum of 200 mg; prednisolone Gradual dose reduction starting at a maximum of 70 mg for patients who showed no improvements in their subjective symptoms after steroid treatment

Authors (Year) Study Design Risk of Bias	Setting Country Study Period	Study Population Inclusion Criteria Exclusion Criteria	Eligible Study Arms (sample size)
Pilgramm et al., 1985[30] RCT High	Otorhinolaryngology department of a federal army hospital Germany NR	Soldiers with AAT occurring within the last 48 hours Soldiers with onset of AAT in the last 48 hours The following parameters led to exclusion of patients from the study: (a) acoustic trauma occurring more than 48 h before examination; (b) loss of hearing not reaching 40 dB in any frequency; (c) loss of hearing of 40 dB no longer detectable in any frequency on audiometric control 24 hours after admission, or spontaneous improvement in hearing of more than 20 dB in any frequency in the first 24 hours after admission; (d) history of acoustic trauma (or "retrauma"); (e) involvement of the middle ear as in explosion trauma; and (f) other severe general illnesses, especially of the respiratory organs (second vital capacity or vital capacity severely restricted), known tendency to convulsions or hyperventilation tetany, or other medical contraindications.	HBOT + infusions 1; n=29 1 session per day at 2.8 bar with 60 minutes per session for 10 successive days (10 sessions total), plus IV 10% dextran-40 solution and 5% sorbitol solution (40 drips/minute for 3-5 hours) for 14 days and IV dextran-1 (3 g) before each first infusion Infusions 1; n=33 IV 10% dextran-40 solution and 5% sorbitol solution (40 drips/minute for 3-5 hours) for 14 days and IV dextran-1 (3 g) before each first infusion HBOT + infusions 2; n=32 1 session per day at 2.8 bar with 60 minutes per session for 10 successive days (10 sessions total), plus IV 10% dextran-40 solution and 5% sorbitol solution (40 drips/minute for 3-5 hours) for 14 days, IV dextran-1 (3 g) before each first infusion, and 24 mg oral betahistine Infusions 2; n=26 IV 10% dextran-40 solution and 5% sorbitol solution (40 drips/minute for 3-5 hours) for 14 days, IV dextran-1 (3 g) before each first infusion, and oral betahistine (24 mg daily)

Authors (Year) Study Design Risk of Bias	Setting Country Study Period	Study Population Inclusion Criteria Exclusion Criteria	Eligible Study Arms (sample size)
Salihoglu et al., 2015[31] NRSI Critical	Otolaryngology service at a training hospital Turkey January 2011 to April 2013	Male adult soldiers with unilateral or bilateral AAT after training with a G3 rifle (caliber 7.62 mm) with onset in the last 30 days Having sensorineural hearing loss due to AAT; having detailed otolaryngological examination records and pure-tone audiometry measurements (values for 0.5, 1, 2, 4, 6, 8, 10, 12.5, 14, and 16 kHz) before, 10 days and 6 weeks after initiation of the treatment; and having combined steroid therapy and HBO2 therapy. Age younger than 18 years; intracranial malignancy; hypertension; comorbid upper respiratory disease; and history of hearing impairment before firearms use	Early HBOT + steroids; n=37 ears Treatment initiated within first 10 days of onset. 1 session per day at 2.4 ATM with 90 minutes per session for a total of 10 days (10 sessions), plus oral deflazakort (90 mg, tapered 15 mg in 3-day intervals) for 18 days and oral pantoprazol (40 mg). If an incomplete improvement was observed on pure-tone audiometry after 10 sessions, HBOT continued up to 20 sessions. Late HBOT+ steroids; n=36 ears Treatment initiated 11 to 30 days after onset. 1 session per day at 2.4 ATM with 90 minutes per session for a total of 10 days (10 sessions), plus oral deflazakort (90 mg, tapered 15 mg in 3-day intervals) for 18 days and oral pantoprazol (40 mg). If an incomplete improvement was observed on pure-tone audiometry after 10 sessions, HBOT continued up to 20 sessions.
Vavrina et al., 1995[32] NRSI Critical	Otorhinolaryngology department of a hospital Switzerland NR	Adults with unilateral or bilateral AAT with onset in the last 72 hours Unilateral and/or bilateral AAT with onset in the last 72 hours Acoustic trauma occurring longer then 72 hours before treatment, spontaneous improvement of hearing before treatment, preexisting inner ear disease, pathological tympanogram and negative Valsalva manoevre and severe general illness	HBOT + drugs; n=36 5-10 sessions (average of 7.2 sessions) at 1.4-2.2 ATA with 60 minutes per session, plus cortisone (150 mg via IV on the first day and 80 mg initial dose orally from second day onward), IV Ginkgo extracts in saline or dextran, and IV prednisone Drugs, n = 42 Cortisone (150 mg via IV on the first day and 80 mg initial dose orally from second day onwards), IV Ginkgo extracts in saline or dextran, and IV prednisone

Authors (Year) Study Design Risk of Bias	Setting Country Study Period	Study Population Inclusion Criteria Exclusion Criteria	Eligible Study Arms (sample size)
Ylikoski et al., 2008[4] NRSI Serious	Military hospital Finland HBOT: August 1, 1993, to March 31, 1996; NBOT: January 1, 1984, to March 31, 1989	Male adult military conscripts with AAT HBOT: (1) previously normal hearing as revealed by the patient history and initial screening audiometry at the beginning of the military service; (2) a temporary threshold shift of 30 dB or more, at least at 1 frequency; (3) the causative weapon was a 7.62 caliber attack rifle; (4) the delay from the exposure to the first audiogram was <48 hours; and (5) no previous history of AAT or tinnitus NBOT (control): (1) similar acute exposure (approximately the same number of shots by an assault rifle); (2) equal delay of time from the AAT to the first audiogram (in the limit of 3 hours); and (3) similar amount and audiogram configuration of the initial hearing impairment (PTA), HPTA, maximal hearing loss (max HL) with a difference 55 dB) NR	HBOT, n = 58 patients (60 ears) 1 session per day from Monday to Friday at 240 kPa with 90 min per session, for a mean (SD) total of 6.1 (1.9) sessions (incudes normobaric sessions) and mean total of 3.5 days (ranging from 1 to 8 days). During the weekend days when HBOT was not available, patients breathed 100% oxygen in a normobaric environment for 90 min twice daily. Number of HBOT session was 3.2 (1.4) NBOT, n = 60 patients (60 ears) NBOT 2 sessions per day with 90 min per session, for a mean (SD) total of 6.2 (1.9) sessions.

Abbreviations: AAT = acute acoustic trauma; ATA = atmosphere absolute; ATM = atmosphere; HBOT = hyperbaric oxygen therapy; HPTA = high pure-tone average; IV = intravenous; NBOT = normobaric oxygen therapy; NR = not reported; NRSI = nonrandomized study of intervention; OS = oral steroids; PTA = pure-tone average; RCT = randomized controlled trial; SSNHL = sudden sensorineural hearing loss; TT5 = Treatment Table 5; TT9 = Treatment Table 9.

Table B-8. Population Characteristics for AAT

Authors (Year) Study Design Risk of Bias	Mean Age (SD)	N (%) Female	N (%) Race/Ethnicity	Hearing Loss at Baseline PTA Hearing Loss
Bayoumy et al., 2020[3] NRSI Serious	HBOT + steroids: 26.1 (4.8) Steroids only: 24.9 (4.0)	NR	NR	Mean (SD) pretreatment absolute hearing loss (relative to the contralateral ear) measured as PTA in dB (including both affected and nonaffected frequencies) HBOT + steroids: 26.7 dB (16.8) Steroids only: 26.6 dB (15.0) No significant between-group difference Mean (SD) initial absolute hearing loss in PTA dB (affected frequencies only) HBOT + steroids: 46.1 dB (14.4) Steroids only: 38.6 dB (11.3) *p*<0.05 at 3000 Hz and 4000 Hz NR
Lafere et al., 2010[28] NRSI Serious	Total: 20.9 (4.6)	NR	NR	Mean (SD) pretreatment hearing loss (relative to PTA at entry to the military) measured as PTA in dB at affected frequencies HBOT + IV + OS: 31.4 (19.0) HBOT + OS: 29.7 (15.7) OS: 25.8 (11.7) *p*=0.6603 NR
Oya et al., 2019[29] NRSI Critical	HBOT TT5: 23.9 (10.7), range: 16 to 48 years HBOT TT9: 27.7 (8.4); age range: 17 to 45 years	HBOT TT5: 0 (0) HBOT TT9: 3 (calculated 10.7)	NR	Mean (SD) pretreatment PTA across all groups and all frequencies (dB): 32.9 (16.0) Mean (SD) pretreatment PTA (mean of the values for 500 Hz, 1,000 Hz, and 2,000 Hz) (dB) HBOT TT5: 19.6 (11.7) HBOT TT9: 29.7 (18.8) Mean (SD) pretreatment HPTA (mean of the values for 4,000 and 8,000 Hz) (dB) HBOT TT5: 35.4 (19.1) HBOT TT9: 51.4 (21.2) NR

Authors (Year) Study Design Risk of Bias	Mean Age (SD)	N (%) Female	N (%) Race/Ethnicity	Hearing Loss at Baseline PTA Hearing Loss
Pilgramm et al.,1985[30] RCT High	Total: 21.2 (4.6)	Total: 0 (0)	NR	NR N (%) perceived hearing loss categories None: 21 (17) Slight: 39 (32) Significant: 56 (46) Absolute: 6 (5) Calculated N (%) with symptoms 24 hours after hospital admission No tinnitus: 4 (3) Right ear tinnitus: 28 (23) Left ear tinnitus: 59 (48) Tinnitus in both ears: 32 (26) Dizziness: 4 (3) Vestibular vertigo: 2 (1) Mean (SD) tinnitus noise level HBOT + infusions 1: 8 (11) Infusions 1: 5 (3) HBOT + infusions 2: 8 (12) Infusions 2: 5 (2)
Salihoglu et al., 2015[31] NRSI Critical	Overall: 25.8 (3.9) Age range: 21 to 36 years	Early HBOT + steroids: 0 (0) Late HBOT+ steroids: 0 (0)	NR	PTA (dB) reported for each frequency only Calculated mean for early HBOT: 41.1 (18.1) Calculated mean for late HBOT: 45.9 (18.1) N (calculated %) with unilateral hearing loss Total: 23 (47.9) N (calculated %) with bilateral hearing loss: Total: 25 (52.1)
Vavrina et al., 1995[32] NRSI Critical	HBOT + drugs: 24.9 (6.3) Drugs: 22.7 (7.6)	NR	NR	NR other than no difference between the groups Both groups scored their self-estimated tinnitus levels between moderate and severe before treatment (only shown on bar graph with no exact values reported).

Authors (Year) Study Design Risk of Bias	Mean Age (SD)	N (%) Female	N (%) Race/Ethnicity	Hearing Loss at Baseline PTA Hearing Loss
Ylikoski et al., 2008[4] NRSI Serious	HBOT: 19.9 (1.5) NBOT (normobaric treatment): 20.3 (2.4)	HBOT: 0 (0) NBOT: 0 (0)	NR	Mean (SD) pretreatment PTA (dB measured at 0.5, 1, 2 kHz) HBOT: 13.2 (9.2) NBOT: 13.7 (9.2) p=NS Mean initial high frequency hearing loss (measured as HPTA in dB at 4, 6, 8 kHz) HBOT: 37.1(14.4) NBOT: 37.3 (15.2) *p*=NS Mean (SD) initial maximal hearing loss (measured at PTA in dB typically at 6 kHz) HBOT: 53.5 (12.1) NBOT: 51.8 (15.7) *p*=NS

Abbreviations: AAT = acute acoustic trauma; HBOT = hyperbaric oxygen therapy; HPTA = high pure-tone average; IV = intravenous; NBOT = normobaric oxygen therapy; NR = not reported; NRSI = nonrandomized study of intervention; NS = not significant; OS = oral steroids; PTA = pure-tone average; RCT = randomized controlled trial; SD = standard deviation; SS = systemic steroids; TT5 = Treatment Table 5; TT9 = Treatment Table 9.

Table B-9. Intervention Characteristics for AAT

Authors (Year) **Study Design** **Risk of Bias**	**Time to Treatment** **Duration of Follow-up**	**HBOT Regiment** Number of HBOT Sessions Length of Session Total duration of treatment Pressure	**Steroid Regiment** Steroid Mode of administration Dosage Duration of treatment	**Adherence to Intervention**
Bayoumy et al., 2020[3] NRSI Serious	Time to treatment: HBOT + Steroids: HBOT treatment: 4.4 (2.7) days Steroid treatment: 2.7 (2.9) days Steroids : 5.9 (2.7) days Duration of Follow-up: 1 year (if 1-year follow-up data missing, included 3-month or 6-month follow-up data)	10 sessions 90 minutes per session, with 3, 5 minute "air breaks" 2 weeks (Monday to Friday) 253 kPa	Prednisone Oral 60 mg 7 days	NR

Authors (Year) **Study Design** **Risk of Bias**	**Time to Treatment** **Duration of Follow-up**	**HBOT Regiment** Number of HBOT Sessions Length of Session Total duration of treatment Pressure	**Steroid Regiment** Steroid Mode of administration Dosage Duration of treatment	**Adherence to Intervention**
Lafere et al., 2010[28] NRSI Serious	Time to treatment: Early HBOT + steroids: < 36 hrs Delayed HBOT treatment: 36 to 43 hrs Time to steroid treatment: NR Steroid only: Immediate Duration of follow-up: 10 days	13 sessions 70 minutes per session 10 days (twice daily for 3 consecutive days, followed by once daily for 7days) 253 kPa 10 sessions 70 minutes per session 10 days (daily sessions) 253 kPa	Methylprednisolone IV 125 mg decreasing to 40 mg daily 5 consecutive days Piracetam IV 12 g over 15 minutes daily 5 consecutive days Methylprednisolone Oral 32 mg decreasing to 40 mg, 3 times per day 5 days Piracetam Oral 2400 mg 3 times per day 5 days (HBOT + IV + OS); 10 days (HBOT + OS and OS groups) Methylprednisolone Oral decreasing daily dosage, 64 mg reducing to 8 mg 10 days	NR
Oya et al., 2019[29] NRSI Critical	Time to treatment: Mean days (SD): 10.3 (7.6) Mean days (SD): 27.8 (53.7) Duration of follow-up: >3 weeks after treatment	NR 2 hours, 15 minutes Mean (SD): 6.5 (1.1) days 180 kPa to 90 KPa NR 1 hour, 45 minutes Mean (SD): 8.5 (2.4) days 135 kPa	Methylprednisolone IV 500 mg NR Prednisolone IV gradual dose reduction starting at maximum of 200 mg NR Prednisolone IV gradual dose reduction starting at a maximum of 70 mg NR	33 of the 35 patients (94.4%) (37 of 39 ears) successfully completed the HBOT.

Authors (Year) **Study Design** **Risk of Bias**	**Time to Treatment** **Duration of Follow-up**	**HBOT Regiment** Number of HBOT Sessions Length of Session Total duration of treatment Pressure	**Steroid Regiment** Steroid Mode of administration Dosage Duration of treatment	**Adherence to Intervention**
Pilgramm et al. (1985)[30] RCT High	Time to treatment: 24 to 72 hours Duration of follow-up: 42 days	10 sessions 60 min per session 10 successive days 2.8 bar	Dextran-40 IV 50 g 10% solution at 40 drips/minute for 3-5 hours 14 days Sorbitol IV 500 ml, 25 g 5% solution at 40 drips/minute for 3-5 hours 14 days Betahistine Oral 24 mg daily NR Dextran-1 IV 3 g before each first infusion 14 days	NR
Salihoglu et al., 2015[31] NRSI Critical	Time to treatment: Early HBOT mean (SD) days: 7.4 (2.0) Late HBOT mean (SD) days: 18.9 (7.0) Duration of follow-up: 6 weeks	10 to 20 sessions (depending on treatment response) 90 minutes per session 10 to 20 days (daily sessions) 2.4 ATM	Deflazakort Oral 90 mg, tapered 15 mg in 3-day intervals 18 days Pantoprazol (Proton pump inhibitor to address GI symptoms of steroids) Oral 40 mg NR	All patients completed HBOT therapy.

Authors (Year) **Study Design** **Risk of Bias**	**Time to Treatment** **Duration of Follow-up**	**HBOT Regiment** Number of HBOT Sessions Length of Session Total duration of treatment Pressure	**Steroid Regiment** Steroid Mode of administration Dosage Duration of treatment	**Adherence to Intervention**
Vavrina et al., 1995[32] NRSI Critical	Time to treatment: 15 to 72 hours Duration of follow-up: 6.5 days	5-10 sessions, average of 7.2 sessions 60 minutes per session 5-10 days (daily sessions) 1.4-2.2 ATA	Prednisone IV NR NR Cortisone IV 150 mg 1 day Ginkgo extracts in saline or dextran IV NR NR Cortisone Oral 80 mg initial dose from second day onwards NR	NR
Ylikoski et al., 2008[4] NRSI Serious	Time to treatment: HBOT mean (SD) hours: 16.8 (10.2) NBOT mean (SD) hours: 16.5 (11.7) Duration of follow-up: End of the therapy (on day 7 if the treatment lasted until the 7th day) or the last measurement at the end of the military service if some degree of damage was present on day 7	Mean (SD) sessions: 3.2 (1.4) 90 minutes per session Mean (range) days: 3.5 (1-8), daily sessions on weekdays 240 kPa	NA	NR

Abbreviations: AAT = acute acoustic trauma; ATA = atmosphere absolute; ATM = atmosphere; IV = intravenous; HBOT = hyperbaric oxygen therapy; NA = not applicable; NR = not reported; NRSI = nonrandomized study of intervention; OS = oral steroids.

Table B-10. Efficacy Outcomes for AAT

Authors (Year) Study Design Risk of Bias Comparison	Definition of Hearing Recovery Outcomes	Efficacy Outcomes
Bayoumy et al., 2020[3] NRSI Serious Steroids only vs. HBOT + steroids	Absolute hearing recovery defined as change in PTA Absolute [in decibels] = PTApre-PTApost Relative hearing improvement defined as change in PTA relative [in %] = 100% PTApre-PTApost / PTApre-PTAcontralateral Clinical recovery: Maximal hearing impairment of 20 dB at frequencies lower than 3000 Hz and maximal hearing impairment of 30 dB at frequencies equal or higher than 3000 Hz; patients were further grouped according to the hearing classification system used by the Committee on Hearing and Equilibrium-Clinical Outcome Score of A-D	Mean (SD) absolute hearing improvement across all frequencies combined, 1-year, HBOT + OS = 29 ears; OS = 24 ears HBOT + OS: 23.5 dB (12.1) OS:12.5 dB (12.5) *p*=0.002 Mean (SD) absolute hearing improvement across all frequencies combined excluding patients with an audiogram measured within 1 day after trauma, 1-year, HBOT + OS = 17; OS = 22 HBOT + OS: 21.3 dB (14.0) OS: 11.6 dB (12.6) *p*=0.030 Total mean relative (to the contralateral ear) hearing improvement across all frequencies combined, % (SD) HBOT + OS: 57.6% (31.6) OS: 31.4% (32.9) *p*<0.05 Returned to clinically acceptable levels[a] HBOT + OS: 11 of 18 (61%) OS: 1 of 12 (8%) *p*<NR Mean relative (to the contralateral ear) hearing improvement by time to treatment Within 2 days: n=12, 71.4% (27.5) More than 2 days: n=17, 47.9% (31.6) *p*<0.05 Taking the start of the therapy into account, the HBO group showed a higher mean hearing improvement than patients in the control group at all different time frames. However, these subgroups were small and the differences were not statistically significant.

Authors (Year) Study Design Risk of Bias Comparison	Definition of Hearing Recovery Outcomes	Efficacy Outcomes
Lafere et al., 2010[28] NRSI Serious Steroids only vs. HBOT + steroids	NR	Mean (SD) hearing improvement from pretreatment (dB) HBOT + IV + OS: 20.6 (17.7) HBOT + OS: 17.0 (14.0) OS: 5.6 (3.6) *p*=0.001 between all 3 groups *p*<0.05 any HBOT vs. OS only Mean (SD) residual hearing loss (dB) HBOT + IV + OS: 2.4 (10.7) HBOT + OS: 5.0 (8.0) OS: 14.7 (8.3) *p*=0.001 between all three groups *p*<0.05 any HBOT vs. OS only Calculated mean standard difference in residual hearing loss for HBOT + OS vs. OS (95% CI): -9.7 (-15.2 to -4.1)
Oya et al., 2019[29] NRSI Critical HBOT Treatment Protocol A vs. HBOT Treatment Protocol B	Complete recovery: hearing restored to within <20 dB Partial recovery: mean loss improved by 10 dB at the follow-up Unchanged: observed improvement was <10 dB or the patient's hearing had deteriorated	Mean (SD) recovery % posttreatment PTA HBOT TT5: 37.9 (29.6) HBOT TT9: 41.7 (28.9) *p*=0.738 Mean (SD) recovery % posttreatment HPTA HBOT TT5: 17.1 (25.9) HBOT TT9: 43.6 (31.5) *p*=0.028 N (calculated %) ears with complete recovery posttreatment HBOT TT5: 0 (0) HBOT TT9: 4 (13.3) N (calculated %) ears with partial recovery posttreatment HBOT TT5: 2 (28.6) HBOT TT9: 20 (66.7) N (calculated %) ears with unchanged posttreatment HBOT TT5: 5 (71.4n) HBOT TT9: 6 (20) There were statistically significant differences in the recovery grade (*p*=0.016) between the cases treated using HBOT TT5 and HBOT TT9.

Authors (Year) Study Design Risk of Bias Comparison	Definition of Hearing Recovery Outcomes	Efficacy Outcomes
Pilgramm et al., 1985[30] RCT High Control or usual care (other than steroids) vs. HBOT	NR	Proportion with hearing recovery after treatment (day 42) HBOT + infusions 1: 83 Infusions 1: 87 HBOT + infusions 2: 92 Infusions 2: 62 Improvement of all groups from baseline: *p*=0.001 Difference between groups: *p*=0.001 Mean (SD) tinnitus development of noise after treatment (day 42) Difference between HBOT and non-HBOT groups: *P*<0.001 Calculated N (%) with deterioration in hearing or an increase in tinnitus after discharge from hospital (4 weeks) HBOT + infusions 1: 2 (6) Infusions 1: 7 (21) HBOT + infusions 2: 1 (3) Infusions 2: 9 (34) *p*=NR
Salihoglu et al., 2015[31] NRSI Critical Other	Complete recovery: hearing restored to within ≤20 dB HL Partial recovery: average loss at follow-up was improved by ≥10 dB HL Unchanged: difference of ≤10 dB HL or deteriorated after treatment	NR
Vavrina et al., 1995[32] NRSI Critical Steroids only vs. HBOT + steroids	NR	Mean (SE) hearing cumulative improvement (dB) across frequencies from pretreatment to posttreatment HBOT + drugs: 121.3 (10.3) Drugs: 74.3 (8.9) For each frequency, the mean hearing improvement of the HBOT plus steroids group was 15.2 dB vs. 9.3 dB for the steroid alone group. *p*<0.004 After treatment (4 days follow-up), the HBOT group showed a lower tinnitus level, but the differences between the 2 groups were not statistically significant (*p*>0.07).

Authors (Year) Study Design Risk of Bias Comparison	Definition of Hearing Recovery Outcomes	Efficacy Outcomes
Ylikoski et al., 2008[4] NRSI Serious Control or usual care (other than steroids) vs. HBOT	Relative hearing improvement (recovery percentage): absolute hearing improvement in decibels divided by initial hearing loss Normal hearing: a threshold shift of 15 dB or less at any frequency	Mean (SD) recovery % posttreatment PTA[b] HBOT: 74.1 (19.9) NBOT: 60.2 (28.9) *p*=0.0240 Calcuated mean standard difference in % posttreatment PTA (95% CI): 13.9 (4.8 to 23.0)[c] Mean (SD) recovery % posttreatment HPTA[b] HBOT: 69.3 (17.1) NBOT: 56.2 (20.3) *p*<0.001 N ears (%) with normal hearing posttreatment[b] HBOT: 42 (70) NBOT: 24 (40) *p*<0.01 N ears (%) with tinnitus present at the time of discharge from military service (1-4 months after AAT) HBOT: 3 (5) NBOT: 11 (18) *p*<0.05

[a] Unable to access supplementary files to determine what these sample sizes represent and we received no response to our outreach from the author; therefore' data is not graded**.**
[b] Follow-up audiograms were done at the end of the therapy (on day 7 if the treatment lasted until the 7th day) and the last measurement at the end of the military service if some degree of damage was present on day 7.
[c] Used OpenEpi to calculate the mean standard difference and confidence intervals for % PTA recovery posttreatment.

Abbreviations: AAT = acute acoustic trauma; dB HL = decibels in hearing level; IV = intravenous; HBOT = hyperbaric oxygen therapy; HPTA = high pure-tone average; NBOT = normobaric oxygen therapy; NR = not reported; NRSI = nonrandomized study of intervention; OS = oral steroids; PTA = pure-tone average; RCT = randomized controlled trial; SE = standard error; TT5 = Treatment Table 5; TT9 = Treatment Table 9.

Table B-11. Subgroup Outcomes for AAT

Authors (Year) Study Design Risk of Bias Comparisons	Subgroups Reported	Subgroup Outcomes
Oya et al., 2019[29] NRSI Critical HBOT Treatment Protocol A vs. HBOT Treatment Protocol B	Other	N (%) of ears whose subjective symptoms improved (out of 31) HBOT TT5: 6 (19.4) HBOT TT9: 25 (80.6) Mean (SD) recovery % posttreatment PTA among steroid-treated ears HBOT TT5: 42.6 (32.4) HBOT TT9: 45.9 (29.3) N (calculated %) ears with complete recovery posttreatment among steroid-treated ears (total N=30) HBOT TT5: 0 (0) HBOT TT9: 4 (16.7) N (calculated %) ears with partial recovery posttreatment among steroid-treated ears (total N=30) HBOT TT5: 2 (33.3) HBOT TT9: 17 (70.8) N (calculated %) ears with unchanged posttreatment among steroid-treated ears (total N=30) HBOT TT5: 4 (66.7) HBOT TT9: 3 (12.5) N (calculated %) ears that improved with steroids among steroid-treated ears (total N=30) HBOT TT5: 6 (100) HBOT TT9: 20 (83.3)
Salihoglu et al., 2015[31] NRSI Critical Other	Time to treatment from symptom onset	N (%) with complete treatment response Early HBOT + steroids: 1 (2.7) Late HBOT + sSteroids: 0 (0) N (%) with partial treatment response Early HBOT + steroids early: 7 (18.9) Late HBOT + steroids: 3 (8.3) N (%) with unchanged treatment response Early HBOT + steroids: 29 (78.4) Late HBOT + steroids: 33 (91.7) There was no statistically significant difference between the 2 groups (*P*=0.095).

Abbreviations: AAT = acute acoustic trauma; HBOT = hyperbaric oxygen therapy; NRSI = nonrandomized study of intervention; PTA = pure-tone average; TT5 = Treatment Table 5; TT9 = Treatment Table 9.

Table B-12. Safety Outcomes for AAT

Authors (Year) Study Design Risk of Bias Comparisons	Safety Outcomes
Bayoumy et al., 2020[3] NRSI Serious Steroids only vs. HBOT + steroids	No side effects of therapy, either from prednisolone or HBOT, were found in this patient population.
Pilgramm et al., 1985[30] RCT High Control or usual care (other than steroids) vs. HBOT	N (calculated %) with reported side effects (i.e., left maxillary barosinusitis, oxygen intoxication) HBOT + infusions 1: 1 (3.0) Infusions 1: 0 (0) HBOT + infusions 2: 1 (3.1) Infusions 2: 0 (0)
Salihoglu et al., 2015[31] NRSI Critical Other	Bilateral myringotomy was performed in 1 patient because of Eustachian tube dysfunction on the 7th day of HBOT therapy; bilateral myringotomy and ventilation tube insertion were performed in one patient because of middle ear effusion, which developed after barotrauma in the HBOT chamber on the 3rd day of HBO2 therapy. Grommet ventilation tubes were removed after HBOT therapy. All patients' tympanic membranes were intact in the control examination 6 weeks after admission.
Vavrina et al., 1995[32] NRSI Critical Steroids only vs. HBOT + steroids	No serious side effects associated with HBO resulting from barometric pressure changes occurred.

Abbreviations: AAT = acute acoustic trauma; HBOT = hyperbaric oxygen therapy; NR = not reported; NRSI = nonrandomized study of intervention; RCT = randomized controlled trial.

Appendix C. Excluded Articles

List of Exclusion Codes

X1: Ineligible population

X2: Ineligible intervention

X3: Ineligible comparator

X4: Ineligible outcomes

X5: Ineligible setting

X6: Ineligible study design

X7: Ineligible language

X8: Duplicate or superseded

X9: Wrong publication type

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Appendix D. Individual Study Risk-of-Bias Assessments

Table D-1. Cochrane RoB 2.0 Risk-of-Bias Rating of RCTs

Authors (Year)	Domain 1 Randomization Process	Domain 2 Deviations from Intervention	Domain 3 Missing Outcome Data	Domain 4 Measurement of Outcomes	Domain 5 Selection of the Reported Result	Overall Risk of Bias	Comments
Attanasio et al., 2015[18]	Some concerns	Some concerns	Some concerns	Some concerns	Some concerns	Some concerns	Some concerns from lack of information on randomization, allocation concealment, baseline characteristics, analysis plan, and missing data
Cavaliere et al., 2022[19]	Some concerns	Low	Low	Low	Some concerns	Some concerns	Some concerns for baseline differences in randomized group, lack of information about intervention adherence and missing data, lack of blinding
Cekin et al., 2009[20]	Some concerns	Low	Low	Low	Some concerns	Some concerns	Some concerns related to baseline differences in time to treatment and lack of an analysis protocol
Chi et al., 2018[21]	Low	Low	Low	Low	Low	Low	None
Cho et al., 2018[22]	Low	Low	Low	Low	Low	Low	None
Cvorovic et al., 2013[23]	Low	Some concerns	Some concerns	Some concerns	Some concerns	Some concerns	Some concerns about possible baseline differences, no reporting on analysis plan, attrition, or missing data.
Dova et al., 2022[24]	Low	Low	Low	Low	Low	Low	None
Kim et al., 2023[25]	Low	Some concerns	Some concerns	Low	Low	Some concerns	Some concerns due to 6 participants (1 to 3 in each group) lost to follow-up or with incomplete treatment who were not included in the analysis
Krajcovicova et al., 2018[26]	Some concerns	Low	Low	Some concerns	Some concerns	Some concerns	Some concerns related to lack of allocation concealment, lack of blinding among outcome assessors, and lack of reporting on whether they study relied on a prespecified analysis plan

Authors (Year)	Domain 1 Randomization Process	Domain 2 Deviations from Intervention	Domain 3 Missing Outcome Data	Domain 4 Measurement of Outcomes	Domain 5 Selection of the Reported Result	Overall Risk of Bias	Comments
Pilgramm et al.,1985 [30]	High	Some concerns	Some concerns	Some concerns	Some concerns	High	High RoB due to lack of information about baseline differences or allocation concealment and some concerns regarding outcome selection and lack of blinding for outcome assessors
Topuz et al., 2004[27]	High	Some concerns	Some concerns	Some concerns	Some concerns	High	High RoB due to possibility of inadequate randomization, lack of reporting of baseline differences and choice of primary outcome.

Abbreviations: RCT = randomized controlled trial; RoB = risk of bias.

Table D-2. ROBINS-I Ratings of NSRIs

Authors (Year)	Domain 1 Bias Due to Confounding[a]	Domain 2 Bias in Selection of Participants	Domain 3 Bias in Classification of Intervention	Domain 4 Bias Due to Deviations from Intended Interventions	Domain 5 Bias Due to Missing Data	Domain 6 Bias in Measurement of Outcomes	Domain 7 Bias in Selection of Reported Result	Overall Risk of Bias Judgment	Comments
Bayoumy et al., 2020[3]	Serious	Low	Low	Low	Moderate	Low	Moderate	Serious	Serious concerns regarding limited attempts to control for only a small number of potential confounders, lack of information about missing data and how missing data were handled, selective reporting of outcomes for frequencies with significant results, and important differences between initiation of steroid treatment
Lafere et al., 2010[28]	Serious	Low	Low	Moderate	Moderate	Serious	Moderate	Serious	Serious risk of bias due to likely baseline differences between the groups and lack of control for confounding
Oya et al., 2019[29]								Critical	Critical concerns due to no attempt to control for confounding (e.g., no use of stratification, matching) and lack of information regarding why which participants received which interventions
Salihoglu et al., 2015[31]								Critical	Critical concerns due to no attempt to control for confounding and potential for major differences in those for whom data were available

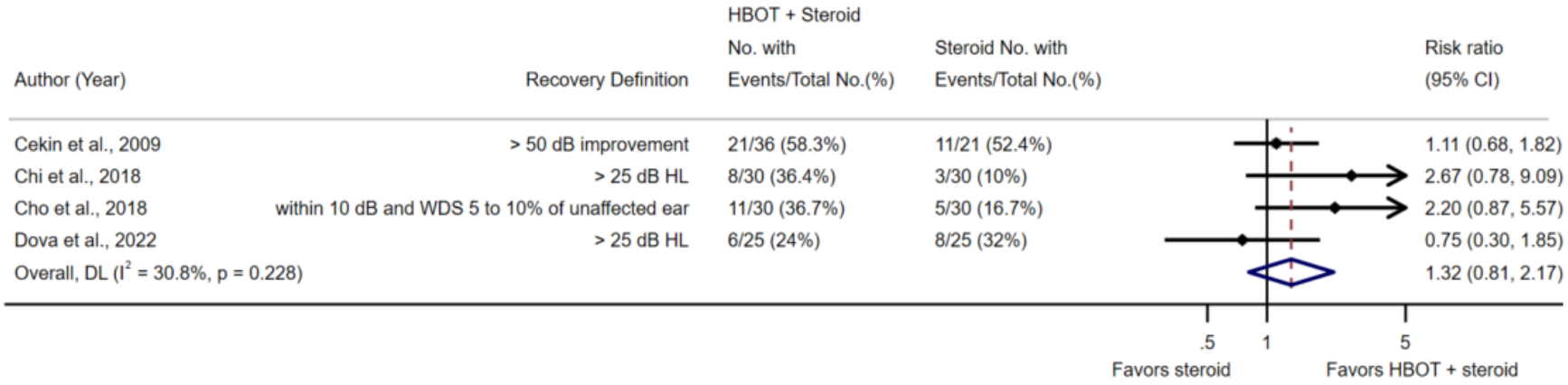
Authors (Year)	Domain 1 Bias Due to Confounding[a]	Domain 2 Bias in Selection of Participants	Domain 3 Bias in Classification of Intervention	Domain 4 Bias Due to Deviations from Intended Interventions	Domain 5 Bias Due to Missing Data	Domain 6 Bias in Measurement of Outcomes	Domain 7 Bias in Selection of Reported Result	Overall Risk of Bias Judgment	Comments
Vavrina et al., 1995[32]								Critical	Critical concerns due to no attempts to control for confounding between groups; no baseline characteristics apart from age and no baseline audiometry results were provided
Ylikoski et al., 2008[4]	Serious	Serious for hearing recovery; low for tinnitus	Low	No information	No information	Serious	Low	Serious	Critical concerns for confounding bias for the outcome of hearing recovery; serious concerns for confounding bias for the outcome of tinnitus

[a] If we assessed a study as critical due to no attempt to control for confounding with sufficient potential for confounding that an unadjusted result should not be considered further.

Abbreviation: NRSI = nonrandomized study of intervention.

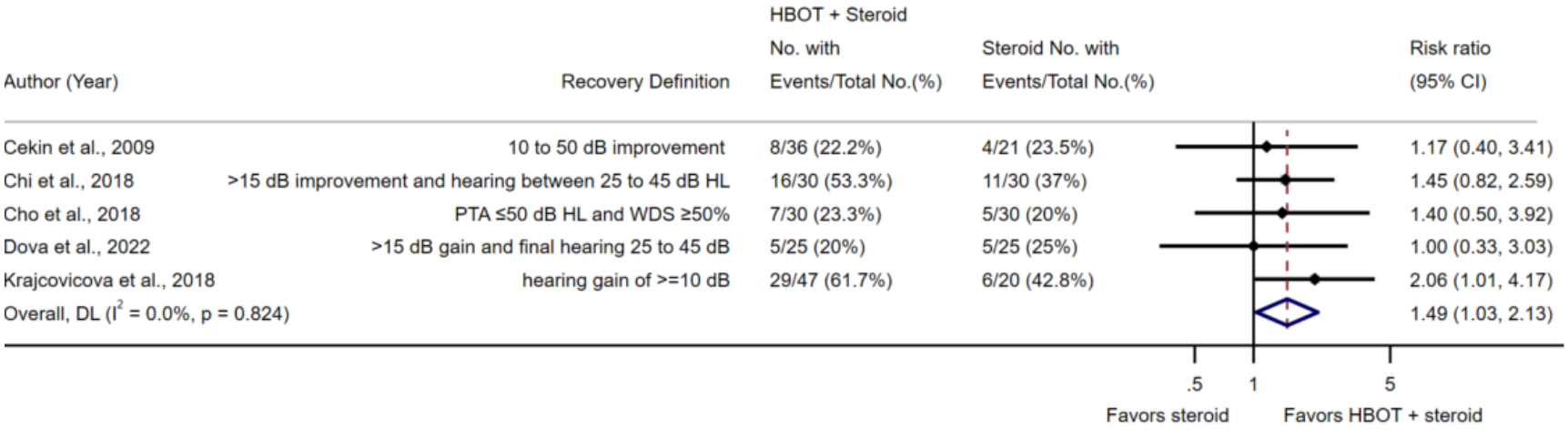
Appendix E. Additional Results

Figure E-1. Effect of HBOT and Steroid vs. Steroid on Complete Recovery



Abbreviation: HBOT = hyperbaric oxygen therapy.

Figure E-2. Effect of HBOT and Steroids vs. Steroids on Partial Recovery



Abbreviation: HBOT = hyperbaric oxygen therapy.