Supplementary Online Content

Rhee T-M, Hwang D, Lee J-S, Park J, Lee JM. Addition of hyperbaric oxygen therapy vs medical therapy alone for idiopathic sudden sensorineural hearing loss: a systematic review and meta-analysis. *JAMA Otolaryngol Head Neck Surg*. Published online September 27, 2018. doi:10.1001/jamaoto.2018.2133

This supplementary material has been provided by the authors to give readers additional information about their work.

eMethods. Supplementary Methods

Search Strategy

Pubmed*			EMBASE†			Cochrane Library		
#18	#11 and #17	**113**	**#18**	#11 and #17	**138**	**#19**	Select 'trials' in #18	**24**
#17	#12 or #13 or #14 or #15 or #16	**13417**	**#17**	#12 or #13 or #14 or #15 or #16	**17570**	**#18**	#11 and #17	**38**
#16	'HBOT'	**576**	**#16**	'HBOT'	**792**	**#17**	#12 or #13 or #14 or #15 or #16	**2442**
#15	'HBO'	**2718**	**#15**	'HBO'	**4107**	**#16**	'HBOT'	**125**
#14	'hyperbaric oxygenation'	**2361**	**#14**	'hyperbaric oxygenation'	**2672**	**#15**	'HBO'	**252**
#13	'hyperbaric oxygen'	**7094**	**#13**	'hyperbaric oxygen'	**9157**	**#14**	'hyperbaric oxygenation'	**548**
#12	'hyperbaric'	**12833**	**#12**	'hyperbaric'	**16222**	**#13**	'hyperbaric oxygen'	**1077**
#11	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10	**11020**	**#11**	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10	**13369**	**#12**	'hyperbaric'	**2406**
#10	'ISHL'	**36**	**#10**	'ISHL'	**43**	**#11**	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10	**811**

#9	‘ISNHL’	**4**
#8	‘SHL’	**344**
#7	‘SNHL’	**1244**
#6	‘sensorineural hearing loss’	**10568**
#5	‘ISSHL’	**106**
#4	‘ISSNHL’	**136**
#3	‘SSHL’	**122**
#2	‘SSNHL’	**279**
#1	‘sudden sensorineural hearing loss’	**1239**

#9	‘ISNHL’	**5**
#8	‘SHL’	**416**
#7	‘SNHL’	**1535**
#6	‘sensorineural hearing loss’	**12783**
#5	‘ISSHL’	**126**
#4	‘ISSNHL’	**149**
#3	‘SSHL’	**134**
#2	‘SSNHL’	**318**
#1	‘sudden sensorineural hearing loss’	**1447**

#10	‘ISHL’	**67**
#9	‘ISNHL’	**1**
#8	‘SHL’	**29**
#7	‘SNHL’	**45**
#6	‘sensorineural hearing loss’	**718**
#5	‘ISSHL’	**23**
#4	‘ISSNHL’	**30**
#3	‘SSHL’	**22**
#2	‘SSNHL’	**32**
#1	‘sudden sensorineural hearing loss’	**220**

* Search options were limited to title or abstract by using commands as shown: ([Title/Abstract])

† Search options were limited to title, keyword, or abstract by using commands as shown: ([Title/Keyword/Abstract] : “:ti,ab,kw”)

Characteristics of the Excluded Studies

No.	Title	First Author	Journal	Main Reason for Exclusion
1	Sudden hypoacusis treated with hyperbaric oxygen therapy: A controlled study[1]	Fattori et al.	Ear Nose Throat, 2001	The protocol and main point of the study is irrelevant. The control group used vasodilator instead of steroids.
2	Sudden sensorineural hearing loss: Our experience in diagnosis, treatment, and outcome[2]	Cadoni et al.	J Otolaryngol, 2005	Results were not available as a suitable form for meta-analysis.
3	Comparison of simultaneous systemic steroid and hyperbaric oxygen treatment versus only steroid in idiopathic sudden sensorineural hearing loss[3]	Callioglu et al.	Int J Clin Exp Med, 2015	Results were not available as a suitable form for meta-analysis.
4	Hyperbaric oxygen therapy as salvage therapy for sudden sensorineural hearing loss[4]	Ajduk et al.	J Int Adv Otol, 2017	Results were not available as a suitable form for meta-analysis.

5	The place of hyperbaric oxygen therapy and ozone therapy in sudden hearing loss[5]	Tasdoven et al.	Braz J Otorhinolaryngol, 2017	The protocol and main point of the study is irrelevant. This study mainly investigated the efficacy of ozone therapy for sudden hearing loss.

eTable 1. Checklist of items to include when reporting a systematic review or meta-analysis (PRISMA guidelines)

Section/topic		Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	5
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	5
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	8
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	6
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	6

Section/topic		Checklist item	Reported on page #
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	6 and eMethods
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	6
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	7
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	7
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	7 and eMethods
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	8
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	7-8
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	9 and eTable 2 and 3
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	7-8
RESULTS			

Section/topic		Checklist item	Reported on page #
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	8-9 and Figure 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	9 and Table 1
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome-level assessment (see Item 12).	9 and eTable 2 and 3
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group and (b) effect estimates and confidence intervals, ideally with a forest plot.	9-11
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	9-11, Figure 1-2
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	10, eFigure 1
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	10-11, Figure 3-4, eFigure 2-5
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., health care providers, users, and policy makers).	11-13
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review level (e.g., incomplete retrieval of identified research, reporting bias).	15-16
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	16

Section/topic		Checklist item	Reported on page #
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	N/A

eTable 2. The Cochrane Collaboration's tool for assessing risk of bias of 3 randomized clinical trials in meta-analysis

Study	Domain	Support for judgment & review authors' judgment
Topuz et al. (2004)[6]	Random sequence generation	Unclear risk of bias. No indication of the method of random sequence generation.
	Allocation concealment	Unclear risk of bias. No indication of an attempt at the allocation concealment.
	Blinding of participants and personnel	High risk of bias. No attempt was described for blinding any party.
	Blinding of outcome assessment	High risk of bias. No attempt was described for blinding of outcome assessment.
	Incomplete outcome data	Low risk of bias. All patients at each randomization group were completely followed, and 100% of each group received allocated intervention.
	Selective reporting	Low risk of bias. All outcomes of interest have been reported in the manuscript.
	Other sources of bias	Low risk of bias. The study appears to be free of other sources of bias.
Cekin et al. (2009)[7]	Random sequence generation	Low risk of bias. Patients were randomly allocated using a computer-based method.
	Allocation concealment	Unclear risk of bias. No indication of an attempt at the allocation concealment.
	Blinding of participants and personnel	High risk of bias. No attempt was described for blinding any party.
	Blinding of outcome assessment	High risk of bias. No attempt was described for blinding of outcome assessment.
	Incomplete outcome data	Low risk of bias. All patients at each randomization group were completely followed, and 100% of each group received allocated intervention.
	Selective reporting	Low risk of bias. All outcomes of interest have been reported in the manuscript.
	Other sources of bias	Low risk of bias. The study appears to be free of other sources of bias.
Cvorovic et al. (2013)[8]	Random sequence generation	Unclear risk of bias. No indication of the method of random sequence generation.

Allocation concealment	Unclear risk of bias. No indication of an attempt at the allocation concealment.
Blinding of participants and personnel	High risk of bias. No attempt was described for blinding any party.
Blinding of outcome assessment	High risk of bias. No attempt was described for blinding of outcome assessment.
Incomplete outcome data	Low risk of bias. All patients at each randomization group were completely followed, and 100% of each group received allocated intervention.
Selective reporting	Low risk of bias. All outcomes of interest have been reported in the manuscript.
Other sources of bias	Low risk of bias. The study appears to be free of other sources of bias.

eTable 3. The Newcastle-Ottawa Scale for assessing the quality of 16 non-randomized studies in meta-analysis

No.	Author	Year	Selection	Comparability	Outcome
1	Cavallazzi et al.[9]	1996	★★★★	★	★★
2	Aslan et al.[10]	2002	★★★★	★	★★★
3	Narozny et al.[11]	2004	★★★★	★	★★
4	Desloovere et al.[12]	2006	★★★★	★	★★★
5	Satar et al.[13]	2006	★★★★	★	★★
6	Dundar et al.[14]	2007	★★★★	★	★★
7	Fujimura et al.[15]	2007	★★★★	★	★★★
8	Ohno et al.[16]	2010	★★★★	★	★★★
9	Alimoglu et al.[17]	2011	★★★★	★	★★
10	Liu et al.[18]	2011	★★★★	★	★★★
11	Yang et al.[19]	2013	★★★★	★	★★★
12	Capuano et al.[20]	2015	★★★★	★	★★★
13	Pezzoli et al.[21]	2015	★★★★	★	★★★
14	Psillas et al.[22]	2015	★★★★	★	★★★
15	Hosokawa et al.[23]	2017	★★★★	★	★★★

The Newcastle-Ottawa Scale

Selection (Maximum of one star for each numbered item)

1. Representativeness of the exposed cohort

   a) truly representative of the average _____ (describe) in the community *

   b) somewhat representative of the average _____ in the community *

   c) selected group of users eg nurses, volunteers

   d) no description of the derivation of the cohort

2. Selection of the non exposed cohort

   a) drawn from the same community as the exposed cohort *

   b) drawn from a different source

   c) no description of the derivation of the non exposed cohort

3. Ascertainment of exposure to implants

   a) secure record (eg surgical records) *

   b) structured interview *

   c) written self report

   d) no description

4. Demonstration that outcome of interest was not present at start of study

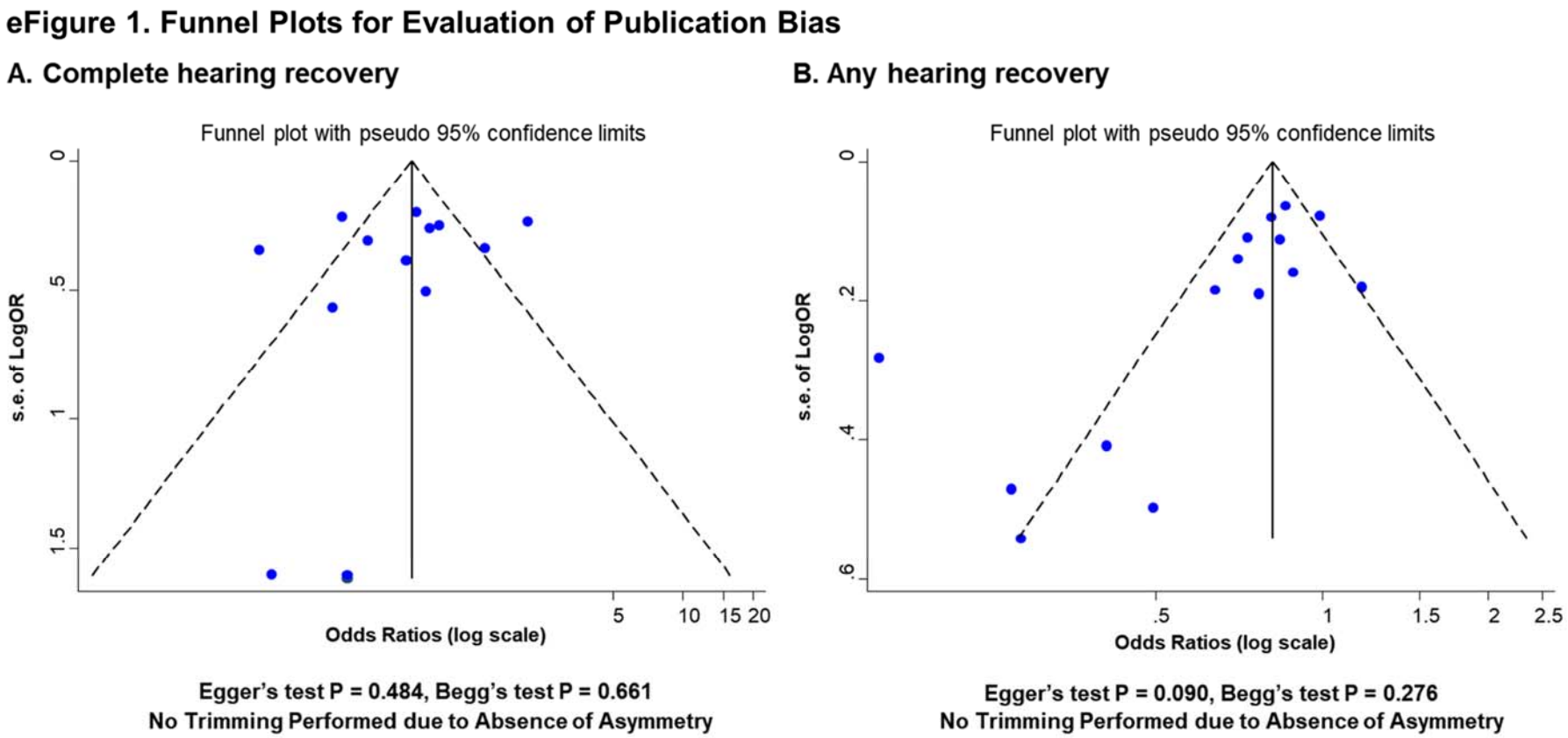
   a) yes * b) no

16	Ricciardiello et al.[24]	2017	★★★★	★	★★

eTable 4. Demographics of the Overall Population

Source	Demographics of the Overall Population				
	Mean Age, y	Male, %	Initial Hearing Level, dB	Severe to Profound Hearing Loss, %	Vertigo, %
Cavallazzi et al,[22] 1996	48.2	51.6	NR	NR	NR
Aslan et al,[23] 2002	47.3	64.0	NR	NR	NR
Narozny et al,[9] 2006	40.8	47.4	66.4	NR	34.6
Topuz et al,[6] 2004	41.5	60.0	70.4	25.5	NR
Desloovere et al,[10] 2006	45.6	46.5	43.6	NR	NR
Satar et al,[11] 2006	45.5	66.7	72.5	37.0	NR
Dundar et al,[12] 2007	NR	56.3	NR	80.0	NR
Fujimura et al,[13] 2007	52.6	NR	68.9	27.7	16.2
Cekin et al,[7] 2009	46.0	64.9	86.8	NR	7.0
Ohno et al,[14] 2010	49.0	50.0	60.7	40.2	32.6
Alimoglu et al,[15] 2011	NR	NR	67.8	NR	NR
Liu et al,[16] 2011	45.8	48.4	NR	54.8	NR
Cvorovic et al,[8] 2013	50.5	NR	69.0	NR	NR
Yang et al,[17] 2013	51.1	46.9	86.2	NR	30.6
Capuano et al,[18] 2015	53.6	57.0	69.6	41.0	8.0
Pezzoli et al,[19] 2015	50.7	NR	66.9	38.6	NR
Psillas et al,[20] 2015	49.1	42.2	69.8	60.0	24.4
Hosokawa et al,[21] 2017	62.0	52.9	NR	30.0	42.8
Ricciardiello et al,[24] 2017	46.1	55.6	53.8	NR	24.1

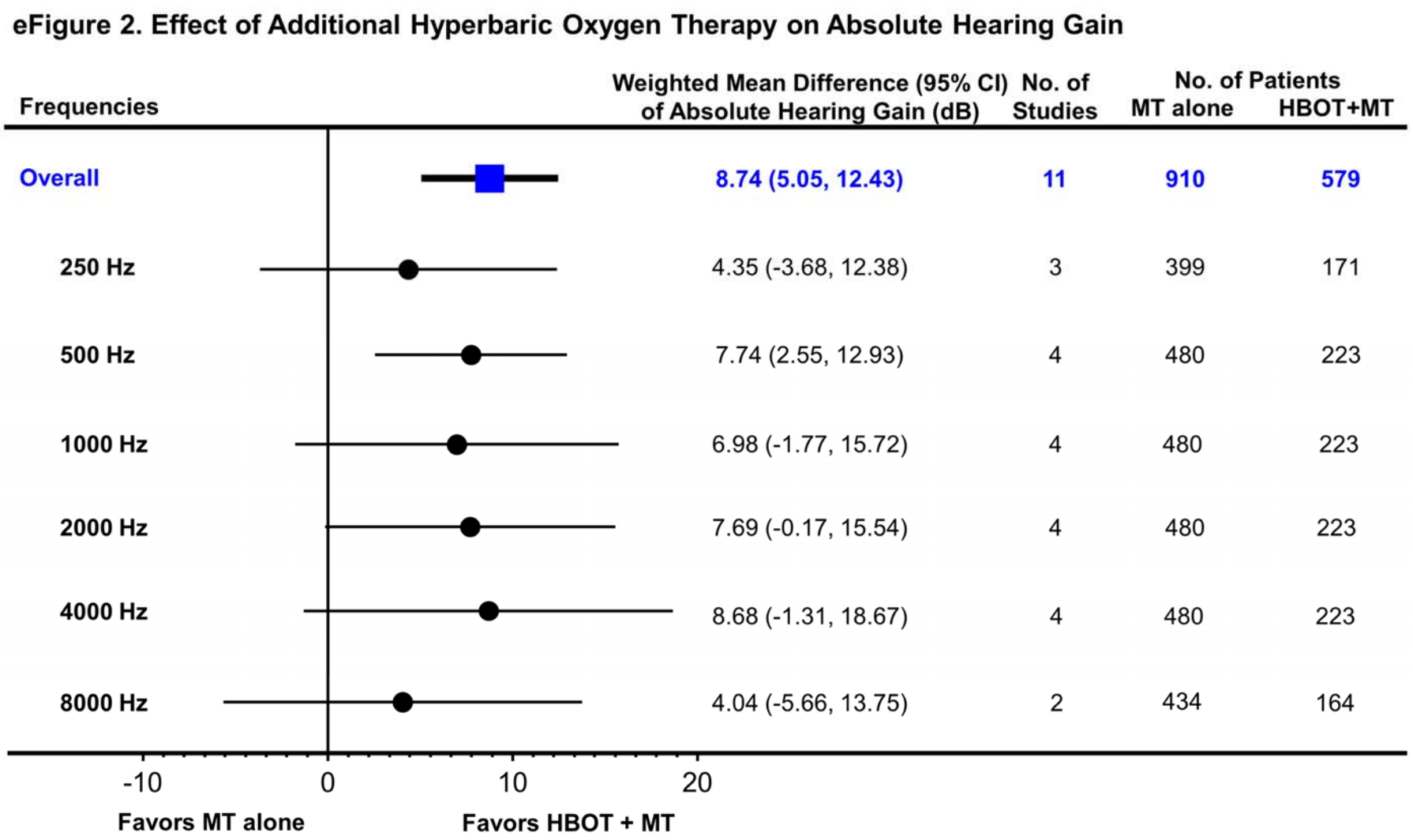
Abbreviation: NR, not reported.



eFigure 1. Funnel plots for evaluation of publication bias

The results of Egger's and Begg's tests are presented. Using the trim-and-fill method, no trimming was done due to absence of asymmetry for funnel plots of **(A)** complete hearing recovery and **(B)** any hearing recovery.

Abbreviations: OR, odds ratio.

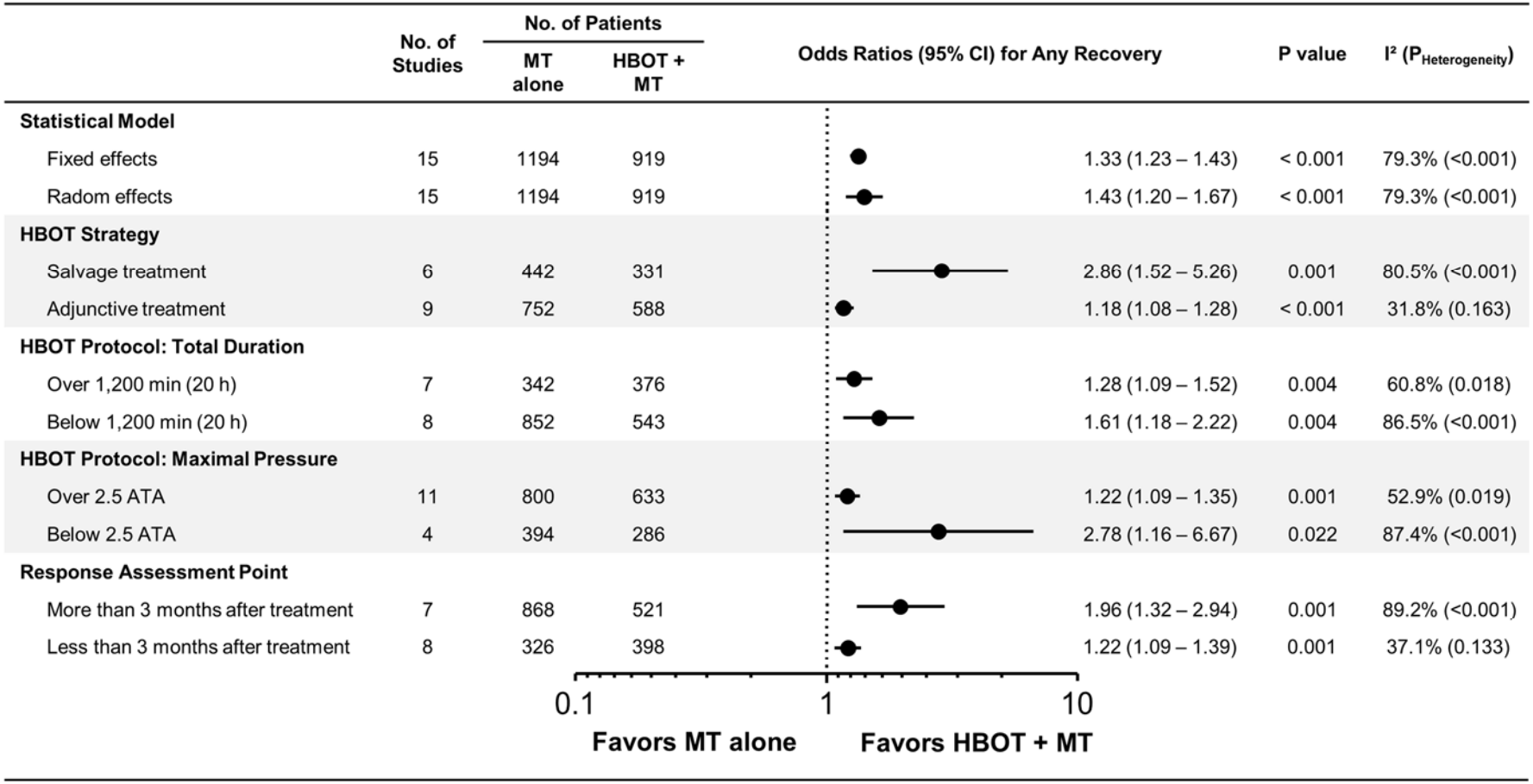


eFigure 2. Effect of additional hyperbaric oxygen therapy on absolute hearing gain

Mean difference with 95% confidence intervals of absolute hearing gain is displayed according to the frequency levels.

Abbreviations are as in Figure 2.

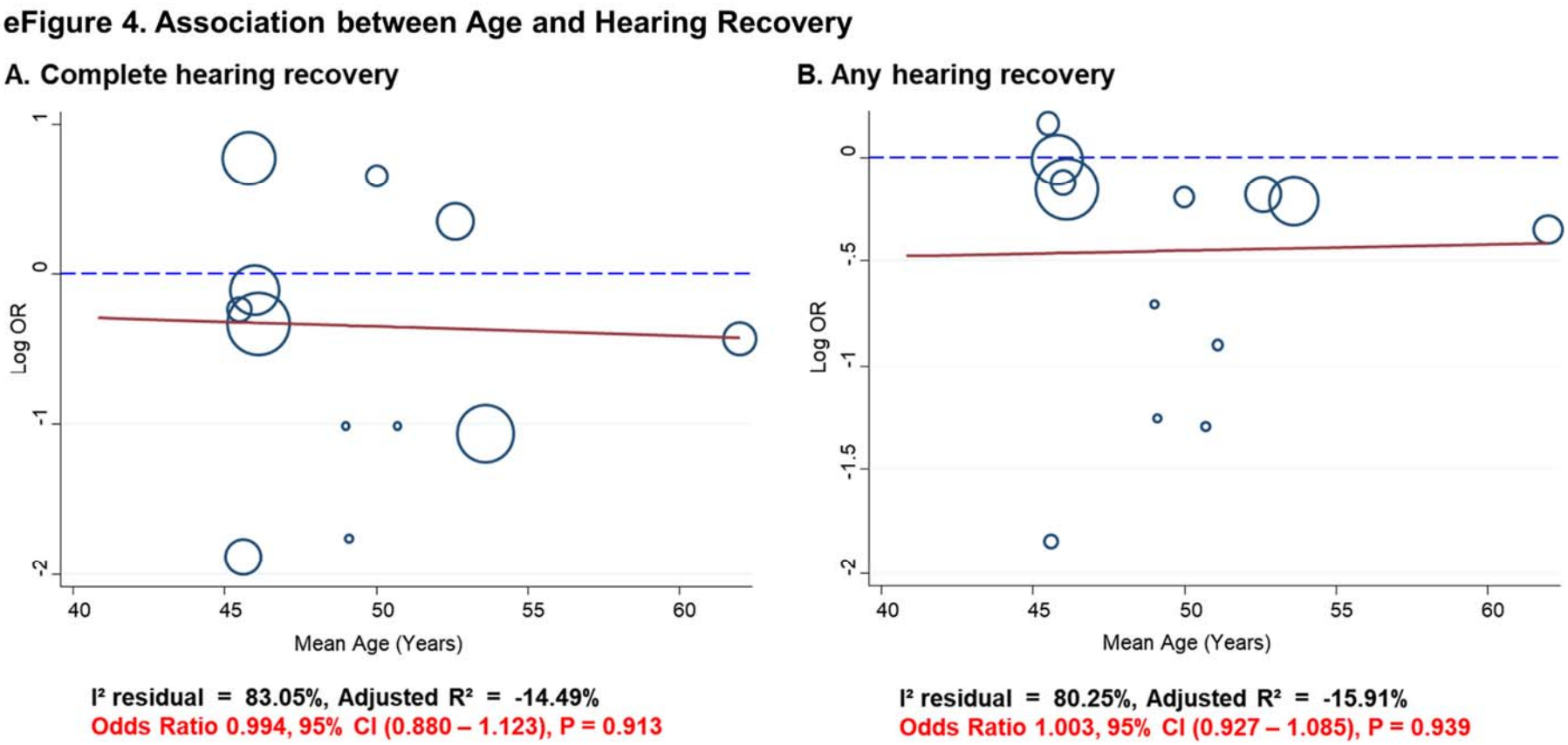
eFigure 3. Subgroup Analysis for Any Hearing Recovery



eFigure 3. Subgroup analysis for any hearing recovery

Effect of hyperbaric oxygen therapy on any hearing recovery according to the various subgroups is presented.

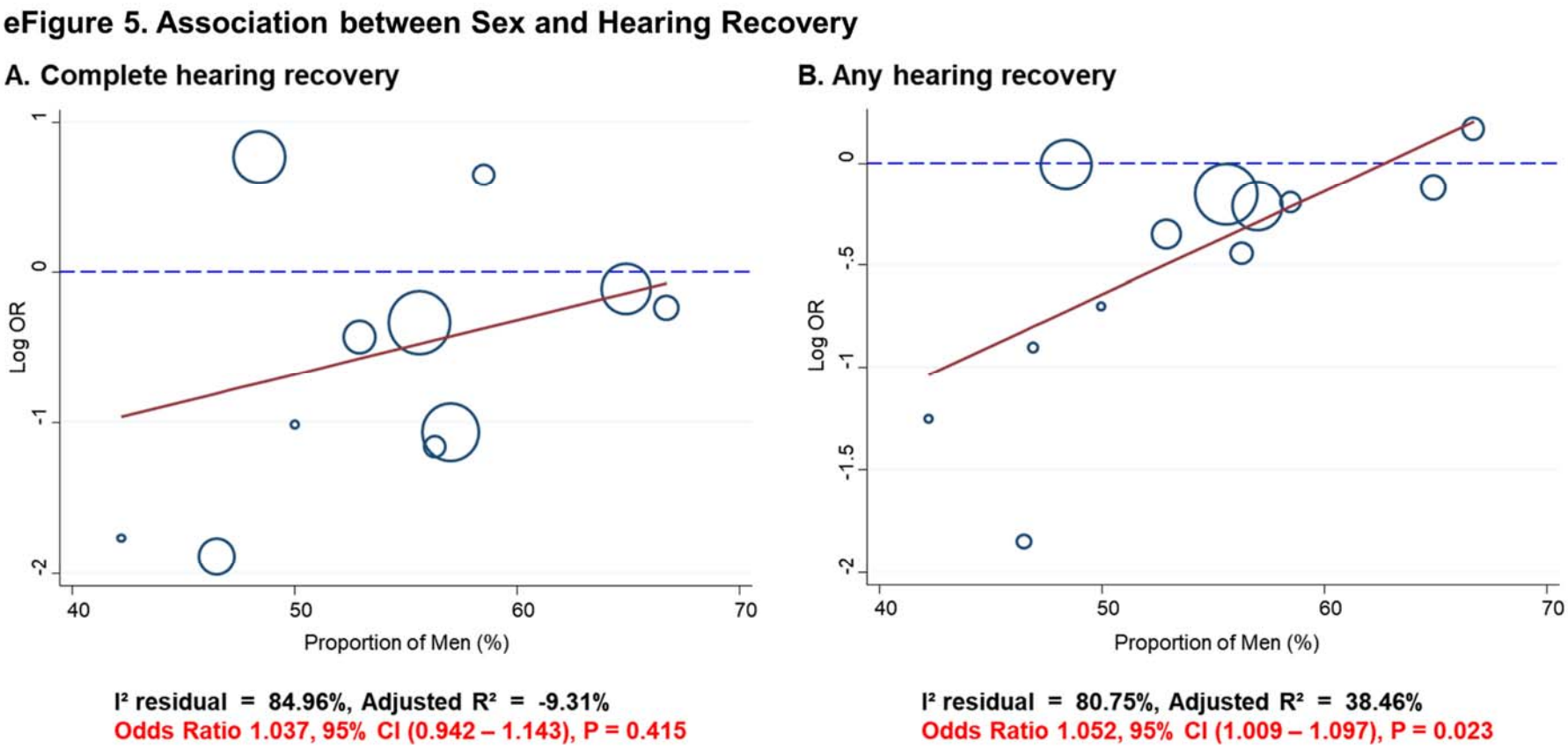
Abbreviations are as in Figure 5.



eFigure 4. Association between age and hearing recovery

Log values of odds ratios for **(A)** complete hearing recovery and **(B)** any hearing recovery are plotted according to the mean age of each enrolled study, using random-effects meta-regression. Each circle indicates a trial which was proportionately weighed in meta-analysis.

Abbreviations: CI, confidence interval.



eFigure 5. Association between sex and hearing recovery

Log values of odds ratios for **(A)** complete hearing recovery and **(B)** any hearing recovery are plotted according to the proportion of men of each enrolled study, using random-effects meta-regression. Each circle indicates a trial which was proportionately weighed in meta-analysis. Abbreviations: CI, confidence interval.

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