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Otology

Hearing preservation surgery for vestibular schwannoma: a systematic review and meta-analysis

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SUMMARY

The aim of this systematic review is to analyse the role of hearing preservation surgery for vestibular schwannoma. The complications and hearing outcomes of the single surgical techniques were investigated and compared with those of less invasive strategies, such as stereotactic radiotherapy and wait and scan policy. This systematic review and meta-analysis was performed according to the PRISMA guidelines. All included studies were published in English between 2000 and 2022. Literature data show that hearing preservation is achieved in less than 25% of patients after surgery and in approximately half of cases after stereotactic radiotherapy, even if data on long-term preservation are currently not available.

KEY WORDS: vestibular schwannoma, acoustic neuroma, hearing preservation, microsurgery, retrosigmoid approach, middle fossa approach, stereotactic radiosurgery

Introduction

Vestibular schwannomas (VSs) or "acoustic neuromas" are benign, slowly growing tumours arising from the vestibulo-cochlear nerve and account for 6-7% of all intracranial neoplasms and 80% of the cerebellopontine angle lesions [1]. They arise from the inferior vestibular nerve in 73% of cases and from the superior vestibular nerve in 27% [2]. The neural area of origin is mainly localised at the Obersteiner-Redlich junction, which is the transition point from central (glial cells) to peripheral (Schwann cells) myelin sheath. Unilateral progressive or sudden sensorineural hearing loss and tinnitus are the main symptoms of presentation [3]. Less frequent symptoms include vertigo or dizziness, headache, ataxia, and cranial nerve palsy. The gold standard for VS diagnosis is gadolinium enhanced magnetic resonance (MR) of the internal auditory canal (IAC) and cerebello-pontine angle (CPA), whose easier access in the last decades has allowed earlier diagnosis [4].

At present, treatment options include a conservative approach (wait and scan [W&S] policy), stereotactic radiosurgery (SRS), and microsurgery with or without hearing preservation [5-11]. The choice depends on different factors, such as patient's age and comorbidities, size and location of the tumour, and hearing status. W&S is based on systematic follow-up by serial gadolinium enhanced MR and hinges on the often negligible growth of VSs and slow progression of symptoms [9, 12]. The goal of conservative treatment is to minimise the risks and complications and to preserve an optimal quality of life in selected patients, such as the elderly, those with minimal symptoms, or with a small or middle-sized tumour. Borsetto et al. have proposed a surveillance protocol consisting in a 10-year minimum follow-up by MR [12].

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SRS provides high doses of ionising radiation precisely delivered to a target, while limiting irradiation of healthy tissues [13]. It is administered in a single session (SRT) or fractionated over several days (FSRT) [14], and performed with Gamma Knife, linear accelerators (LINAC) or Cyber Knife. The choice among the different techniques and modalities is based on tumour size, hearing function, and performance status. Growth control rates after SRS have been reported to be from 90% to 98% at 10 years [14-16]. SRS does not represent an option in young patients due to the risk, though minimal (1:1000), of developing radiation-induced cancers [17-20].

Surgical treatment of VS can be performed through different approaches, depending on tumour size, location, age, and hearing status. The trans-labyrinthine (TL) approach allows a large exposure of the IAC and CPA with minimal cerebellar retraction and complete control of the facial nerve. However, it does not preserve residual hearing [5] and will not be discussed further in the present review. The retro-sigmoid (RS) approach is a potentially hearing preserving technique that offers a large view of the CPA. However, it requires relevant cerebellar retraction, especially in large and anterior tumours. It is usually indicated in patients with good preoperative hearing and small VS (< 1.5 cm in the CPA), not reaching the midline and fundus of the IAC [21]. The retro-labyrinthine approach (RLA) is a trans-mastoid surgical avenue that allows hearing preservation; however, it offers a reduced exposure of the CPA compared to the TL and RS approaches and is nowadays rarely used [22]. The middle fossa (MF) or sub-temporal approach allows hearing preservation by reaching the IAC from above. It is indicated in young patients with good preoperative hearing function affected by VSs limited to the IAC or with only minimal (< 0.5 cm) extra-meatal extension [11].

The aim of the present systematic review was to evaluate early- and long-term hearing preservation rates after VS hearing preservation surgery (HPS) by comparing them with more conservative approaches such as W&S and SRS.

Materials and methods

This systematic review was performed in agreement with the PRISMA 2020 Statement Guidelines [23]. A specific PICOS question (Population: individuals with unilateral VS and with serviceable hearing function; Intervention: microsurgical approaches with hearing preservation techniques; Comparator: W&S or SRS strategies; Outcomes: hearing preservation; Study design: prospective studies) was constructed. Focused PICOS questions of this review are: 'is HPS an effective strategy to preserve hearing in specific and tailored cases of VS?' and 'is there any difference in terms of early and late hearing preservation rates between HPS, W&S, and SRS?'.

Search strategy

An electronic literature search was independently conducted by two authors using the PubMed/MEDLINE database as follows: ("vestibular schwannoma" OR "acoustic neuroma") AND "hearing preservation" AND (randomized OR randomized OR random OR randomly OR randomization OR RCT OR RCTs OR "clinical trial" [Publication Type] or "clinical trials as topic" [MeSH Terms]). The request was done on September 15, 2023 with no time limitations.

Study selection

Initially, titles and abstracts were independently screened by three authors (VP, VF and FSa) for eligible papers. Next, full-text papers were independently screened and those fulfilling eligibility criteria were included. Reference lists of original studies were hand-searched to identify articles that could have been missed during the electronic search. Any disagreement was resolved by consensus.

Articles were included in this systematic review if they met the following inclusion criteria: prospective randomised clinical trial or clinical study; article in English; patients with VS undergoing W&S, SRS or MF, RS or RLA approaches; evaluation of serviceable hearing preservation defined through pure tone and speech audiometry or by the American Academy of Otolaryngology – Head and Neck Surgery (AAO-HNS) [24] or Gardner-Robertson (GR) [25] classification systems.

In vitro studies, case series, case reports, animal studies, letters to the editor, opinion articles, abstracts, review papers, book chapters, pre-print and unpublished articles were excluded, together with studies reporting on patients with bilateral VS or type 2 neurofibromatosis (NF2), cases treated by a TL approach or without the specific aim of hearing preservation, patients undergoing dual treatment (gross or near total resection followed by SRS), and patients with less than 3 months of follow-up.

Data extraction and comparison

The authors performed data extraction individually. Information from the included studies were tabulated according to the study designs, study period, demographics, tumour size, type of treatment, complications, and hearing preservation. Collected data were primarily based on the focused questions outlined above. Series with heterogeneous procedures and methods were carefully screened in order to consider only those cases that met the inclusion criteria. The authors cross-checked all extracted data. Any disagreement

was resolved by discussion until consensus was reached. When possible, data were eventually aggregated in subgroups in order to estimate and compare the hearing preservation rates between the different strategies and techniques.

Statistical analysis

Statistical analysis of the different rates of hearing preservation in the two subgroups (surgery vs. SRS) was performed using the Chi-square test. Results were considered significant for p values < 0.05. The IBM software SPSS Statistics version 26 was used for the analysis.

Results

Study selection

Our initial search yielded 40 records. After initial screening of titles and abstracts, 23 full-text articles were selected for reading. Of these, 13 were further excluded since they did not meet the inclusion criteria. After the final selection stage, 10 studies were included in the present review, of which 3 reporting on surgical approaches, 6 on SRS, and one of both surgical and SRS. No studies reporting data on W&S strategies fulfilled the inclusion criteria. The selection process is shown in Figure 1.

General characteristics of studies included

Table I shows general characteristics of the included studies [14-15, 26-33]. All were unicentric prospective studies published in English between 2000 and 2022, and involved a total of 869 cases, of which 513 treated by hearing preservation microsurgical techniques and 356 by SRS. Mean age of patients ranged between 35 and 66 years. The male to female ratio was not reported in all studies; for this reason, these data were not included in the analysis. The individual studies used different hearing classifications: some authors [14,26-27,29] used the AAO-HNS classification, while others [15,28,30-33] used the GR classification. Similarly, when ambiguity over the concept of 'serviceable hearing preservation' was found, these data were standardised by including under this definition only Class A and B according to the AAO-HNS classification, and Class I and II according to the GR classification (pure tone audiometry average threshold lower or equal to 50 dB and word recognition at speech audiometry greater or equal to 50%). Thus, only patients with serviceable pre-treatment hearing and for whom a hearing preserving procedure was attempted were included in the analysis.

Results of hearing preservation surgery

Surgical results of the studies included in this review are summarised in Table II.

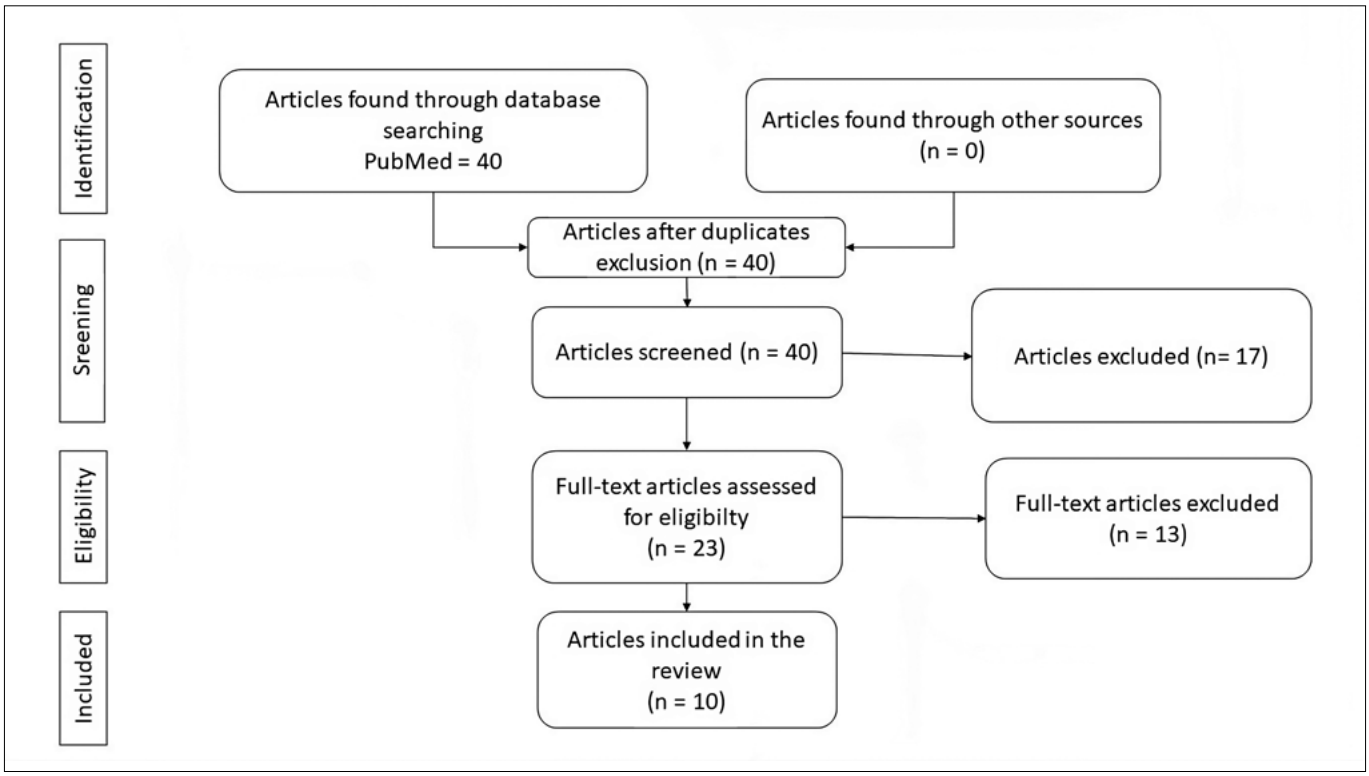

Figure 1. Flow-chart showing selection strategy.

Table I. General characteristics of the studies included.

#	Author (year)	Study design	No. of patients	Mean age (years)	Treatment	Surgical technique/SRS modality	Hearing classification
1	Bento et al. (2022) [26]	Unicentric prospective	22	35	Surgery	RLA	AAO-HNS
2	Colletti et al. (2005) [27]	Unicentric prospective	70	53	Surgery	35 RS 35 MF	AAO-HNS
3	Tonn et al. (2000) [28]	Unicentric prospective	399	51	Surgery	RS	GR
4	Pollock et al. (2006) [29]	Unicentric prospective	52	51	22 Surgery 30 SRS	RS/MF GKRS	AAO-HNS
5	Saraf et al. (2022) [30]	Unicentric prospective	20	64	SRS	FSRS (proton)	GR
6	Putz et al. (2020) [14]	Unicentric prospective	34	66	SRS	6 SSRS 28 FSRS	AAO-HNS
7	Niranjan et al. (2008) [31]	Unicentric prospective	51	54	SRS	GKRS	GR
8	Chopra et al. (2007) [15]	Unicentric prospective	106	56	SRS	GKRS	GR
9	Tamura et al. (2009) [32]	Unicentric prospective	74	47	SRS	GKRS	GR
10	Ikonomidis et al. (2015) [33]	Unicentric prospective	41	55	SRS	LINAC	GR

AAO-HNS: American Academy of Otolaryngology – Head and Neck Surgery classification; GR: Gardner-Robertson classification; RS: retro-sigmoid approach; RLA: retro-labyrinthine approach; MF: middle cranial fossa approach; SRS: stereotactic radiosurgery; GKRS: Gamma-knife radiosurgery; FSRS: fractioned stereotactic radiosurgery; SSRS: single-session stereotactic radiosurgery; LINAC: linear accelerator.

Table II. Results of hearing preservation surgery.

Author (year)	Surgical technique	No. of patients	Koos stage	Complications	Postoperative FP	Short-term hearing preservation (≤ 12 months)	Long-term hearing preservation (> 12 months)	Mean follow-up (months)
Bento et al. (2022) [26]	RLA	22	I: 36% II: 64%	5.5%	5.5%	31.8%	NA	3
Colletti et al. (2005) [27]	RS	35	I: 100%	35%	20%	40%	NA	12
	MF	35	I: 100%	23%	23%	51.4%	NA	12
Tonn et al. (2000) [28]	RS	399	II: 54.5% III: 44.2% NA 1.3%	NA	NA	19%	NA	6
Pollock et al. (2006) [29]	RS/MF	22	NA	NA	15%	5%	5%	42

RS: retro-sigmoid approach; RLA: retro-labyrinthine approach; MF: middle cranial fossa approach; FP: facial palsy; NA: not available.

Bento et al. [26] included 22 patients in their analysis operated by a RLA for small VSs (36% Koos I, 64% Koos II) with serviceable preoperative hearing. All patients were young (mean age, 35 years) and preoperative hearing levels were AAO-HNS Class A in 2 cases (9%) and Class B in 20 cases (91%). Complete macroscopic tumour removal was obtained in all cases with low rate of complications (1 patient with House-Brackmann grade II facial paralysis). Postoperatively, a serviceable hearing level (Class A and B) was maintained in 31.8% of patients at 3 months.

An RS approach was used by Colletti et al. [27] on 35 middle-aged patients (mean age, 52 years) with small intracanalicular (Koos I) VSs and preserved hearing (46% AAO-HNS Class A and 54% Class B), while Tonn et al. [28] used the

same approach on 399 middle-aged patients (mean age, 52 years) with larger VSs (Koos II 54% and Koos III 44%) and serviceable hearing. The two authors obtained divergent results in terms of hearing preservation (40% vs. 19%), confirming the likely predictive role of tumour size in cochlear nerve integrity. However, in the series by Tonn et al. [28] a possible bias must be discussed. In fact, only 229 of 399 patients were operated on after the introduction of intraoperative cochlear function monitoring. Thus, when considering only the latter subgroup, better hearing preservation rates were registered (26.8%), but still not remotely comparable to those of the series by Colletti et al. [27]. Furthermore, when extracting Tonn's [28] data in relationship with tumour size, those with extra-meatal diameter < 15 mm were correlated with better hearing preservation rates (22%) compared with larger tumours (15% in tumours with an extra-meatal diameter between 16 and 30 mm; 0% in tumours with an extra-meatal diameter larger than 30 mm).

The MF approach was analysed by Colletti et al. [27] on a series of 35 middle-aged patients (mean age, 54 years) with small intra-canalicular (Koos I) VSs and preserved hearing (43% AAO-HNS Class A and 57% Class B). They obtained even better hearing preservation rates (51.4%) compared to the RS subgroup, with a similar rate of complications (23% *vs* 20% of facial paralysis).

Finally, Pollock et al. [29] included 22 patients in their series operated on by RS or MF, obtaining very low rates of hearing preservation (5%). However, no categorisation in terms of technique or tumour size were specified in the manuscript, thus preventing any possible interpretation and analysis of results.

Results of stereotactic radiosurgery

Results of the different types of SRS of the studies included are summarised in Table III.

The traditional delivery modality of SRS is by a single session (SSRS). However, this technique is routinely used in patients with small tumours and non-serviceable hearing level (AAO-HNS Classes C or D) [14]. The only 6 cases in which this technique was surprisingly used for patients with serviceable hearing were described by Putz et al. [14], administering on large VSs (mean volume, 13.9 cm^3) a total dose of 12-13 Gy. Unluckily, hearing outcomes were presented by the authors in combination with those of 28 patients treated by fractioned SRS (FSRS), with an excellent but not-interpretable long-term hearing preservation rate of 53%.

Fractioned proton radiosurgery was administered by Saraf et al. [30] to 20 patients with smaller VSs (median volume, 0.81 cm^3) with a good hearing preservation at the short- (53% at 1 year) and long-term (57% at 3 years).

Gamma-knife radiosurgery (GKRS) was the most widely used technique in the included studies. Pollock et al. [29] administered a mean dose of 26.4 Gy to 30 patients affected by small to medium-sized VSs, with a satisfying tumour control and a serviceable hearing preservation of 77% at 3 months and 63% at last follow-up (mean, 42 months). Similar results were obtained with GKRS by Niranjan et

Table III. Results of stereotactic radiosurgery.

Author (year)	SRS modality	No. of patients	Mean volume (cm^3)	Total dose (Gy)	Max cochlear dose (Gy)	Tumour growth control	Early-term hearing preservation (≤ 12 months)	Long-term hearing preservation (> 12 months)	Mean follow-up (months)
Pollock et al. (2006) [29]	GKRS	30	1.5	26.4	NA	96%	77%	63%	42
Saraf et al. (2022) [30]	FSRS (proton)	20	0.81	50.4-54	50.7	100% at 4 years	53%	57%	36
Putz et al. (2020) [14]	SSRS	6	13.9	12-13	13.7	100% at 10 years	NA	53%	36
	FSRS	28	13.4	50.4-55.8	51.1	93.8% at 10 years			
Niranjan et al. (2008) [31]	GKRS	51	0.000112	18.7-36	NA	99% at 3 years	NA	64.5%	42
Chopra et al. (2007) [15]	GKRS	106	1.3	20-26	NA	98.3% at 10 years	NA	56.6%	68
Tamura et al. (2009) [32]	GKRS	74	1.3	NA	NA	93.2% at 5 years	NA	78.4%	56
Ikonomidis et al. (2015) [33]	LINAC	41	2.1	15.23	11.4	75% at 2 years	51.2%	36.6%	39

Gy: Gray; NA: not available; SSRS: single-session stereotactic radiosurgery; FSRS: fractioned stereotactic radiosurgery; GKRS: Gamma-knife radiosurgery; LINAC: linear accelerator.

al. [31] on 51 intra-canalicular VSs (64.5% of hearing preservation at 42 months), by Chopra et al. [15] on 106 patients (56.6% at 68 months), and by Tamura et al. [32] on 74 patients (78.4% at 56 months).
Ikonomidis et al. [33] performed LINAC SRS on 41 patients with preserved serviceable hearing and with Koos I to III VSs (median volume, 2.1 cm^3). Hearing preservation was registered in 51.2% of cases at 6 months and in 36.6% of cases at the last observation (mean, 39 months).

Hearing preservation surgery vs stereotactic radiosurgery

When aggregating the results of all the studies (Tab. IV), SRS showed significant better overall hearing preservation rates in comparison to the surgical approaches considered (57.8% *vs* 23.4%, p value < 0.0001). When comparing single surgical and radiosurgical techniques, the best results were found in the MF and GKRS groups. However, no statistical analysis was performed to confirm this finding, due to the high heterogeneity between the different subgroups.

Table IV. Data aggregation and meta-analysis.

Treatment	Hearing preservation (%)	P value	Technique	Hearing preservation (%)
Surgery	23.4	< 0.0001	MF [27]	51.4
			RLA [26]	31.8
			RS [27,28]	20.7
Stereotactic radiosurgery	57.8		GKRS [15,29,31,32]	62
			Proton FSRS [30]	57
			LINAC [33]	36.6

MF: middle cranial fossa approach; RLA: retro-labyrinthine approach; RS: retro-sigmoid approach; FSRS: fractioned stereotactic radiosurgery; GKRS: Gamma-knife radiosurgery; LINAC: linear accelerator.

Discussion

VSs are benign tumours, but their progressive growth can lead to severe and life-threatening sequelae. In recent decades, the easier access to MR has allowed VSs to be diagnosed more frequently at a smaller and scarcely symptomatic stage. Furthermore, it has been demonstrated that only one-third of all VSs have the tendency to grow, while approximately 50% of patients maintain their hearing during an observation period of 5 years [10]. In this panorama, hearing sparing surgical approaches have gained increasing interest, while the evolution of SRS and the development of W&S strategies have added further options to the current therapeutic armamentarium for management of small and middle-sized VSs.
The aim of this review was to analyse the role of HPS for VS by investigating the outcomes of single techniques and comparing them with those of less invasive strategies, such as SRS and W&S. To the best of our knowledge, no other systematic reviews with the same purposes has been published to date. Surgery has demonstrated to provide an adequate rate of hearing preservation (23.4%) when used with the correct principles and indications. The most frequently used hearing sparing approaches are MF and RS, among which the choice depends on the surgeon's familiarity, preference, and tumour size. The only study comparing these two techniques in terms of hearing preservation is that by Colletti et al. [27]. The authors found that the RS approach offers better chances of keeping serviceable hearing in case of adverse anatomic conditions and IAC enlargement greater than 7 mm, while the MF approach provides better preservation rates when the tumour fills the IAC fundus (distance less than 3 mm). Unfortunately, a direct comparison between these three techniques in the included studies was not feasible, since each author used different indication criteria and parameters. However, when looking for a potential predictive factor for hearing preservation in selected series, it is quite easy to speculate over the fact that smaller and intra-canalicular VSs [27] may be correlated with better outcomes (Tab. II). This hypothesis was also confirmed by other authors who found significantly better preservation rates in patients with smaller tumours in both surgical [26, 28] and SRS series [14,31-32].
SRS was shown in our review to provide excellent hearing preservation rates (overall 57.8% after a mean follow-up of 53 months) with high rates of growth control (93.2% to 100%). LINAC [33] reported worse results of hearing preservation compared to the other techniques (Tab. IV). However, the large variability in tumour size, and total, marginal and cochlear doses makes it impossible to compare the different techniques routinely in use.
Hearing impairment after microsurgery with cochlear nerve integrity preservation is thought to be ascribable to mechanical or thermal neural microvascular damage and is assumed to occur immediately after surgery. On the contrary, hearing deterioration after SRS tends to be progressive over 6 to 24 months and seems to be caused by ischaemic neural damage secondary to tumour swelling, or progressive radiation-induced neural oedema and demyelination [18,38]. For this reason, the best results of SRS when compared to microsurgery should be verified over a longer follow-up period. Moreover, the risk of radiation-induced malignant transformation should be always considered in the decision-making process and patient counselling [19].
We believe that a comparison of hearing preservation rates among microsurgery and W&S strategies is not reasonable, since they have very different indication criteria. However, literature data show that approximately 50% of patients

maintain their hearing over a period of 5 years with a W&S policy [10].

One of the main limitations of our review was the high heterogeneity of the different series, which made impossible to compare in detail the data of individual studies. Further randomised clinical trials may be therefore necessary to develop a decisional algorithm based on different patient- and disease-related patterns.

Conclusions

In the past, surgery was the only possible treatment for VS; today, the development of SRS and other non-surgical conservative strategies has considerably expanded the range. In addition, hearing preservation has become a major challenge. The present review found satisfying preservation rates after both microsurgery and SRS, especially when dealing with intra-canalicular and small-sized VSs. In particular, SRS showed slightly better results, but the observational period of the reviewed series was not long enough to arguably claim the superiority of this approach. Hence, further randomised controlled trials are needed to compare long-term hearing outcomes of the different treatment options.

Conflict of interest statement

The authors declare no conflict of interest.

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Author contributions

VP, NQ: conceived, designed, wrote and revised the work; VF, FSa, VP: independently screened, read and selected the articles; VP: realised meta-analysis; VF, FSA, VP, MTB, RM, FSI, NQ: took part to the writing of the present paper.

Ethical consideration

Not applicable.

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