Washington State Health Care Authority

Hyperbaric Oxygen Therapy for Sudden Sensorineural Hearing Loss

Peer review and public comment on draft evidence report

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Health Technology Assessment Program (HTA)

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This document was created in response to peer review and public comments on a Draft Health Technology Assessment (HTA) report prepared by the RTI-UNC Evidence-based Practice Center through a contract to RTI International from 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 necessarily represent the views of the State of Washington HCA and no statement in this document should be construed as an official position of the State of Washington HCA.

The information in the document is intended to help the State of Washington's independent Health Technology Clinical Committee make well-informed coverage determinations. This document and its associated Evidence Report are 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 document and the associated Evidence 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).

Acknowledgments

The following individuals contributed to the report associated with this document:
Lead Investigator: Sara M. Kennedy, MPH
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Peer Review Comments and Responses

Two independent, external peer reviewers were invited to provide comments on the Draft Evidence Report and were provided with an honorarium for their review. The peer reviewer's name, affiliations, and conflicts of interest are reported in ***Table 1***.

Table 1. External Peer Reviewer of the Draft Evidence Report

Name	Title/Affiliation	Summary of Conflicts of Interest Reported
Desmond A Nunez, MD, MBA, FRCSEd, FRCSC	Professor, Division of Otolaryngology-Head and Neck Surgery Department of Surgery, Faculty of Medicine The University of British Columbia Diamond Health Care Centre	Published systematic review on this topic; Member of American Academy of Otolaryngology Head and Neck Surgery, treats patients with sudden sensorineural hearing loss.
Seth Roslow Schwartz, MD, MPH	Otology, Neurotology, and Skull Base Surgery Co-Director: The Listen For Life Center at Virginia Mason Section Head for Otolaryngology Head and Neck Surgery Virginia Mason Franciscan Health Associate Clinical Professor Otolaryngology at The University of Washington Methodologist for Guidelines: The American Academy of Otolaryngology Head and Neck Surgery	Author of American Academy of Otolaryngology Clinical Practice Guideline that evaluated HBOT for SSNHL; author of retrospective study on HBOT as salvage therapy; organization offers HBOT but does not have a stated position on the topic.

The peer reviewers did not identify any missing studies and did not identify any studies that should have been excluded from the report. We addressed most of the comments submitted by the reviewers in the Final Evidence Report. We provide a rational below for any comments we did not fully address. Meaningful revisions included additional information about how we assessed confounding in non-randomized studies of interventions, greater focus on hearing outcomes at high-frequencies for acute acoustic trauma (ATA), clarification that all included studies were conducted at hospitals with medical grade hyperbaric oxygen therapy (HBOT) chambers so findings are not generalizable to non-medical chambers, and acknowledgement of potential barriers to timely HBOT treatment. We considered other revisions made based on peer review comments as minor revisions. Specific peer review comments and responses are provided in ***Table 2***.

Table 2. Peer Reviewer Comments on Draft Evidence Report and Response

Item	Comment	Response
Introduction		
Are there any additional issues you think we should cover in the introduction?	**Reviewer 1:** The introduction is comprehensive. **Reviewer 2:** I completely agree that HBOT should be analyzed separately for sudden SNHL and AAT. ES1.2 Therapeutic pressure levels of HBOT are different. Non medical chambers only deliver up to 1.2 atm and are not regulated like medical HBOT. Medical HBOT delivers greater than 1.5 Atm. All of the evidence reviewed is for Medical grade HBOT chambers and the conclusions should not be generalized to non Medical chambers Fig ES-1: In the analytic framework there should be a decision node for HBOT with or without steroids	Thank you. No response required. We have added a note in ES 1.2 and 1.2 of the full report to explain this. Based on PICOTs, HBOT here refers to HBOT with or without steroids.
Do you see anything inaccurate, superfluous, or unclear?	**Reviewer 1:** The introduction is clear and accurately reflects the existing literature on Hyperbaric Oxygen therapy for Sudden Sensorineural Hearing loss. The variation in the pure tone audiomte. **Reviewer 2:** No.	No response required. No response required.
Any additional comments?	**Reviewer 1:** None. **Reviewer 2:** No.	No response required. No response required.
Methods		
Do you see any problems with our methods?	**Reviewer 1:** The risk of bias assessment tools selected are appropriate. However, it is not possible to appraise the reviewers use of these tools specifically in the risk of bias due to confounding domain. Note, the preamble to the ROBINS I V2 states 'Before undertaking a ROBINS-I assessment (or series of assessments, e.g. in the context of a systematic review), users of the tool should specify the important confounding factors that are likely to influence the association between the intervention and the outcome (see section "At planning stage").' https://methods.cochrane.org/bias/risk-bias-non-randomized-studies-interventions The HTA will be improved if this list of factors is included in the text of the report or as an appendix. **Reviewer 2:** No specific problems. The methods are clearly written and appropriate.	Thank you for this comment. We have added text to the methods section of the full report to list the important confounding factors that we identified prior to conducting ROBINS-I assessments. No response required.

Any additional comments about the Methods section?	**Reviewer 1:** None.	No response required.
	Reviewer 2: Methods: Study selection. Any age. Should the data for children be looked at independently. In the CPG on sudden hearing loss, children were called out as a special population as the mechanism for sudden hearing loss can be different and consequently the response to treatment can be different.	Children were included. If studies had reported data separately for children, we would have reported findings for this population separately. But the two studies that include older children (>13 years) and did not report results separately for children.
	Population: Was the primary condition unilateral SNHL or were bilateral cases included? Bilateral is often a different etiology and again may have differential response to therapy.	We included studies that enrolled participants with unilateral or bilateral hearing loss. Most studies only enrolled those with unilateral hearing loss. No studies reported outcomes by unilateral or bilateral hearing loss, but we would have reported these findings if they had been reported.
	Comparator: By different HBO treatments, does that include different pressures (ie, were low pressure therapy like 1.2 atm grouped with higher pressure treatments?)	We included HBOT at any pressure. If a study compared HBOT administered at different pressures, we included that within EQ1a on varying HBOT protocols. We reported ATA for all studies and note that all studies in the meta-analyses were done at > 2.0 ATA.
	Time to treatment. The study specifies under 15 days. Clearly there is more evidence for those treated immediately. There is significant interested in steroids for salvage between 14-31 days. This is partially of importance as a relatively low percentage of people respond to initial therapy and more importantly because logistically it can be very difficult to initiate treatment that quickly and many patients are unable to start treatment prior to 14 days post symptom onset.	We did not exclude any studies based on time to treatment but, yes, the evidence is concentrated among those treated quickly. We have added a sentence to the discussion noting that this is an area to consider for future research for this reason.
	Salvage therapy EQ2: This looks at a comparison of HBO alone to intratympanic steroids alone. In current practice, the evidence for intratympanic steroids for salvage is compelling enough that the AAO/HNS guideline on sudden hearing loss recommends salvage IT steroids. HBO is often used in combination with it, but very rarely alone. There is evidence (albeit not RCT level) comparing HBOT with IT steroids to IT steroids alone. That evidence may be worth looking at here.	We have added a paragraph to the discussion to highlight the AAO/HNS guideline on delayed treatment and a systematic review of salvage therapy that included non-randomized studies that found evidence for offering HBOT + intratympanic steroids.

Results		
Are there any studies you believe we may have missed?	**Reviewer 1:** No. **Reviewer 2:** There are no specific studies, but as mentioned above, when looking at HBOT for salvage treatment the included RCTs only compared HBOT to IT steroids, but did not compare HBOT with IT steroids to IT steroids alone. There are some non randomized trials that make this analysis and might be worth evaluating as there are no RCTs that make this comparison, but it is a more important clinical question.	No response required. We agree that this is an important point and we have added a paragraph to the discussion to highlight this evidence.
Are there studies that you believe we should have excluded?	**Reviewer 1:** No. **Reviewer 2:** No.	No response required. No response required.

Do you believe we have inaccurately described any studies?	Reviewer 1: Yilikoski et al was not fully accurately described. 3.3.3.1, Page 35, HBOT vs. Control or Usual Care (other than steroids): EQ1, final sentence 'critical RoB for the outcome of hearing improvement due to poor control for confounding and the exclusion of some participants from analysis' I am uncomfortable with the critical RoB allocation, however I do not have insight into the reviewers' choice of confounding factors. See my comments on confounding bias ascertainment in my B.1 response, and for hearing recovery in this article below. Page 37, Hearing recovery, penultimate sentence 'Notably, particpants without any abnormal threshold level in PTA range were excluded from the statistical analysis when calculating the hearing recovery percentage PTA.' Please revise this sentence to reflect that all high frequency aduiometic data in the study was subject to statistical analysis. Rationale: While the sentence accurately reflects Yilikoski et al's (2008) report of PTA as the authors defined it, it can be misinterpreted and is not the clinically important audiometeric frequency difference to consider in AAT. A Pure tone audiometric threshold shift maximal at 6 kHz is the early characteristic of all forms of noise induced hearing loss including AAT. Therfore all emphasis in my view needs to be given to audiometric findings at frequencies of 4 kHz and above. Yilikoski et al' also report 'All patients had a trauma at least in one frequency in HPTA range'. HPTA range was defined as 4,6 and 8 kHz in their paper. Importantly the statistical significance of the inter-group differences identified in the HPTA range is $p<0.001$ while it is only $p=0.024$ in the PTA range, consistent with the lower impact expected in lower audiometric test frequencies from noise exposure. **Reviewer 2:** No.	Thank you for this comment and explanation. We agree and have revised the RoB rating for Yilkoski et al and revised our results to focus on high-PTA findings. Thank you for this comment. We have rephrased the results to clarify that all participants were included in the HPTA analysis. No response required.

Any additional comments about the Results?	**Reviewer 1:** Acute Acoustic Trauma Section 3.3.2.1, Pg. 29, penultimate sentence '…; 2 studies were assessed as RoB[3,28] and' I recommend inserting 'serious' before RoB for consistency with the summary of Study Characteristics reported in Table 14.	Thank you for catching this, we have added the word serious.
	Reviewer 2: ES3.2.6 The second point of pressure differential is key. The lower level was 1.5 atm which is still only available in appropriate chambers. There are lifestyle HBO chambers not run by Hyperbaric medicine physicians that can deliver up to 1.2 atm. It should be clear that this is not the same thing as true HBO at the therapeutic levels offered by most hyperbaric medicine providers	We have added a note to this section to reminde the reader that 1.5 ATA is below the pressure typically used in medical grade HBOT.
	AAT ES 3.3.2.2 Determining the difference between starting at 1 day vs 2 days is difficult to assess as these would both be considered early treatment.	Agreed, we would also consider treatment initiation at 1 and 2 days early treatment. This is how the included study reported time to iniation so we've included the comparison they reported.
	ES 3.3.3.1 What are the infusions being referred to?	We've added that these were infusions of dextran and sorbitol (plasma expanders) with and without betahisine (anti-vertigo medication).
	ES 3.3.5 What is meant by alternative protocols?	We've added detail about the protocols to the ES.
	Full report section 1.2: Again, I think it is important to distinguish that while anything over 1atm is considered hyperbaric, the definitions for therapeutic treatment typically involve higher pressures and should be distinguished from homeopathic treatments offered in non medical settings (less than 1.2Atm).	We have added a note to this section to clarify this.
	Page 24, HBOT vs IT steroids for salvage. There is some non randomized data suggesting that combining HBOT with IT steroids leads to better hearing recovery than either alone. Since clinical practice is to offer IT steroids based on CPG from AAO/HNS, it may be worth looking at that data (although the conclusions of favoring HBOT over steroids alone for salvage would likely not be changed. AAT	We have added a paragraph to the discussion to include the AAO/HNS guideline and included findings from a broader systematic review on salvage threapy.

	Page 29 3.3.2.1 It says two studies were assessed as RoB and one was assessed as critical RoB. What was the RoB level for the first 2 studies? Page 35 Study and Population characteristics Betahistine is used as an anti-vertigo medication, but its mechanism of action is as a vasodialator	Thank you for catching this; the word serious was missing and has been added. Thank you, we've added this information.
Discussion		
Do you think we missed any important points?	**Reviewer 1:** No. The discussion reflects the literature. **Reviewer 2:** No.	No response required. No response required.
Do you disagree with any of the discussion items?	**Reviewer 1:** I have no serious concerns. **Reviewer 2:** No.	No response required. No response required.
Any additional comments about the Discussion?	**Reviewer 1:** Limitations of Evidence Base 4.2.1, pg. 44. Sentence 4 'some studies defined recovery based on PTA, while others used different frequency combinations or categorical definitions of hearing improvement.' Expand on the meaning of PTA here and/or in the Introduction. Rationale: PTA describes an averaged measure. Pure tone audiometric thresholds at three or four frequencies are commonly averaged, usually 0.5, 1, 2, 3 or 4 kHz. However, the frequencies used in any particular study should be stated by each study's investigators. The frequencies being averaged is especially important in a review of SSNHL and AAT. **Reviewer 2:** A general comment related to duration of follow up. Many of the studies had very short follow up times (end of treatment, two weeks, etc.).While these results are valid, longer term follow up (ie 2-3 months or longer) to determine if the differences found early persist would be helpful. Comparing results in studies with short term follow up to those with longer follow up could be worthwhile.	We have elaborated on this point in the limitations section. We added a note to the limitaitons to include this research gap.
Other Sections		

Any comments on the structured abstract, conclusion, figures, tables and appendices?	**Reviewer 1:** The figures and tables are of high quality and appropriately supplement the text. References Since the HTA is intended primarily for a US audience, consider using American reference sources to support the definition of PTA such as 1. Guide for the evaluation of hearing handicap. JAMA. 1979 May 11;241(19):2055-9. PMID: 430800. 2.Monsell EM. New and revised reporting guidelines from the Committee on Hearing and Equilibrium. American Academy of Otolaryngology-Head and Neck Surgery Foundation, Inc. Otolaryngol Head Neck Surg. 1995 Sep;113(3):176-8. doi: 10.1016/S0194-5998(95)70100-1. PMID: 7675474. **Reviewer 2:** The structured abstract is useful and concise. The conclusions, figures, and tables are well constructed and clear for the most part.	Thank you. We have added these references to the background section on PTA. Thank you.
General Comments		
Is the report clearly written, adequately detailed and of an appropriate length?	**Reviewer 1:** The report is clearly written and adequately detailed. **Reviewer 2:** Yes.	No response required. No response required.
Please make any additional comments you feel would help us improve the report.	**Reviewer 1:** I commend the HTA authors for undertaking a comprehensive review. I have no additional comments. **Reviewer 2:** This is overall a nice report that well captures the literature on the topic. The only point that is not made in the report is the logistical challenges of actually getting patients into the HBO chamber quickly. Insurance authorization can take weeks for a condition with a window of treatment that closes or at least diminishes in efficacy in days. This is likely outside of the scope of this report, but is a crucial issue in practice. These logistical concerns are one reason why the AAO guideline panel allowed for treatment out to one month despite the weaker evidence for benefit after 2 weeks.	Thank you. Thank you. We have added a comment about this point in the future research section of the discussion.

Public Comments and Responses

The Draft Evidence Report was posted for public comment from January 7 to February 6, 2025. No public comments were submitted.