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Supplementary appendix

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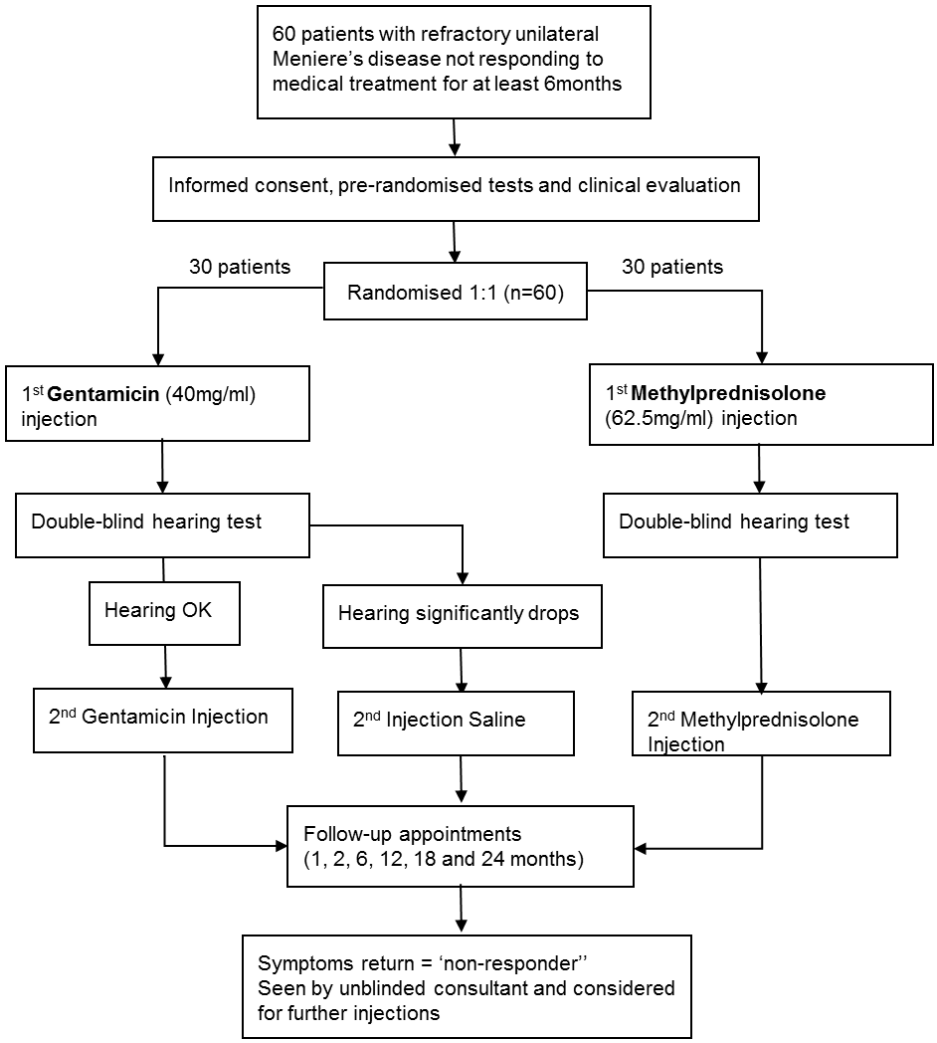
Supplement to: Patel M, Agarwal K, Arshad Q, et al. Intratympanic methylprednisolone versus gentamicin in patients with unilateral Ménière's disease: a randomised, double-blind, comparative effectiveness trial. *Lancet* 2016; published online Nov 16. http://dx.doi.org/10.1016/S0140-6736(16)31461-1.

Appendix

Supplement to Patel M, Agarwal K, Arshad Q et al., **“**Intratympanic steroids vs. gentamicin in unilateral Ménière's disease: a randomised double-blind comparative effectiveness trial**”**

Supplementary Methods

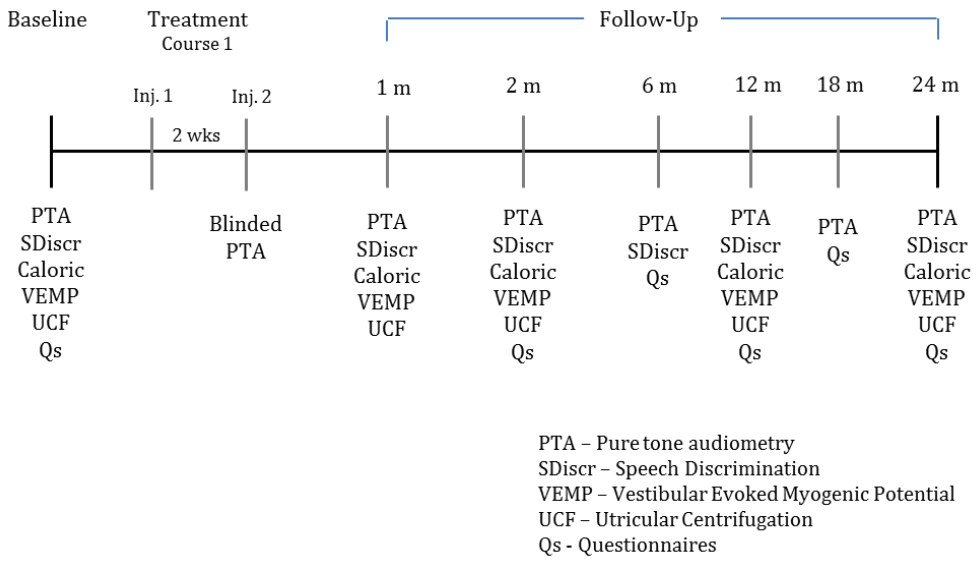
Figure S1: Trial design



Follow-up information
Three patients recruited from Leicester Royal Infirmary were followed-up at Charing Cross Hospital (main site) and the same individual (MP) conducted all follow-ups and all tests at both sites.

Injection procedure
The patients lay supine on a couch with the head turned away from the treated ear. The ear canal was sprayed with 2 to 3 squirts of Lidocaine spray (Xylocaine spray™ 10mg/spray). After 60 seconds the ear canal was completely aspirated. All patients were told before injection that it might sting. The injection syringe was attached to a 22Gauge spinal needle which, under microscopic control, was inserted in the inferior aspect of the pars tensa. The injection continued until a fluid level could be seen to fill the tympanic cavity. Volume injected was recorded after each injection; which ranged between 0·3 to 1ml. The patient was asked not to swallow or speak for 20 minutes. Immediately after treatment, all 60 patients were issued the same (Cawthorne-Cooksey) rehabilitation exercises and instructed to begin performing them after 3 days, twice daily, beginning slowly and grading their intensity progressively over 4 weeks.

Figure S2: Treatment and testing follow-up schedule.



Recommended AAO-HNS outcome measures [1]

Class of vertigo control: The number of attacks of vertigo were categorised into the following Classes A-F [1]: Complete Control (A), Substantial Control (B), Limited Control (C), Insignificant Control (D), Worse Control (E) and Secondary treatment required (F). In line with the AAO-HNS committee recommendations, we categorised response to treatment using the following formula [1]:

$$\frac{\text{average number of attacks per month in the final six months of treatment}}{\text{average number of vertigo attacks per month for the six months before treatment}} \times 100$$

Where 0 = Complete Control, 1-40= Substantial Control, 41-80 Limited Control, 81-120 Insignificant Control and >120 Worse Control of vertigo.

Functional Level Scale: The Functional Level Scale (FLS) was reported as improved, unchanged or worse at two years compared to baseline [1].

Pure-tone Audiometry: A meaningful hearing loss was reported as a decrease by 10dB in ipsilesional pure-tone threshold across 0.5, 1, 2 and 3KHz (mean value) before treatment (baseline) and for the worse audiogram between 18-24 months after treatment [1].

Speech Discrimination: A 15% change in speech discrimination from baseline compared to 24 months was considered clinically meaningful [1]. We report speech discrimination as 'decreased', 'unchanged' or 'improved'.

Statistical Analysis: We compared the number of patients for steroid or gentamicin in each category. Groups were compared with Chi-Square analysis and Fisher's Exact Test. All analyses were performed with SPSS version 22. All results except class of vertigo control are analysed per protocol[1] i.e. with the two treatment failures removed.

Methodological details of vestibular function tests

Caloric Test

Bithermal (30 & 44°C) water caloric tests were conducted providing the percentage of caloric paresis (Jongkees formula: 100 x [(LC + LW) - (RC + RW)/(LC + LW + RC + RW)], directional preponderance [(LC+RW)-(RC+LW)/(LC + LW + RC + RW)] from slow phase velocity eye movements (GN Otometrics, Taastrup, Denmark).

Cervical Vestibular Evoked Myogenic Potential (VEMP)

A custom system delivered air-conducted sound monaurally via audiological headphones and captured ipsilateral electromyographic (EMG) activity. Sound was delivered as 500Hz tone bursts at 110dB (normal hearing level (nHL)) of positive polarity. EMG signals were averaged over two hundred sweeps and rectified. Electrical resistance across electrodes was <5KΩ. The electrode montage comprised the right and left sternocleidomastoid muscle bellies, the right and left ipsilateral mid-clavical bones (reference) and sternum (ground).

Subjects lay on an examination bed, upper torso elevated with backrest at 30°, lower body flat. Patients were asked to elevate their heads from the support and turn the head either to the left (right ear test) or to the right (left ear test) to increase tonic neck muscle activity. A biofeedback device monitored contraction strength (approximately 30 μV). The p13 was the first distinctive peak in waveform and n23 the first trough and percentage amplitude asymmetry attained.

Utricular Centrifugation (UCF)

Utricular centrifugation (UCF, to measure utricular function via tilts of the subjective visual vertical (SVV) was performed with a vertical axis rotation chair (NeuroKinetics Inc, Pittsburugh, USA) capable of lateral chair translation for eccentric displacement in total darkness and with the subject's head, torso, legs and feet secured into the chair. Centred (on axis) head position was ensured with a vertically calibrated laser. Attached to the chair were two arms holding a thin wooden plaque 1m from participants onto which a laser projected an illuminated static red dot or line (160mm x 3mm). The line could be rotated about its centre using a wheel joy-pad given to patients who were instructed to position the straight line to their perceived gravitational vertical (SVV). Upon doing so, the patient was asked to give a vocal cue that the line was vertical ("yes" or "ok"). Line angle was saved, and the line re-orientated to a new angle. During the test, SVV was repeatedly measured in 30s intervals in stationary and central, right and left chair positions during rotation. The UCF sequence was: 1). Chair stationary. 2). Chair accelerated at $3^{o}/s^{2}$ up to a constant velocity of 400º/s over 120s and maintained in the on-axis position for 60s. 3). Translation from centre to the right laterally (4cm, 0·2cm/s) over 30s. 4). Translation back to centre over 30s. 5). Translation from centre to the left laterally (4cm, 0·2cm/s) over 30s 6). Translation back to the central position for 30s and decelerated at 2·5º/s to rest. During rotation with head-aligned to earth-vertical, lateral displacement of the seated body by 4 cm from the rotation axis stimulates the eccentrically positioned utricle unilaterally through the resultant centrifugal force. The resulting utriculo-ocular reflex causes ocular counter-roll in an opposite direction to the translation direction. At 400°/s the stimulated utricle is exposed to a centrifugal acceleration of $\omega 2r=0{\cdot}40$ g, where ω is the angular velocity and r the distance between the axis of rotation and the stimulated utricle, giving rise to a tilt sensation of $11{\cdot}2°$ [2]. UCF was scored as median utricular percentage weakness [3].

Six patients never performed the utricular UCF assessment owing to availability of equipment (5 cases) or refusal (1 case). Three patients (two in the gentamicin arm) were unable to perform a caloric test owing to previous grommet insertion (2 cases) or a thin tympanic membrane (1 case).

Supplementary Results

Intention-to-treat Analysis

All the intention-to-treat analysis has been presented in the main body of the manuscript, except for the Vertigo and Autonomic sub-scales of the Vertigo Symptom Scale questionnaire presented below.

There was no significant difference between drugs for the Vertigo Symptom Scale sub-scores (vertigo scores: drug; F[1,58]0·77; P=0·38, *drug x time interaction;* F[1,58]0·06; P=0·81, autonomic scores: drug; F[1,58]2·6; P=0·11; *drug x time interaction*; F[1,58]0·07; P=0·79).Vertigo (*time*; F[1,58]82·9; P<0·0001) and Autonomic scores were significantly lower at 24 months compared to baseline (*time*; F[1,58]60·1; P<0·0001).

Per- Protocol Analysis

This is the secondary analysis conducted after the two 'non responder' patients were crossed over from the steroid to the gentamicin arm.

There were no differences between the statistical analyses for intention-to-treat and per-protocol. The statistical analyses per- protocol are presented here:

Primary Outcomes

Number of vertigo attacks in final six months

There was no significant difference between drugs for the number of attacks of vertigo in the final six months compared to six month baseline (*drug*; F[1,56]1·15; P=0·29; *drug x time interaction*; F[1,56]0·21; P=0·65). The secondary analysis omitting the two failures from the steroid group showed that the number of attacks in the 6 months before treatment (baseline) was 16·8 $\pm$ 12·8 which fell significantly to 1·2 $\pm$ 3·1 in the final 6 months of the 24 month follow-up (*time;* F[1,56]64·8; P<0·001).

Secondary Outcomes

Number of attacks in one month

There was no difference between drugs for number of attacks at 24 months compared to one month baseline (drug; F[1,56]0·70; P=0·41, *drug x time* interaction; F[1,56]0·38; P=0·54). Number of attacks in the one month before treatment which fell significantly over time (time; F[1,56]34·8; P<0·001).

Vertigo Symptom Scale and Dizziness Handicap Inventory scores

There was a marginal drug effect for mean Vertigo Symptom Scale scores (*drug;* F[1,56]4·17; P=0·051) but no significant difference between arms for the interaction (*drug x time interaction*; F[5,54]1.1; P=0·37). Vertigo Symptom Scale mean scores significantly decreased over time (*time*; F[5,52]22·06; P<0·001).

There was no significant difference between drug arms for Dizziness Handicap Inventory scores (*drug;* F[1,56]3.7; P=0.06, *drug x time interaction*; F[5,52]0·10; P=0·99). Dizziness Handicap Inventory mean scores significantly decreased over time (*time*; F[5,52]36·1; P<0·001).

Vertigo and autonomic subscale symptoms

There was no significant difference between gentamicin and steroid arms for the Vertigo (*drug*; F[1,56]2·5; P=0·12, *drug x time interaction*; F[1,56]0·07; P=0·80) or Autonomic subscales (drug; F[1,56]0·71;P=0·41, *drug x time interaction*; F[1,56]0·13; P=0·72. The Vertigo subscale mean score was significantly lower at 24 months compared to baseline (*time*; F[1,56]79·9; P<0·001) as was the Autonomic subscale mean score (*time*; F[1,56]57·9; P<0·001).

Functional Level Scale

There was a marginal drug effect for the mean Functional Level Scale scores (*drug;* F[1,56]4·11; P=0·052) but no significant interaction between the drug arms (*drug x time interaction;* F[5,52]0·20; P=0·97). Functional level Scale mean scores significantly decreased over time (time; F[5,52]25·65; P<0·001).

Pure-tone Audiometry

Hearing level was taken as the mean pure-tone audiometry threshold across 0.5, 1, 2 and 3KHz. There was no significant difference between drug arms for hearing levels (*drug;* F[1,56]0·43; P=0·84, *drug x time interaction*; F[6,52]1·90; P=0·10). We found a significant overall improvement in hearing level over time (*time*; F[6,52]2·45; P=0·04).

Speech Discrimination

There was no significant difference between drugs for speech discrimination (*drug;* F[1,56]0·013; P=0·91; *drug x time interaction*; F[5,52]2·25; P=0·06). There was a decrease in speech discrimination with respect to baseline for gentamicin over time and an overall improvement for steroids over time (*time*; F[5,52]2·56; P=0·04).

Tinnitus Handicap Inventory and Aural Fullness Scale

There was no significant difference between arms for Tinnitus Handicap Inventory scores (*drug;* F[1,56]2·68;P=0·11, *drug x time interaction*; F[5,52]0·88; P=0·50). Tinnitus Handicap Inventory mean scores significantly decreased over time (*time*; F[5,52]13·66; P<0·001).

There was no significant difference between arms for Aural Fullness Scale scores (drug; F[1,56]3·34; P=0·07, *drug x time interaction*; F[5, 52]0·72; P=0·61). Aural Fullness Scale mean scores significantly decreased over time (*time*; F[5,52]7·71; P<0·001).

Statistical information

We also performed non-parametric (Mann-Whitney U) tests which confirmed that where ANOVA revealed significant changes over time, these were also shown by non-parametric tests. We also tested for any differences at 24 months follow-up using non-parametric methods. The findings confirmed those using the ANOVA i.e., that there were no significant differences between steroid and gentamicin.

AAO-HNS outcomes

The American Academy for Otolaryngology and Head and Neck Surgery (AAO-HNS) produced an updated set of recommended guidelines for intervention studies in Ménière's disease in 1995 [1]. In their guidelines, the AAO-HNS stated that all intervention studies should have a two-year follow-up and outcomes should be based on the final six months of treatment (18-24 months). Unlike previous double-blind, randomised RCTs [4-6], an advantage of the current study is that we have complied with these recommendations.

The AAO-HNS outcomes, class of vertigo control, change in functional level scale, change in pure-tone audiometry and change in speech discrimination, are presented in Appendix tables S1-4. These outcomes tell us how many patients in each drug arm experienced a worsening, no change or improvement of symptoms and this will be presented below. Essentially, these results showed no difference between gentamicin and steroid for the class of vertigo control or pure tone hearing levels. However, a significantly higher number of patients experienced improvement and fewer patients experienced a meaningful worsening in speech discrimination after steroid as shown in table S5 and reported in the main paper under Speech Discrimination. Thus, in summary, the analysis presented in the main paper and the one recommended by the AAO-HNS (1995) provide the same result except for speech discrimination.

All AAO-HNS outcomes apart from the class of vertigo control were analysed for the intention-to-treat population and per-protocol. Results were the same whichever way the data were analysed i.e., the cross-over patients did not affect the result. However, as drug differences were greater for per-protocol than for intention-

to-treat, the data presented here are for per-protocol apart from speech discrimination which is presented for both intention-to-treat and per-protocol.

Class of vertigo control

In the gentamicin arm: 25/30 experienced Complete Control (Class A, 83·3%), 3/30 Substantial Control (Class B, 10%) and 2/30 Limited Control (Class C, 6·6%). In the steroid arm: 21/30 experience Complete Control (Class A, 70%), 3/30 Substantial Control (Class B, 10%), 4/30 Limited Control (Class C, 13·3%) and 2/30 required secondary treatment (Class F, 6·6%). Chi-square analysis showed no significant difference between gentamicin and steroid for quality of vertigo control (P=0·39), Table S1.

Table S1: Class of vertigo control to gentamicin or steroid treatment according to the AAO-HNS committee classification for gentamicin and steroid.

	Complete (Class A)	Substantial (Class B)	Limited (Class C)	Failures (Class F)
Gentamicin (/30)	25 [83·3%]	3 [10%]	2 [6·6%]	0
Steroid (/30)	21 [70%]	3 [10%]	4 [13·3%]	2 [6·6%]

Functional Level Scale

After gentamicin treatment, the FLS score improved in 25/30 patients, there was no change in 4 patients and 1 patient experienced a worse score. After steroid treatment, and omitting the two Class F drug failures, FLS score improved in 22/28 patients, there was no change in 3 patients and a worse score in 3 patients. Chi-square analysis showed no significant difference between gentamicin and steroid for functional outcome (P=0·36), Table S2.

Table S2: AAO-HNS Functional level scale categories for gentamicin and steroid

	Improvement	No Change	Worsening
Gentamicin (/30)	25 [83·3%]	4 [13·3%]	1 [3·3%]
Steroid (/28)	22 [78·5%]	3 [10·7%]	3 [10·7%]

Pure-tone audiometry

A decrease by 10dB in the mean across 0.5, 1, 2 and 3 KHz pure-tone threshold level between 18-24 months represented a clinically meaningful reduction in hearing as defined by the AAO-HNS. Although fewer patients experienced a clinically meaningful hearing worsening following steroid treatment compared to gentamicin (9 patients *versus* 4 patients respectively), there was no significant difference between arms with chi-square analysis (P=0·29), Table S3.

Table S3: AAO-HNS hearing level categories to gentamicin or steroid.

	Improvement	No Change	Worsening
Gentamicin (/30)	9 [30%]	12 [40%]	9 [30%]
Steroid (/28)	8 [28·7%]	16 [57·1%]	4 [14·2%]

Speech Discrimination

Following steroid treatment, more patients experienced a clinically meaningful improvement in speech discrimination compared to gentamicin (8 patients *versus* 3 patients respectively) and fewer patients experienced a clinically meaningful worsening (1 patient *versus* 9 patients, Table S4). Chi-square analysis showed a significant difference between gentamicin and steroid treatments (P=0·01) and confirmed with post-hoc testing (Fisher's Exact Test, P=0·008). There was also a significant difference between drugs when results were analysed for intention-to-treat. A clinically meaningful improvement in speech discrimination was found in 8 patients for steroid versus 3 patients for gentamicin and a clinically meaningful worsening in 3 patients for steroid and 9 patients for gentamicin. Chi-square analysis showed a significant difference between gentamicin and steroid treatments (P=0·02) and confirmed with post-hoc testing (Fisher's Exact Test, P=0·039).

Table S4: AAO-HNS Speech discrimination categories to gentamicin and steroid

	Improvement	No Change	Worsening
Gentamicin (/30)	3 [10%]	18 [60%]	9 [30%]
Steroid (/28)	8 [28·5%]	19 [67·8%]	1 [3·6%]

Vestibular tests

Vestibular tests showed ablation of vestibular function after gentamicin whereas there was maintenance of vestibular function after steroid. Accordingly, vestibular function was significantly different between gentamicin and steroid groups, as shown in Figure S3, for all tests (Caloric canal paresis, Vestibular evoked myogenic potentials (VEMPs) and Utricular Centrifugation).

As shown in Figure S3, for intention-to-treat, there was a significant drug *arm* effect for caloric paresis (*time x drug interaction;* F[4,52]15·89, P<0.001), caloric directional preponderance (*drug;* F[1,7·237; P=0·01).VEMP amplitude asymmetry (*drug time x interaction*; F[4,55]5·04, P=0·002), or UCF weakness (*time x drug interaction*; F[4,49]3·37; P=0·02).

After removing the patient failures the statistics were unchanged. There was a significant drug effect for caloric paresis (*drug x time interaction;* F[4,50]16·27; P<0·001), caloric directional preponderance (*drug*; F[1,6·736; P=0·012), VEMP asymmetry (*time x drug interaction*; F[4,53]4·74, P=0·002), or UCF weakness (*time x drug interaction;* F[4,47]3·12; P=0·02).

Figure S3: Mean vestibular functions (± SD) over the 24months follow up A. Caloric Paresis, B. Caloric Directional Preponderance, C. VEMP asymmetry, and D. Utricular Centrifugation (UCF) Weakness.

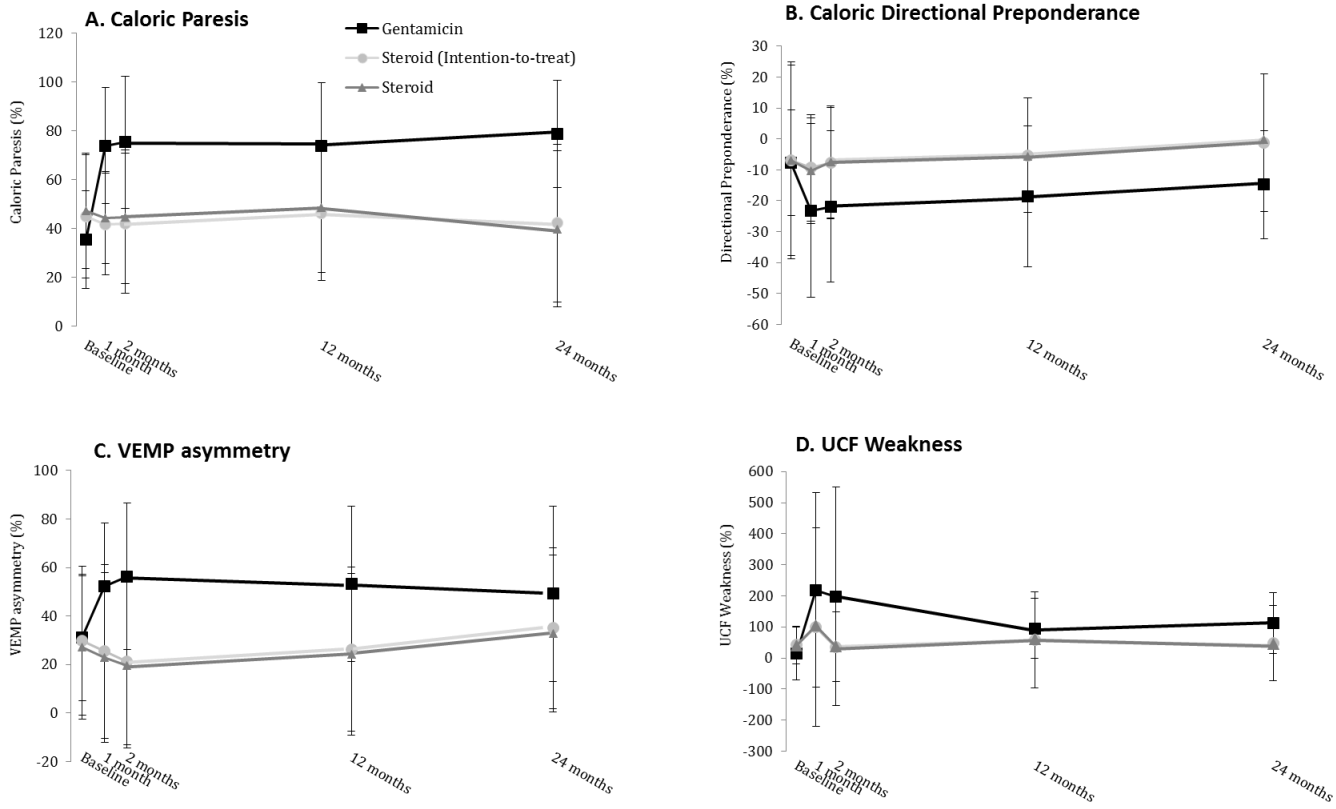


Table S5: Study raw data Mean (± SD) for A). Gentamicin, B). Methylprednisolone intention-to-treat population and C). Methylprednisolone per-protocol population.

A). Gentamicin (n=30)

Characteristic (Mean (± SD))	Baseline	1 month	2 months	6 months	12 months	18 months	24 months
Vertigo attacks over six months (n)	19·9 (16·7)						2·5 (5·8)
Vertigo attacks over one month (n)	6·9 (7·3)						0·7 (2·8)
Vertigo Symptom Scale (/60)	24·7 (12·6)		10·4 (9·8)	12·5 (14·6)	10·8 (13·7)	10·1 (11·3)	8.2 (11·3)
Dizziness Handicap Scale (/100)	59·3 (20·6)		35·3 (22·2)	30·2 (24·3)	29·5 (26·0)	29·5 (25·0)	24·5 (26·7)
Functional Level Scale (/6)	4·0 (0·9)		2·6 (1·2)	2·6 (1·3)	2·4 (1·3)	2·3 (1·3)	2·2 (1·3)
Tinnitus Handicap Inventory (/100)	45·7 (30·3)		26·8 (22·3)	31·1 (27·4)	31·5 (29·2)	27·1 (27·2)	25·9 (29·5)
Aural Fullness Scale (/10)	6·6 (3·1)		4·1 (2·9)	4·2 (3·3)	4·5 (2·9)	3·4 (2·5)	3·5 (2·8)
Pure-tone average (dB)	51·5 (11·3)	52·2 (15·8)	49·0 (16·9)	45·5 (17·7)	47·3 (19·2)	44·8 (18·8)	49·4 (18·1)
Speech discrimination (%)	71·1 (21·7)	69·4 (22·9)	74·3 (23·4)	76·6 (25·9)	71·6 (24·7)		65·0 (30·1)
Caloric asymmetry (%)	35·3 (20·1)	73·9 (23·7)	75·3 (27·0)		73·6 (26·1)		78·7 (22·0)
Caloric directional preponderance (%)	-7·7 (17·1)	-23·1 (28·1)	-21.9 (24·5)		-18·6 (22·7)		-14·8 (17·5)
VEMP asymmetry (%)	31·1 (26·0)	52·2 (26·1)	56·4 (30·3)		53·2 (32·0)		49·2 (36·2)
UCF weakness (%)	14·3 (84·6)	218·9 (313·7)	198·2 (351·2)		94·7 (96·3)		113·1 (98·0)

B). Methylprednisolone (Intention-to-treat, n=30)

Characteristic (Mean (± SD))	Baseline	1 month	2 months	6 months	12 months	18 months	24 months
Vertigo attacks over six months (n)	16·4 (12·5)						1·6 (3·4)
Vertigo attacks over one month (n)	5·5 (6·5)						0·5 (1·4)
Vertigo Symptom Scale (/60)	21·8 (10·5)		7·2 (7·7)	5·9 (8·0)	6·9 (7·2)	7·9 (10·7)	5·3 (6·3)
Dizziness Handicap Scale (/100)	51 (20·5)		26·1 (22·2)	22·3 (20·0)	20·6 (22·1)	15·3 (17·0)	16·3 16·7)
Functional Level Scale (/6)	3·5 (0·9)		2·2 (1·0)	2·1 (1·1)	2·1 (1·0)	1·9 (0·9)	1·9 (1·1)
Tinnitus Handicap Inventory (/100)	39·4 (25·4)		22·7 (21·4)	20·3 (20·1)	19·1 (21·1)	17·3 (18·5)	18·1 (20·8)
Aural Fullness Scale (/10)	5·3 (3·0)		3·3 (2·5)	2·6 (2·4)	3·3 (3·9)	3·1 (2·7)	2·9 (2·6)
Pure-tone average (dB)	53·3 (21·2)	49·3 (22·2)	49·8 (22·3)	46·7 (23·3)	47·0 (24·0)	48·4 (22·1)	46·9 (24·0)
Speech discrimination (%)	65·0 (29·3)	71·8 (26·5)	76·1 (24·4)	75·6 (26·4)	73·4 (27·2)		76·3 (29·4)
Caloric asymmetry (%)	44·9 (25·1)	41·7 (20·8)	42 (28·7)		46·1 (27·4)		42·1 (32·2)
Caloric directional preponderance (%)	-6·9 (30·8)	-9·3 (17·2)	-7·7 (18·0)		-5·3 (18·5)		-1·2 (22·2)
VEMP asymmetry (%)	29·9 (30·6)	25·4 (35·8)	21·3 (34.4)		26·3 (33·9)		35·1 (33·2)
UCF weakness (%)	41·4 (60·4)	99·1 (319·2)	35·8 (112·5)		57·1 (154·6)		46·9 (121·2)

C). Methylprednisolone (Per-Protocol, n=28)

Characteristic (Mean (± SD))	Baseline	1 month	2 months	6 months	12 months	18 months	24 months
Vertigo attacks over six months (n)	16·8 (12·8)						1·2 (3·1)
Vertigo attacks over one month (n)	5·3 (6·7)						0·4 (1·4)
Vertigo Symptom Scale (/60)	22 (10·3)		6·9 (7·2)	4·6 (6·4)	6·6 (7·1)	7·2 (10·4)	5·2 (6·3)
Dizziness Handicap Scale (/100)	52·5 (20·0)		25·9 (21·7)	20·4 (19·1)	20·3 (22·2)	14·5 (17·1)	15·7 (15.7)
Functional Level Scale (/6)	3·5 (0·8)		2·3 (1·0)	2·0 (1·0)	2·0 (1·0)	1·9 (0·9)	1·8 (1·1)
Tinnitus Handicap Inventory (/100)	38·5 (25·8)		22·2 (21)	18·5 (19·3)	18·6 (21·3)	16·0 (18·0)	17·3 (19·9)
Aural Fullness Scale (/10)	5·4 (3.1)		3·2 (2·5)	2·6 (2·4)	3·3 (4·1)	2·9 (2·8)	3·0 (2·6)
Pure-tone average (dB)	54·8 (21·0)	50·4 (22.5)	50·9 (22·7)	46·9 (24·1)	48·0 (24·5)	49·1 (22·7)	46·5 (23·7)
Speech discrimination (%)	63·8 (29·7)	69·9 (26·4)	75·0 (24·9)	74·6 (27·1)	72·4 (27·8)		77·3 (28·5)
Caloric asymmetry (%)	47·3 (23·6)	44·3 (18·8)	44·7 (27·5)		48·4 (26·5)		39·7 (31·9)
Caloric directional preponderance (%)	-7·0 (31·9)	-10·3 (17·2)	-7·6 (18·3)		-5·6 (18·3)		-0·3 (22·5)
VEMP asymmetry (%)	27·1 (29·6)	22·9 (35·0)	19·7 (34·3)		24·1 (33·4)		32·8 (32·2)
UCF weakness (%)	41·0 (61·9)	105·6 (331·3)	37·3 (117·0)		60·4 (157·1)		46·2 (126·0)

Table S6: Study raw data Median (± interquartile range (IQR) 75th percentile) for A). Gentamicin, B). Methylprednisolone intention-to-treat population and C). Methylprednisolone per-protocol population.

A). Gentamicin (n=30)

Characteristic (Median (IQR 75th percentile))	Baseline	1 month	2 months	6 months	12 months	18 months	24 months
Vertigo attacks over six months (n)	16·5 (30)						0 (1·25)
Vertigo attacks over one month (n)	4·5 (10·5)						0 (0)
Vertigo Symptom Scale (/60)	20·5 (38·25)		7 (15·8)	5·5 (22)	5 (12·5)	5 (18)	4 (13)
Dizziness Handicap Scale (/100)	60 (74)		33·5 (51)	23 (42·5)	20 (41)	16 (31)	12 (28)
Functional Level Scale (/6)	4 (5)		2 (3)	2 (3)	2 (3)	2 (3)	2 (3)
Tinnitus Handicap Inventory (/100)	43 (74)		17 (40)	23 (44)	20 (46)	12 (34)	10 (30)
Aural Fullness Scale (/10)	7·5 (9)		4 (6.25)	5 (7·25)	4 (7)	3 (5)	3 (5)
Pure-tone average (dB)	51·3 (61·3)	55 (61·6)	53·1 (60)	48·1 (57·5)	51·3 (61·9)	43·8 (60)	51·3 (61·9)
Speech discrimination (%)	75 (90·8)	73·3 (86·7)	80 (93·25)	83·3 (96·7)	73·3 (93·3)		70 (96·6)
Caloric asymmetry (%)	37·5 (50·3)	82 (88·8)	85·5 (89·5)		85 (89)		86 (91)
Caloric directional preponderance (%)	-7 (6)	-19·5 (-11.8)	-21·5 (-5.3)		-20 (2)		-11 (-3)
VEMP asymmetry (%)	36·2 (42·9)	55·05 (70·2)	63·7 (79·5)		59·8 (79·1)		59 (75)
UCF weakness (%)	-6 (23)	149 (199)	85 (171)		77·5 (141)		97·5 (143·8)

B). Methylprednisolone (Intention-to-treat, n=30)

Characteristic (Median (IQR 75th percentile))	Baseline	1 month	2 months	6 months	12 months	18 months	24 months
Vertigo attacks over six months (n)	12 (24)						0 (1·25)
Vertigo attacks over one month (n)	3 (6·25)						0 (0)
Vertigo Symptom Scale (/60)	23 (28·25)		5 (9·25)	3·5 (6·5)	4·5 (11·25)	4 (9)	2·5 (10)
Dizziness Handicap Scale (/100)	49 (64)		18 (43·5)	20 (42)	12 (40)	8 (29·75)	12 (25)
Functional Level Scale (/6)	3 (4)		2 (3)	2 (3)	2 (3)	2 (3)	1·5 (3)
Tinnitus Handicap Inventory (/100)	38 (59)		15 (44·5)	13 (34·5)	9 (31·5)	10 (28·5)	9 (33)
Aural Fullness Scale (/10)	5 (7)		3·5 (5·25)	2·5 (4)	3 (5)	2 (5·25)	3 (5)
Pure-tone average (dB)	52·5 (65)	52·5 (58·8)	55 (64·1)	45 (62·8)	48·8 (61·9)	48·8 (61·4)	48·1 (59·1)
Speech discrimination (%)	66·7 (91·7)		76·7 (96·7)	83·3 (93·3)	90 (96·7)	86·7 (94·1)	85 (100)
Caloric asymmetry (%)	44 (68·5)	42 (55·5)	40 (63·5)		46 (72)		47 (69)
Caloric directional preponderance (%)	-10 (-1)	-9 (0)	-9 (6)		-10 (4)		-3 (17)
VEMP asymmetry (%)	31·9 (54·3)	33·2 (48·8)	14·8 (44·9)		26·7 (49·9)		39·3 (57·2)
UCF weakness (%)	28 (82)	24 (84)	11 (50)		9 (70)		17 (87)

C). Methylprednisolone (Per-Protocol, n=28)

Characteristic (Median (IQR 75th percentile))	Baseline	1 month	2 months	6 months	12 months	18 months	24 months
Vertigo attacks over six months (n)	12 (24)						0 (1)
Vertigo attacks over one month (n)	3 (6·75)						0 (0)
Vertigo Symptom Scale (/60)	23 (28)		5 (8·75)	2·5 (5)	4 (11)	4 (7·75)	2·5 (9·75)
Dizziness Handicap Scale (/100)	51 (64)		18 (41)	18 (38)	12 (38·5)	6 (25·25)	12 (24)
Functional Level Scale (/6)	3 (4)		2 (3)	2 (3)	2 (3)	2 (2·75)	1 (2·75)
Tinnitus Handicap Inventory (/100)	37 (57·5)		15 (43·5)	10 (33·25)	8 (29·5)	9·5 (27·5)	9 (31·5)
Aural Fullness Scale (/10)	5·5 (7)		3·5 (5)	2·5 (4)	3 (5)	2 (5·75)	3 (5)
Pure-tone average (dB)	53·1 (65)	53·8 (58·8)	55·6 (64·7)	45·6 (63·4)	53·1 (63·1)	49·4 (61·8)	48·1 (58·4)
Speech discrimination (%)	66·7 (90)	75 (85·8)	83·3 (93·3)	85 (96·7)	81·7 (95·8)		85 (100)
Caloric asymmetry (%)	48 (69)	44 (57)	40 (64)		47 (72)		40 (68)
Caloric directional preponderance (%)	-10 (-5)	-9 (0)	-9 (7)		-10 (1)		-3 (21)
VEMP asymmetry (%)	29·6 (47·8)	32·6 (46·2)	13·7 (42·7)		23·5 (49)		37·3 (56·3)
UCF weakness (%)	28 (79·5)	24 (89)	11 (56)		9 (70·5)		6 (98)

Figure S4: Median ± range number of attacks of vertigo 6 months before treatment and in the final 6 months (18-24 months post-injection).

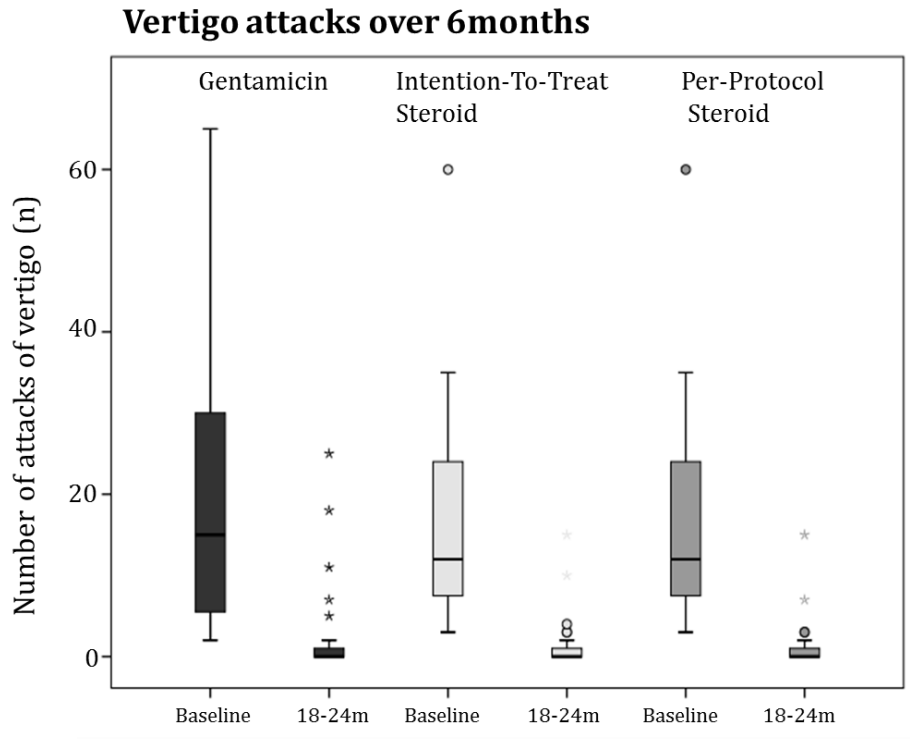


Figure S5: Median ± range number of vertigo attacks for gentamicin and steroid in the one month before treatment and at 24 months.

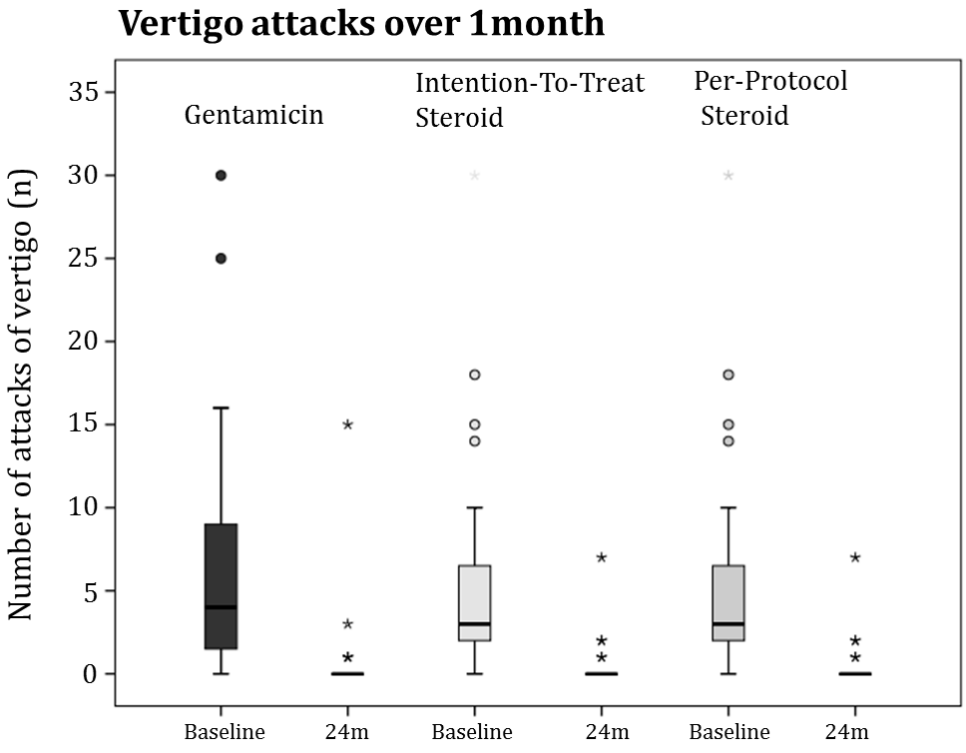


Figure S6: Median ± range for A. Vertigo Symptom Scale and B. Dizziness Handicap Inventory

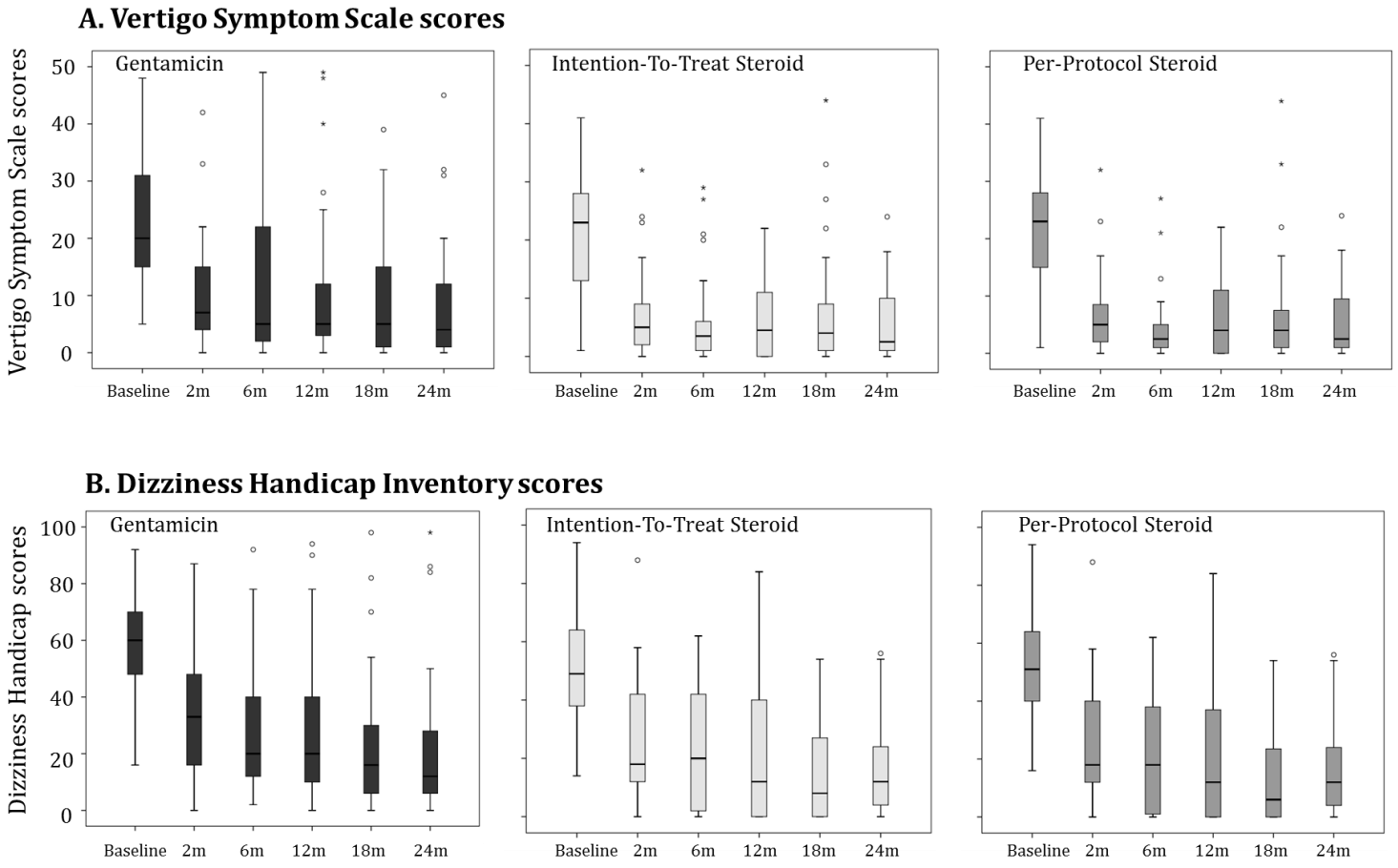


Figure S7: Median ± range for the Functional Level Scale scores at each time point.

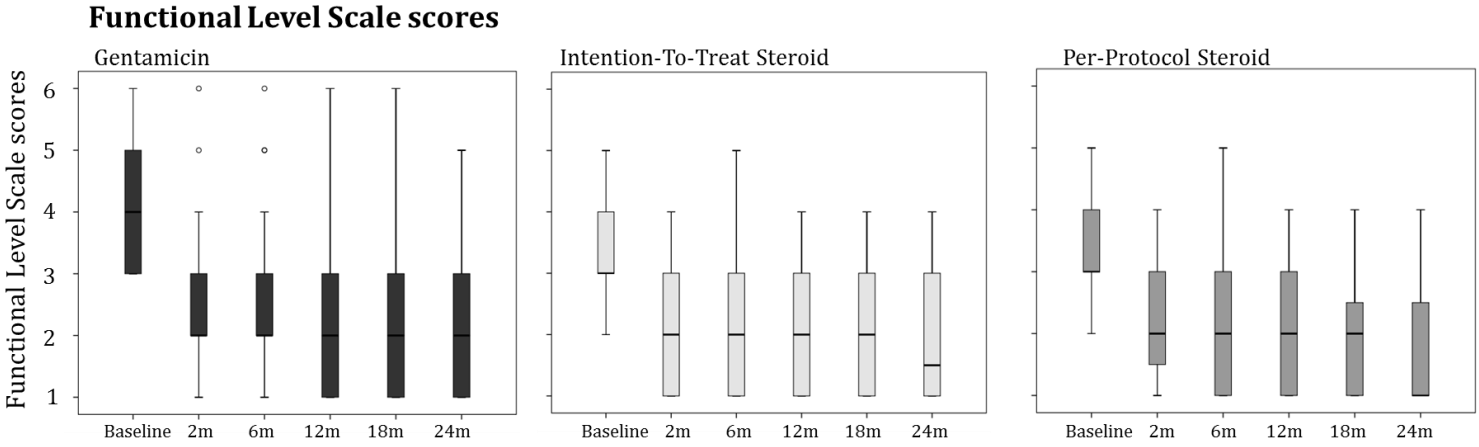


Figure S8: Median ± range for A. Tinnitus Handicap Inventory and B. Aural Fullness Scale

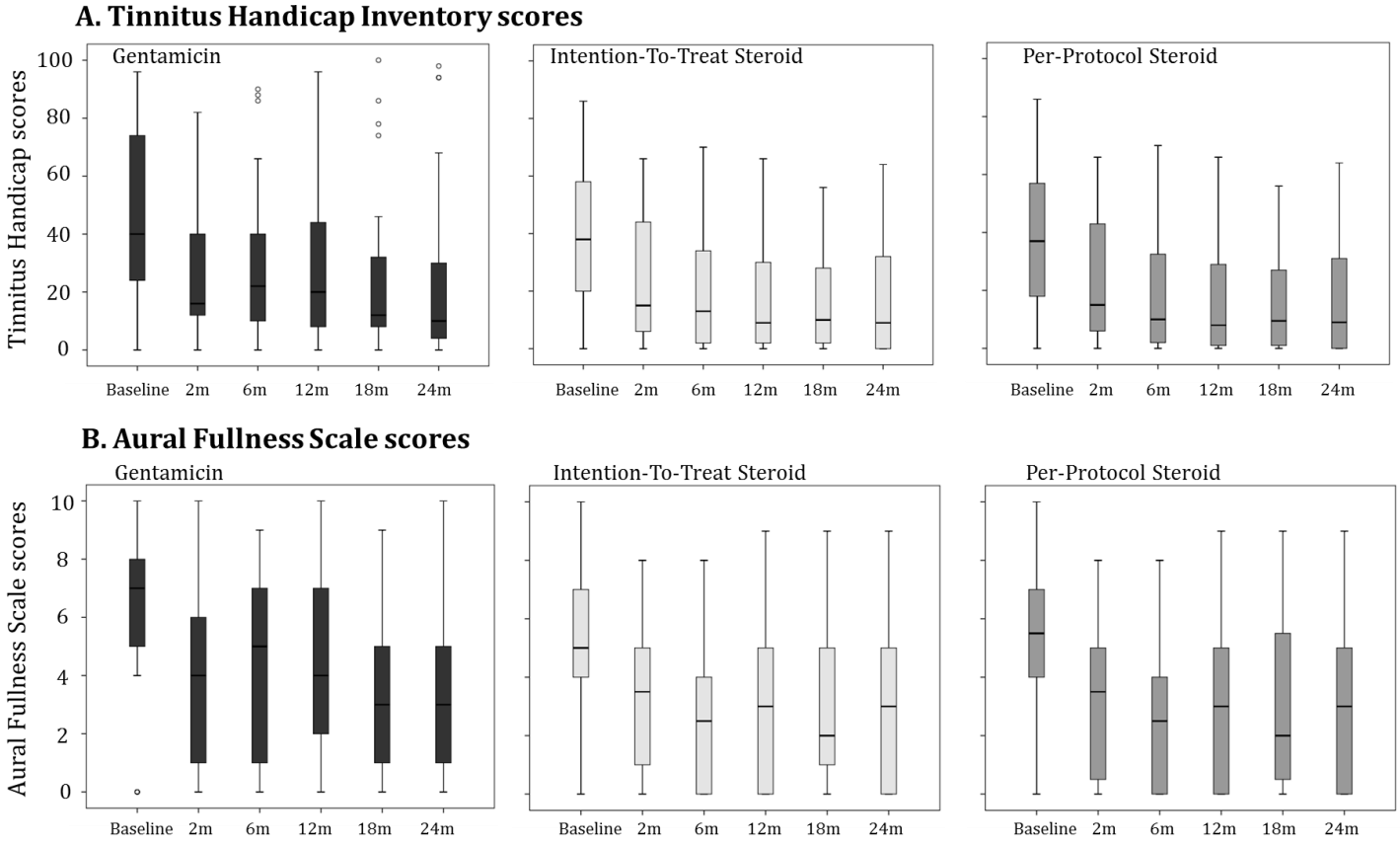
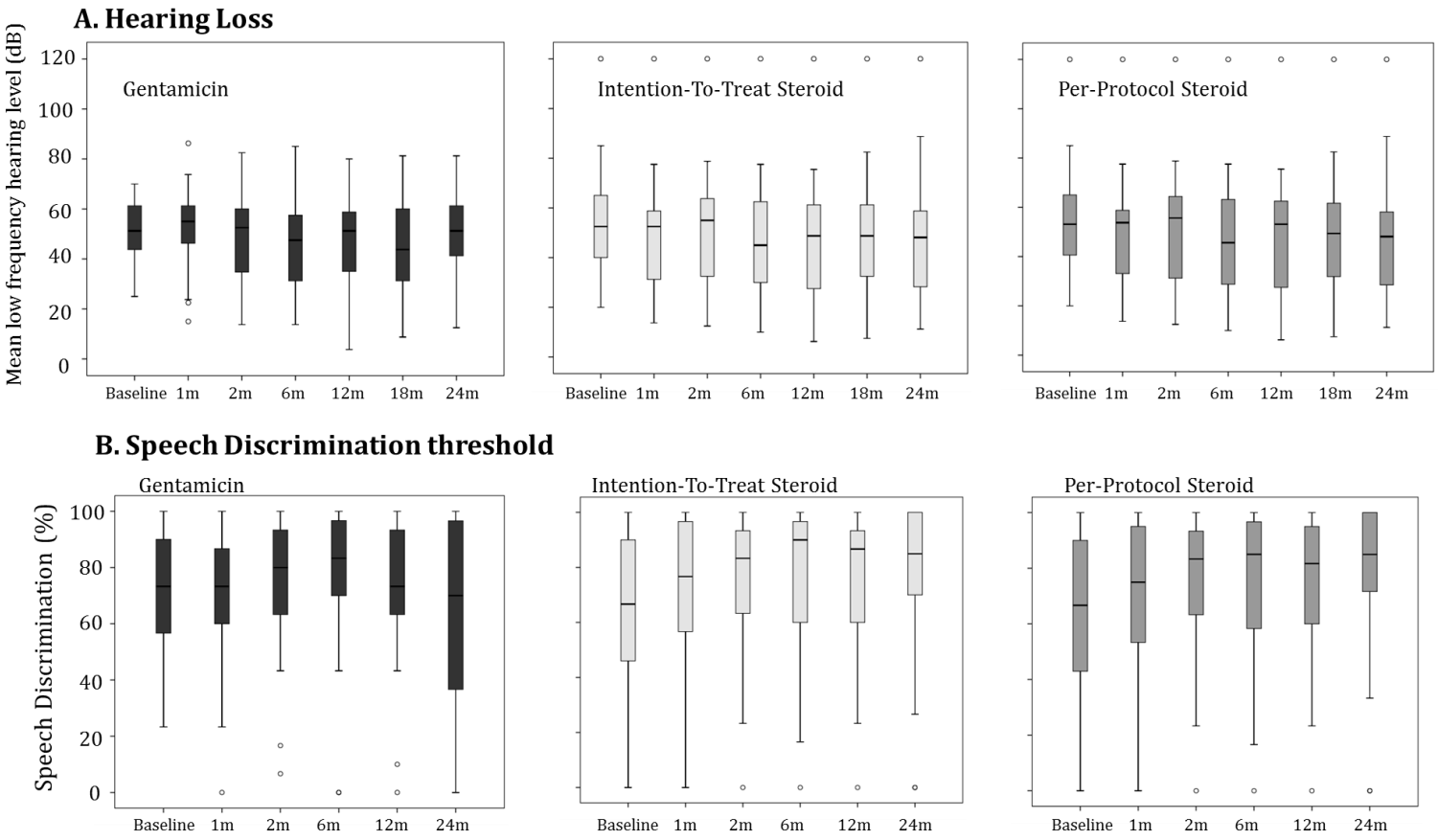


Figure S9: Median ± range for A. Mean low-frequency (average 0·5, 1, 2 and 3KHz) pure tone audiometry level and B. Mean speech discrimination threshold over the 24months follow-up.



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