

# **1365 Partially Implantable Active Middle Ear Implant for Sensorineural Hearing Loss**

**Submission to MSAC**

**MSAC Application 1365**

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## **MAIN BODY OF THE SUBMISSION**

**Submission prepared by:**

MED-EL Implant Systems Australasia Pty Ltd  
Suite 2.07, 90-96 Bourke Rd  
Alexandria NSW 2015  
Australia

**Contact person:**

Mrs Robyn Shakes / Managing Director  
Ph: 0431 570 389  
[robyn.shakes@medel.com](mailto:robyn.shakes@medel.com)

**Ms Matylda Jaworski / Regulatory Affairs**

**Ph: 0415 539 206**  
[matylda.jaworski@medel.com](mailto:matylda.jaworski@medel.com)

## Executive Summary

This application is seeking Medicare Benefits Schedule (MBS) listing of “Partially Implantable Active Middle Ear Implant for Sensorineural Hearing Loss”. The Australian Medical Services Advisory Committee (MSAC) has reviewed before (Application 1137, 2010).

In Australia, the insertion of a partially implantable Middle Ear Implant is not offered as a treatment option so far, resulting in a very niche population of people with a SNHL and a medical condition preventing the use of conventional hearing aids (CHA) that is currently left untreated.

The Australian Medical Services Advisory Committee (MSAC) has reviewed Implantable Active Middle Ear Implant once before and compared it to cochlea implants (CI) and bone anchored hearing aids (BAHA). MSAC noted MEI will augment existing options of BAHA and CI when conventional hearing aids do not work or cannot be tolerated.

MSAC’s conclusions from the 2009 review were as follows:

- **Safety:** due to the absence of comparative evidence it is not possible to accurately compare the rates of adverse events between patients receiving MEI, CI or BAHA, although a total of 1,222 patients were used to inform the safety of MEI. MSAC agreed there are no long term safety data available for MEI but on the limited available evidence, MEI is likely to be at least as safe as BAHA and CI. Surgical complexity of MEI is similar to CI and greater than BAHA. CI is a more risky procedure than BAHA, and BAHA site problems are not experienced with MEI. The current submission contains new clinical evidence and also requests MBS listing at the same fee as for CC which represents a reduction in cost versus previous submissions.
- **Clinical effectiveness:** MSAC noted there was a paucity of high level evidence with which to assess the effectiveness of the MEI. In the absence of any comparative studies, MSAC could not be confident of the comparative effectiveness of MEI versus BAHA, and thus could not conclude that MEI is more effective than BAHA in any patient group. The majority of the available studies assessed MEI in patients with SNHL. This is reflective of the anticipated Australian practice suggested by the clinical experts. MSAC cautioned against the very small number of studies of highly variable quality, and agreed that superior effectiveness of MEI over CI or BAHA could not be demonstrated.
- **Economic evaluation:** Due to insufficient data on comparative effectiveness to support a full cost-effectiveness analysis, a cost comparison was conducted for the

different costs associated with each of the three procedures. MSAC noted there was no measure of the magnitude of clinical benefit included in the economic analysis. In addition, MSAC noted that substantial co-payment/out of pocket expenses would be likely for some MBS items. MSAC noted there would be major out-of-pocket expenses for in-hospital services but that these do not contribute to the Safety Net accumulations. MSAC did not agree with expert opinion and the numbers suggested in the application, that MEI would replace current CI and BAHA use, or that there would be a large pool of unmet need of those with hearing loss due to the cosmetic attraction of MEI versus BAHA, but rather noted, the selection of MEI over BAHA or CI is determined on a case-by-case basis and depends on the patient's individual circumstances and options. MSAC noted that individuals who currently persist with hearing loss or a less than optimal hearing aid, may consider MEI implantation but would not consider BAHA or CI. Sensitivity analysis suggests that if one percent of the estimated pool of individuals with moderate or severe hearing loss elected to have MEI, the additional cost would be AUD 2,291,787. These estimates are based on prevalence data of hearing loss in Australia and include a large proportion of older Australians for whom an MEI would not be suitable. MSAC agreed that the main reason for implantation of a MEI is not cosmetic, but rather medical reasons in subjects with chronic external otitis who cannot tolerate occlusion of the external ear canal. MSAC also accepted that some patients would 'choose' MEI due to greater convenience than BAHA and CI. MSAC noted the base case assumed full substitution giving a cost saving per patient of AUD 5,878 in the current pool of patients, and that substitution of MEI for CI would be cost saving (76% of current pool have CI), whilst substitution for BAHA would be cost-increasing (24% of current pool have BAHA). Therefore, the net effect is cost saving with full substitution if MEI results in patients being at least as well off as, or better off than, after BAHA or CI. MSAC noted the outcomes depend on the type and severity of HL, and presence of therapy-resistant external otitis (or any other medical conditions that may arise out of using BAHA or CI), and would therefore influence the level of substitution across categories. However, the evidence suggests that full substitution is unlikely (low usage to date) and MEI does not appear to be superior to CI. MSAC concluded that MEI is more expensive than BAHA, but less expensive than CI. MSAC was unable to identify any particular sub group of patients who would be suitable for MEI due to failure of hearing aids and other conservative treatment.

- Budgetary impacts: MSAC estimated the first year cost of an MEI, BAHA and CI is AUD 23,873, AUD 15,207 and AUD 34,466 respectively. However, MSAC found uncertainty around the utilisation estimates, but acknowledged the applicant's

response to the final Assessment Report stressed the importance of enforcing appropriate medical indications for use of MEI. Based on 2006-07 MBS data, the total cost of BAHA would be AUD 1,611,957 (106 patients) and the total cost of CI would be AUD 11,270,250 (327 patients). This gives a total cost of AUD 12,882,207. If MEI were used instead of BAHA and CI, the total cost would be AUD 10,336,916. Hence, the cost savings of performing MEI as a direct replacement for BAHA and CI would be over AUD 2.5 million.

- MSAC's advice to the minister: After considering the strength of the available evidence in relation to the safety, effectiveness and cost-effectiveness of the middle ear implant as a treatment for hearing loss, MSAC does not support public funding for middle ear implants.

### ***Description of new technology***

The **only partially implantable** active middle ear implant indicated for sensorineural hearing loss plus medical condition is the Vibrant Soundbridge. This hearing implant system comprises of two components:

An internal component that includes a magnet, an electronics housing, and a transducer; and an external audio processor containing a power source (battery), microphone and digital signal processor. The signal from the audio processor is transmitted to the internal component and transformed into vibrations. The transducer which is called the Floating Mass Transducer (FMT) is crimped or otherwise attached to the long process of the incus at a single point and mechanically drives the ossicular chain. The amplified vibrations can be adjusted via an external auditory processor (AP) to suit different degrees of hearing losses. Battery life of the AP is 6 days. Patients can place new batteries in or charge their existing batteries.

Implantation of the proposed Vibrant Soundbridge for SNHL + medical condition is carried out by an otolaryngologist (ENT surgeon) under general anaesthesia on an outpatient or inpatient basis. The surgical procedure lasts 1.5 to 2 hours after preparing the patient. This involves administering anaesthetics and intravenous antibiotics 30 minutes before surgery, marking the incision site and shaving the hair over the expected incision site. The surgery involves the following steps:

- Creating the incision behind the ear in a posterior-superior direction
- Performing a full or partial mastoidectomy via the facial recess route or the transmeatal route (depends on the medical status of the patient's ear and on the surgeon's preferences)

- Drilling a bone bed and tie-down holes for placing the implant, the transition to the FMT and the demodulator
- Accessing and visualising the middle ear by either posterior tympanotomy through the facial recess, or by lifting the tympanomeatal flap of the outer ear canal (depends on surgical approach used)
- Fixing the implant, transition and the demodulator into the previously drilled bone bed
- Placing/crimping the FMT on to the long process of the incus
- Placing the excess conductor link in the excavated mastoid
- Closing the wound

6 to 8 weeks after surgery the patient is fitted with the audio processor (AP) and initial programming is carried out. The patient is followed-up on a regular basis and the AP is re-programmed when necessary.

### ***The main indication and proposed MBS item descriptions***

Treatment options for sensorineural hearing loss involve amplifying the incoming sound through a range of conservative management therapies including hearing aids. However, when patients also have a medical condition in their outer ear they are unable to wear hearing aids. Hearing aid use has been proven to exacerbate their conditions. Current treatment options for such patients include no treatment or treatment with an active middle ear implant. The only active MEI currently available and indicated for this population is the Vibrant Soundbridge.

### ***Indications for other fully implantable active middle ear implants***

Currently, there are three active middle ear implants: Esteem and the Carina are both indicated for adults who have:

- Stable bilateral moderate to severe sensorineural hearing loss
- Unaided speech discrimination tests score greater than or equal to 40%
- Normal middle ear function and anatomy
- Minimum 30 days of experience with appropriately fit hearing aids

Both of these devices are **contraindicated** in patients who present with chronic outer, middle or inner ear pathologies.

**Indications for partially implantable active middle ear implants****a) Vibrant Soundbridge:**

- Pure-tone air-conduction threshold levels at or within the levels listed below in Table 1 .Pure-tone air-conduction thresholds for both ears within 20 dB HL of each other at frequencies 0.5 to 4 kHz Air-bone gap at 0.5, 1, 2 and 4 kHz no greater than 10 dB HL at two or more of these frequencies.
- Normal tympanometry.
- No previous middle ear surgery.
- The patient shall have no history of post-adolescent, chronic middle ear infections or inner ear disorders such as vertigo or Meniere's syndrome.
- Speech audiometry curve adequate to the respective PTA. Speech understanding >65% (at 65dB SPL) for word lists with amplification or at most comfortable level under earphones.
- Unable to wear or benefit from a conventional hearing aid for medical reasons.
- The ear selected for implantation of the VSB shall be equal to or worse than the un-implanted ear.

**Table 1 - Air conduction threshold levels for SNHL indication (CE marked countries)**

<b>Frequency (kHz)</b>	0.5	1	1.5	2	3	4
<b>Lower Limit (dB HL)</b>	10	10	10	15	25	40
<b>Upper Limit (dB HL)</b>	65	75	80	80	85	85

Vibrant Soundbridge candidates cannot use conventional hearing aids for a variety of medical reasons. These may include but are not limited to conditions such as chronic otitis externa, psoriasis, exostosis of the ear canal, persistent excessive cerumen blocking the ear canal, absent or deformed pinnae following skin cancer, unusual morphology affecting the ear canal or pinna that prevent the use of conventional hearing aids.

**b) Ototronix MAXUM:**

- For use in adults, 18 years of age or older,
- Present with a moderate to severe sensorineural hearing loss
- unaided word recognition score of 60% or greater
- Desire an alternative to an acoustic hearing aid.
- Experience with appropriately fit hearing aids.

In conclusion, the only partially implantable active middle ear implant that offers

management for the target population is the Vibrant Soundbridge.

The details of the proposed MBS listing as agreed by PASC are as follows:

Proposed MBS item descriptor for partially implantable MIDDLE EAR IMPLANT, Insertion of, including a mastoidectomy	
Category 3 – Therapeutic Procedures	
MBS [item number]	partially implantable MIDDLE EAR IMPLANT, insertion of, including mastoidectomy, for patients with:
	<p>sensorineural hearing loss that is stable, bilateral and symmetrical; and</p> <p>air conduction thresholds in the mild to severe range with PTA4 below 80 dB HL; and</p> <p>have speech perception discrimination of <math>\geq 65\%</math> correct with appropriately amplified sound; and</p> <p>cannot wear conventional hearing aid because of outer ear pathology; and</p> <p>no history of inner ear disorders such as Meniere's syndrome</p> <p>a normal middle ear (no history of middle ear surgery or of post-adolescent, chronic middle ear infections; and normal tympanometry; and on audiometry the air-bone gap is <math>\leq 10</math> dBHL at two or more of the following frequencies: 0.5, 1, 2 and 4 kHz).</p>
	Fee: \$1,876.59 (based on mastoidectomy item).
	(Anaes)

Rationale for the proposed listing and clinical management algorithm

Insertion of a partially implantable MEI is not reimbursed by the MBS. This treatment is proposed as an additional option to the current practice for a sub-population of patients that are currently left untreated.



**Fig 1 - Clinical Management Algorithm**

### **Comparator**

The appropriate comparator is No Treatment.

### **Clinical evidence**

The present review relies on best available evidence on Middle Ear Implants to draw conclusions about their relative effectiveness and safety.



Overall, an assessment of the study characteristics that could potentially influence test validity showed that the following studies demonstrated notable characteristics that differed from all studies:

- Memari (Memari et al., 2011) is unique in that it represents a different geographical location (Iran) and may reflect differences in the provision of health care.
- In three studies, Pok et al. (2010), Sziklai et al. (2011) and Gerard et al. (2012), the length of follow-up was not specified. The first two studies are of prospective design and it could be assumed that data was collected at initial fitting. The latter is a retrospective study where a longer follow-up could be assumed (Gerard et al., 2012; Pok et al., 2010; Sziklai I, 2011).

Keeping these studies in mind, the literature available on middle ear implants demonstrates that implantation of the VSB:

- Results in a significant improvement in sound-field hearing thresholds
- Results in significantly better speech recognition/comprehension in quiet and noisy situations
- Leads to few difficulties in understanding speech in relatively easy listening conditions, as compared to noisy conditions; and improves health in general
- Is a safe procedure with minor adverse events resolving on their own or with local treatment

Assessment of VSB outcomes at a long-term follow-up demonstrate:

- A small but non-significant shift in bone conduction thresholds over time
- Constant functional gain
- Slight decrease in recognition/comprehension over time, yet still significantly better outcomes than baseline
- Sustained subjective benefit

In the field of middle ear implants it can be concluded that the VSB is;

- At least as effective as other partially or fully implantable MEI
- At least as safe as other partially implantable MEI
- Superior in terms of safety in regard to fully-implantable MEI

The evidence base used to reach the conclusions above are summarised in Table 28 with respect to important features of the evidence outlined in Section B.8 of the PBAC Guidelines.

**Table 2 - Non-randomised studies assessing the safety and efficacy of middle ear implants**

Author	Reports
Fully implantable device: ESTEEM	
Barbara (2014)	Delayed facial nerve palsy after surgery for the Esteem. <i>Acta Otolaryngol.</i> , Early Online, 1–4, 2014.
Chen (2004)	Phase 1 clinical trial results of the Envoy System: a totally implantable middle ear device for sensorineural hearing loss. <i>Otolaryngol.Head Neck Surg.</i> 131 (6):904-916, 2004.
Gerard (2012)	Esteem 2 middle ear implant: our experience. <i>Audiol.Neurotol.</i> 17 (4):267-274, 2012.
Kraus (2011)	Envoy Esteem Totally Implantable Hearing System: phase 2 trial, 1-year hearing results. <i>Otolaryngol.Head Neck Surg.</i> 145 (1):100-109, 2011.
Llanos-Méndez (2013)	Esteem® totally implantable hearing device for treatment of sensorineural hearing loss. Systematic review. ISBN:978-84-15600-26-8, 2013.
Memari (2011)	Safety and patient selection of totally implantable hearing aid surgery: Envoy system, Esteem. <i>Eur.Arch.Otorhinolaryngol.</i> 268 (10):1421-1425, 2011.
Monini (2013)	Esteem middle ear device versus conventional hearing aids for rehabilitation of bilateral sensorineural hearing loss. <i>Eur.Arch.Otorhinolaryngol.</i> 270 (7):2027-2033, 2013.
Fully implantable device: CARINA	
Bruschini (2010)	Fully implantable Otologics MET Carina device for the treatment of sensorineural and mixed hearing loss: Audio-otological results. <i>Acta Otolaryngol.</i> 130 (10):1147-1153, 2010.
Jenkins	Otologics fully implantable hearing system: Phase I trial 1-year results. <i>Otol.Neurotol.</i> 29 (4):534-541, 2008.
Tringali (2010)	Otologics middle ear transducer with contralateral conventional hearing aid in severe sensorineural hearing loss: evolution during the first 24 months. <i>Otol.Neurotol.</i> 31 (4):630-636, 2010.
Partially implantable device: VIBRANT SOUNDBRIDGE	
Boeheim (2010)	Active middle ear implant compared with open-fit hearing aid in sloping high-frequency sensorineural hearing loss. <i>Otol.Neurotol.</i> 31 (3):424-429, 2010.

Boheim (2007)	Rehabilitation of high frequency hearing loss: use of an active middle ear implant]. HNO 55 (9):690-695, 2007.
Bruschini (2009)	Exclusive Transcanal Surgical Approach for Vibrant Soundbridge Implantation: Surgical and Functional Results.[Miscellaneous Article]. Otology & Neurotology 30 (7):950-955, 2009.
Edfeldt (2014)	Evaluation of cost-utility in middle ear implantation in the Nordic School. Acta Otolaryngol. 2014 Jan;134(1):19-25., 2014.
Fisch (2001)	Clinical experience with the Vibrant Soundbridge implant device. Otol.Neurotol. 22 (6):962-972, 2001.
Fraysse (2001)	A multicenter study of the Vibrant Soundbridge middle ear implant: early clinical results and experience. Otol.Neurotol. 22 (6):952-961, 2001.
Garin (2005)	Hearing in noise with the Vibrant Soundbridge middle-ear implant. Proceedings of the 4th International Symposium on Electronic Implants in Otolaryngology, pg 72-73, 2005
Ihler (2013)	Mastoid cavity obliteration and vibrant soundbridge implantation for patients with mixed hearing loss. Laryngoscope, DOI: 10.1002/lary.24180, 2013.
Ihler (2014)	Long-term functional outcome and satisfaction of patients with an active middle ear implant for sensorineural hearing loss compared to a matched population with conventional hearing aids. Otolology & Neurotology, 35:211-215. 2014
Labassi (2005)	Retrospective of 1000 patients implanted with a Vibrant Soundbridge middle-ear implant. <b>Proceedings</b> of the 4th International Symposium on Electronic Implants in Otolaryngology, pg 74-75. 2005
Lenarz (2001)	Vibrant Sound Bridge System. A new kind hearing prosthesis for patients with sensorineural hearing loss. 2. Audiological results]. Laryngorhinotologie 80 (7):370-380, 2001.
Luetje (2002)	Phase III clinical trial results with the Vibrant Soundbridge implantable middle ear hearing device: a prospective controlled multicenter study. Otolaryngol.Head Neck Surg. 126 (2):97-107, 2002.
Luetje (2010)	Vibrant Soundbridge implantable hearing device: critical review and single-surgeon short- and long-term results. Ear Nose Throat J. 89 (9):E9-E14, 2010.
Mosnier (2008)	Benefit of the Vibrant Soundbridge Device in Patients Implanted For 5 to 8 Years.[Report]. Ear & Hearing 29 (2):281-284, 2008.

Pok (2010)	Clinical experience with the active middle ear implant Vibrant Soundbridge in sensorineural hearing loss. <i>Adv.Otorhinolaryngol.</i> 69:51-58, 2010.
Saliba (2005)	Binaural hearing, Digital hearing aid, Middle ear implant, Stereophony, and Vibrant Soundbridge. Binaurality in Middle Ear Implant Recipients Using Contralateral Digital Hearing Aids.[Miscellaneous Article]. <i>Otology &amp; Neurotology</i> 26 (4):680-685, 2005.
Schmutziger (2006)	Long-Term Assessment after Implantation of the Vibrant Soundbridge Device. <i>Otology &amp; Neurotology</i> 27:183–188 2006.
Snik (1999)	First audiometric results with the Vibrant soundbridge, a semi-implantable hearing device for sensorineural hearing loss. <i>Audiology</i> 38 (6):335-338, 1999.
Snik (2001)	Multicenter audiometric results with the Vibrant Soundbridge, a semi-implantable hearing device for sensorineural hearing impairment. <i>Otolaryngol.Clin.North Am.</i> 34 (2):373-388, 2001.
Snik (2001)	Vibrant semi-implantable hearing device with digital sound processing: effective gain and speech perception. <i>Arch.Otolaryngol.Head Neck Surg.</i> 127 (12):1433-1437, 2001.
Snik (2006)	Estimated cost-effectiveness of active middle-ear implantation in hearing-impaired patients with severe external otitis. <i>Arch.Otolaryngol.Head Neck Surg.</i> 132 (11):1210-1215, 2006.
Sterkers (2003)	A middle ear implant, the Symphonix Vibrant Soundbridge: retrospective study of the first 125 patients implanted in France. <i>Otol.Neurotol.</i> 24 (3):427-436, 2003.
Sziklai (2014)	Functional gain and speech understanding obtained by Vibrant Soundbridge or by open-fit hearing aids. <i>Acta Otolaryngol., Acta Otolaryngologica</i> ; 131: 428–433. 2014.
Todt (2002)	Comparison of different vibrant soundbridge audioprocessors with conventional hearing AIDS. <i>Otol.Neurotol.</i> 23 (5):669-673, 2002.
Todt (2005)	Hearing benefit of patients after Vibrant Soundbridge implantation. <i>ORL J.Otorhinolaryngol.Relat Spec.</i> 67 (4):203-206, 2005.
Truy (2008)	Vibrant soundbridge versus conventional hearing aid in sensorineural high-frequency hearing loss: a prospective study. <i>Otol.Neurotol.</i> 29 (5):684-687, 2008.
Uziel (2003)	High-frequency sensorineural hearing loss, Middle ear implant, Rehabilitation, SIGNIA, and Symphonix Vibrant Soundbridge. Rehabilitation for High-Frequency Sensorineural Hearing Impairment in Adults with the Symphonix Vibrant Soundbridge: A Comparative Study.[Miscellaneous Article]. <i>Otology &amp; Neurotology</i> 24 (5):775-783, 2003.

Vincent (2004)	A longitudinal study on postoperative hearing thresholds with the Vibrant Soundbridge device. Eur.Arch.Otorhinolaryngol. 261 (9):493-496, 2004.
Partially implantable device: MAXUM	
NO LITERATURE AVAILABLE FOR THE MAXUM DEVICE	
Partially implantable device: SOUNDTEC	
Hough (2002)	Middle ear electromagnetic semi-implantable hearing device: results of the phase II SOUNDTEC direct system clinical trial. Otol.Neurotol. 23 (6):895-903, 2002.
Roland (2001)	Verification of improved patient outcomes with a partially implantable hearing aid, The SOUNDTEC direct hearing system. Laryngoscope 111 (10):1682-1686, 2001.
Silverstein (2005)	Electromagnetic hearing device, Ossicular magnet, Semi-implantable hearing device, and SOUNDTEC. Experience with the SOUNDTEC Implantable Hearing Aid.[Miscellaneous Article]. Otology & Neurotology 26 (2):211-217, 2005.
SYSTEMATIC REVIEW	
Alberta Health and Wellness (2011)	Middle Ear Implants for the Treatment of Hearing Loss, Final STE Report: December 2011
Butler (2013)	Efficacy of the active middle-ear implant in patients with sensorineural hearing loss. J.Laryngol.Otol. 127 Suppl 2:S8-16, 2013.
CEDIT (2002)	Middle ear implants - systematic review, expert panel. Anonymous. 2002.
Kahue (2014)	Middle ear implants for rehabilitation of sensorineural hearing loss: a systematic review of FDA approved devices (Provisional abstract). Otol Neurotol. Aug;35(7):1228-37, 2014.
Klein (2012)	Hearing aid, Hearing loss, and Middle ear implant. A Systematic Review of the Safety and Effectiveness of Fully Implantable Middle Ear Hearing Devices: The Carina and Esteem Systems.[Review]. Otology & Neurotology 33 (6):916-921, 2012.
MSAC (2010)	Middle ear implant for sensorineural, conductive and mixed hearing losses. MSAC, 2010

***The type of economic evaluation presented***

Using the grid provided in Table 12 and Table 13, the most appropriate method for comparing the proposed medical service against its main comparator No intervention is a cost effectiveness analysis. The same method was used for comparing the two types of partially implantable middle ear implants, the Vibrant Soundbridge and MAXUM. A modelling approach was taken as analysis was based on the data available from the non-randomised studies identified in the literature. A decision tree with embedded Markov processes was built that represented the pathways by which a person may decide to receive middle ear implantation or not, and the clinical events that may occur following their decision. The clinical events in the model are defined as events that can affect the costs and course of treatment in the short or long-term. These include recurring medical conditions in the No intervention arm; and adverse events, device failure, explantation/reimplantation and ceasing MEI use in the intervention arm. The model is illustrated in figure 11. The Markov model built to represent the pathway for receiving the proposed medical service was cloned for the MAXUM and the two middle ear implants were compared. Both models were populated with cost data (mostly) from the MBS and effectiveness data obtained from the literature. The comparison of VSB against no intervention was based upon utility values; and the comparison of the two MEI was based upon patient benefit scores measured by the APHAB. The time horizon of the model was 10 years with a cycle length of 6 months; and costs and effectiveness outcomes were discounted at a 5% rate.

***The cost per patient***

The estimated costs of partially implantable MEIs per procedure was calculated to be AUD 24.468 for the VSB and AUD 13.850 for the MAXUM/SOUNDTEC (see Section D.4). Compared to no intervention, the provision of the Vibrant Soundbridge AMEI results in an improvement of 1.41 QALYs at An incremental cost of AUD 21.927 per patient. The Vibrant Soundbridge is more costly than the MAXUM implant system with an increment of AUD 10.619 and also proves to be more beneficial for the patient with effectiveness improved by 199 units.

***Sustainability of the proposed MBS fee for insertion of a partially implantable Middle Ear Implant***

The addition of the insertion of a partially implantable MEI to the MBS as proposed in this application will lead to an increase in direct treatment costs. The results of the cost-effectiveness analysis clearly indicate that the VSB is a highly cost-effective treatment when compared to No Treatment with an incremental cost-effectiveness ratio of 15.575

AUD/QALY. When compared to the MAXUM the incremental cost-effectiveness ratio is 53.25 AUD/effectiveness. This is a much smaller ICER however as effectiveness outcomes are inverted it represents a significant improvement in patient perceived benefit.

Deterministic sensitivity analysis demonstrated the results of the base-case analysis to be generally robust against variations in the input values of single variables. Results were most sensitive to the total cost of MEI(VSB) provision, and to a lesser extent to the probability of revision surgery and ceasing to use MEI. Comparing the VSB against the MAXUM also revealed cost and effectiveness results that were generally robust to variation in the value of input parameters. The cost outcomes were most sensitive to the costs of VSB and MAXUM provision, and then to a lesser extent to the probability of ceasing to use MAXUM and VSB, and revision surgery following implantation with either device.

The variables found to be effective in DSA were entered into a probabilistic sensitivity analysis. PSA results indicated similar results to base-case outcomes. Providing a partially implantable MEI, namely the Vibrant Soundbridge, as associated with increased QALY ranging from 1,19 to 1,52 but also increased costs ranging from AUD 21.881,48 to AUD 22.265,86, when compared to receiving no intervention. When compared to the MAXUM, the Vibrant Soundbridge was associated with increased effectiveness ranging from 176 to 211,9 but also increased costs ranging from AUD 10.505,87 to AUD 10.745,28.

Based on further sensitivity analysis where the discount rate was varied, the total cost per patient for the Vibrant Soundbridge over the implant lifetime of 10 years would be AUD 26.059,55 and AUD 24.468,43 using 0 % and 5 % discounting. The QALY associated with MEI was more influenced with a decrease from 1.75 to 1.41. The resulting ICER for the VSB against no intervention can thus be calculated as 13.160,06 and 15.575,26, respectively. Similar outcomes were seen when comparing the VSB to the MAXUM: Discounting over a 10-year time period did not influence incremental costs too much while effectiveness outcomes were significantly decreased. The resulting ICER was 45,75 and 53.25, at 0 % and 5 % discounting rates.

The time horizon of the model was also extended to a 20 year time period. The total cost per patient for the Vibrant Soundbridge increased from AUD 24.468,43 at 10 years to AUD 31.149,79 at 20 years. The QALY associated with MEI was more influenced with a decrease from 10.27 to 15.5. The resulting ICER for the VSB against no intervention can thus be calculated as 15.575,25 and 12.986,73, respectively. Comparing the VSB to the MAXUM showed that over a 20-year time horizon differences in the cost and effectiveness of the two interventions become more apparent. The incremental cost was AUD 10.618,57 at 10 years and AUD 13.981,69 at 20 years; and the incremental effectiveness improved from 199.41 to 306.85.

**Estimated extent of Use and Financial Implications**

Based on the prevalence data provided in Section E.1, within the first year after listing, between 33 and 103 cases of insertion of a partially implantable Middle Ear Implant are to be expected. A further annual increase of 1.7 % per year is to be expected in accordance with the population growth. The calculation of number of services each year is based on the assumption that the existing pool of eligible patients could be implanted over a 10 to 15 year period, with 10 years representing a maximum and 15 years representing a minimum number of services per year. Of course this assumption may be influenced by patients' preferences, their willingness to undergo a surgical procedure and their ability to pay out-of-pocket for additional services or non-covered device costs. Taking a mean number of 71 implanted patients into account, in the first year a cost of AUD 133.263 is expected to the MBS for the proposed item. Total costs to the MBS for the associated items, pre-, post- and reimplantation related items, are estimated to sum up to AUD 144.895 in the first year of implementing the proposed service. Total non-MBS associated costs for the proposed intervention include the costs for hospital stay, counselling, batteries as well as the implant and processor, although the sum of AUD 1.062.435 may be covered by the patient or private insurances. The overall total costs of the proposed intervention is therefore AUD 1.340.594 in the first year. Taking the population growth into account, these costs will rise to AUD 1.4537.883 in the fifth year of implementation. Considering the deterministic sensitivity analysis provided in section E5, the number of procedures varies by  $\pm 10$  around the base case values presented for each year.



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# List of Attachments

<b>Attachment</b>	<b>Title</b>	<b>Numbers of copies provided</b>
<b>Attachment A</b>	Review summary on clinical studies	Electronic only
<b>Attachment B</b>	VSB clinical outcomes	Electronic only
<b>Attachment C</b>	Comparators clinical outcomes	Electronic only
<b>Attachment D</b>	Summary of input parameters for the economic evaluation	Electronic only
<b>Attachment E</b>	Variables included in probabilistic sensitivity analysis	Electronic only
<b>Attachment F</b>	Budget impact analysis	Electronic only
<b>Attachment G</b>	DSA for BIA	Electronic only

## List of Volumes

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2. Attachments volume	4
3. References volume	4

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# Abbreviations

Abbreviation	Full term
AC	Air conduction
AMEI	Active Middle Ear Implant
AP	Audio Processor
APHAB	Abbreviated Profile of Hearing Aid Benefit
AR-DRG	Australian Refined Diagnostic Related Group
ARTG	Australian Register of Therapeutic Goods
AUD	Australian Dollar
BAHA	Bone anchored hearing aid
BC	Bone conduction
BIA	Budget impact analysis
CBAs	controlled before and after studies
C/MHL	Conductive and mixed hearing loss
CEA	Cost effectiveness analysis
CEDIT	Comite d'Evaluation et de Diffusion des Innovations Technologiques
CI	Cochlear Implant
CHA	Conventional Hearing Aid
COSI	Client-orientated scale of improvement
CRD	Cochrane Library, and The Centre of Reviews and Dissemination
CUA	cost-utility analysis
DAP	Decision Analytical Protocol
dB	Decibel
DALYs	Disability Adjusted Life Years
DRG	diagnosis-related group
DSA	Deterministic sensitivity analysis
DVA	Department of Veteran Affairs
ENT	Ear, Nose & Throat
FDA	United States Food and Drug Administration

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FG	Functional Gain
FMT	Floating Mass Transducer
FU	Follow up
GBA	Gemeinsamer Bundesausschuss (Federal Joint Committee)
G-DRG	German Diagnosis Related Group
GHABP	Glasgow Hearing Aid Benefit Profile
GP	General Practitioner
HA	Hearing aid
HDSS	Hearing Device Satisfaction Scale
HICP	the harmonized consumer price index
HL	hearing loss/ hearing level
HTA	Health technology assessment
HUI	Health Utilities Index
ICER	Incremental Cost-Effectiveness Ratio
IOI-HA	International Outcome Inventory for Hearing Aids
ITS	Interrupted time series
MBS	Medicare Benefits Schedule
MEI	Middle Ear Implant
N/A	Not Applicable
n.a.	Not available
n.d.	Not determined
nCBAs	not controlled before and after studies
NHB	Net Health Benefit
NIHL	Noise induced hearing loss
NMB	Net Monetary Benefit
OFIA	Operational and Financial Impact Analysis
OPS	Operationen- und Prozedurenschlüssel (Operating Procedures)
OW	Oval window
PHAB	Profile of Hearing Aid Benefit
PHAP	Profile of Hearing Aid Performance

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PICO	Population – Indication – Comparator – Outcome(s)
PL	Prosthesis List
PSA	Probabilistic sensitivity analysis
QALY	Quality Adjusted Life Year
RCT	Randomized Controlled Trial
RW	Round window
SHACQ	Soundbridge Hearing Aid Comparison Questionnaire
SNHL	Sensorineural Hearing Loss
SNR <sub>50</sub>	signal-to-noise ratio where 50% of the presented test material is understood
SPL	Sound Pressure Level
UAMC	University of Arizona Medical Center
VORP	Vibrating Ossicular Prosthesis
VS	Vibrant Soundbridge
WHO	World Health Organization
WRS	word recognition score in quiet

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## A. Details of the proposed intervention and its intended use on the MBS

### A.1 Requested MBS listing and details of the intervention

This application is seeking Medicare Benefits Schedule (MBS) listing for insertion of Active Middle Ear Implants (AMEI) in Sensorineural Hearing Loss (SNHL) plus a medical condition. The Vibrant Soundbridge (VSB) was first implanted in 1996. The device was approved with the CE marking in February 1998 and by the FDA in August 2000. Due to favorable results in adults affected by mixed and conductive hearing loss (Beltrame et al., 2009; Colletti et al., 2009; Colletti et al., 2006; Huttenbrink et al., 2008; Kiefer et al., 2006) VSB-candidacy indications were extended to include not only sensorineural but also mixed and conductive hearing losses in patients 18 years of age or older. As of November 2008, the VSB had been implanted in more than 60 children and adolescents in countries throughout the world with favourable results. In June 2009, the VSB received approval for patients younger than 18 years of age in the European Union and all other countries accepting the CE marking (Cremers et al., 2010) audiologic results and the risk profile are comparable to the adult population (Claros and Pujol, 2013; Colletti et al., 2013; Roman et al., 2012; Zernotti et al., 2012). Middle ear implants have been implanted in children under the age of 5 with favourable results (Frenzel et al., 2010; Mandala et al., 2011).

This application intends to treat patients with active middle ear implants, with a hearing loss who cannot wear hearing aids because of a medical condition which precludes wearing hearing aids. These patients need to be aided, but their hearing is not at a level which requires a cochlear implant, and is ineligible for a bone conduction implant. Therefore an active middle ear implant represents their only alternative for restoring hearing.

Category [3 ] – [Therapeutic Procedures]
MBS [item number (Note: this will be assigned by the Department if listed on the MBS)] [Proposed item descriptor] MIDDLE EAR IMPLANT, Insertion of, including a mastoidectomy, for patients who have:  Air conduction thresholds in the mild to severe range with PTA4 below 80 dB HL; Sensorineural hearing loss and cannot wear conventional hearing aids for a variety of reasons. However, these individuals can still benefit from the amplification of sounds; Medical conditions precluding the use of hearing aids, such as chronic otitis externa, psoriasis, exostosis of the ear canal, persistent excessive cerumen blocking the ear canal,

absent or deformed pinnas following cancer treatment, unusual morphology affecting the ear canal or pinna;

Speech perception discrimination of at least 65% correct with appropriately amplified sound.

Fee: \$[1,876.59 - Proposed fee] - based on Mastoidectomy item

[(Anaes.) - Proposed relevant explanatory notes]

The **internal components** of the proposed medical service are currently being funded through surgical budgets, private health fund exgratia applications (and subsequent approval) and occasionally by patients themselves. The external audio processor, upgrades, programming and maintenance is publicly funded through Australian Hearing to eligible clients. Otherwise the service is either self-funded or funded through the exgratia private health fund application.

## Details of the intervention

The only **partially implantable** active middle ear implant indicated for sensorineural hearing loss plus medical condition is the Vibrant Soundbridge

### **Materials**

The materials in the VSB were selected to be inert with respect to body tissue. For the implanted parts, commonly used long-term implant materials were used. The materials in direct tissue contact are:

For the implant itself, the VORP502, the materials in direct body contact are:

NuSil MED-4750,

Titanium Grade 1 (ASTM F67), and

Loctite Hysol.

For the AP Amadé, the material in direct body contact is:

Xylex® ResinHX8300HP (Colors formulated for Dark Chocolate, Terra Brown, Golden Sand, Silver Grey).

For the Vibroplasty Couplers, the Vibroplasty-OW-Coupler, the Vibroplasty-CliP-Coupler, the Vibroplasty-Bell-Coupler, and the Vibroplasty-RW-Coupler the material in direct body contact is:

Titanium Grade 2 (ASTM F67).

For the generic tools, the materials in direct body contact are:

Medical Grade Stainless Steel (Forming Forceps),

Non-magnetic Medical Grade Stainless Steel (Skin Flap Gauge 7).

The VORP Sizer Kit underwent a change to the product materials. Originally the product was made of:

Polypropylene (both, VORP template and FMT Sizer).

The currently marketed VORP Sizer Kit is made of:

Medical Grade Thermoplastic Elastomere (VORP template)

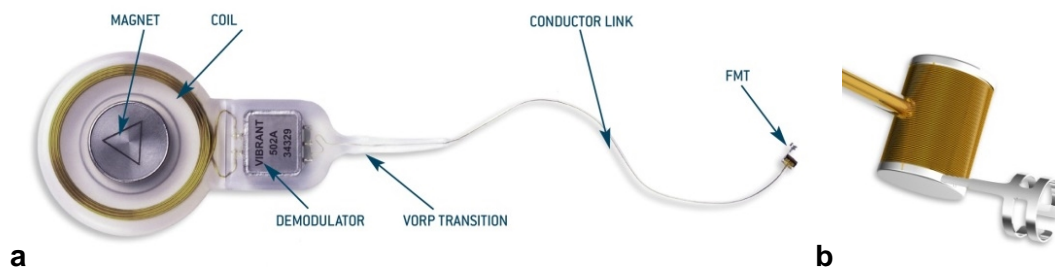
Medical Grade Polypropylene (FMT Sizer).

The biological safety of these materials was preclinically established according to ISO 10993.

### Device Components

The VSB System consists of **an internal part** (VORP502), an **external audio processor** (AP Amadé), the Vibroplasty Couplers, generic tools (accessories to facilitate the implantation), and the fitting system of the AP (application software SYMFIT).

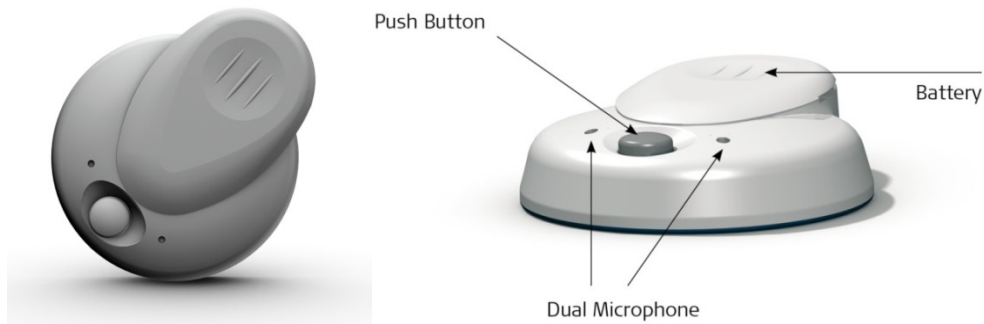
The internal part is surgically implanted. It consists of the FMT, conductor link, electronic package (demodulator) and a magnet surrounded by an internal coil. The AP is held onto the intact skin by magnetic attraction over the implant. It contains a microphone, processing electronics and a battery for power. The following is a depiction of the main internal and external system components:



**Fig 2 - VORP502**

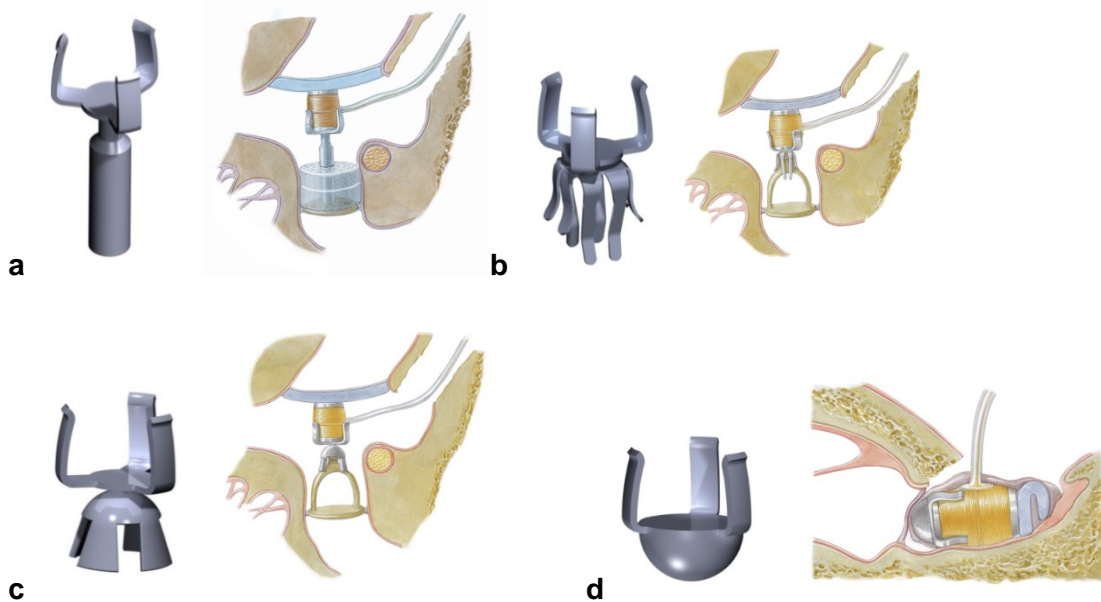
(a) entire implant, (b) enlarged view of the FMT





**Fig 3 - AP Amadé**

The Vibroplasty Couplers provide additional placement options for the FMT in subjects affected by conductive or mixed hearing loss. They are specifically designed to be used in concert with the FMT. Four Vibroplasty Couplers are available: the Vibroplasty-OW-Coupler (oval window), the Vibroplasty-CliP-Coupler, the Vibroplasty-Bell-Coupler, and the Vibroplasty-RW-Coupler (round window) – see Fig 4. All Couplers, except for the Vibroplasty-RW-Coupler are available in four different sizes. Depending on the design, the Vibroplasty Couplers may be placed either on the stapes footplate in the oval window, the stapes head, or the round window. As can be seen from Fig 4, the different types account for the anatomic variability in compromised middle ears.

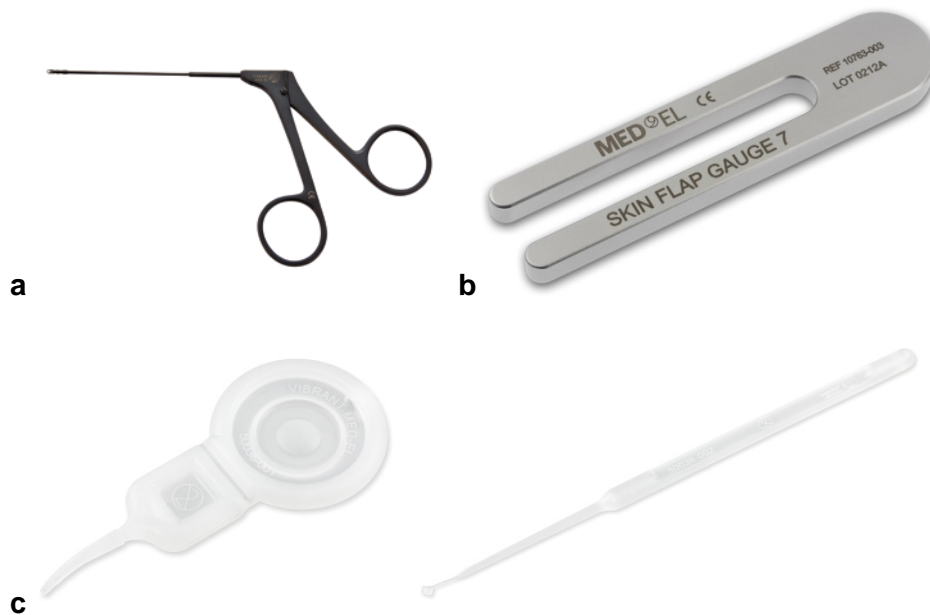


**Fig 4 - Vibroplasty Couplers**

(a) Vibroplasty-OW-Coupler (oval window), (b) Vibroplasty-CliP-Coupler, (c) Vibroplasty-Bell-Coupler, and (d) Vibroplasty-RW-Coupler (round window)

Several optional surgical tools are available for use with the VSB. These include: the Forming Forceps, the Skin Flap Gauge 7, and the VORP Sizer Kit. The Forming Forceps can be used to form the FMT attachment around the incus and the Skin Flap Gauge 7 can

be used to evaluate the thickness of the skin flap in the area covering the coil section of the implant. The VORP Sizer Kit, consisting of VORP template and FMT Sizer, is intended to be used during implantation to support a safe and effective procedure: the VORP template can be used to facilitate positioning of the implant on the skull and creation of the bone bed. The FMT Sizer is intended to be used during surgery to determine the volumetric requirements of the Floating Mass Transducer and assure adequate access for the FMT in the middle ear.



**Fig 5 - Surgical tools for intraoperative application**

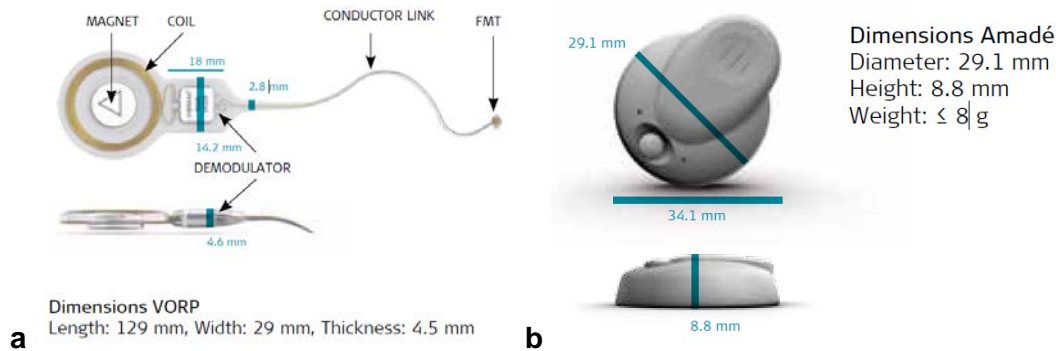
(a) Forming Forceps, (b) Skin Flap Gauge 7, and (c) VORP Sizer Kit containing VORP template and FMT Sizer.

Prior to use, the AP Amadé is programmed to meet the particular hearing needs of the patient. Programming hardware and software are similar to hearing aid programming equipment, and programming typically takes about 30 minutes. Programming is done by trained hearing professionals. Standard fitting hardware are a PC, a hearing aid interface modem - HiPro box, and a standard programming cable that usually are available at implant centers and hearing professional practices.

The fitting is performed in the off-the-shelf hearing instrument fitting software, CONNEXX 6.4.3 or higher (Siemens). To enable CONNEXX to recognize the AP, the database SYMFIT is needed. The SYMFIT is used to program the APs of the VSB System as a single fitting user interface.

## Mechanical Characteristics

The VORP502 is an elongated silicone and titanium implant. Its weight is 9.30 g. The weight of the AP Amadé is 8.00 g including the battery and the magnet. Key dimensions are supplied in the following illustration.



**Fig 6 - Mechanical characteristics of (a) VORP502 and (b) AP Amadé.**

## Other Characteristics

### Power Supply

The implant system is powered by one hearing aid (type 675) battery in the audio processor (AP). As described in section 4.0, the processed audio signal and the energy required for generating the vibration is coupled to the implant via an inductive link. The implant has been intentionally designed to be passive when not activated with the AP and therefore does not require an energy source of its own.

### Electrical Characteristics

Unlike other hearing implants such as cochlear implants, neither the AP nor the implant itself is capable of delivering electrical signals to the patient. Electricity is exclusively needed to operate the circuits within the AP, which then supplies signals to the implant via electronic induction. The implant system is only active in the way that it creates mechanical (vibrational) energy, which is passed to the inner ear.

### Signal Processing Capabilities

Audio signal processing is exclusively performed by the AP. The following key features have to be present in the AP to ensure that effective bone conduction stimulation can be achieved:

- Frequency response equalization: The audio signal picked up by the microphone is processed through a filter bank. The filter bank is used to equalize the frequency

response of the bone conduction pathway. In addition, it is used to adapt the signal processing to the individual patient's degree of hearing loss.

- Dynamics processing: Due to the constrained dynamic range of the bone conduction pathway (compared to the normal auditory pathway via the tympanic membrane) dynamics processing (specifically compression) is needed. As with frequency response equalization, the patient's degree of hearing loss influences the setting of the dynamics processor.

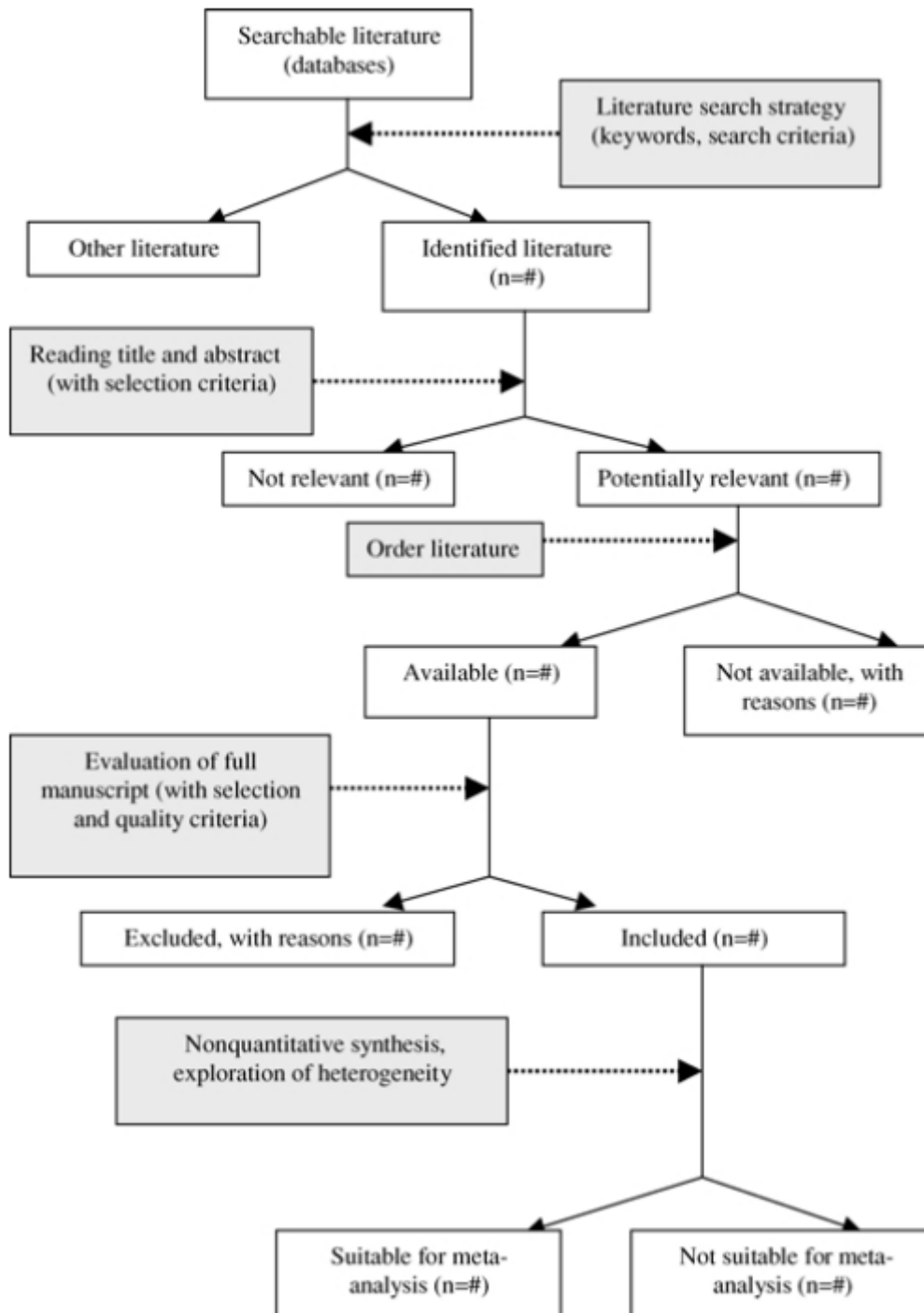
Additional features may be available in different models of the AP. They can be used to increase listening comfort in certain situations, but do not contribute to the clinical benefit of the VSB established within this report.

### **Individual Programming**

The key features - frequency response equalization and dynamics processing settings - have to be individually programmed for each patient. This programming is performed with a software application (Symfit) and a fitting interface (e.g. HiPro or NOAHlink). The programming is done by trained hearing specialists at each center and settings cannot be changed by the individual VSB user.

## **A.1.1 Health technology assessment background**

Health technology assessment (HTA) is a multidisciplinary activity that systematically examines the technical performance, safety, clinical efficacy, and effectiveness, cost, cost effectiveness, organizational implications, social consequences, legal, and ethical considerations of the application of a health technology. HTA activities are characterized by a systematic and structured way of answering questions by evaluating and synthesizing available evidence from the literature (Fig 7).



**Fig 7 - Flow diagram of literature selection process**

(adapted from Khan et al.)

The proposed medical service has been considered under MSAC application 1137 in 2010. While the assessment compared the MEI to Cochlear implants and BAHA as comparators, which have been excluded for the current application 1365, the main conclusions were:

- **SAFETY:** Overall, absolute evidence from case series studies suggests that MEI appears to be as safe as CI and BAHA. Certain adverse events are likely to be more

commonly seen in children, specifically with the BAHA, paediatric bone is softer than that of adults, and has a longer osseointegration time, and hence may be more susceptible to device loosening or damage. Additionally, children may be likely to sustain head trauma during rambunctious play. Children may also be less reliable at cleaning and maintaining their implant site. This may be especially important in the case of the BAHA.

- **EFFECTIVENESS:** Generally, MEI implantation and/or activation led to improvements in patients with MHL and CHL. Only one comparative study assessed the MEI versus the CI, and no comparative studies assessed the MEI versus the BAHA. Functional gain provided by the MEI was usually of clinical significance ( $\geq 10$  dB). Other effectiveness outcomes were varied and not uniformly reported across the studies. Where reported, quality of life and patient satisfaction outcomes showed improvements after MEI implantation or activation. Where reported, technical outcomes generally showed improvements after MEI implantation or activation but statistical analyses were generally not supplied. Generally the MEI appears to be as effective as the HA in patients with MHL.
- **COST-EFFECTIVENESS:** The estimated costs of MEI, BAHA and CI were taken from a number of sources (MBS, Australian Refined Diagnostic Related Group (AR-DRG), manufacturer's implants and the median charged MBS fee). A one-night hospital stay would be necessary for all MEI (compare to 90% for CI and none for BAHA); **MEI can be performed as day surgery and under local anaesthetic.** Only costs incurred in the 1<sup>st</sup> year were considered. Although the MEI was shown to provide an overall cost saving if used as a direct replacement for CI/BAHA, it was indicated that if MEI replaces BAHA there will be an increase in cost. However, this did not take into account the treatment costs of infection rates in the long term associated with a percutaneous character of the BAHA abutment.

However, it was also indicated that there was:

- Significant risk of residual hearing loss in MEI implantation compared to no risk in BAHA implantation; Unlike the CI literature, the MEI literature included many patients with mild or moderate HL. In these patients, any further deterioration in hearing may be of greater clinical importance compared with losses in patients with severe or profound HL. Patients with CHL did not report significantly worse residual hearing after implantation. **Proposed reconsideration is based on the fact that MEI cannot be compared to CI as the audiological criteria for the two implants are**

**mutually exclusive. There is a sizable body of research showing the risk of loss of residual hearing with MEI is negligible.**

- A sizeable unaddressed pool of patients who may be eligible for MEI, not presently accessing implantable devices, and may represent the largest uptake for leakage of MEI. Therefore no cost saving with MEI, only growth; **Proposed reconsideration is based on the fact MEI implants remain an important option for a group of patients who cannot benefit from conventional hearing aids or other prosthesis.**

In addition, other international health technology assessment (HTA) agencies have reviewed insertion of partially implantable Middle Ear implants.

- The systematic literature review by Butler et al. (Butler et al., 2013) which was funded by MSAC reports about the effectiveness of active middle-ear implants in subjects affected by sensorineural hearing loss and compared the outcomes with external hearing aids. The authors performed a systematic search of several electronic databases, including PubMed and Embase, in order to identify relevant studies for inclusion. The active middle ear implants under evaluation include the VSB, the Otologics MET, the Envoy Esteem and the Ototronix Maxum (formerly, Soundtec Direct Drive Hearing System). A total of 14 comparative studies were included. 9 articles reported on the primary outcome of functional gain: one publication found that the middle-ear implant worked better than external hearing aids, while another found that external hearing aids were generally significantly better than middle-ear implants. 6 of the 7 remaining studies found that middle-ear implants were better than external hearing aids, although generally no clinically significant difference was seen. The authors concluded that in general, active middle ear implants appear to be as effective as external hearing aids for patients with sensorineural hearing loss.
- Another systematic review was published in the Journal of Otology & Rhinology (Klein et al., 2013). The article is based on the final STE Report of the University of Alberta (Alberta Health and Wellness Report, 2011). The main objective was to examine the current state of the science related to the safety and effectiveness of the Vibrant Soundbridge middle ear implant in the treatment of hearing loss. Several data bases including MEDLINE, EMBASE, The Cochrane Library, Web of Science, CINAHL, PsycINFO and the Centre for Reviews and Dissemination were searched without date or language limits. Finally, 44 studies involving a total 832 patients met

the study's eligibility criteria. The authors concluded that the majority of studies which compared the VSB to conventional hearing aids, reported statistically significant improvements in functional gain, speech reception, and quality of life with the VSB. Regarding speech recognition, the findings were mixed. Among studies that compared the VSB to the unaided condition, there was clinical benefit observed in all categories with the device. Adverse event rates were reasonably low, although VSB implantation poses a significant risk compared to non-invasive treatment with conventional hearing aids. The Vibrant Soundbridge middle ear implant appears to offer a safe and effective alternative for patients able and unable to wear conventional hearing aids.

- The STE report for the province of Alberta (Alberta Health and Wellness Report, 2011) is a systematic review of the evidence on middle ear implants (MEI) for the treatment of hearing loss. The objectives of this review were to determine the safety, effectiveness and cost-effectiveness of MEI in comparison to external hearing aids, bone anchored hearing aids (BAHA), or cochlear implants; to identify particular subgroups of patients who might benefit most from MEI, and to summarize the current criteria for using MEI versus alternative treatments for hearing loss. Main outcomes were:
  - Safety: The partially implantable Vibrant Soundbridge and fully implantable Carina appear to be relatively safe. There were few reports of major complications, and these occurred at rates similar to those with BAHA. A greater number of major complications was reported with the fully implantable Esteem, including high rates of nerve damage. Revision surgeries and explantations were more frequent with the Esteem and Carina MEIs. No significant safety issues associated with conventional hearing aids were found. While in this review, the safety of MEI was not specifically compared to that of cochlear implants because of differences in eligible patient populations (cochlear implants are typically indicated for more severe hearing loss), based on previously published reviews of cochlear implants, MEI appears to be at least as safe as cochlear implants.
  - Effectiveness Evidence: Middle ear implants offer functional gains comparable to those achieved with hearing aids. Based on limited evidence, MEIs appear to provide greater improvements in the perception of speech in noisy situations and in sound quality. Due to differences in the severity of hearing loss in patients eligible for cochlear implants and those eligible for



MEI, the comparative effectiveness of these two devices could not be assessed

- Economical Evidence: A cost-effectiveness analysis could not be conducted because for patients who are not medically able to wear a hearing aid, and who are ineligible for a BAHA, there are currently no alternative treatment options. Based on an estimated 20 patients receiving MEI per year in Alberta, the total budget impact over 5 years would be \$2,677,497.
- In conclusion, the authors state that although the technology has been in use for over 10 years, good quality evidence on MEI is still lacking. In patients medically able to wear conventional hearing aids, the evidence indicates that MEI offers a similar improvement in functional gain to that achieved with conventional hearing aids, but may offer greater improvement with respect to perception of speech in noise and sound quality. In the small group of patients who are medically unable to use conventional hearing aids, MEI appears to offer a viable treatment option.
- In the UK, the Vibrant Soundbridge is approved for SNHL according to the Clinal Commissioning Policy Statement: Active Middle Ear Implant, December 2012, Reference; NHSCB/D9/b/2: "Active middle ear implants are not routinely commissioned except under the following circumstances, as no other alternative treatment is available: Patients with bilateral sensorineural hearing loss in whom conventional hearing aids have been used and found to be medically unsuitable due to conditions of the external ear".

### **A.1.2 SNHL + medical condition and screening background**

Individuals suspected of having a hearing loss are referred for a full audiometric evaluation of their hearing. This evaluation consists of pure tone audiometry and speech testing. Pure tone audiometry is divided into air conduction and bone conduction testing where the first indicates the sensitivity of the entire hearing system, and the latter indicates the sensitivity of the inner ear only. Thresholds of audibility, also named hearing thresholds, are determined at frequencies from 250 to 8000 Hz which is the range of sound that the human ear is most sensitive to. Normal hearing is represented by air and bone conduction thresholds below 25 dB HL. Anything greater than 25 dB HL represents various levels of hearing loss. Without public funding, these patients who would be respective AMEI candidates are currently left untreated.

## A.2 Indications and Contraindications

### A.2.1 Indications for active middle ear implants

Out of the three active middle ear implants the Esteem and the Carina are both indicated for adults who have:

- Stable bilateral moderate to severe sensorineural hearing loss
- Unaided speech discrimination tests score greater than or equal to 40%
- Normal middle ear function and anatomy
- Minimum 30 days of experience with appropriately fit hearing aids

**Both of these devices are contraindicated in patients who present with chronic outer, middle or inner ear pathologies.**

These criteria represent a population who could alternatively be treated by conventional HAs, or by a cochlear implant when amplification is insufficient. The only active middle ear implant that offers management for the target population is the Vibrant Soundbridge.

**The indications for the Vibrant Soundbridge are:**

- Pure-tone air-conduction threshold levels at or within the levels listed below in Table 3. Pure-tone air-conduction thresholds for both ears within 20 dB HL of each other at frequencies .5 to 4 kHz Air-bone gap at 0.5, 1, 2 and 4 kHz no greater than 10 dB HL at two or more of these frequencies.
- Normal tympanometry.
- No previous middle ear surgery.
- The patient shall have no history of post-adolescent, chronic middle ear infections or inner ear disorders such as vertigo or Meniere's syndrome.
- Speech audiometry curve adequate to the respective PTA. Speech understanding >65% (at 65 dB SPL) for word lists with amplification or at most comfortable level under earphones.
- Unable to wear or benefit from a conventional hearing aid for medical reasons.
- The ear selected for implantation of the VSB shall be equal to or worse than the un-implanted ear.

**Table 3 - Air conduction threshold levels for SNHL indication (CE marked countries)**

<b>Frequency (kHz)</b>	0.5	1	1.5	2	3	4
<b>Lower Limit (dB HL)</b>	10	10	10	15	25	40
<b>Upper Limit (dB HL)</b>	65	75	80	80	85	85

Vibrant Soundbridge candidates cannot use conventional hearing aids for a variety of medical reasons. These may include but are not limited to conditions such as chronic otitis externa, psoriasis, exostosis of the ear canal, persistent excessive cerumen blocking the ear canal, absent or deformed pinnae following skin cancer, unusual morphology affecting the ear canal or pinna that prevent the use of conventional hearing aids.

## A.2.2 Definition and incidence of the medical condition

### Clinical need

Hearing loss is among the most frequent physical impairments in industrialized nations. According to the statistics of the WHO, approximately 51 million adults in developed countries suffer from a moderate or greater hearing loss, 13 million of whom have a severe to profound hearing loss.<sup>1</sup> This represents 6.6% of the population. This number is considerably higher in the adult population, where the share of persons with hearing loss is estimated to range from 17% to more than 20%

Although the methodologies of available epidemiological surveys differ, these numbers correspond roughly to data compiled on the basis of a survey in Germany for the year 2011. According to this study (Deutscher Schwerhörigenbund e.V., 2012), approximately 21 percent of the population over 14 years of age suffer from mild to profound hearing loss.

The epidemiological data for Germany are comparable to data in other European countries, with age-specific prevalence rates of hearing loss (as measured in dB) varying by  $\pm 2\%$ . However, direct comparison of the data is limited due to differences in the methods and tools employed to collect and tabulate data and to classify results (Roth et al., 2011).

**Table 4 - Prevalence of hearing loss in selected European countries**

<b>Country</b>	<b>Survey</b>	<b>21-39 dB</b>	<b>40-69 dB</b>	<b>70-94 dB</b>	<b>&gt;95 dB</b>	<b>Total</b>
Italy	2170 pers over 18	17.1%	4.0%	1.2%	0.3%	22.5%

<sup>1</sup> Moderate hearing loss is defined as a hearing threshold level in the better ear of 41 dBHTL or more (averaged over 0.5, 1, 2, 4kHz). Severe to profound hearing loss is a hearing threshold level in the better ear of 61 dBHTL or more (averaged over 0.5, 1, 2, 4kHz).

Finland	3518 pers over 25	17.2%	4.3%	0.5%	0.04%	22.1%
Denmark	705 pers age 30-50	3.4%	0.2%			
Sweden	590 pers over 20	18.1%	4.5%	0%	0%	22.6%
UK	2662 pers over 18	16.8%	4.9%	0.7%	0.2%	22.6%
Germany	2031 pers over 16	11.0%	7.0%	1.4%	0.3%	19.7%
Germany	18+ years	11.7%	7.3%	1.5%	0.3%	20.8%
Germany	20+ years	11.9%	7.4%	1.5%	0.3%	21.1%
Germany	25+ years	12.7%	7.9%	1.6%	0.4%	22.6%

Source: Deutscher Schwerhörigenbund [www.schwerhoerigen-netz.de](http://www.schwerhoerigen-netz.de) „Internationale Statistikvergleiche" and <http://www.oesb-dachverband.at/schwerhoerigkeit/statistik/>

Surveys also reveal that hearing loss is increasing among children and adolescents. According to the data of the U.S. National Health and Nutrition Examination Survey, the prevalence of hearing loss among adolescents aged 12-19 years increased from 14.9% to 19.5% between 1994 and 2006, representing an increase of 31% (Kahue et al., 2014; Shargorodsky et al., 2010).

### **Hearing loss and its consequences**

Hearing loss may be caused by interference with the transmission of sound from the outer to the inner ear (conductive hearing loss), damage within the inner ear or to the auditory nerve or auditory centres in the brain (sensorineural hearing loss). In some cases, hearing loss may be the result of both sensorineural and conductive hearing loss and is then referred to as mixed hearing loss.

Sensorineural hearing loss is the most common type of hearing loss and its most common form is aged-related hearing loss, or presbycusis. This progressive condition is caused by the loss of function of hair cells in the inner ear, a gradual process that ultimately leads to deafness. Hearing loss in adults may also be caused by excessive exposure to noise or ototoxic drugs, metabolic disorders, infections or genetic factors.

Partial hearing loss is the term used to describe types of hearing loss that are mild to severe, thus permitting the person with hearing loss to hear some sounds. In general partial hearing loss affects high-frequency hearing more than low-frequency hearing.

In children, hearing loss may have a genetic aetiology or have prenatal, perinatal or postnatal causes. The latter include conditions such as meningitis and viral infection of the

inner ear (for example, rubella or measles), as well as premature birth and congenital infections. Deafness that occurs before the development of language is described as prelingual, whereas deafness that occurs after the development of language is described as postlingual.

Studies of age-specific differences in speech-recognition performance in noise indicate that there are significant age-related deficits related to high frequency hearing loss (Dubno et al., 1984). The Beaver Dam Epidemiology of Hearing Loss Study shows significant age effects in word recognition scores in competing messages for both men and women, with performance consistently poorer in men than in women at all age groups and hearing loss categories (Cruickshanks et al., 1998).

In children, even mild hearing loss can impair speech and language development, have negative effects on academic achievement and impair social and emotional development (Borg et al., 2007; Moeller et al., 2007; Stevenson et al., 2010). In addition to the immediate effects on the ability to hear and understand speech, age-related hearing loss and partial hearing loss can have grave consequences for mental health and overall quality of life. However, deafness and hearing loss are not typically associated with increased mortality, and need not be associated with significant morbidity. Furthermore, some people who are deaf identify with a cultural model of deafness that does not consider deafness to be an impairment. For hearing-impaired individuals who use sign language as their preferred language and grow up as members of the 'Deaf Community', deafness may not have a major impact on quality of life. However, for a child who is born deaf within a hearing family or for a person who becomes deaf and is accustomed to functioning in a hearing environment, deafness usually does have a significant impact on quality of life. In children, deafness typically has significant consequences on linguistic, cognitive, emotional, educational and social development. In adults, the loss of hearing affects the ability to hear environmental noises and to understand speech. This, in turn, can affect the ability to take part in daily activities and engage in the accustomed social and professional networks, thus leading to isolation and, in some cases, psychological problems (Meinzen-Derr et al., 2011; Stevenson et al., 2010). In the case of partial hearing loss as described above, patients can "hear" but they typically cannot understand voices when they are in a "difficult" acoustic environment; i.e. an environment in which there is background noise. This often leads to social isolation and may have a number of other negative effects on the quality of life as well as on psychological and physical well-being.

A recent study of 496 elderly patients (over 85 years) in Linköping, Sweden found that mental health problems and depression were more likely among patients with hearing loss who didn't use their hearing aids than among those who used hearing aids regularly (Oberg et al., 2012). In a representative cohort study of 604 patients in the 60- to 69-year-old age

group of non-institutionalized subjects who underwent both audiometric and cognitive tests, Lin (Lin et al., 2011) found that greater hearing loss is associated with poorer cognitive functioning: a 25 dB increase in hearing loss is associated with a reduction in cognitive performance of 7 years. In a larger prospective study of a cohort of 1985 elderly patients (mean age = 77.8 years), hearing loss was found to be independently associated with accelerated cognitive decline and cognitive impairment (Lin et al., 2011). Other studies have found that adults with acquired hearing loss report a significantly lower quality of life than persons with normal hearing (Fellinger et al., 2007; Hallberg et al., 2008). "The literature ... clearly demonstrates that hearing loss is associated with physical, emotional, mental and social well-being. Depression, anxiety, emotional instability, phobias, withdrawal, isolation, lessened health status and lessened self-esteem are not "just quality of life" issues. For many people, uncorrected hearing loss is a serious "life or death" issue." (Kochkin, 2010).

The loss of hearing at adult age also results in the degradation of the peripheral and central nervous system; including the degeneration of spiral ganglion cells, changes in the sensitivity of neurons and the reorganization of sound representation (Leake et al., 1999; Leake et al., 2008). Numerous studies show that the degree of degradation in the nervous system and other negative effects on the neural system and cognitive ability are correlated with the duration of deafness or hearing loss (Blamey, 1997; Blamey et al., 2013).

Hearing loss in general has been related to a number of quality of life issues:

- lower earning power, especially among persons with severe to profound hearing loss;
- strained personal relationships (especially for age-related mild-moderate hearing loss) and negative dysfunctional communication;
- discrimination;
- communication problems
- behaviors to compensate hearing loss;
- increased incidence of depression and depressive symptoms;
- reduced emotional stability;
- increased anxiety and social phobias;
- poorer cognitive functioning;
- poorer health status;
- societal isolation.

In light of the aging of the population in almost all countries, hearing loss will pose an ever greater problem at individual level and in a public health framework.

Statistics Canada's 2006 Participation and Activity Limitation Survey found that hearing impairment may affect an individual's education in various ways, including the choice of educational and training options, the time required to complete courses, and the level of

education attained. One out of five people who reported hearing limitations said that they had discontinued their education because of their condition. People with severe hearing difficulties were much more likely than those with mild hearing impairment (43.5% versus 16.8%) to withdraw from school. The survey responses also indicated that hearing difficulties limited both the type of work and number of hours worked. Many individuals with hearing limitations believed that their condition made it more difficult for them to advance in their career, change jobs, or find work (Brennan et al., 2009). A recent Australian study found an association between hearing loss and walking ability. The authors speculated that this may be due to problems with balance caused by hearing problems, together with a fear of falling, and a decline in physical and social involvement. Limited social interactions may also affect the cognitive decline associated with hearing loss (Karpa et al., 2010). A systematic review of health-related quality of life in individuals with sensorineural hearing loss and hearing aids concluded that most studies which used a disease-specific quality of life measure (i.e., specific to hearing loss as opposed to generic health measures) found improved emotional and social well-being in hearing aid users. However, findings from studies that used generic quality of life measures varied. Nevertheless, the authors concluded that hearing aids provide a low-risk, relatively non-invasive treatment that improves quality of life by reducing “psychological, social and emotional effects of SNHL” (Chisolm et al., 2007). A systematic review of bone-anchored hearing aids found similar differences in quality of life reported by studies that used generic versus disease-specific measures (Colquitt et al., 2011).

There are many causes of acquired sensorineural hearing loss after birth. The majority are listed below:

- Meningitis, malaria, cytomegalovirus, or other infections such as mumps, toxoplasmosis and measles occur. These are particularly common in poor developing countries.
- Iodine deficiency leading to endemic cretinism – one sixth of the world population is at risk of iodine deficiency; the numbers with related hearing loss are not known.
- Noise induced hearing loss (NIHL) due to excessive noise exposure, either social or industrial. Most developed countries have legislation limiting the noise exposure at work to no more than 90dB. In recent years, the impact of social noise has become apparent and studies indicate that young people are losing some high frequency hearing from loud music in enclosed places such as dance clubs, or when using personal stereos. Much talk is made about the need to raise awareness of the problem but very few countries have sufficiently robust legislation to protect the public.

- Ototoxicity is a common cause of hearing loss. It is well known that many powerful drugs such as some antibiotics, or cytotoxics (anti-cancer drugs) can damage the hearing with some people being more susceptible than others. However, in life threatening conditions hearing loss may be a lesser consideration.
- Presbycusis is the hearing impairment caused by aging of hair cells in the cochlea. There is no direct cause and there is no specific treatment apart from hearing rehabilitation. Since the world population is aging, more and more adults are affected.
- Sudden hearing loss, sporadic occurrence often idiopathic.
- A recent systematic review estimated that 30% of European men, and 20% of European women over the age of 70, had age-related hearing loss (of 30 dB HL or more in their better ear), and by the age of 80, this increased to 55% of men and 45% of women (Roth et al., 2011). In the US, one study found a prevalence rate of hearing loss (of 25 dB HL or more) of 63% in US adults over the age of 70 (Lin et al., 2011). Inconsistencies in the definitions of hearing loss, ear (better ear or worse ear) in which the hearing level is measured, and the age ranges used to distinguish age-related hearing loss exist across the few available studies on adult onset hearing loss, making it difficult to determine the prevalence of hearing loss more precisely (Lin et al., 2011).
- In children, the prevalence of sensorineural hearing loss (>40dB) is estimated to be 1 in 1,000 live births (Carney and Moeller, 1998). Children seem to be developing noise-induced hearing loss at increasing rates, possibly due to the use of musical instruments, audio equipment, fireworks, toy guns and telephones.
- Middle ear implants are significantly more expensive than external hearing aids and involve a technically difficult surgical procedure – as a result they may not appeal to many patients (Shohet et al., 2011).

### **A.2.3. Existing arrangements**

Individuals are identified through audiometric testing to identify mild to severe sensorineural hearing loss with a PTA4 below 80 dB HL, unaided speech recognition above 65%, and the presence of an outer ear pathology. Outer ear pathologies are treated conservatively by an ENT doctor, even though the results may not always be successful. Patients with sensorineural hearing loss are usually treated by conventional HAs, or by a cochlear implant when amplification is insufficient.

The patient population being proposed in this application consists of individuals who have



moderate to severe sensorineural hearing loss and a medical condition precluding the use of conventional hearing aids. These patients need to be aided, but their hearing is not at a level which requires a cochlear implant.

Also, bone conduction implants are not indicated for this degree and type of hearing loss. Therefore an active middle ear implant represents their only alternative for restoring hearing. Without public funding, these patients who would be respective AMEI candidates are currently left untreated.

Otherwise the MEI treatment option is either self-funded or funded through exgratia private health funding.

Other devices as the Vibrant Soundbridge, classified as an active middle ear implant indicated for sensorineural hearing loss are the Esteem (Envoy) and Carina (Otologics) and are fully implantable hearing implants and as such excluded from this application. All of the device systems are on the Australian Register of Therapeutic Goods (ARTG). All of these devices have received CE Mark approval as well as United States Food and Drug Administration (FDA) approval, but for none of the systems a MBS item descriptor has been assigned yet.

Relevant existing MBS item that the proposed medical service would most closely resemble in terms of complexity and time:

Category [3 ] – [Therapeutic Procedures]
MBS 41554 MASTOIDECTOMY, intact wall technique, with myringoplasty and ossicular chain reconstruction (Anaes.) (Assist.) Fee: \$1,876.95 Benefit: 75% = \$1,407.75

### A.2.4 Market approval status of Vibrant Soundbridge

The VSB System is a long-standing technology: in 1998, the VSB was approved for mild to severe sensorineural hearing loss in the European Union and markets accepting the CE mark. The respective clinical data were collected in the course of two multicenter studies, one performed in the United States of America (Luetje et al., 2002), the other one performed in Europe (Fisch et al., 2001; Snik et al., 2001). Subsequent to the VSB-approval for patients younger than 18 years of age in the European Union and all other countries accepting the CE marking in 2009. As of November 2008, the VSB has been implanted in more than 60 children and adolescents in countries throughout the world with favourable results (Cremers

et al., 2010;Mandala et al., 2011;Sia, 2012).

## A.2.5 Reimbursement status of middle ear implants

The insertion of an active middle ear implant (AMEI) by any method is not reimbursed on the MBS and the device is not listed on the Prosthesis List (PL). AMEI's however are currently registered under the Australian Register of Therapeutic Goods (ARTG) and the implantation procedure is performed in public and private hospitals throughout Australia and may be funded by public hospital surgical budgets, private health fund ex-gratia payments and occasionally is self-funded by patients.

**Table 5 - MEI components listed on the ARTG**

ARTG No	Product	Indication
170179	Amade audio processor - Middle ear implant system sound processor	The Amade audio processor is an external part of the Vibrant Soundbridge system. The Vibrant Soundbridge system is indicated for use in patients who have mild to severe hearing impairment and cannot achieve success or adequate benefit from traditional therapy.
161702	Vibrating Ossicular Prosthesis (VORP) 502X - Hearing aid, middle ear implant.	For use in adults, adolescents and children who have mild to severe hearing impairment and cannot achieve success or adequate benefit from traditional therapy. For sensorineural HL, the VORP is crimped to the long process of the incus to directly drive the ossicular chain.
185533	Vibroplasty Coupler - Hearing aid, middle ear implant.	The Vibroplasty Couplers are intended to be used in combination with the Vibrant Soundbridge to facilitate the coupling between the FMT and a Vibratory Structure of the middle ear. The prosthesis type is chosen on the basis of the ossicular remnants once all primary disease has been removed from the middle ear.

## A.2.6 Proposed listing of partially implantable active middle ear implants

### Rationale for the proposed listing

Adult onset hearing loss ranked eighth in the 20 leading specific causes of burden of disease and injury in Australia in 2003. This burden of disease is calculated using an estimate of years of healthy life lost due to disability caused by disease and is measured in Disease Adjusted Life Years (DALYs). One DALY represents the loss of the equivalent of one year of full health. Using DALYs, the burden of diseases that cause early death but little disability (e.g. drowning or measles) can be compared to that of diseases that do not cause death but do cause disability (e.g. cataract causing blindness). In 2003, Adult onset hearing loss contributed to 64,853 DALYs, equating to 2.5% of the total DALYs for Australia that year. For

2005, Access Economics reported an estimated 95,005 DALYs were lost due to hearing loss, representing 3.8% of the total burden of disease from all causes of disability and premature death (WHO report; Global Burden of Disease: DALYs, Part 4 (2004)).

Prevalence of hearing loss in the better ear (Hearing thresholds  $\geq 25$  dB) in Australia was reported in a study of Wilson et al (Wilson et al., 1999) to be on the overall population 22.2%. Treatment options for sensorineural hearing loss involve amplifying the incoming sound through a range of conservative management therapies including hearing aids. However, when patients also have a medical condition in their outer ear they are unable to wear hearing aids - HA use has been proven to exacerbate their conditions. Current treatment options for such patients include no treatment or treatment with an active middle ear implant.

The only partially implantable active middle ear implant that offers management for the target population is the Vibrant Soundbridge.

Proposed MBS listing(s)

The details of the MBS listing agreed by PASC are as follows:

<b>Proposed MBS item descriptor for partially implantable MIDDLE EAR IMPLANT, Insertion of, including a mastoidectomy</b>	
Category 3 – Therapeutic Procedures	
MBS [item number]	
partially implantable MIDDLE EAR IMPLANT, insertion of, including mastoidectomy, for patients with:	
sensorineural hearing loss that is stable, bilateral and symmetrical; and	
air conduction thresholds in the mild to severe range with PTA4 below 80 dB HL; and	
have speech perception discrimination of $\geq 65\%$ correct with appropriately amplified sound; and	
cannot wear conventional hearing aid because of outer ear pathology; and	
no history of inner ear disorders such as Meniere’s syndrome	
a normal middle ear (no history of middle ear surgery or of post-adolescent, chronic middle ear infections; and normal tympanometry; and on audiometry the air-bone gap is $\leq 10$ dBHL at two or more of the following frequencies: 0.5, 1, 2 and 4 kHz).	
Fee: \$1,876.59 (based on mastoidectomy item).	
(Anaes)	

## **A.3 Intervention details**

### **A.3.1 Clinical management pre-intervention**

Individuals suspected of having a hearing loss are referred for a full audiometric evaluation of their hearing. This evaluation consists of pure tone audiometry and speech testing. Pure tone audiometry is divided into air conduction and bone conduction testing where the first indicates the sensitivity of the entire hearing system, and the latter indicates the sensitivity of the inner ear only. Thresholds of audibility, also named hearing thresholds, are determined at frequencies from 250 to 8000 Hz which is the range of sound that the human ear is most sensitive to. Normal hearing is represented by air and bone conduction thresholds below 25 dB. Anything greater than 25 dB HL represents various levels of hearing loss. Sensorineural hearing loss is indicated by equal air and bone conduction thresholds above 25 dB, and means that the outer hair cells of the cochlea are damaged. Speech testing is carried out to support the audiological results in determining treatment options for hearing loss.

Treatment options for sensorineural hearing loss involve amplifying the incoming sound through a range of conservative management therapies including hearing aids. However, when patients also have a medical condition in their outer ear they are unable to wear hearing aids. Hearing aid use has been proven to exacerbate their conditions. Current treatment options for such patients include no treatment or treatment with an active middle ear implant. The only active MEI currently available and indicated for this population is the Vibrant Soundbridge.

#### **Indications for other active middle ear implants**

Currently, there are three active middle ear implants: Esteem and the Carina are both indicated for adults who have:

- Stable bilateral moderate to severe sensorineural hearing loss
- Unaided speech discrimination tests score greater than or equal to 40%
- Normal middle ear function and anatomy
- Minimum 30 days of experience with appropriately fit hearing aids

Both of these devices are contraindicated in patients who present with chronic outer, middle or inner ear pathologies.

These criteria represent a population who could alternatively be treated by conventional HAs, or by a cochlear implant when amplification is insufficient. The only active middle ear implant that offers management for the target population is the Vibrant Soundbridge.

### Indications for the Vibrant Soundbridge:

- Pure-tone air-conduction threshold levels at or within the levels listed below in Table 1 .Pure-tone air-conduction thresholds for both ears within 20 dB HL of each other at frequencies 0.5 to 4 kHz Air-bone gap at 0.5, 1, 2 and 4 kHz no greater than 10 dB HL at two or more of these frequencies.
- Normal tympanometry.
- No previous middle ear surgery.
- The patient shall have no history of post-adolescent, chronic middle ear infections or inner ear disorders such as vertigo or Meniere's syndrome.
- Speech audiometry curve adequate to the respective PTA. Speech understanding >65% (at 65dB SPL) for word lists with amplification or at most comfortable level under earphones.
- Unable to wear or benefit from a conventional hearing aid for medical reasons.
- The ear selected for implantation of the VSB shall be equal to or worse than the un-implanted ear.

**Table 6 - Air conduction threshold levels for SNHL indication (CE marked countries)**

Frequency (kHz)	0.5	1	1.5	2	3	4
Lower Limit (dB HL)	10	10	10	15	25	40
Upper Limit (dB HL)	65	75	80	80	85	85

Vibrant Soundbridge candidates cannot use conventional hearing aids for a variety of medical reasons. These may include but are not limited to conditions such as chronic otitis externa, psoriasis, exostosis of the ear canal, persistent excessive cerumen blocking the ear canal, absent or deformed pinnae following skin cancer, unusual morphology affecting the ear canal or pinna that prevent the use of conventional hearing aids.

### A.3.2 Clinical management intervention

The **only partially implantable** active middle ear implant indicated for sensorineural hearing loss plus medical condition is the Vibrant Soundbridge. This hearing implant system comprises of two components:

An internal component that includes a magnet, an electronics housing, and a transducer; and an external audio processor containing a power source (battery), microphone and digital

signal processor. The signal from the audio processor is transmitted to the internal component and transformed into vibrations. The transducer which is called the Floating Mass Transducer (FMT) is crimped or otherwise attached to the long process of the incus at a single point and mechanically drives the ossicular chain. The amplified vibrations can be adjusted via an external auditory processor (AP) to suit different degrees of hearing losses. Battery life of the AP is 6 days. Patients can place new batteries in or charge their existing batteries.

Implantation of the proposed Vibrant Soundbridge for SNHL + medical condition is carried out by an otolaryngologist (ENT surgeon) under general anaesthesia on an outpatient or inpatient basis. The surgical procedure lasts 1.5 to 2 hours after preparing the patient. This involves administering anaesthetics and intravenous antibiotics 30 minutes before surgery, marking the incision site and shaving the hair over the expected incision site. The surgery involves the following steps:

- Creating the incision behind the ear in a posterior-superior direction
- Performing a full or partial mastoidectomy via the facial recess route or the transmeatal route (depends on the medical status of the patient's ear and on the surgeon's preferences)
- Drilling a bone bed and tie-down holes for placing the implant, the transition to the FMT and the demodulator
- Accessing and visualising the middle ear by either posterior tympanotomy through the facial recess, or by lifting the tympanomeatal flap of the outer ear canal (depends on surgical approach used)
- Fixing the implant, transition and the demodulator into the previously drilled bone bed
- Placing/crimping the FMT on to the long process of the incus
- Placing the excess conductor link in the excavated mastoid
- Closing the wound

6 to 8 weeks after surgery the patient is fitted with the audio processor (AP) and initial programming is carried out. The patient is followed-up on a regular basis and the AP is re-programmed when necessary.

### **A.3.3 Clinical management post-intervention**

#### **Post-Implantation of the Vibrant Soundbridge**

Activation of audio Processor (AP) and Follow-up Fittings with audiologists take place approximately eight weeks after implantation of the AMEI. The AP fitting is performed using the VIBRANT MED-EL SYMFIT 6.0 software and off-the-shelf hearing instrument fitting software, CONNEXX 6.4 (Siemens) or higher version. The fitting software products are used in conjunction with an off-the-shelf hearing aid interface modem, Hi-Pro Box or the Noah Link (GN Otometrics) and a Personal Computer. The VIBRANT MED-EL SYMFIT 6.0 software provides a parameter database, which enables the audio Processor to be programmed with the CONNEXX software. The programming process is performed by a trained hearing professional (audiologist) and typically takes about 30 minutes. The workflow during the activation visit is as follows: The patient's audiogram is entered in the CONNEXX software.

- CONNEXX uses the air conduction thresholds to propose a “first fit” based on the DSL I/O gain prescription rule (Select the appropriate acclimatization level 1 to 4; based on the level of experience with hearing aids).
- The audiologist has the opportunity to fine-tune the settings (frequency response and dynamic range compression) and enable features to enhance listening comfort (e.g., wind noise reduction), keeping in mind that it may be too early to obtain objective measurements as the healing may not be complete.

All follow up visits (FU) are referred to the activation visit and take place at 1, 6 and 12 months post activation.

**One month post activation** aims to optimize the first fitting and to achieve quick information about the audiological benefit from the devices:

- AC and BC pure tone audiometry to control the hearing thresholds
- Optimization of the fitting
- Warble tone thresholds in sound field in unaided and aided conditions at 500, 750, 1000, 1500, 2000, 3000, 4000, 6000, and 8000 Hz. If necessary, the contralateral ear has to be masked (not plugged; to avoid the occlusion effect) by using a second loudspeaker.

#### **Six months post activation**

- AC and BC pure tone audiometry

- Warble tone thresholds in sound field in unaided and aided conditions at 500, 750, 1000, 1500, 2000, 3000, 4000, 6000, and 8000 Hz. Free field masking if necessary
- Unaided/ aided speech perception in quiet: SRT for 50% speech understanding and WRS in sound field. If required, the contralateral ear is masked, using a free field speech noise.
- Unaided/ aided speech in noise: to find out the signal-to-noise ratio where 50% of the presented test material is understood (SNR50) in unaided vs. aided condition. The measurement is performed at 1 meter away in front of the subject (S0N0)
- Optimization of fitting: only if necessary

#### **Twelve months post activation**

- AC and BC pure tone Audiometry
- Warble tone thresholds in sound field in unaided and aided condition at 500, 750, 1000, 1500, 2000, 3000, 4000, 6000, and 8000 Hz. Free field masking if necessary  
speech audiometry with headphones

## **A.4 Main comparator**

PASC agreed in the latest “1365 Ratified meeting outcomes from the August 2014 PASC meeting” protocol, that the comparator is no treatment for the proposed subgroup of patients with SNHL. PASC advised that eligible partially implantable active middle ear implants should also be compared with each other in order to assess whether they achieve similar safety and clinical effectiveness outcomes.

To our opinion, the only partially implantable, active middle ear implant that offers management for the target population is the Vibrant Soundbridge, but for the sake of completeness and to compile a generic assessment of the evidence for the medical service associated with Middle Ear Implants we extended our evaluation to the following comparators: partially implanted middle ear implant, (Maxum, Ototronix/Soundtec) as well as fully implantable middle ear devices such as Carina (Otologics LLC) and Esteem (Envoy Medical).

Furthermore, we do feel the need to point out that, although having included the Maxum system in this assessment report, the device set-up is a contraindication to our intended treatment group. This is based on the fact that the Maxum system is placing the sound processor in the ear canal. As stated by the company itself the system comprises of an ‘External component: a deep insertion, completely-in-the-canal, open-fit, electromagnetic sound processor (IPC) that is worn in the external auditory canal, similar to a conventional hearing aid’.



The **Vibrant Soundbridge** is for Patients with stable, sensorineural hearing loss with an outer ear pathology that prevents the wearing of a hearing aid and who have:

PTA4 below 80 dB HL with one of the following air conduction thresholds:

- mild hearing loss -  $25 \text{ dB} \leq \text{BEHL}_{0.5-4\text{kHz}} < 40 \text{ dB}$ ; or
- moderate hearing loss -  $40 \text{ dB} \leq \text{BEHL}_{0.5-4 \text{ kHz}} < 70 \text{ dB}$ ; or
- severe hearing loss -  $70 \text{ dB} \leq \text{BEHL}_{0.5-4 \text{ kHz}} < 95 \text{ dB}$ ; and
- speech perception discrimination of  $\geq 65\%$  correct with appropriately amplified sound; and
- bilateral, symmetrical hearing loss with PTA thresholds in both ears within 20 dBHL<sub>0.5-4 kHz</sub> of each other; and
- a normal middle ear (no history of middle ear surgery or of post-adolescent, chronic middle ear infections); and
- normal tympanometry;
- on audiometry, the air-bone gap is  $\leq 10 \text{ dBHL}_{0.5-4 \text{ kHz}}$  at two or more frequencies.
- no history of other inner ear disorders such as Meniere's disease.

Patient Contraindications:

- A patient is known to be intolerant of the materials used in the implant (medical grade silicone elastomer, medical grade epoxy and titanium).
- A patient with retrocochlear, or central auditory disorders.
- A patient with nonresponsive active ear infection and/or chronic fluid in or about the ear.
- A patient whose hearing loss has demonstrated an improving and decreasing fluctuation over a two year period of 15 dB in either direction.
- A patient with any physical, psychological, or emotional disorder that would interfere with surgery or the ability to perform on test and rehabilitation procedures.
- A patient with a skin or scalp condition that may preclude attachment of the Audio Processor with a magnet.

**Table 7 - Summary of indications and contraindications for the Vibrant Soundbridge**

	<b>Targets of the proposed medical service</b>	<b>Excluded medical services within AMEI criteria</b>	<b>Excluded medical services beyond AMEI criteria</b>
<b>Population</b>	Individuals who have: <ul style="list-style-type: none"> <li>• mild to moderate sensorineural hearing loss</li> <li>• stable bilateral symmetrical hearing loss</li> <li>• a medical condition in the outer ear and a normal middle ear</li> <li>• unable to wear or benefit from HAs due to medical reasons</li> <li>• no previous middle ear surgery</li> <li>• no history of post-adolescent, chronic middle ear infections or inner ear disorders such as vertigo or Meniere's syndrome.</li> <li>• unaided speech recognition above 65%</li> </ul>	Individuals who have: <ul style="list-style-type: none"> <li>• up to severe sensorineural hearing loss</li> <li>• stable unilateral or bilateral symmetrical hearing loss</li> <li>• normal outer and middle ear</li> <li>• previously used HAs but received no or limited benefit</li> <li>• no history of otitis externa or eczema for the outer ear canal</li> <li>• no history of post-adolescent, chronic middle ear infections or inner ear disorders such as vertigo or Meniere's syndrome.</li> <li>• unaided speech recognition above 40 dB for AMEI</li> </ul>	Individuals who have: <ul style="list-style-type: none"> <li>• severe to profound sensorineural hearing loss</li> <li>• stable unilateral or bilateral, symmetrical or asymmetrical hearing loss</li> <li>• normal outer and middle ear for CI; normal or pathological outer or middle ears for BCI</li> <li>• previously used HAs but received no or limited benefit</li> <li>• no previous middle ear surgery</li> <li>• no history of post-adolescent, chronic middle ear infections or retrocochlear disorders</li> <li>• unaided speech recognition below 65%</li> </ul>
<b>Intervention</b>	AMEI	Hearing aids, AMEI	CI, BCI
<b>Comparator(s)</b>	No treatment	-	-
<b>Outcomes affected</b>	Hearing thresholds, speech perception in quiet and noise, sound localisation, quality of life and other subjective benefits	Hearing thresholds, speech perception in quiet and noise, sound localisation, quality of life and other subjective benefits	Hearing thresholds, speech perception in quiet and noise, sound localisation, quality of life and other subjective benefits

The only other partially implantable middle ear device is the **Maxum Systems, Ototronix/Soundtec**

- Manufactured by Ototronix®, LLC, Houston, TX
- Based on original SoundTec™ technology and FDA approved

The Maxum system uses a rare-earth magnet implanted on the middle ear bones, and a sound processor worn in the ear canal. The minimally invasive implant procedure can be performed in a procedure room or outpatient clinic under a local anaesthetic. The sound processor sends electric signals to a transceiver coil and these signals are transferred by electromagnetic energy across the eardrum to the MAXUM implant which causes the ossicles to vibrate, thereby directly stimulating the cochlea (inner ear).

Patient Indications:

- For use in adults, 18 years of age or older,
- Present with a moderate to severe sensorineural hearing loss
- unaided word recognition score of 60% or greater
- Desire an alternative to an acoustic hearing aid.
- Experience with appropriately fit hearing aids.

Patient Contraindications:

- For subjects who have conductive hearing loss,
- Retrocochlear or central auditory disorder,
- Active middle ear infections,
- Tympanic membrane perforations associated with recurrent middle ear infections,
- Disabling tinnitus.

Other, but **fully implantable** active middle ear implants are the Esteem and the Carina system, both are indicated for adults who have:

- Stable bilateral moderate to severe sensorineural hearing loss
- Unaided speech discrimination tests score greater than or equal to 40%
- Normal middle ear function and anatomy
- Minimum 30 days of experience with appropriately fit hearing aids

Both of these devices are contraindicated in patients who present with chronic outer, middle or inner ear pathologies. These criteria represent a population who could alternatively be treated by conventional HAs, or by a cochlear implant when amplification is insufficient. MEI implants are an important option for a small group of patients who cannot wear conventional hearing aids or other prosthesis for medical reasons.

**Table 8 - Summary of research questions that the assessment will investigate**

Population	Intervention	Comparator	Outcomes to be assessed
<p>Patients with stable, sensorineural hearing loss with an outer ear pathology that prevents the wearing of a hearing aid and who have:</p> <ul style="list-style-type: none"> <li>• a PTA<sub>4</sub> below 80 dBHL with one of the following air conduction thresholds:                             <ul style="list-style-type: none"> <li>- mild HL - 25 dB ≤ BEHL<sub>0.5-4kHz</sub> &lt; 40 dB; or</li> <li>- moderate HL - 40 dB ≤ BEHL<sub>0.5-4 kHz</sub> &lt; 70 dB; or</li> <li>- severe HL - 70 dB ≤ BEHL<sub>0.5-4 kHz</sub> &lt; 95 dB; AND</li> </ul> </li> <li>• have speech perception discrimination of ≥65% correct with appropriately amplified sound; and</li> <li>• bilateral, symmetrical SNHL with PTA thresholds in both ears within 20 dBHL<sub>0.5-4kHz</sub> of each other; and</li> <li>• a normal middle ear (no history of middle ear surgery or of post-adolescent, chronic middle ear infections); and</li> <li>• normal tympanometry; and</li> <li>• on audiometry the air-bone gap is ≤10 dBHL<sub>0.5-4kHz</sub> at two or more frequencies); and</li> <li>• no history of other inner ear disorders such as Meniere’s disease.</li> </ul>	<p>Middle ear implant</p>	<p>No treatment</p>	<p><u>Effectiveness outcomes:</u></p> <ul style="list-style-type: none"> <li>- Abbreviated Profile of Hearing Aid Benefit</li> <li>- Client-orientated scale of improvement</li> <li>- Functional gain</li> <li>- Speech recognition</li> <li>- Sound-field assessment</li> <li>- Speech comprehension scores</li> <li>- Self-assessment scales</li> <li>- Patient preference</li> </ul> <p><u>Safety outcomes:</u></p> <ul style="list-style-type: none"> <li>- Complications</li> <li>- Adverse events</li> <li>- Infection rates</li> <li>- Taste disturbance</li> <li>- Fibrosis</li> <li>- Aural fullness</li> <li>- Acoustic trauma</li> <li>- Dizziness</li> <li>- Damage to the middle ear</li> <li>- Revision surgery</li> <li>- Explant rate</li> <li>- Device failure</li> <li>- Mortality</li> </ul>
<p><b>Clinical Questions</b></p> <p>1. In patients with outer ear pathology that prevents use of a conventional hearing aid, who have mild, moderate or severe SNHL that is stable, bilateral and symmetrical and who meet all other criteria set out in Table 7, is the MEI <b>more effective</b> compared to no treatment?</p> <p>2. In patients with outer ear pathology the prevents use of a conventional hearing aid, who have mild, moderate or severe SNHL that is stable, bilateral and symmetrical and who meet all other criteria set out in Table 7, is the middle ear implant <b>as safe</b> as no treatment?</p>			

In terms of overall clinical claims for the proposed medical service against its main comparator presenting consequences for health outcomes VSB compared to no treatment, the following can be summarised:

- Bone conduction thresholds after VSB implantation are no worse than before. The mean change in thresholds is 1-3 dB which is clinically non-significant.
- Air conduction hearing thresholds are superior with the VSB. The functional gain with the VSB ranges from 12,5 dB HL to 33 dB HL.
- VSB is superior in terms of speech understanding, especially in noisy indications. Compared to no treatment the VSB provides 30 to 50% improvement, depending on the test used and the presentation level.

- Long-term postoperative patient satisfaction and quality of life results are superior to no treatment.

In the previous MSAC assessment (application 1137, Conductive, Mixed and Sensorineural Hearing Loss) CI (item 41617) and BCI (items 41603 and 41604 – osseointegration procedures) were used as comparators. However, the intended population hearing is not at a level which requires a cochlear implant and is out of criteria of the BCI treatment range (Ref.: Cochlear website: BAHA not indicated for pure SNHL). Thus the population intended for MEI would otherwise be left untreated. In contrast to cochlear implants, an active middle ear implant is not inserted into the inner ear. Instead, the direct drive amplification process maximizes the potential of an individual's residual cochlear function via the middle ear. Unlike bone conduction hearing implants (where sound is routed to the cochlear with the best cochlear reserve), an active middle ear implant can improve the hearing in the implanted ear thus providing true binaural hearing. Binaural hearing is essential to optimize hearing potential and develop auditory skills such as sound localization, hearing in background noise and spatial awareness.

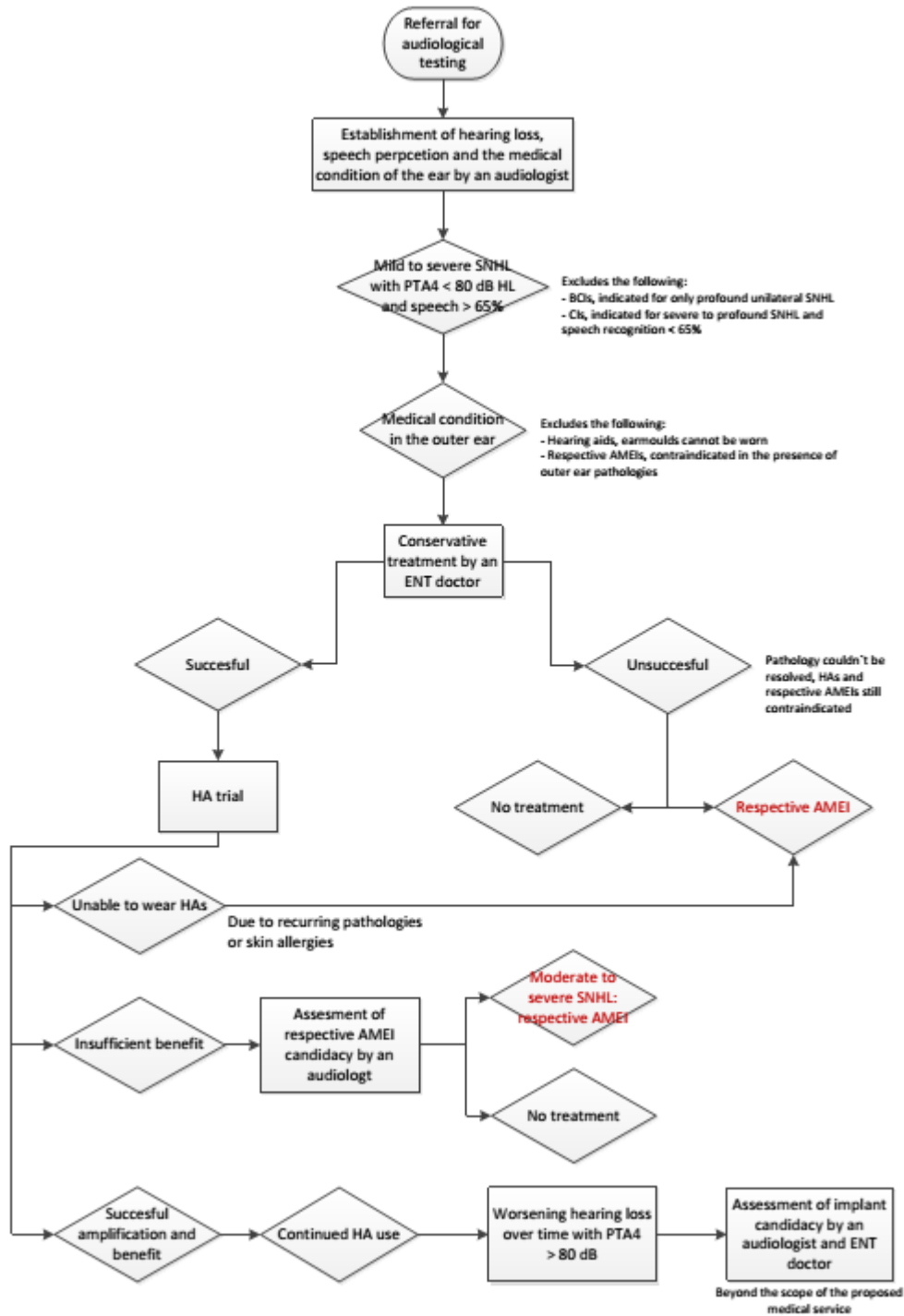
MSAC's Recommendation in 2010 for 1137 after considering the then in force compiled evidence was that MEI was for people who could not tolerate occlusion of the ear canal. It was agreed on that patients may opt for the MEI out of convenience. It was concluded that, substituting the MEI for the BCI and CI services would lead to an overall cost saving. MSAC agreed that the MEI was more expensive than the BCI, but less expensive than the CI. MSAC furthermore concluded that substituting the MEI for the CI would lead to a cost saving but the outcome may be less effective; and that the MEI for the BCI would lead to a cost increase but with no increase in effectiveness.

## **A.5 Clinical management algorithm**

The proposed medical service is highlighted presenting the only treatment option for the target population.

These individuals are identified through audiometric testing to identify mild to severe sensorineural hearing loss with a PTA4 below 80 dB HL, unaided speech recognition above 65%, and the presence of an outer ear pathology. Outer ear pathologies are treated conservatively by an ENT doctor, even though the results may not always be successful. As a result the respective AMEI, the Vibrant Soundbridge, is provided. When conservative treatment is successful it can be followed by a Hearing Aid trial which may exacerbate the previous ear pathology, leading again to the treatment options of the respective AMEI or no treatment. Hearing aids may not provide sufficient benefit for all patients, who could then receive an AMEI for pure moderate to severe sensorineural hearing loss or have to be left untreated.

Without public funding, these patients who would be respective AMEI candidates are currently left untreated. Otherwise the MEI treatment option is either self-funded or funded through exgratia private health funding.



**Fig 8 - Clinical Management Algorithm**

## A.6 Differences between the proposed intervention and main comparator

As the only comparator is NO TREATMENT this section is not applicable.

## **B. Systematic evaluation of the evidence for the proposed medical device**

A systematic review of the literature was carried out to evaluate the following questions;

1. In patients with outer ear pathology preventing the use of a conventional hearing aid, who have mild, moderate or severe SNHL that is stable, bilateral and symmetrical and who meet all other indication criteria, is the MEI more effective compared to no treatment?
2. In patients with outer ear pathology preventing the use of a conventional hearing aid, who have mild, moderate or severe SNHL that is stable, bilateral and symmetrical and who meet all other indication criteria, is the middle ear implant as safe as no treatment?

Other middle ear implant systems that are FDA approved or CE marked for patients with moderate or severe SNHL that is stable, bilateral and symmetrical and who meet all other relevant indication criteria, were included in the review to provide a better picture of the performance of the proposed medical service.

### **B.1 Description of the search strategy**

A structured search strategy was developed (Table 9) to search several online databases to identify studies published before the study inception date of 17.09.2014. The databases searched included Pubmed and OVIDSP (MEDLINE); Embase, BIOSIS Previews, Deutsche Arzteblatt and SciSearch from the German Institute of Medical Documentation and Information (DIMDI); the Cochrane Library, and The Centre of Reviews and Dissemination (CRD) database. The search was extended to full texts of articles and included papers published in English or German; and excluded studies published before 1996. The list of study titles was supplemented with potentially relevant publications already known by the research team; and the bibliographic references of reviews were searched to locate additional relevant materials.



**Table 9 - Search strategy for identifying studies on middle ear implants in treating sensorineural hearing loss**

Search term	
1	Soundbridge.tw
2	floating mass transducer.tw
3	middle ear implant
4	implantable hearing aid
5	implantable hearing device
6	1 or 2 or 3 or 4 or 5
7	6 AND hearing loss, sensorineural[MeSH Terms]

## B.2 Listing of included non-randomised studies

The citations identified by the literature search were evaluated against the PICOS criteria detailed below. Unrelated citations were removed and the full texts of the remaining were obtained for further screening. Studies were excluded if they still did not fulfil the eligibility criteria, or if the study design or reporting was of low quality. Screening of citations and of the full texts was conducted by two reviewers working independently from each other, with any uncertainties resolved by discussion or through consultation with a third researcher.

**Participants:** Subjects of any age, gender or ethnicity; with mild, moderate or severe sensorineural hearing loss of any aetiology in one or both ear(s), who have failed all other conservative medical, surgical, pharmaceutical treatment and could not benefit from conventional hearing aids (CHA) were included in this review. Subjects with a mixed or conductive hearing loss, or with a profound unilateral hearing loss were excluded.

**Intervention:** The intervention included was unilateral implantation with the Vibrant Soundbridge middle ear implant by means of incus Vibroplasty. Any surgical approach was considered. Bilateral VSB implantation was excluded.

**Comparators:** Unilateral VSB implantation was compared to receiving no surgical intervention; and presented against the Maxum (formerly SOUNDTEC Direct Drive) partially implantable MEI, and the Esteem and Carina fully implantable hearing devices.

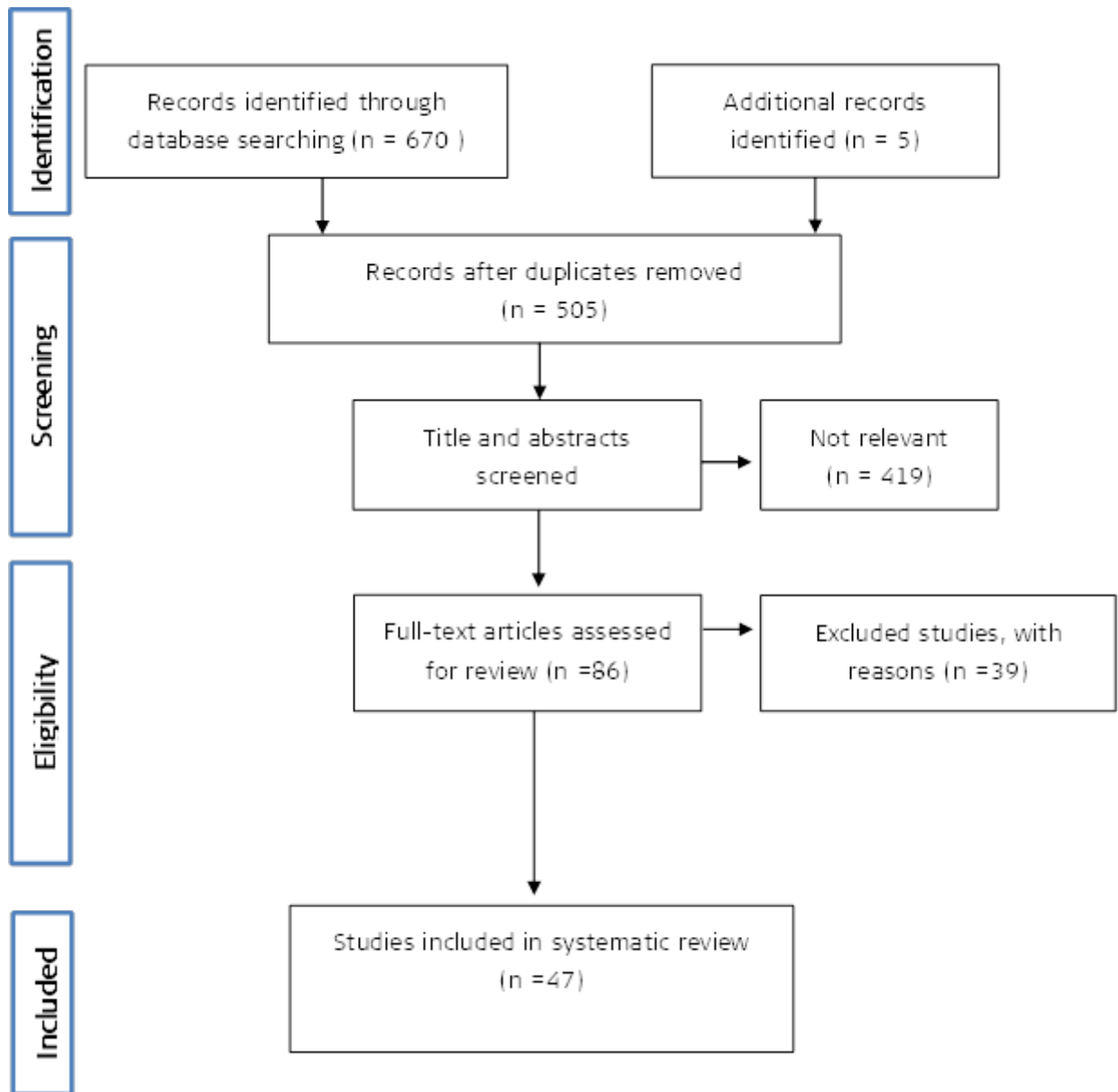
**Outcomes:** Data was searched on safety, efficacy and economical outcomes with the VSB. Safety-oriented outcomes included complication/adverse event rates, damage to the middle ear / inner ear revision surgery/explant rate/device failure and mortality. Efficacy

outcomes were divided into audiological outcomes including hearing thresholds, functional gain, speech perception in quiet and noise, speech recognition thresholds; and subjective outcomes determined by questionnaires, patient-oriented scales of improvement and satisfaction scales. Data related to quality of life (QALY, ICER) were considered under economical outcomes.

**Study Design:** Systematic reviews and meta-analyses, clinical studies including randomized or nonrandomized comparative studies, case series, case-control studies, controlled/not controlled before-and-after studies (CBAs and nCBAs) and interrupted time series (ITS) analyses) were included in this review. Non-systematic reviews, case reports, letters, editorials; and animal, in-vitro and laboratory studies were excluded. Clinical studies with sample sizes less than 5 were also excluded.

The results of the database search and study selection is depicted in [Fig 9](#). Out of a total of 670 citations, 86 were found to be matching the PICOS criteria. Upon screening the full-texts 39 were excluded due to: unavailable full-tests (2), overlapping samples (5), small sample size (5), sample out of criteria (3), wrong study design (5), wrong comparator (1), low quality data reporting (9), unrelated outcomes (4), no outcome data (3), data collapsed across conditions (1). 42 studies remained to be included in the submission. These are listed in Table 10.

The manual search for relevant studies yielded in the inclusion of 6 more publications. Four of these were identified from study bibliographies; one was a recent publication not picked up by the database search; and another was a HTA report from Alberta, Canada. Overall, the data from 47 studies are presented in this submission.



**Fig 9 - Flow chart of data selection**

### **Non-randomised studies**

A list of all non-randomised studies is presented in Table 10. Most studies compare MEI performance against that obtained in the unaided condition pre- or post-operatively. Some studies have included a baseline condition aided with hearing aids; this data has however been excluded from the submission. Results of the individual studies are summarised through the following sections.

**Table 10 - Non-randomised studies assessing the safety and efficacy of middle ear implants**

Author	Reports
<b>Fully implantable device: ESTEEM</b>	
Barbara (2014)	Delayed facial nerve palsy after surgery for the Esteem. Acta Otolaryngol., Early Online, 1–4, 2014.
Chen (2004)	Phase 1 clinical trial results of the Envoy System: a totally implantable middle ear device for sensorineural hearing loss. Otolaryngol.Head Neck Surg. 131 (6):904-916, 2004.
Gerard (2012)	Esteem 2 middle ear implant: our experience. Audiol.Neurotol. 17 (4):267-274, 2012.
Kraus (2011)	Envoy Esteem Totally Implantable Hearing System: phase 2 trial, 1-year hearing results. Otolaryngol.Head Neck Surg. 145 (1):100-109, 2011.
Llanos-Méndez (2013)	Esteem® totally implantable hearing device for treatment of sensorineural hearing loss. Systematic review. ISBN:978-84-15600-26-8, 2013.
Memari (2011)	Safety and patient selection of totally implantable hearing aid surgery: Envoy system, Esteem. Eur.Arch.Otorhinolaryngol. 268 (10):1421-1425, 2011.
Monini (2013)	Esteem middle ear device versus conventional hearing aids for rehabilitation of bilateral sensorineural hearing loss. Eur.Arch.Otorhinolaryngol. 270 (7):2027-2033, 2013.
<b>Fully implantable device: CARINA</b>	
Bruschini (2010)	Fully implantable Otologics MET Carina device for the treatment of sensorineural and mixed hearing loss: Audio-otological results. Acta Otolaryngol. 130 (10):1147-1153, 2010.
Jenkins	Otologics fully implantable hearing system: Phase I trial 1-year results. Otol.Neurotol. 29 (4):534-541, 2008.
Tringali (2010)	Otologics middle ear transducer with contralateral conventional hearing aid in severe sensorineural hearing loss: evolution during the first 24 months. Otol.Neurotol. 31 (4):630-636, 2010.
<b>Partially implantable device: VIBRANT SOUNDBRIDGE</b>	
Boeheim (2010)	Active middle ear implant compared with open-fit hearing aid in sloping high-frequency sensorineural hearing loss. Otol.Neurotol. 31 (3):424-429, 2010.
Boheim (2007)	Rehabilitation of high frequency hearing loss: use of an active middle ear implant]. HNO 55 (9):690-695, 2007.

Bruschini (2009)	Exclusive Transcanal Surgical Approach for Vibrant Soundbridge Implantation: Surgical and Functional Results.[Miscellaneous Article]. <i>Otology &amp; Neurotology</i> 30 (7):950-955, 2009.
Edfeldt (2014)	Evaluation of cost-utility in middle ear implantation in the Nordic School. <i>Acta Otolaryngol.</i> 2014 Jan;134(1):19-25., 2014.
Fisch (2001)	Clinical experience with the Vibrant Soundbridge implant device. <i>Otol.Neurotol.</i> 22 (6):962-972, 2001.
Fraysse (2001)	A multicenter study of the Vibrant Soundbridge middle ear implant: early clinical results and experience. <i>Otol.Neurotol.</i> 22 (6):952-961, 2001.
Garin (2005)	Hearing in noise with the Vibrant Soundbridge middle-ear implant. <i>Proceedings of the 4th International Symposium on Electronic Implants in Otology</i> , pg 72-73, 2005
Ihler (2013)	Mastoid cavity obliteration and vibrant soundbridge implantation for patients with mixed hearing loss. <i>Laryngoscope</i> , DOI: 10.1002/lary.24180, 2013.
Ihler (2014)	Long-term functional outcome and satisfaction of patients with an active middle ear implant for sensorineural hearing loss compared to a matched population with conventional hearing aids. <i>Otology &amp; Neurotology</i> , 35:211-215. 2014
Labassi (2005)	Retrospective of 1000 patients implanted with a Vibrant Soundbridge middle-ear implant. <b>Proceedings</b> of the 4th International Symposium on Electronic Implants in Otology, pg 74-75. 2005
Lenarz (2001)	Vibrant Sound Bridge System. A new kind hearing prosthesis for patients with sensorineural hearing loss. 2. Audiological results]. <i>Laryngorhinootologie</i> 80 (7):370-380, 2001.
Luetje (2002)	Phase III clinical trial results with the Vibrant Soundbridge implantable middle ear hearing device: a prospective controlled multicenter study. <i>Otolaryngol.Head Neck Surg.</i> 126 (2):97-107, 2002.
Luetje (2010)	Vibrant Soundbridge implantable hearing device: critical review and single-surgeon short- and long-term results. <i>Ear Nose Throat J.</i> 89 (9):E9-E14, 2010.
Mosnier (2008)	Benefit of the Vibrant Soundbridge Device in Patients Implanted For 5 to 8 Years.[Report]. <i>Ear &amp; Hearing</i> 29 (2):281-284, 2008.
Pok (2010)	Clinical experience with the active middle ear implant Vibrant Soundbridge in sensorineural hearing loss. <i>Adv.Otorhinolaryngol.</i> 69:51-58, 2010.

Saliba (2005)	Binaural hearing, Digital hearing aid, Middle ear implant, Stereophony, and Vibrant Soundbridge. Binaurality in Middle Ear Implant Recipients Using Contralateral Digital Hearing Aids.[Miscellaneous Article]. <i>Otology &amp; Neurotology</i> 26 (4):680-685, 2005.
Schmutziger (2006)	Long-Term Assessment after Implantation of the Vibrant Soundbridge Device. <i>Otology &amp; Neurotology</i> 27:183–188 2006.
Snik (1999)	First audiometric results with the Vibrant soundbridge, a semi-implantable hearing device for sensorineural hearing loss. <i>Audiology</i> 38 (6):335-338, 1999.
Snik (2001)	Multicenter audiometric results with the Vibrant Soundbridge, a semi-implantable hearing device for sensorineural hearing impairment. <i>Otolaryngol.Clin.North Am.</i> 34 (2):373-388, 2001.
Snik (2001)	Vibrant semi-implantable hearing device with digital sound processing: effective gain and speech perception. <i>Arch.Otolaryngol.Head Neck Surg.</i> 127 (12):1433-1437, 2001.
Snik (2006)	Estimated cost-effectiveness of active middle-ear implantation in hearing-impaired patients with severe external otitis. <i>Arch.Otolaryngol.Head Neck Surg.</i> 132 (11):1210-1215, 2006.
Sterkers (2003)	A middle ear implant, the Symphonix Vibrant Soundbridge: retrospective study of the first 125 patients implanted in France. <i>Otol.Neurotol.</i> 24 (3):427-436, 2003.
Sziklai (2014)	Functional gain and speech understanding obtained by Vibrant Soundbridge or by open-fit hearing aids. <i>Acta Otolaryngol., Acta Otolaryngologica</i> ; 131: 428–433. 2014.
Todt (2002)	Comparison of different vibrant soundbridge audioprocessors with conventional hearing AIDS. <i>Otol.Neurotol.</i> 23 (5):669-673, 2002.
Todt (2005)	Hearing benefit of patients after Vibrant Soundbridge implantation. <i>ORL J.Otorhinolaryngol.Relat Spec.</i> 67 (4):203-206, 2005.
Truy (2008)	Vibrant soundbridge versus conventional hearing aid in sensorineural high-frequency hearing loss: a prospective study. <i>Otol.Neurotol.</i> 29 (5):684-687, 2008.
Uziel (2003)	High-frequency sensorineural hearing loss, Middle ear implant, Rehabilitation, SIGNIA, and Symphonix Vibrant Soundbridge. Rehabilitation for High-Frequency Sensorineural Hearing Impairment in Adults with the Symphonix Vibrant Soundbridge: A Comparative Study.[Miscellaneous Article]. <i>Otology &amp; Neurotology</i> 24 (5):775-783, 2003.
Vincent (2004)	A longitudinal study on postoperative hearing thresholds with the Vibrant Soundbridge device. <i>Eur.Arch.Otorhinolaryngol.</i> 261 (9):493-496, 2004.

Partially implantable device: MAXUM	
NO LITERATURE AVAILABLE FOR THE MAXUM DEVICE	
Partially implantable device: SOUNDTEC	
Hough (2002)	Middle ear electromagnetic semi-implantable hearing device: results of the phase II SOUNDTEC direct system clinical trial. <i>Otol.Neurotol.</i> 23 (6):895-903, 2002.
Roland (2001)	Verification of improved patient outcomes with a partially implantable hearing aid, The SOUNDTEC direct hearing system. <i>Laryngoscope</i> 111 (10):1682-1686, 2001.
Silverstein (2005)	Electromagnetic hearing device, Ossicular magnet, Semi-implantable hearing device, and SOUNDTEC. Experience with the SOUNDTEC Implantable Hearing Aid.[Miscellaneous Article]. <i>Otology &amp; Neurotology</i> 26 (2):211-217, 2005.

### **Systematic reviews and HTA reports**

Citation details of the systematic reviews and HTA reports identified in the literature search are provided in Table 11. Due to the heterogeneity in the data collected by the included studies a meta-analysis was not possible in any systematic review. Only the economical data available from the HTA reports are included in this submission.

**Table 11 - Systematic reviews and HTA reports**

<b>SYSTEMATIC REVIEW</b>	
Kahue (2014)	Middle ear implants for rehabilitation of sensorineural hearing loss: a systematic review of FDA approved devices (Provisional abstract). <i>Otol Neurotol.</i> Aug;35(7):1228-37, 2014.
Butler (2013)	Efficacy of the active middle-ear implant in patients with sensorineural hearing loss. <i>J.Laryngol.Otol.</i> 127 Suppl 2:S8-16, 2013.
Klein (2012)	Hearing aid, Hearing loss, and Middle ear implant. A Systematic Review of the Safety and Effectiveness of Fully Implantable Middle Ear Hearing Devices: The Carina and Esteem Systems.[Review]. <i>Otology &amp; Neurotology</i> 33 (6):916-921, 2012.
Alberta Health and Wellness (2011)	Middle Ear Implants for the Treatment of Hearing Loss, Final STE Report: December 2011
Medical Services Advisory Committee (2010)	Middle ear implant for sensorineural, conductive and mixed hearing losses.MSAC, 2010
Comite d'Evaluation et de Diffusion des Innovations Technologiques (2002)	Middle ear implants - systematic review, expert panel. Anonymous. 2002.

#### **Kahue (2014)**

This systematic review by Kahue 2014 evaluates safety and efficacy of middle ear implant (MEI) systems for the rehabilitation of sensorineural hearing loss. Systematic data search used MEDLINE and Cochrane Library databases. Initial study inclusion required the publication to be in the English language; the use of the Vibrant Soundbridge, SOUNDTEC Direct, or Esteem MEI; independent reporting of patients with purely SNHL; at least 5 implanted ears; and comparative data between preoperative and postoperative audiometric performance. An initial search yielded 3,020 articles that were screened based on title and abstract. A full manuscript review of the remaining 80 articles was performed, of which 17 unique studies satisfied inclusion criteria and were evaluated. Variables including functional gain, speech recognition score improvement, audiometric



threshold shift following surgery, adverse events, and patient reported outcome measures were recorded. Study quality was appraised according to author conflict of interest, prospective or retrospective study design, inclusion criteria, number of patients, proper use of study controls, outcome measures reported, length of follow-up, and level of evidence. Heterogeneous outcome reporting precluded meta-analysis; instead a structured review was performed using best available data. Kahue 2014 concluded that the majority of studies evaluating the safety and efficacy of MEIs are retrospective in nature with limited follow-up. To date, no prospective randomized controlled trial exists comparing contemporary air conduction hearing aid performance and MEI outcomes. Furthermore he concluded that, middle ear implants offer an effective method of rehabilitating moderate-to-severe SNHL. Functional gain and speech recognition improvement appears on par with optimally fitted HAs, whereas patient-perceived outcome measures suggest that MEIs provide enhanced sound quality while reducing occlusion effect. Kahue 2014 summarizes that the future of MEIs is promising; however, further improvements in device reliability, safety, and insurance coverage are needed.

#### Butler (2013)

A systematic review was conducted by Butler et al (2013) to advise on the effectiveness of the active middle-ear implant in patients with sensorineural hearing loss, compared with external hearing aids. Several electronic databases, PubMed, Embase Cochrane Library and Current Contents databases, in order to identify relevant studies and reviews for the period between database inception and March 2012 have been screened. Only comparative studies were eligible for inclusion. Initial eligibility on the basis of study citation was conservatively determined by one reviewer (if unclear from the abstract, the full text paper was obtained). The bibliographies of all included studies were hand searched for any relevant references which may have been missed by the literature search. The Literature search resulted in fourteen comparative studies identified for inclusion, employing a variety of middle-ear implant devices, including the Envoy Esteem, Otologics Middle Ear Transducer, Soundtec Direct Drive Hearing System and Vibrant Soundbridge. Nine studies reported on the primary outcome of functional gain: one found that the middle-ear implant was significantly better than external hearing aids ( $p < 0.001$ ), while another found that external hearing aids were generally significantly better than middle-ear implants ( $p < 0.05$ ). Six of the seven remaining studies found that middle-ear implants were better than external hearing aids, although generally no clinically significant difference (i.e.  $\geq 10$  dB) was seen. Commonly reported adverse events following device implantation included middle-ear effusion, haematoma of the ear canal or tympanic

membrane, and pain. In the three studies reporting adverse events, device malfunction occurred in 5.7 per cent of patients. Butler 2013 concluded from evidence compiled in this review that the active middle-ear implant is as effective as the external hearing aid in improving hearing outcomes in patients with SNHL.

#### Klein (2012)

Klein 2012 performed a systematic review of evidence from existing research on the safety and efficacy of the Esteem Hearing System (Envoy, Minneapolis, MN, USA) and the Carina Fully Implantable Hearing Device (Otologics, Boulder, CO, USA). Systematic search was performed after The Cochrane Collaboration guidelines and the PRISMA statement. Sources used were MEDLINE, EMBASE, The Cochrane Library, Web of Science, CINAHL, PsycINFO, and the Centre for Reviews and Dissemination. Titles and abstracts of 7,700 citations were screened, and 30 articles were selected for full review, of which, 7 articles on the Esteem and 13 on the Carina met the study's eligibility criteria. Information was extracted using a pretested data abstraction form, and study quality was assessed using the Oxford Centre for Evidence-Based Medicine Levels of Evidence. Klein 2014 concluded that the majority of studies were quasi-experimental, pre- post comparisons of aided and unaided conditions. Complication rates with the Esteem were higher than with the Carina, and most commonly included taste disturbance. However, device failure was common with the Carina, predominately related to charging difficulties. For both devices, clinically significant improvements in functional gain, speech reception, and speech recognition over the unaided condition were found. In studies comparing the Esteem or Carina to hearing aids, findings were mixed. Although improvements in functional gain were similar to those for hearing aids, speech recognition and quality of life were greater with the implants. Despite limited evidence, these devices seem to offer a relatively safe and effective treatment option, particularly for patients who are medically unable to wear conventional hearing aids.

#### Alberta Health and Wellness (2011)

This STE report is a systematic review of the evidence on middle ear implants (MEI) for the treatment of hearing loss. The objectives of this review were to determine the safety, effectiveness and cost-effectiveness of MEI in comparison to external hearing aids, bone anchored hearing aids (BAHA), or cochlear implants; to identify particular sub-groups of patients who might benefit most from MEI, and to summarize the current criteria for using MEI versus alternative treatments for hearing loss. A budget impact analysis and economic decision model were also prepared based on the published literature,

information provided by the manufacturers, expert clinical opinion, and Alberta Health and Wellness administrative data. MEIs reviewed and licensed by Health Canada were the Vibrant Soundbridge® (Med-El) and the Esteem® (Envoy Medical). A third MEI, the Carina® fully implantable hearing aid (Otologics), was still in the process of obtaining licensing in Canada. All three devices are included in this assessment. A literature search was conducted for published and unpublished studies on middle ear implants, bone-anchored hearing aids and cochlear implants in the international literature before September 2011. The review of the Vibrant Soundbridge (VSB), Esteem, and Carina middle ear implants included 60 studies representing a total of 1009 patients. There were 25 studies meeting the inclusion criteria for BAHA, which collectively included 638 patients. The compiled Evidence of Safety data on the partially implantable Vibrant Soundbridge and fully implantable Carina appear to be relatively safe. There were few reports of major complications, and these occurred at rates similar to those with BAHA. A greater number of major complications were reported with the fully implantable Esteem, including high rates of nerve damage. Revision surgeries and explanations were more frequent with the Esteem and Carina MEIs. No significant safety issues associated with conventional hearing aids were found. While in this review, the safety of MEI was not specifically compared to that of cochlear implants because of differences in eligible patient populations (cochlear implants are typically indicated for more severe hearing loss), based on previously published reviews of cochlear implants, MEI appears to be at least as safe as cochlear implants. The Evidence of Effectiveness showed for middle ear implants offer comparable functional gains to those achieved with hearing aids. Based on the limited evidence, MEIs appear to provide greater improvements in the perception of speech in noisy situations and in sound quality. MEI also appears to be at least as effective as BAHA in patients who may be eligible for both devices. Due to differences in the severity of hearing loss in patients eligible for cochlear implants and those eligible for MEI, the comparative effectiveness of these two devices could not be assessed. A cost-effectiveness analysis could not be conducted because for patients who are not medically able to wear a hearing aid, and who are ineligible for a BAHA, there were no alternative treatment options. Only three economic evaluations have been published on MEIs. The quality of these studies was low. They also differed in the assumptions made, conditions around the use of comparators, and sources of cost data. Budget Impact calculations were based on an estimated 20 patients receiving MEI per year in Alberta (based on Expert Advisory Group discussions), the total budget impact over 5 years would be \$2,677,497. Concluding remarks were that, although the technology has been in use for over 10 years, good quality evidence on MEI is still lacking. In patients medically able to

wear conventional hearing aids, the evidence indicates that MEI offers a similar improvement in functional gain to that achieved with conventional hearing aids, but may offer greater improvement with respect to perception of speech in noise and sound quality. In the small group of patients who are medically unable to use conventional hearing aids, MEI appears to offer a viable treatment option.

#### Medical Services Advisory Committee (2010)

The Medical Service Advisory Committee 2010 performed a systematic review on clinical comparators for MEI according to the type and severity of hearing loss: In patients with mild or moderate sensorineural, conductive or mixed hearing losses, the comparator is the bone anchored hearing aid (BAHA). In patients with severe sensorineural or mixed hearing losses, the comparator is the cochlear implant (CI). In patients with severe conductive hearing loss, the comparator is the BAHA. The evidence presented in the selected studies was assessed and classified using the dimensions of evidence defined by the National Health and Medical Research Council (NHMRC 2000) including strength of the evidence, size of the effect and relevance of the evidence. The included studies presented a variety of MEI devices. While most studies assessed the VSB MEI, the Otologics MET, Envoy Esteem, Rion device, SOUNDTEC DDHS, and TICA MEIs were also assessed. Additionally, some studies described instances in which the MEI attachment method or the devices themselves had been modified to permit implantation. Hence, differences in components and attachment occurred between the six identified different MEI devices and also between patients receiving the same MEI. MSAC concluded for the MEI device safety outcomes, drawn from comparative, case series and case report data for a total of 1222 patients. There were no deaths associated with MEI implantation. Most adverse events were relatively rare and of low severity with the Vibrant Soundbridge (VSB). Residual hearing loss (RHL) after implantation was an important adverse event which was only reported in MEI patients. Most of the evidence for the effectiveness of the MEI has been derived from level IV evidence. Generally, MEI implantation and/or activation led to improvements in patients with mild, moderate and severe sensorineural hearing loss (SNHL); SNHL of undefined severity; mild, moderate and severe mixed hearing loss (MHL); MHL of undefined severity; and CHL. The MEI appears to be at least as effective as the HA. While most studies assessed the VSB MEI, the Otologics middle ear transducer (MET), Envoy Esteem, Rion device, SOUNDTEC Direct Drive Hearing System (DDHS) and TICA MEIs were also assessed. Expert opinion of the Advisory Panel stated that although there were slight differences between the MEI devices, their method of implantation was similar enough for pooled outcomes to be

reported. The majority of the available studies assessed the MEI in patients with SNHL. This is reflective of the anticipated Australian practice suggested by clinical experts. The reporting of effectiveness outcomes was compromised by the lack of uniform outcome measurements. The economic evaluation was to performed to compare the cost-effectiveness of MEI relative to BAHA and CI. In the absence of conclusive effectiveness data, a cost analysis was conducted to compare the different costs associated with each of the three procedures on which MSAC noted that MEI is more expensive than BAHA, but MEI is less expensive than CI.

#### Comite d'Evaluation et de Diffusion des Innovations Technologiques (2002)

This review was performed by horizon scanning documents and gives a concise overview of the MEIs which were available in that market at the time (CEDIT 2002). Neither a search strategy nor a list of references was provided. The devices considered were the Vibrant Soundbridge, the Otologics Middle Ear Transducer and the SOUNDTEC Direct Drive Hearing System. The population considered by this document is limited. A simple economic analysis was performed which stated that the cost of hospital based management of the MEI in adults is approximately €10,000, of which 56 per cent was the cost of the device itself. This document noted that the undebatable medical indications for receiving the MEI are skin pathology or anatomical abnormality in the ear canal, due to the fact that this makes the use of the HA more difficult. It recommended the establishment of the defined audiological parameters for the use of the MEI.

### **B.3 Assessment of the measures taken by investigators to minimise bias in the direct randomised trials**

Bias is any systematic error in the design, conduct or analysis of a study which results in estimates which depart from true values. An unbiased study is free from systematic error. Many types of bias have been named, but three general types can be identified which were screened for: selection bias, information bias and confounding bias. Selection bias is a systematic error in a study caused by the individuals selected into the study being different from the entire target population in an important way (ie the instance of selecting or the fact of having been selected is insufficient or not stated at all; a carefully chosen or representative collection of patients with beneficial outcomes regarding study hypothesis). The Berkson's bias, is a type of selection bias which may occur in case-control studies

which are based entirely on hospital studies. Information bias is a systematic error in a study caused by errors in the data which are collected in the study, or in the analysis of the data (ie details derived from study, experience, or instructions are insufficient; knowledge of specific events or situations are insufficiently reported; a collection of facts or data (statistical information) presented insufficient or not at all or data is published several times; a numerical measure of the uncertainty of an experimental outcome). The converse of an unpublished study is a study that is published several times. This is often, but not always, obvious (ie Barbara et al 2009, 2011 and 2014; excluded) If duplicate publications represent several updates of the data, then the most recent was used. Uncertainty' covers concepts such as inadequate minimization of important sources of bias, lack of statistical significance in an underpowered trial, detecting clinically unimportant therapeutic differences, inconsistent results across trials, and trade-offs within the comparative effectiveness and/or the comparative safety considerations. Various randomization procedures /collapse of data or patient groups were used across the trials (Zwartenkot 2013; excluded). An uneven distribution of patients between the studies can be reported for almost all studies, but does not result in biased outcomes. Whether the differences were significant or whether statistical adjustments of results were conducted was only reported in few trials. Not all evidence carries the same weight of truth that is systematically collected from a carefully crafted sufficient sample that decreases biases and promotes generalization. For example in none of the studies the outcome assessor, audiologist or ENT surgeon, was blinded to the post-operative audiological or subjective test evaluations, which is in this application not relevant as outcomes cannot be biased. Not all evidence tests a hypothesis in the most relevant and effective way that demonstrates that differences seen did not happen by chance alone.

The methodological quality of each included study was critically appraised. Each study was assessed according to the likelihood that bias, confounding and/or chance may have influenced its results. To evaluate the rigor and weight of the evidence necessary for evidence based practice and independent research we used the Cochrane Consumers & Communication review group, study quality guidelines, quality criteria levels as summarized in Table 12 and Table 13.

**Table 12 - Summary of comparator study characteristics included in the evaluation**

Study	level of evidence		n	Follow-up	Outcomes	Conclusion
	Oxford ebM	NHMRC				
Fully implantable device: ESTEEM						
Barbara et al. 2011 Italy Prospective, pre/post study	III	III-3	18 adults	1.5-2 months	AC and BC pure tone thresholds, Speech recognition in quiet, Quality of life	beneficial results in subjects suffering from high frequency, severe bilateral sensorineural hearing loss (SNHL)
Barbara et al. 2014 Italy Prospective, cross-sectional study	IV	IV	34 adults	3 months	Adverse events	delayed facial nerve (FN) impairment and taste disturbances were found in a limited number of subjects.
Chen et al. 2004 USA Prospective, multicenter study	III	III-2	7 adults	4 months	AC and BC pure tone thresholds, Functional gain, Speech recognition in quiet and noise, Quality of life, Adverse events	feasibility of a totally implantable middle-ear device for sensorineural hearing loss was proven
Gerard et al. 2012 Belgium Retrospective, pre/post study	III	III-3	13 adults	not stated	AC and BC pure tone thresholds, Functional gain, Speech recognition in quiet and noise, Quality of Life, Adverse events	offers good functional and satisfaction results; however, careful selection of patients is required. The implant is safe and only associated with classic auditory implant complications
Monini et al. 2013 Germany Retrospective, cohort study	III	III-3	15 adults	3 months	Functional gain, Speech recognition in quiet, Quality of life	possible beneficial role for rehabilitation of SNHL in selected candidates and improvement of quality of life was concluded
Memari et al. 2011 Iran Prospective, pre/post study	III	III-2	10 adults	19-40 months	AC and BC pure tone thresholds, Functional gain, Adverse events	surgery seems to be relatively safe. Correct selection of patients is very important and influences postoperative results. Hearing gain in current devices is similar to conventional hearing aids, but with better subjective hearing quality.

Study	level of evidence		n	Follow-up	Outcomes	Conclusion
	Oxford ebM	NHMRC				
Kraus et al. 2011 USA	III	III-2	57 adults	12 months	AC and BC pure tone thresholds, Functional gain, Speech recognition in quiet and noise, Quality of life, Adverse events	hearing results are statistically superior to baseline, best-fit HAs for SRT and WRS and the Esteem system is safe.
Prospective, multicenter study						
Fully implantable device: CARINA						
Bruschini et al. 2010 Italy	IV	III-3	7 adults	12-21 months	AC and BC pure tone thresholds, Functional gain, Speech recognition in quiet, Quality of life	is a viable treatment for moderate to severe SNHL and for mixed hearing loss and that in selected cases it could represent an alternative to conventional hearing aids. Implantation without affecting residual cochlear hearing levels and auditory performance could be shown to be similar or better than that reported with Ha's. Device proved to be well tolerated.
Prospective, pre/post study						
Jenkins et al. 2008 USA	III	III-1	20 adults	12 months	AC and BC pure tone thresholds, Functional gain, Speech recognition in quiet and noise, Quality of life, Adverse events	feasibility and lack of deleterious effects on native hearing was shown. Significant challenges in its clinical application have been encountered, and the company is addressing these issues in design revisions. Patient subjective questionnaires demonstrated improved naturalness of sound and functional hearing that are similar to their baseline hearing aids.
Prospective multicenter study						
Tringali et al. 2010 France	III	III-2	7 adults	24 months	AC and BC pure tone thresholds, Functional gain, Speech recognition in quiet, Quality of life	MET seems to be a suitable and successful treatment option resulting in significant improvement in speech comprehension, especially after 6 months, in patients with severe sensorineural hearing loss. During the 24-month follow-up of this study, the MET has been a safe and effective treatment for severe hearing loss
Prospective, longitudinal study						
Partially implantable device: SOUNDTEC						
Hough et al. 2002 USA	III	III-2	103 adults	4-5 months	AC and BC pure tone thresholds, Functional gain, Speech recognition in quiet and noise, Quality of life, Adverse events	significant improvement in outcomes
Prospective, multicenter trial						



Study	level of evidence		n	Follow-up	Outcomes	Conclusion
	Oxford ebM	NHMRC				
Roland et al. 2001 USA Prospective, pre/post study	III	III-3	23 adults	6 months	AC pure tone threshold, Functional gain, Quality of life	increased high-frequency gain without feedback. Patient satisfaction
Silverstein et al. 2005 USA Retrospective, pre/post study	III	III-3	64 adults	3 months	AC and BC pure tone thresholds, Functional gain, Speech recognition in quiet. Quality of life	well tolerated in the majority of patients, with a significant increase in functional gain over conventional hearing aids and reduces occlusion effect and feedback. Magnet instability and noise were the most frequent complaints.

**Table 13 - Summary of Vibrant Soundbridge study characteristics included in the evaluation**

Study	level of evidence		n	Follow-up/Testing interval	Outcomes	Conclusions
	Oxford EbM	NHMRC				
Partially implantable device: VIBRANT SOUNDBRIDGE						
Boeheim et al. 2010 Austria Prospective, with/without	IV	III-3	10 adults	5-56 months	Unaided and aided sound field thresholds, Speech recognition in quiet and noise	Significant improvement
Böheim et al. 2007 Austria Retrospective pre/post study	IV	III-3	9 adults	6 months	Unaided and aided PTA4 , Speech recognition in quiet and noise	Significant Improvement

Study	level of evidence		n	Follow-up/Testing interval	Outcomes	Conclusions
	Oxford EbM	NHMRC				
Fisch et al. 2001 Europe	III	III-2	47 adults	3 months	Unaided pure tone audiometry, Subjective impressions of sound quality - not reported	Safety of the surgical procedure was demonstrated
Prospective, single arm trial						
Frayse et al. 2001 France	IV	III-2	25 adults	22 months	Unaided and aided sound field thresholds (PTA4), Speech recognition, Subjective outcomes using the APHAB	Measurable benefit from the VBS in comparison with HA (superior amplification, greater ease in communication in noise)
Prospective, pre/post study						
Garin et al. 2005 Belgium	III	III-2	11 adults	9-24 months	Speech intelligibility in noise (55 dB)	Improvement in Outcomes
Retrospective, with/without						
Labassi et al 2005 France	IV	IV	1100 adults	7 years	Adverse events during/after surgery	Reliable middle ear implant
Retrospective study						
Lenarz et 2001 Germany	IV	III-3	34 adults	6 months	Unaided and aided sound field audiometry, Speech intelligibility in quiet and noise, Subjective outcomes using the PHAB questionnaire	Significant improvement
Retrospective, pre/post study						

Study	level of evidence		n	Follow-up/Testing interval	Outcomes	Conclusions
	Oxford EbM	NHMRC				
Luetje et al 2002 USA	III	III-2	53 adults	18 weeks	Unaided and aided pure tone audiometry, Tympanometry and acoustic reflex measurement, Speech reception in quiet and noise, Subjective outcomes using APHAB, HDSS and SHACQ	Safe and effective treatment
Prospective, single arm trial						
Luetje et al. 2010 USA	III	III-3	31 adults	1-11 years	Unaided and aided pure tone audiometry, Degree of device use using a questionnaire	Sustained gain
Retrospective, pre/post study						
Mosnier et al 2008 France	III	III-2	100 adults	5-8 years	Unaided and aided sound field audiometry, Speech intelligibility in quiet (65 dB), Subjective outcomes using Vibrant Questionnaire and GBI, Adverse events	Safe and effective treatment
Prospective, single arm trial						
Pok et al. 2010 Austria	IV	III-3	54 adults	not stated	Unaided and aided pure tone audiometry, unaided and aided sound field audiometry, Speech intelligibility in quiet (65 dB, 80 dB)	In cases of SNHL with unsatisfying benefit from conventional HAs, the VSB system offers an attractive and effective hearing solution
Retrospective, with/without						

Study	level of evidence		n	Follow-up/Testing interval	Outcomes	Conclusions
	Oxford EbM	NHMRC				
Saliba et al. 2005 Canada and France	III	III-3	8 adults	5-8 weeks	Unaided and aided pure tone audiometry, unaided and aided sound field audiometry, Speech intelligibility in quiet and noise les at various levels with constant noise (65 dB), Subjective outcomes using APHAB	Improvement in Outcomes
Prospective, with/without						
Schmuziger et al. 2006 Switzerland	IV	III-3	20 adults	not stated	Pre and post op pure tone thresholds, Speech intelligibility in quiet using Freiburger monosyllables at 65 dB, Speech intelligibility in noise (70 dB) SPL, Subjective outcomes using the IOI-HA and GBI and a not validated questionnaire	VSB was not superior to conventional hearing aids in audiologic terms, but should be considered for patients were HA are contraindicated
Retrospective chart review						
Snik et al. 2006 Netherlands	IV	III-1	13 adults	6-24 months	Direct cost of the middle ear implant, Patients satisfaction, Quality adjusted life years, Cost per QALY	Based on the cost per QALY, middle-ear implantation proved to be a cost-effective and justified health care intervention in the Netherlands
Prospective, cost utility study						

Study	level of evidence		n	Follow-up/Testing interval	Outcomes	Conclusions
	Oxford EbM	NHMRC				
Snik et al. 2001 Europe	IV	III-3	63 adults	7 months	Unaided and aided pure tone audiometry, unaided and aided sound-field speech testing in noise and quite	overall benefit from VSB treatment, but subpopulation with no benefit remains
Retrospective, multicenter study						
Snik et al. 2001 Netherlands	IV	III-2	14 adults	7 months	Aided and unaided warble tone thresholds, Speech recognition tests	Most of patients benefit from VSB treatment but subgroup presented with low gain
Prospective						
Sterkers 2003 France	IV	III-2	125 adults	4 years	Unaided and aided, pre and post surgery pure tone thresholds, Sound Field Warble tone to determine functional gain, Speech intelligibility in quiet, Subjective outcomes using the GBI and a Vibrant benefit not validated questionnaire	significant improvement, high level of satisfaction with the VSB
Retrospective survey						
Sziklai et al. 2011 Hungary	III	III-2	7 adults	not stated	Warble tone functional gain, Speech recognition scores	no significant difference
Self control prospective study						

Study	level of evidence		n	Follow-up/Testing interval	Outcomes	Conclusions
	Oxford EbM	NHMRC				
Todt et al. 2005 Germany	IV	III-3	23 adults	5 years	unaided and aided thresholds pre - post implantation, Speech discrimination in quiet and noise, Subjective outcomes using an open Questionnaire	Improvement in Outcomes
Retrospective, with/without						
Todt et al. 2002 Germany	IV	III-3	5 adults	1 year	Unaided and aided pure tone thresholds under headphones and BC, pre- post implantation, Speech discrimination in quiet (Freiburger monosyllables test), Speech discrimination in noise, Subjective outcomes using the APHAB Questionnaire	The Symphonix Soundbridge device can improve the hearing benefit of moderately to severely hearing handicapped patients— particularly in those with a high-frequency hearing loss— when compared with the conventional hearing aids
Prospective within-subjects						
Uziel et al. 2003 France	IV	III-2	6 adults	6 months	Warble tone thresholds, Speech comprehension in quiet and noise, Subjective outcomes using the APHAB and HDSS Questionnaire	Suitable treatment option offering advantages over conventional amplification to the hearing-impaired person with a high-frequency hearing loss
Prospective, cross-sectional within-subjects						
Vincent et al. 2004 France	IV	III-2	39 adults	2- 24 months	Unaided and aided pure tone thresholds, Residual hearing pre- and post implantation	Significant Improvement
Retrospective, with/without						

Study	level of evidence		n	Follow-up/Testing interval	Outcomes	Conclusions
	Oxford EbM	NHMRC				
Ihler et al 2014 Germany	IV	III-2	22 adults	3-6 months	Pure tone audiometry, Speech Audiometry in quiet and in noise, Subjective outcomes using Quality of life assessment questionnaire GBI	Improvement in Outcomes compared to HA
Retrospective study						

## B.4 Characteristics of the non-randomised studies

### B4.1 Eligibility criteria

Eligibility for inclusion in a non-randomised trial depended on the candidacy criteria defined by the manufacturers. The candidacy criteria are presented in Table 14 : Accordingly, adults aged 18 years and above were included in the studies. Inclusion was not restricted by age, gender or other demographic variable. Some studies selected patients who were implanted with a middle ear implant within a specified time frame in their clinic.

**Table 14 - Eligibility criteria**

	<b>Eligibility criteria</b>	<b>Exclusion criteria</b>
<b>VIBRANT SOUNDBRIDGE</b>	stable bilateral symmetric sensorineural hearing loss with mild to severe hearing levels; air-bone gap at 500, 1000, 2000, and 4000 Hz was to be no greater than 10 dB at 2 or more frequencies; air conduction pure tone average at 500, 1000, 2000 and 4000 Hz between 25 and 80 dB HL; speech understanding of at least 65% for word lists with appropriately amplified sound; normal middle ear with: no history of middle ear surgery; no history of post-adolescent, chronic middle ear infections; and no history of other inner ear disorders such as Meniere's disease.	Pure unilateral hearing loss; conductive, retrocochlear, or central auditory disorders; hearing loss fluctuating more than 15 dB in either direction within a period of 2 years; physical, psychological, or emotional disorders that would interfere with subjects' ability to undergo testing or surgery; subjects who were mentally retarded or had organic brain disorders
<b>SOUNDTEC Direct Drive</b>	bilateral symmetric sensorineural hearing loss with moderate to moderately severe sensorineural hearing impairment; bone conduction thresholds within 10 dB of air thresholds, high-frequency pure tone average of 1000, 2000, and 4000 Hz between 35 and 70 dB hearing level (HL), discrimination scores greater than or equal to 60% for NU-6 words, duration of hearing loss of at least 2 years without fluctuation, at least 6 months of recent hearing aid experience, use of an optimally fit NAL-R compliant hearing aid for at least 45 days in the ear to be implanted, age 21 to 80 years, sufficient cognitive skills and motivation to participate, adequate ear canal size to accommodate the deep ear mold coil assembly, dissatisfaction with conventional hearing aids, and absence of otitis externa, otitis media, and retrocochlear pathology	Exclusion criteria included a malformed or inflamed ear, perforated tympanic membrane, acute otitis media, otosclerosis, previous middle ear surgery, and disabling tinnitus.



	<b>Eligibility criteria</b>	<b>Exclusion criteria</b>
<b>ESTEEM</b>	mild to severe sensorineural hearing loss between 500 and 4000 Hz in the ear implanted that is equal to or worse than the nonimplanted ear, air conduction pure tone average of 500, 1000, 2000, 3000 and 4000 Hz between 38 and 85 dB HL, previous use of a properly functioning hearing aid for at least 4 hours per day in the ear to be implanted for at least 3 months, healthy middle ear with normal middle ear anatomy, normal-functioning eustachian tube, adequate space for the Envoy System via fine cut CT scan, speech discrimination (unaided, in the ear to be implanted) of at least 60% or better with recorded delivery at 80 dB, psychological and emotional stability, with realistic expectations of the benefits and limitations of the device	Subjects with vestibular or osteodegenerative disorders, middle ear pathology, a history of recurrent otitis media, conductive or mixed hearing loss, nonorganic hearing loss, retrocochlear hearing loss, central auditory nervous system disorder, and prelinguistic onset of hearing loss
<b>CARINA</b>	bilaterally symmetric sensorineural hearing loss with moderate to moderately severe sensorineural hearing impairment;(within 20 dB) hearing, pure-tone or high-frequency pure-tone average between 40 and 80 dB hearing level (HL), and NU-6 scores greater than 40% at 80 dB HL or 40 dB sensation level in the ear to be implanted	Subjects with vestibular or osteodegenerative disorders, middle ear pathology, a history of recurrent otitis media, conductive or mixed hearing loss, nonorganic hearing loss, retrocochlear hearing loss, central auditory nervous system disorder, and prelinguistic onset of hearing loss were excluded from the study.

## B4.2 Patient baseline characteristics

Patient baseline characteristics provided by most studies included age and gender. Some also specified the use of pre-operatively worn hearing aids. Eight studies did not however provide gender information. One longitudinal study on post-operative hearing thresholds by Vincent (2004) and a study by Labassi (2005), which was a conference proceeding, did not specify any patient baseline characteristics. The baseline characteristics can be seen in Table 15.

### Age

Patients' age ranged from 18 up to 86 years.

### Gender

The distribution of males to females across all studies was balanced (52% males and 48% females).

**Table 15 - Characteristics of study participants and duration of follow-up compared in trials**

Study	n	Age (yrs)	Sex	Follow-up
<b>VIBRANT SOUNDBRIDGE</b>				
Boenheim et al. (2010)	10	59 (44-73)	not stated	5-56 months
Böheim et al. (2007)	30	52 (30-75)	16 male,14 female	6 months
Fisch et al. (2001)	47	48.4 (19-80)	23 male,24 female	8 -12 weeks
Fraysse et al. (2001)	25	49.3 (20-73)	8 male,17 female	6-22 months
Garin et al. (2005)	11	59 (37-69)	7 male,4 female	9-24 months
Garin et al. (2003)	9	63 (37-72)	4 male,5 female	9-24 months
Labassi et al. (2005)	1450	not stated	not stated	not stated
Lenarz et al. (2001)	34	47.2 (18.9-80.3)	16 male,18 female	6 months
Luetje et al. (2002)	53	58.8 (28 - 86)	26 male,27 female	18 weeks
Luetje et al. (2010)	31	56 (28-74)	19 male,12 female	1-11 yrs.
Mosnier et al. (2008)	100	51 (19-79)	not stated	5-8 yrs.
Pok et al. (2010)	54	52.3 (30-75)	29 male,25 female	not stated
Saliba et al. (2005)	8	58 (45-68)	3 male,5 female	5-8 weeks
Schmuziger et al. (2006)	20	59 (37-75)	16 male,4 female	24 month
Snik et al. (2006)	13	52.4 ± 13.9 (18-79)	9 male,12 female	not stated
Snik et al. (2001)	14	33-67	not stated	not stated
Sterkers et al. (2003)	95	56 ± 13 (24-81)	45 male, 50 female	not stated
Sziklai et al. (2011)	7	21-62	not stated	not stated
Todt et al. (2005)	23	54-69	not stated	not stated
Todt et al. (2002)	5	54-69	not stated	not stated
Uziel et al. (2003)	6	56 (32-67)	4 male,2 female	not stated
Vincent et al. (2004)	39	not stated	not stated	not stated
<b>ESTEEM</b>				
Barbara et al. (2011)	18	not stated	not stated	1.5-2 months
Barbara et al. (2014)	34	not stated	23 men, 11 females	3 months
Chen et al. (2004)	7	64.4 (42 -88 )	5 men, 2 women	4 months
Gerard et al. (2012)	13	21-64	4 males, 9 females	not stated
Monini et al. (2013)	15	18 - 74	7 male, 8 female	3 months
Memari et al. (2011)	10	32.7+/-12.9	3 male, 7 female	19-40 months
Kraus et al. (2011)	57	52.9 (18-77)	38 male, 19 female	12 months
<b>CARINA</b>				
Bruschini et al. (2010)	8	46.4 (34-66)	7 males, 1 female	12-21 months
Jenkins et al. (2008)	20	62.8 (31.6-82)	10 male, 10 female	12 months
Tringali et al. (2010)	7	65 (53-77)	5 male, 2 female	24 months
<b>SOUNDTEC DIRECT DRIVE</b>				
Hough et al. (2002)	103	65.1	68 male, 35 female	4-5months
Roland et al. (2001)	23	67.1 +/-11.4	10 male, 13 female	6 months
Silverstein et al. (2005)	64	40-86	19 male, 18 female	3 months

### B4.3 Interventions in the non-randomised studies

In addition to the Vibrant Soundbridge, three comparable middle ear implant systems were included in the systematic review. All MEI were activated, or the sound processor was fitted within 4-8 weeks after the implantation. Audiological testing was carried out on initial fitting and then at regular intervals. The amount follow-up specified by each study is presented in Table 15.

## B.5 Outcome measures and analysis of the literature

A range of outcomes have been identified as relevant to the research questions: The category of outcomes required to address the research questions proposed in the DAP are:

- Is the partially implantable MEI **superior in effectiveness** compared to no treatment?
- Is the partially implantable MEI **as safe** as no treatment?

Because there are no head-to-head comparisons between partially implantable active middle ear implants and no treatment a comparison between partially implanted devices was conducted. We have been seeking data on patient-oriented outcomes, including: effectiveness, e.g., the subject perspective determined by questionnaires, patient-oriented scale of improvement, functional gain, speech recognition, real ear insertion gain, sound-field assessment and speech comprehension scores as well as satisfaction with communication and data related to quality of life (QALY, ICER). Safety-oriented outcomes included complication/adverse event rates, damage to the middle ear / inner ear revision surgery/explant rate/device failure and mortality. For measurements of safety and effectiveness as well as quality of life related outcomes, systematic reviews and clinical studies including randomized and nonrandomized comparative studies, Case-control studies, controlled/not controlled before-and-after studies (CBAs and nCBAs) and interrupted time series (ITS) analyses) have been included in the analysis. Non-systematic reviews, case reports, letters, editorials, and animal, in-vitro and laboratory studies have been excluded. A summary of the PICOS is presented in Table 7. Although non-randomized studies may be more prone to bias, randomized trials may not always be possible or practical. For example, it seemed unlikely that randomized controlled trials (RCT) have been conducted and therefore RCTs were not available for inclusion.

As agreed by the Protocol Advisory Subcommittee (PASC) of MSAC in their advice and final DAP (August 2014) the following outcomes are presented in the submission to address the review questions:

### **Effectiveness outcomes:**

SUBJECTIVE: (patient outcomes)

- **Abbreviated Profile of Hearing Aid Benefit (APHAB)**

quantifies the disability caused by hearing loss, and the reduction of that disability achieved with hearing aids. The APHAB uses 24 items covering 4 subscales: ease of communication, reverberation, background noise, and aversiveness to sounds. The

APHAB has been normed on 128 elderly adults with mild to moderate hearing loss. The APHAB can be downloaded from the University of Memphis Hearing Aid Research Lab (HARL) web site ([www.ausp.memphis.edu/harl/applications.html](http://www.ausp.memphis.edu/harl/applications.html)).

- **Client-orientated scale of improvement (COSI)**

is an open-ended scale in which the patient targets up to five listening situations for improvement with amplification. The patient is able to choose up to 5 listening situation from a list of 16. The COSI was normed on 1770 adults with hearing loss in Australia. The goal of the COSI is for the patient to target up to five specific listening situations and report the degree of benefit obtained compared to that expected for the population in similar listening situations. Many hearing aid manufacturers now include the COSI in their fitting software. The COSI can be downloaded for free from the NAL web site ([http://www.nal.gov.au/nal\\_products\\_front\\_page.htm](http://www.nal.gov.au/nal_products_front_page.htm)).

- **Glasgow Hearing Aid Benefit Profile (GHABP)**

examines six dimensions of outcome including disability, handicap, hearing aid use, benefit, satisfaction, and residual disability. The GHABP consists of four predetermined and four patient-nominated items. The GHABP was normed on 293 adults. Based on the normative findings, it is an appropriate instrument for clinicians who want to use self-report data to measure improvement in audibility. The Hearing Aid Benefit Interview, a completely open-ended questionnaire, is the precursor to the GHABP.

- **Glasgow Benefit Inventory (GBI)**

measures the change in health status produced by surgical interventions (here, "health status" is the general perception of well-being, including total psychological, social, and physical well being). The GBI is generic and \*not\* limited to audiological or ENT use. The GBI is a post-intervention questionnaire which assesses the interventions effects on the health status of the patients. The questionnaire contains 18 questions which can be completed either in an interview or filled-in by the patient.

- **Profile of Hearing Aid Performance (PHAP)**

consists of 66 items measuring two aspects of hearing aid performance: 1) speech communication in a variety of everyday listening situations, and 2) reactions to loudness or quality of environmental sounds in seven subscales. The goal of the PHAP is to measure aided performance rather than benefit. Normative data for test-retest reliability were completed on 30 subjects.

- **Profile of Hearing Aid Benefit (PHAB)**

consists of 66 items in seven subscales including familiar talkers, ease of communication, reverberation, reduced cues, background noise, aversiveness of sounds, and distortion of sounds. The goal of the PHAB is to measure hearing-aid benefit (unaided vs. aided) across those seven dimensions. The PHAB has been normed on 42 hearing aid users.

- **Patient preference**

- **Self-assessment scales (not indicated in the DAP)**

#### AUDIOLOGICAL:

- **Functional gain**

Is defined as the difference in sound field thresholds (AC) from unaided to aided listening conditions and is an indicator of functional benefit from an amplification device (measurements performed at different frequencies).

- **Speech audiometry (ie Speech recognition, Speech comprehension scores, SPR threshold).**

Is often carried out in free field. The most accepted measures for speech thresholds are the Speech Recognition Threshold (SRT) and the Speech Detection Threshold (SDT). The most common materials for speech recognition testing are the monosyllabic words, the Central Institute of the Deaf W-22 (**CID W-22**) and the Northwestern University-6 (**NU-6**) word list. There are other materials available for speech testing, ie nonsense material and sentence material. The two sentence procedures that are popular are the Hearing In Noise Test (HINT) and the QuickSIN. Other sentence tests that are available that have particular applications are the Synthetic Sentence Identification test (SSI), the Speech Perception and Noise test (SPIN), and the Connected Speech test. **Quiet vs. Noise testing** in speech recognition testing is another important factor to be measured. The effects of sensorineural hearing loss beyond the threshold loss, such as impaired frequency resolution or impaired temporal resolution, makes speech recognition performance in quiet a poor predictor for how those individuals will perform in noise. Speech recognition in noise is being promoted by a number of experts because adding noise improves the sensitivity of the test and the validity of the test. Giving the test at several levels will provide for a better separation between people who have hearing

loss and those who have normal hearing. Individuals with hearing loss have a lot more difficulty with speech recognition in noise than those with normal hearing, and that those with sensorineural hearing loss often require a much greater signal-to-noise ratio (SNR), 10 to 15 better, than normal hearers.

- Sound-field assessment

Stimuli are presented through loudspeakers and the testing is described as being performed “in (the) soundfield.” The soundfield can comprise different settings: ie free sound field, diffuse sound field or quasi-free sound field. It is important to recognize that soundfield audiometric testing is not ear-specific. That is, thresholds obtained by presenting the stimulus via loudspeakers will be heard by the better-hearing ear, should one ear hear better than the other. For example, an individual may have normal hearing in one ear and a mild to moderate hearing loss in the other ear. When tested in soundfield this individual will hear and respond to pure tones presented at 20 dB HL or lower. A unilateral hearing loss cannot be assessed using soundfield testing.

**Safety outcomes:**

- Complications
- Adverse events
- Infection rates
- Taste disturbance
- Fibrosis
- Aural fullness
- Acoustic trauma
- Dizziness
- Damage to the middle ear
- Revision surgery
- Explant rate
- Device failure
- Mortality

## B.6 Systematic overview of the results of the non-randomised studies

### B.6.1 Efficacy outcomes

This section presents the evidence for the effectiveness of partially-implantable MEI in treating patients with sensorineural hearing loss and a medical condition in the outer ear preventing the use of conventional hearing aids. This will be followed by the evidence for comparable MEI in treating patients with a sensorineural hearing loss only.

#### **Functional gain**

16 studies measured the functional gain of the Vibrant Soundbridge in a total of 377 adult patients. Functional gain was calculated using the hearing thresholds at 0.5, 1, 2 and 4 kHz; and the mean gain measured by individual studies ranged from 9.5 dB to 33.4 dB. The pooled average was 24,04 dB (SD 6,51 dB). Considering a difference of 10 dB or more indicating a clinically significant shift in hearing thresholds, it can be said that the VSB leads to significantly better hearing compared to unaided hearing. The results of individual studies is presented in Table 16 - Functional gain VSB.

**Table 16 - Functional gain VSB**

author	n	follow up	PTA calculation	unaided Thresholds		Device Thresholds				Functional Gain (unaided <sub>mean</sub> - device <sub>mean</sub> )		
				mean [dB]	sd	mean [dB]	sd	range	sd	mean [dB]	sd	p
Böheim 2010	10	5-56 months	no information	45.6	-	32.75	-	-	-	12.85	-	-
Böheim 2007	9	6 months	PTA <sub>4</sub>	-	-	-	-	-	-	26	-	-
Fraysse 2001	25	6-22 months	PTA <sub>4</sub>	-	-	-	-	-	-	27	12-15	-
Ihler 2013	10	1.3–37.5 months	PTA <sub>4</sub>	-	-	37.6	13.9	-	-	9.5	10.6	-
Ihler 2014	10	6.5 - 60 months	no information	-	-	29.9	8.7	-	-	25.2	8.6	-
Lenarz 2001	12	6 months	PTA <sub>4</sub>	-	-	-	-	-	-	32	-	-
Luetje 2002	53	18 weeks	PTA <sub>3</sub>	-	-	-	-	-	-	33.4	-	-
Mosnier 2008	77	1-11 yrs.	PTA <sub>4</sub>	-	-	-	-	-	-	26	-	-
Pok 2010	54	not stated	PTA (all freq.)	-	-	-	-	-	-	25.3	-	-

Saliba 2005	8	5-8 weeks	PTA <sub>4</sub>	-	-	-	-	-	-	18	9.7	-
Sterkers 2003	75	not stated	PTA <sub>4</sub>	-	-	-	-	-	-	27	12-16	-
Todt 2005	7	not stated	PTA <sub>4</sub>	-	-	-	-	-	-	22.8	6.5	-
	16					-	-	-	-	29.8	2.9	-
Todt 2002	5	not stated	PTA (all freq.)	-	-	-	-	-	-	24.3		-
Uziel 2003	6	not stated	PTA <sub>4</sub>	54.75	29.1	33.25	20.3			21.5	6.9	-

3 studies measured the functional gain of the SOUNDTEC, partially implantable MEI including 182 adults. The functional gain was measured using the SF thresholds at 0.5,1,2, and 3 kHz and one study (Silverstein 2005) measured at 0.25 kHz – 6 kHz. Neither unaided nor aided threshold were reported. The reported mean functional gain was presented in graphs ranging from 24.25dB – 40.25dB resulting in a mean of 28.74 dB (SD 7.71dB). The results of individual studies is presented in Table 17.

In total 9 publications for fully implantable devices could be deducted from literature. 3 are Esteem system and 6 Carina device related studies. In 7 studies the functional gain of the fully implantable middle ear implants in a total of 127 adult patients was measured. Functional gain was calculated using different hearing thresholds (0.5, 1, 2 and 4 kHz; 0.5, 1, 2 and 3 kHz; 0.5, 1, 2 kHz; 0.25 – 8 kHz) and the mean gain measured by individual studies ranged from 11.2 dB to 40.25 dB. The pooled average was 24.94 dB (SD 9.65 dB). The results of individual studies is presented in Table 17.



Table 17 - Functional gain comparator

author	n	follow up	PTA calculation	unaided Thresholds		Device Thresholds				Functional Gain (unaided <sub>mean</sub> - device <sub>mean</sub> )		
				mean [dB]	sd	mean [dB]	sd	range	sd	mean [dB]	sd	p
Chen 2004, Esteem	5	4 months	SF .5-1-2-3 kHz	62.25	-	54.25	-	-	-	14.75	-	-
Gerard 2012*, Esteem	13	not stated	PT ,25 to 8 kHz	66.84	-	41.77	-	-	-	25	11	-
Monini 2013, Esteem	15	3 months	SF ,125-8 kHz	-	-	-	-	-	-	30		-
Memari 2011, Esteem	10	19-40 months	SF 0,25-0,5-1-2-4 kHz	-	-	-	-	-	-	11.2	9.61	-
Kraus 2011, Esteem	48	12 months	SF .5-1-2	-	-	-	-	-	-	27		-
Bruschini 2010, Carina	7	12-21 months	SF .5-1-2-3 kHz	62.18	6.26	35.78	4.28	11.25-36.25	8.49	26.4	8.49	p < ,05
Jenkins 2008, Carina		12 months	NO DATA REPORTED									
Tringali 2013*, Carina	7	24 months	SF .5-1-2-3 kHz	-	-	-	-	-	-	40.25		-
Hough 2002*, SOUNDTEC	95	4-5 months	SF .5-1-2-3 kHz	-	-	-	-	-	-	24.45		-
Roland 2001*, SOUNDTEC	23	6 months	SF .5-1-2-3 kHz	-	-	-	-	-	-	24.25		-
Silverstein 2005, SOUNDTEC	64	3 months	SF 0.25 - 6 kHz	-	-	-	-	-	-	26		-

\* estimated from figures

SF: Sound field PT:Pure tone

### Speech recognition/comprehension scores

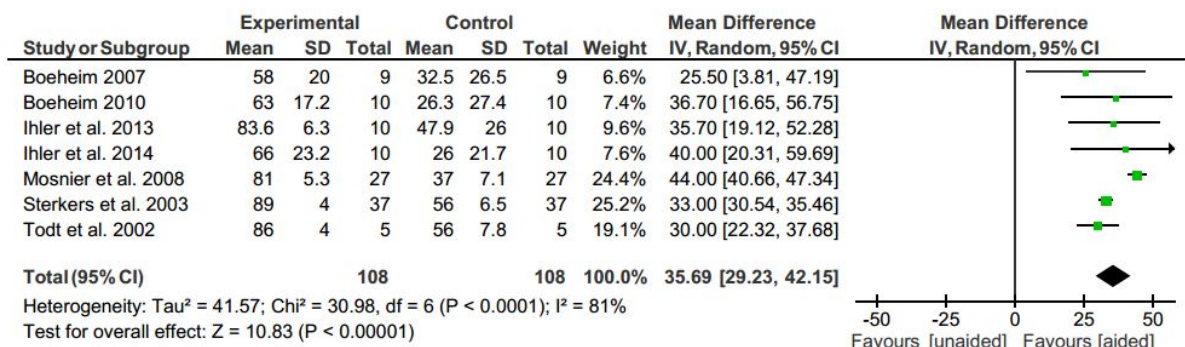
16 studies measured speech recognition in quiet using several different speech tests; with the most frequently used ones being Freiburger monosyllabic word lists and French Fournier disyllabic word lists presented at 65 dB SPL. 11 studies covering 192 patients assessed the word recognition score (WRS) when aided with the VSB and indicated a mean WRS of 57% to 89%. The pooled average across studies was 73.6% (SD 12%). A meta-analysis was possible for seven studies that provided full dataset for aided and unaided performance. The results and the forest plot are given in Fig 10 - Meta-analysis VSB. A random-effects model was chosen due to the test of heterogeneity showing significant results. The mean improvement in the WRS was 35.69% (95% CI levels, 29.23 - 42.15) demonstrating an overall significant of the VSB. Please see Table 18 - Speech in quiet VSB

#### VSB for SNHL

08-Oct-2014

##### 1 unaided vs. aided WRS

##### 1.1 New Outcome



**Fig 10 - Meta-analysis VSB**

**Table 18 - Speech in quiet VSB**

speech in quiet		Baseline unaided			Initial testing/activation		
WRS	Test	unaided			aided		
author		mean [dB]	sd	n	mean [dB]	sd	n
Boeheim 2010	Freiburger mono	26,3	27,4	10	63	17,2	10
Boeheim 2007	Freiburger mono	32,5	26,5	9	58	20	9
Ihler 2013	Freiburger mono	47,9	26,9	10	83,6	6,3	10
Ihler 2014	Freiburger mono	26	21,7	10	66	23,2	10

Lenarz 2001	Freiburger mono	28	-	7	63	-	7
Pok 2010	Freiburger mono	30	-	54	57	-	54
Todt 2005	Freiburger mono	-	-	7	75	10,4	7
				16	73	8	16
Todt 2002	Freiburger mono	56	7,8	5	86	4	5
Mosnier 2008	Freiburger mono	37	7,1	27	81	5,3	27
Sterkers 2003	Freiburger mono	56	6,5	37	89	4	37

<b>SRT</b>	Test	unaided			aided		
		<i>mean [dB]</i>	<i>sd</i>	<i>n</i>	<i>mean [dB]</i>	<i>sd</i>	<i>n</i>
<i>author</i>							
Uziel 2003	French fournier	-	-	6	32,5	-	6
Saliba 2005	French fournier	58	6,8	8	44	8,2	8
Fraysse 2001	French fournier	62	-	25	50	-	25

WRS outcomes in quiet for SOUNDTEC, partially implantable MEI including were reported in 2 studies using NU-6 word testing (n=159 Patients). Baseline/unaided and 3 months outcomes were reported with a mean of 43,9 dB (SD 51.05; 7.8 -80) and a mean of 78.05 dB (SD 5.73; 82.1 – 74). Please see Table 19 - WRS; Speech in quiet comparator.

8 studies measured word recognition score (WRS) in quiet using several different speech tests (CID W-22 word list at 50 dB; Lafon bisyllabic words at 50 dB; disyllabic words at 65 dB; Italian disyllables at 65 dB; Fournier word lists; CNC words); with the most frequently used ones being Lafon bisyllabic words lists and CID W-22 word list, presented at 60 dB SPL and 50 dB SPL respectively. One study (Barbara 2011) did not give any details regarding test used. 51 patients assessed with the WRS when aided with the Device (Carina or Esteem) resulted in a mean WRS of 77.75% (SD 11.15). The unaided score for 92 patients resulted in a mean WRS of 23.72 % (SD 10.46). Resulting in a mean improvement in the WRS of 54.03%. Data summarized in Table 19 - WRS; Speech in quiet comparator.

The 50% speech recognition threshold (SRT) was also investigated in three studies using the French Fournier disyllabic word lists. Fraysse et al. (2001) and Saliba et al. (2005) measured the SRT in the unaided and aided conditions and demonstrated an improvement of 14 dB and 12 dB, respectively. With the VSB switched on, patients achieved an SRT of 44 dB and 50 dB. Statistical testing indicated that the differences observed was significant. In another

study, Uziel et al. (2003) measured an aided SRT of 32.5 dB in six subjects, but did not compare the results to unaided values. Details in Table 18 - Speech in quiet VSB

No SRT measurements in quiet for the SOUNDTEC device were performed.

The 50% speech recognition threshold (SRT) in quiet was also investigated in three studies using CID W-22 word lists and Fournier word lists. The unaided mean SRT was 69.47 dB (SD 15.69) and with the devices switched on, patients achieved a mean SRT of 43.7 dB (SD 11.03). In the study by Tringali et al. (2013) the measured an aided SRT was 57 dB at the initial testing and 44 six months post-op in seven subjects, but did not compare the results to unaided values. Please see Table 20 - SRT, speech in quiet comparator

**Table 19 - WRS; Speech in quiet comparator**

speech in quiet		Baseline unaided			Initial testing/activation			3 months post-op / 1month post-act			4 months post-op / 2 month post-act			3 months post-act			6 months post-op			12 months post-op		
WRS	Test	unaided			aided			aided			aided			aided			aided			aided		
author		mean [dB]	sd	n	mean [dB]	sd	n	mean [dB]	sd	n	mean [dB]	sd	n	mean [dB]	sd	n	mean [dB]	sd	n	mean [dB]	sd	n
Barbara et al. 2011	unknown	36	-	18	76		18															
Chen et al. 2004	CID W-22	21	-	5				56		5	47		5									
Gerard et al. 2012	Lafon bisyllabic				64	33	13															
	Lafon bisyllabic				91	11	13															
Monini et al. 2013	bisyllbic	18.7	21.7	8									66.2	22,6	8							
Kraus et al.2011	CID W-22	10.4		54												69.1		no information	54	68.9		no information
Bruschini 2010	Italian disyllables	32.5		7															68.75			7
Jenkins et al. 2008	CNC words							77		20						77			18	78		10
Tringali et al. 2013	Fournier words				80		7									86			7			
Hough et al. 2002	NU-6 words	7.8	16.6										82.1		95							
Silverstein et al. 2005	NU-6 words	80	3.6CI	64									74	5.4CI	64							

**Table 20 - SRT, speech in quiet comparator**

speech in quite		Baseline unaided			Initial testing/activation			3 months post-op / 1month post-act			4 months post-op / 2 month post-act			3 months post-act			6 months post-op			12 months post-op			
<i>SRT</i>	Test	unaided			aided			aided			aided			aided			aided			aided			
<i>author</i>		<i>mean [dB]</i>	<i>sd</i>	<i>n</i>		<i>mean [dB]</i>	<i>sd</i>	<i>n</i>	<i>mean [dB]</i>	<i>sd</i>	<i>n</i>	<i>mean [dB]</i>	<i>sd</i>	<i>n</i>	<i>mean [dB]</i>	<i>sd</i>	<i>n</i>	<i>mean [dB]</i>	<i>sd</i>	<i>n</i>	<i>mean [dB]</i>	<i>sd</i>	<i>n</i>
Chen et al. 2004	CID W-22	62		5				43		5	45		5										
Kraus et al.2011	CID W-22	58.9		54												30.6		54	29.4				54
Monini et al. 2013	bisyllbic words	87.5	13.1	8										56.9	11,6	8							
Tringali et al. 2013	Fournier words					57		7								44		7					

Speech recognition in noise was assessed by ten studies in a total of 140 patients. Several different speech tests were implemented at different signal-to-noise ratios (SNR), making it difficult to summarise the results. The full list of outcome is presented in Table 21 - Table speech in noise VSB. Studies comparing unaided and aided performance demonstrate a clinically significant improvement in the WRS and SRT with the VSB.

Table 21 - Table speech in noise VSB

Speech in noise author	n	Test	Speech level	Noise level	SNR	Outcome measure	aided		unaided		mean change
							mean [dB]	sd	mean [dB]	sd	
Boeheim 2010	10	OLSA sentences	adaptive	60 dB	various	SRT dB	-1,5	1,4	4,8	5,3	6,3
Böheim 2007	9	Döring sentence test	80 dB	60 dB	20	% word score	63,3	-	35,6	-	27,7
			65 dB	60 dB	5		27,8	-	9,4	-	18,4
Garin 2005	9	Fournier french words	50 dB	55 dB	5	% word score	86	18	62	28	24
			55 dB	55 dB	0		69	27	37	26	32
			60 dB	55 dB	-5		40	28	15	26	25
Lenarz 2001	7	Göttinger sentences	65 dB	55 dB	10	% word score	62	-	28	-	34
Luetje 2002	53	R-SPIN	-	-	8	% word score	NS	-	-	-	-
Saliba 2005	8	Fournier french words	adaptive	65 dB	various	SRT dB	54	5,8	61	7,5	7
Schmuziger 2006	10	Basler sentences	70 dB	adaptive	various	dB SNR for SRT50	5	-	6,2	-	1,2
Todt 2005	7	Freiburger monosyllables	65 dB	60 dB	5	% word score	59,3	11,5	-	-	-
	16						65,7	10,1	-	-	-
Todt 2002	5	Freiburger monosyllables	65 dB	60 dB	5	% word score	74	9	-	-	-
Uziel 2003	6	Fournier french words	adaptive	60 dB	various	% word score	NS	-	-	-	-

NS: not stated



One study measured speech recognition in noise for the SOUNDTEC device (Hough 2002). The test used was the Speech Perception and Noise test (SPIN) under monaural listening condition. In total 95 patients participated, but only a gain of 0.1 was reported, no further details stated.

Speech recognition in noise for the fully implantable devices, Carina and Esteem was assessed in 3 studies, with a total of 48 patients. Several different speech tests were implemented at different signal-to-noise ratios (SNR), making it difficult to summarise the results for the Esteem and Carina outcomes. The full list of outcome is presented in Table 22 - Speech in noise comparator. Furthermore there is no unaided performance measurement, making it difficult to draw assumptions regarding improvement of speech in noise.

**Table 22 - Speech in noise comparator**

disyllables in noise		Listening condition	un-aided	3 - 4 months			6 months			12 months		
author	Test			mean [dB]	sd	n	mean [dB]	sd	n	mean [dB]	sd	n
Chen 2004 Esteem	HINT	S0N0	no information	only one remaining patient for HINT test, series of 5 graphs as stated in text not available								
		S0NR										
		S0NL										
Gerhard 2012 Esteem	Lafon bisyllabic	SNR +10		85	14							
		SNR +0		71	19							
		SNR -5		64	30							
Jenkins 2008 Esteem	HINT	S0N0		5,2		20	9,3			18	3,6	10
Hough 2002 SOUNDTEC	SPIN	monaural		n = 95 , only reported a gain of 0.1								

***Self-assessment scales/patient preference***

Twelve studies were identified that assessed the subjective benefit of the VSB in a total of 398 patients. Most studies implemented only one self-assessment scale, while three studies implemented several. Six different scales were used by the different studies, the most common ones being the (Abbreviated) Profile of Hearing Aid Benefit ((A)PHAB) and Glasgow Benefit Inventory (GBI). In all studies, patients were asked to fill in these questionnaires at one time point post-operatively. Other tests included the Hearing Device Satisfaction Scale (HDSS) and the Soundbridge Hearing Aid Comparison Questionnaire (SHACQ) which are designed for comparing two different hearing devices. Summary of the data is shown in Table 23 - Subjective outcomes VSB.

APHAB: Six studies covering 130 patients reported on the outcomes of the APHAB. One of these studies by Luetje (2002) reported on the number of individuals indicating an improvement on the different subscales of the PHAB, therefore this study was excluded from data synthesis. The data from the remaining five studies were pooled together and are presented in Table 24 - Subjective outcomes VSB pooled. The summary data demonstrate that patients` experienced more difficulty in understanding speech in background noise and less difficulty in the ease of communication.

**Table 23 - Subjective outcomes VSB**

authors	n	Tests used	(A)PHAB for VSB				GBI for VSB				GHABP			
			BN	RV	EC	AS	Total	General	Social	Physical	Unaided		Aided	
											mean	sd	mean	sd
Fraysse 2001	25	APHAB	39	35	22	21								
Lenarz 2001	34	PHAB	47	45	28	29								
Luetje 2002	53	PHAB, HDSS, SHACQ												
Mosnier 2008	77	GBI					17.8	22.8	14.1	1.7				
Saliba 2005	8	APHAB	48	47	33	33								
Schmutziger 2006	20	GBI					14.7	22.1	5	-5				
Snik 2006	21	GBI, NCIQ, SF-36					33.9	41.5	15.7	17.6				
Sterkers 2003	125	GBI					18	20	18	2				
Todt 2002	5	APHAB	25	25	11	26								
Uziel 2003	5	APHAB, HDSS	38	21	18	35								
Edfeldt 2014	15	GHABP									25.7	18,6	96.1	15
Ihler 2014	10	GBI					38.3	47.1	11.7	18.4				

Five studies covering 25 patients reported on the outcomes of the APHAB. The data from these five studies were pooled together and are presented in Table 23. The summary data demonstrate that patients` experienced more difficulty in understanding speech in background noise and less difficulty in the ease of communication.

**Table 24 - Subjective outcomes VSB pooled**

POOLED VSB DATA				
Outcome measure	Subscale	range	<i>mean</i>	<i>sd across studies</i>
(A)PHAB	BN	25 to 48	39,4	9,24
	RV	21 to 47	34,6	11,6
	EC	11 to 33	22,4	8,56
	AV	21 to 35	28,8	5,59
GBI	Total	14,7 to 38,3	24,5	10,8
	General	20 to 47,1	30,7	12,6
	Social	5 to 15,7	12,9	4,98
	Physical	-5 to 17,4	6,94	10,48

Three studies (SOUNDTEC) analyses subjective questionnaires such as the APHAB and a set of custom questions about sound quality, overall satisfaction and recommend to others. In total 94 patients were investigated for subjective outcomes with partially implantable SOUNDTEC device. Hough 2002 reported mean improvement of the APHAB questionnaire outcomes compared to baseline aided scores, but no data was given.

Seven studies were identified that assessed the subjective benefit of fully implantable middle ear implants (Carina and Esteem), in a total of 51 patients. All studies implemented only one self-assessment scale, with the most frequently used being the Profile of Hearing Aid Benefit ((A)PHAB). In all studies, patients were asked to fill in these questionnaires at one time point post-operatively, only one study (Bruschini 2010) provided unaided/ baseline data. Other tests included the *Client-orientated scale of improvement (COSI)* and the Glasgow Benefit Inventory (GBI). Data is summarized in Table 25 - Subjective outcomes comparator

**Table 25 - Subjective outcomes comparator**

author	n	(A)PHAB unaided/baseline								(A)PHAB for Device 20 weeks to 12 months								
		BN	sd	RV	sd	EC	sd	AV	sd	BN	sd	RV	sd	EC	sd	AV	sd	Total
Chen 2004	5	NO DATA REPORTED								22	-	32	-	25	-	-12	-	-
		22#	-	32#	-	25#	-	-12#	-	28#								
Gerard 2012	13	NO DATA REPORTED								-	-	-	-	-	-	-	-	-
Kraus 2001		reporting mean improvement compared to baseline aided scores, NO DATA REPORTED								-	-	-	-	-	-	-	-	-
Bruschini 2010	7	66.08	0.12	78.33	0.11	54.08	0.19	4.33	0.06	19.33*	0.12*	19.83*	0.1*	10.33*	0.09*	2*	0.02*	-
Jenkins 2008		EXTRACTED FROM GRAPH								38	-	35	-	22	-	-32	-	-
										47#	-	40#	-	23#	-	-29#	-	-
Tringali 2013	95	aided with contra HAs compared to unaided								-	-	-	-	-	-	-	-	-
Hough 2002		34.5	18	36.2	17	33.4	14.2	34.7	12.5	38.8	23.7	44.5	21.7	44.0	21.0	42.4	19.4	-
Roland 2001	23	NO DATA REPORTED										41	26	34.8	29	38.2	25.1	28.9

# 12 months and above

Background Noise (BN), Reverberation (RV); Ease of Communication (EC), Aversiveness to Sound (AV)

author	n	GBI score		
		total		
Barbara 2011	18	8.98		
		-		
Monini 2013	8	-		
Silverstein 2006	68	-	-	-

COSI			
in itinere		final score	
-		-	
17.9		19.4	
-		22.7	
-	-	-	-

custom questionnaire							
soundquality		overall satisfaction			recommend to others		
-	-	-	-	-	-	-	-
-	-	-	-	-	-	-	-
-	-	-	-	-	-	-	-
2.9/3.3		2.9/3.3			3.0/3.5		

Data(SI/AI): Silverstein Institute [SI] and Atkins Institute [AI]

*GBI*: Five studies covering 253 patients reported on the outcomes of the GBI. The pooled data across all studies is presented in Table 23 - Subjective outcomes VSB. Results indicate a significant positive impact of aided hearing on general health. The same, however, cannot be said for physical and social health where patients report almost no change in health status.

The GBI score for the SOUNDTEC, given by Barbara 2011 was 8.98. Data is summarized in Table 25 - Subjective outcomes comparator.

Only one study, reporting on 18 patients presented GBI outcomes (total score of 8.98). The data had to be extrapolated from the graph and only showed a total score which does not give any information whether beneficial for the patient or not. The data is presented in Table 25 - Subjective outcomes comparator.

*Client-orientated scale of improvement (COSI)*: No studies were identified implementing the COSI in VSB recipients. In comparison, COSI scales were used in two studies evaluating the subjective benefit of fully-implant MEI. In a group of 18 patients Barbara (2011) measured an in itinere and final scores of 17,9 and 19,4; indicating an improvement with aided hearing. Another study by Monini (2013) also found high degree of improvement reaching a final score of 22.7.

The COSI outcomes for 2 studies (partially implantable SOUNDTEC device) (n=26) for one in itinere timepoint (some time after surgery, not specified) and a final score were 17.9 and 19.4/22.7 respectively.

Two studies were identified implementing the COSI in fully implantable middle ear implant recipients. In a group of 18 patients Barbara (2011) measured an in itinere and final scores of 17,9 and 19,4; indicating an improvement with aided hearing. Another study by Monini (2013) also found high degree of improvement reaching a final score of 22.7. Please see Table 25 - Subjective outcomes comparator

## **B.6.2 Safety Outcomes**

Seven studies covering a total of 1398 patients reported on complications following VSB implantation. The overall rate of complications is given below, followed by the incidence rate of the different adverse events. The full list of complications reported in the literature is presented in Table 26 - Adverse events VSB and Table 27 - Adverse events comparator.

Table 26 - Adverse events VSB

Adverse Events VSB reported	Fisch 2001	Frayse 2001	Labassi 2005	Mosnier 2008	Luetje 2010	Schmuziger, 2006	Sterkers 2003	n studies	Total n of subjects	n cases	incidence when reported	incidence across all studies
<b>taste disturbances</b>	6			6		3	7	4	239	26	10,9	1,86
<b>middle ear effusion</b>							0	1	95	0	0,00	0,00
<b>pain</b>		3					1	2	120	4	3,33	0,29
<b>vertigo / dizziness</b>							0	1	95	0	0,00	0,00
<b>tinnitus</b>	1					2	1	3	162	4	2,47	0,29
<b>facial palsy</b>	0	1	2					3	1172	7	0,60	0,50
<b>limited benefit</b>							3	1	95	3	3,16	0,21
<b>headaches</b>						2	0	2	115	2	1,74	0,14
<b>revision surgery</b>	1		16	12	4	3		5	1278	38	2,97	2,72
<b>skin flap problems</b>			9	9				2	1177	18	1,53	1,29
<b>implant failure</b>			27	7				2	1177	27	2,29	1,93
<b>aural fullnes</b>				21				1	77	21	27,3	1,50
<b>complications</b>	8	4	54	55	4	10	12	7	1398	147	10,5	10,52
<b>TOTAL EVENTS</b>	47	25	1100	77	34	20	95			1398		



Table 27 - Adverse events comparator

Adverse Events Comparator reported	Barbara 2014	Chen 2004	Gerard 2012	Memari 2011	Kraus 2011	n studies	Total n subjects	n subjects	incidence when reported	incidence in literature	Jenkins 2008	incidence	Hough 2002	incidence
	Esteem	Esteem	Esteem	Esteem	Esteem						Carina		SOUNDTEC	
taste disturbances	10		0	1	24	4	111	39	35,1	22,2			2	1,941748
middle ear effusion					18	1	57	18	31,6	10,2	3	15	1	
pain		6			12	2	64	18	28,1	10,2			2	
vertigo / dizziness				0	11	2	67	11	16,4	6,25	1	5	2	1,941748
tinnitus		1		0	10	3	74	14	18,9	7,95	1		1	
nausea													1	
facial palsy/facial nerve damage	3		1	2	4	4	111	14	12,6	7,95				
limited benefit		5		2	4	3	74	14	18,9	7,95				
headaches				1	3	2	67	4	5,97	2,27				
skin flap problems													2	1,941748
aural fullnes											2		1	0,970874
wound infection		1	3	0		3	27	7	25,9	3,98				
TM perforation													1	
external otitis		4				1	7	4	57,1	2,27			1	
deterioration in hearing			3			1	10	3	30,0	1,70				
miscellaneous					30	1	57	30	52,6	17,0				
partial device extrusion											3			
implant malfunction/failure		2		1		2	17	3	17,6	1,7	9	45		
revision surgery			4	1		2	20	5	25,0	2,84			1	0,970874
explantation			2	1		2	20	3	15,0	1,70	6			
<b>TOTAL EVENTS</b>	13	17	8	5	133	5					14		14	
<b>N AFFECTED</b>	13	7	8	4	52			84			14		14	13,59223
<b>N SAMPLE</b>	34	7	10	10	57			118			20		103	

*Complications/Adverse events:* Complications were observed in 142 patients who received a VSB, which is equivalent to 10.5% of the overall sample. The incidence of complications observed for comparable devices were: 71.2% for the Esteem, 70% for the Carina, and 13.6% for the SOUNDTEC Direct Drive.

*Infection rates:* Wound infections were not observed with any partially implantable MEI; but were observed with the Esteem, in which the incidence rate was 3.98%

*Taste disturbance:* Taste disturbances were reported by 26 patients in four studies, indicating an incidence of 1.86% in the literature. In comparable devices the incidence rates were; 22.2% for the Esteem, 0% for the Carina and 1.94% for the SOUNDTEC

*Fibrosis:* No studies reported on the presence of fibrosis. A few skin flap problems were observed in two studies, indicating an incidence rate of 1.29% in the literature for the VSB. The SOUNDTEC partially implantable MEI also lead to skin flap problems in 1.94% of cases.

*Aural fullness:* Aural fullness was reported by 21 patients in a single study, resulting in an incidence of 27.3%. Across all included studies this rate dropped to 1.5%. The incidence rate for comparable devices were: 0% with the Esteem, 10% with the Carina, and 0.9% with the SOUNDTEC.

*Acoustic trauma:* Defined as a damage to the inner ear, acoustic trauma can be demonstrated by a shift in bone conduction pure tone thresholds. Twelve studies were found reporting on BC thresholds following VSB implantation. All except one demonstrated a threshold shift of less than 5 dB. The remaining study demonstrated a mean shift of 8 dB two years after implantation. A change of 10 dB or less is said to be clinically not significant. A threshold shift less than 5 dB was also observed in comparable partially and fully implantable MEI.

*Dizziness:* Dizziness and/or vertigo was addressed as a potential adverse event by Sterkers (2003), and was not observed in any of the included 95 patients. Dizziness was reported following MEI implantation at a rate of 6.25% with Esteem, 5% with the Carina, and 1.94% with the SOUNDTEC.

*Damage to the middle ear:* Damage to the middle ear could be demonstrated by an occurring pathology in the middle ear, or by a shift in air conduction pure tone thresholds. The occurrence of middle ear effusion was rated by Sterkers (2003), and was not observed in any of their patients. Pure tone AC thresholds were not examined by any VSB studies. The incidence of ME effusion observed following comparable devices were: 10.2% with the Esteem, 15% with the Carina, and 0.97% with the SOUNDTEC.

*Revision surgery:* The rate of revision surgery was mentioned in five studies covering a total of 1278 patients. Revision surgery was required in 2.72% of cases in the literature,

and was mostly due to implant failure. Following implantation of comparable devices revision surgery occurred at a rate of 2.84% with Esteem and 0.94% with SOUNDTEC.

Device failure and explantation: The rate of device failure and explantation as reported in two studies was 1.93%. in 1177 patients. In these two studies, Labassi (2005) and Sterkers (2003) indicated device malfunctions or failures of the first generation models of the Vibrant Soundbridge, and that very few were observed with second generation models since 1999. Labassi (2005) further reported a 0.3% failure rate of the new devices. The incidence of device failure or malfunction for comparable fully implantable devices were 1.7% for the Esteem and 45% for the Carina. None have been so far observed with the SOUNDTEC.

Mortality: There was no report of mortality associated with the devices or procedures in the literature of partially or fully implantable middle ear implants.

## **B.7 Extended assessment of comparative harms**

A comprehensive search strategy was used to identify all studies on MEI, and the citations found were complemented by a manual search of the study bibliographies. Bibliographies available from manufacturer websites were also used in this process to identify any publications that were not found by the online database search. Therefore, it can be said all relevant publications were included in this submission and no reports on device safety including patients were missed.

All adverse events associated with the Vibrant Soundbridge have been presented in section B6. The non-randomized trials included in this section present complications observed within a short and long-term follow-up after implantation, and have reported on all complications occurring within the specified time frame. This means that any delayed adverse event, if occurring, would have been reported. No further complications are anticipated to occur in association with receiving a MEI.

## B.8 Interpretation of the clinical evidence

The present review relies on best available evidence on Middle Ear Implants to draw conclusions about their relative effectiveness and safety.

Overall, an assessment of the study characteristics that could potentially influence test validity showed that the following studies demonstrated notable characteristics that differed from all studies:

- Memari (Memari et al., 2011) is unique in that it represents a different geographical location (Iran) and may reflect differences in the provision of health care.
- In three studies, Pok et al. (2010), Sziklai et al. (2011) and Gerard et al. (2012), the length of follow-up was not specified. The first two studies are of prospective design and it could be assumed that data was collected at initial fitting. The latter is a retrospective study where a longer follow-up could be assumed (Gerard et al., 2012; Pok et al., 2010; Sziklai I, 2011).

Keeping these studies in mind, the literature available on middle ear implants demonstrates that implantation of the VSB:

- Results in a significant improvement in sound-field hearing thresholds
- Results in significantly better speech recognition/comprehension in quiet and noisy situations
- Leads to few difficulties in understanding speech in relatively easy listening conditions, as compared to noisy conditions; and improves health in general
- Is a safe procedure with minor adverse events resolving on their own or with local treatment

Assessment of VSB outcomes at a long-term follow-up demonstrate:

- A small but non-significant shift in bone conduction thresholds over time
- Constant functional gain
- Slight decrease in recognition/comprehension over time, yet still significantly better outcomes than baseline
- Sustained subjective benefit

In the field of middle ear implants it can be concluded that the VSB is;

- At least as effective as other partially or fully implantable MEI
- At least as safe as other partially implantable MEI
- Superior in terms of safety in regard to fully-implantable MEI

The evidence base used to reach the conclusions above are summarised in Table 28 with respect to important features of the evidence outlined in Section B.8 of the PBAC Guidelines.

Table 28 - Summary of the evidence base supporting the therapeutic claims

Comparison	Therapeutic claim	The level and quality of the evidence	Statistical precision and size of the effect	Consistency of the results over the trials presented
Partially implantable MEI for patients with SNHL+medical condition vs. no treatment	Significant improvement in sound-field hearing thresholds	Level III to Level IV evidence from non-randomised pre-post or with/without studies. <b>Reference standard</b> in audiology is dedicated clinical follow-up.	Based on clinical significance defined as a shift in threshold > 10 dB HL	Demonstrated in 15/16 studies covering 377 patients
	Significantly better speech recognition/comprehension in quiet		Meta-analysis: mean improvement of 35.69% (95% CI levels, 29.23 - 42.15), Z = 10.83 (P< 0.00001) (see Table 18)	Improvement in speech comprehension scores in all seven included studies
	Significantly better speech recognition/comprehension in noisy situations		Based on clinical significance defined as a mean change of 10% (see Table 21)	Consistent improvement seen in three studies
	Few difficulties in understanding speech in relatively easy listening conditions, as compared to noisy conditions; and improves health in general		No unaided comparison available, statistical analysis not applicable (see Table 21)	Comparable values across included studies
	Is a safe procedure with minor adverse events resolving on their own or with local treatment		Statistical analysis not applicable (see Table 26 )	Not applicable
	Small but non-significant shift in bone conduction thresholds over time		Based on clinical significance defined as a shift in threshold < 10 dB HL	Demonstrated in 5 studies at a long-term follow-up
	Constant functional gain over time		Long-term mean FG:26 dB Short-term mean FG: 27 dB	Single study by Mosnier (2008)
	Slight decrease in recognition/comprehension over time, yet still significantly better outcomes than baseline		Mean WRS at long-term: 81 +/-5.3%; at short-term: 89 +/-4.0% (N=27, paired t-test, p 0.05)	Single study by Mosnier (2008)

Comparison	Therapeutic claim	The level and quality of the evidence	Statistical precision and size of the effect	Consistency of the results over the trials presented
	Sustained subjective benefit		Device satisfaction at: long-term: 77%); short term: 80%. GBI total score at short-term: 15.4 +/-1.68; long-term: 17.8 +/- 2.78	Single study by Mosnier (2008)

### **Form of economic evaluation**

As the main comparator is No Treatment, hearing-related outcome measures for No Treatment are very limited. As such, a cost-effectiveness analysis which incorporates the costs of the partially implantable Middle Ear Implants and the cost for No Treatment (opportunity costs for the society) should be sufficient to determine the cost-effectiveness of insertion of a partially implantable Middle Ear implant relative to No Treatment and to each.

## **C. Translating the clinical evaluation to the listing requested for inclusion in the economic evaluation**

Section C is provided to show that the conclusion of superior effectiveness and equal safety justifies a cost-effectiveness analysis after issues of applicability are addressed.

Strangely enough only few papers follow a coherent presentation of data which reduces the amount of extractable papers from 86 (which met the PICO criteria) to 47 (which finally could be used for data analysis) clearly documenting the missing of generally valid standards of how to describe data in order to make outcomes comparable. We are well aware of the fact that the evidence presented in part B is far away from the quality of randomized controlled trials (RCT), an evidence level that is normally applied in drug applications. To our knowledge, no evidence of higher level than that used in part B is available. Especially RCTs cannot be performed with medical devices of high risk classes or products that require surgery, because any kind of sham surgery is forbidden for aspects of ethics.

Nevertheless, the evidence obtained from systematic literature searches provides a plausible rationale supporting our claims.

Cost-Effectiveness Analysis (CEA) is the evaluation of the costs and consequences of alternative interventions using clinical outcomes in “natural units.” The natural units can include a range of clinical end points such as, life years gained, functional gain, complications avoided, or speech understanding in different conditions. The goal of CEA is to maximize societal health benefits while functioning within a constrained budget. Although there are several advantages of CEA, the major disadvantage is the inability to provide interdisease comparisons; therefore, it cannot measure the opportunity cost of implementing one intervention over another choice. Due to the inherent scarcity of health care resources, the “opportunity cost” refers to the loss of health benefits that would have been created if the resources were used in another health care sector. Another disadvantage of CEA is defining the most important effectiveness end point to report. The appropriate measure should reflect the objective of performing the analysis, and it should consider units that would improve policy decision-making. The quality of effectiveness data is imperative to a strong economic evaluation. The quality of effectiveness study design can be graded based on the NHMRC levels of evidence



(<https://www.nhmrc.gov.au/>). There will always be a certain amount of uncertainty associated with both cost and consequent data collection.

Section B.8 (Discussion) of this submission concluded that partially implantable MEI for SNHL+medical condition (Vibrant Soundbridge) are, when compared to no treatment, superior in terms of effectiveness and non-inferior in terms of safety outcomes; and when compared to other partially implantable MEI is non-inferior/at least as safe and effective. These conclusions are derived from the indirect comparison of non-randomised trials. Due to the nature of the studies and the consequent uncertainty, the economic evaluation of choice for either comparison is a cost-effectiveness model which is presented in Section D.

This section is provided to show that the therapeutic standpoints of the proposed medical device in comparison to no treatment and other partially implantable MEI and the choice of a cost-effectiveness model in either case is valid after issues in the translation of the evidence is considered.

### **C.1.1 Applicability of outcome comparisons**

The clinical setting for the studies included in this submission reflects a population that is intended to be treated with a partially implantable active middle ear implant for sensorineural hearing loss due to the inability to wear or benefit from hearing aids. The degree of hearing loss varied from mild to severe, and the type of an existing outer ear medical condition varied. Therefore, overall the study participants are representative of the target population in Australia.

The age of the study participants ranged from 18 to 86 years; and there were slightly more males than females with the percentages of 53.9 % and 46.1 %. The most informative study of the target population comes from Wilson et al. (1999) who provided prevalence values for different types of hearing loss by age group. This study covered individuals with any type of hearing loss who were aged 15 up to 70+ years, including 55 % males (510) and 45 % females (416). These demographic data may be an overestimation of the target population with sensorineural hearing loss. Nevertheless, there appears to be a good overlap between the study and target populations.

Overall, no issues were seen in the applicability of the study population to the target Australian population.

### **C.1.2 Circumstances of use**

The circumstances of use for a middle ear implant are not expected to change between the studies and the target population due to the following:

- There are universal standards for audiological equipment
- Candidacy assessment is based upon guidelines that are recognized worldwide, and the procedure is thus carried out similarly in different countries
- The decision for providing MEI implantation is made after an individual is assessed against candidacy criteria which are determined by the manufacturer
- MEI implantation is delivered under general anaesthesia by a trained surgeon

It is anticipated that the surgical procedure taken may differ between clinics. This is determined by patient anatomy and surgeon's preference. Effectiveness outcomes remain unaffected by this variety while safety outcomes may slightly, but not significantly, vary between the different approaches. The same variety seen in the literature is expected to be seen in the target population.

### **C.1.3 Extrapolation issues**

All identified studies reported the exact number or proportion of events occurring over a single follow-up period; and as given in Table 15, these periods ranged from a few months up to 11 years. In addition, almost none of the studies reported time-to-event data that would allow the calculation of event rates. In order to use the available information in a base-case cost-effectiveness analysis, the observed probability of events were transformed into time-based probabilities. To reduce uncertainty, studies reporting outcomes at a timeframe shorter than 6 months were excluded from the economic evaluation unless they were the only source of information. The methods implemented and the estimated base-case values are described in Section D.4. No other extrapolation issues were identified.

### **C.1.4 Transformation issues**

Studies investigating outcomes with the Vibrant Soundbridge AMEI reported final outcomes, while those investigating the Maxum/SOUNDTEC AMEI did not report final quality of life outcomes. Instead of measuring utility weights, the proportion of difficulties in everyday life was measured using the APHAB. It was not possible to transform these

outcomes into utility weights and the outcomes were used directly in the economic model comparing the different AMEI.

## **D. Economic evaluation for the main indication**

A US study, published in 2000, on the costs of severe-to-profound hearing loss concluded that direct and indirect costs (including medical, non-medical, educational and lost productivity costs) amounted to an average lifetime cost per individual of US \$297,000. Total costs varied depending on when the hearing loss began. Costs for individuals with prelingual onset of hearing loss exceeded US \$1 million, whereas costs for those with severe-to profound hearing loss acquired later in life averaged US \$43,000 (Mohr et al., 2000). A more recent US study, on age-related hearing loss, estimated direct medical costs and lost productivity costs using national, state and city data for 2002 and projected costs for 2030. In 2002, lost productivity costs due to age-related hearing loss were approximately \$1.4 billion at the national level; this was estimated to reach \$9 billion by the year 2030. Medical costs associated with the first year of treatment for Americans with hearing loss aged 65 and older were estimated at \$1,292 per person, or \$8.2 billion nationally (Stucky et al., 2010).

The requested MBS fee amount represents a cost-effectiveness fee for the Vibrant Soundbridge (VSB, MED-EL Australasia) implantation compared with the Ototronix MAXUM/SOUNDTEC and both compared to No Treatment. This reflects the clinical evidence demonstrating that Middle Ear implantation is superior in terms of clinical effectiveness and the treatment is as safe as comparable surgical treatment options (Section B).

### **D.1 Decision model**

The systematic review of the literature presented in Section B has shown that partially implantable MEI for SNHL+medical condition (Vibrant Soundbridge) are, when compared to no treatment, superior in terms of effectiveness and non-inferior in terms of safety outcomes. Using the grid provided in Table 29 the appropriate economic evaluation is a cost-effectiveness or cost-utility analysis. Considering that the underlying data come from non-randomised studies, a modelling approach was taken.

**Table 29 - Classification of an intervention for determination of economic evaluation to be presented**

		Comparative effectiveness versus comparator				
		Superior		Non-inferior	Inferior	
Comparative safety versus comparator	Superior	CEA/CUA		CEA/CUA	Net clinical benefit	CEA/CUA
					Neutral benefit	CEA/CUA
					Net harms	None
	Non-inferior	CEA/CUA		CEA/CUA	None	
	Inferior	Net clinical benefit	CEA/CUA	None	None	
		Neutral benefit	CEA/CUA			
		Net harms	None			

An economic evaluation of the proposed medical service against other MEI is also carried out in this submission. The evidence from Section B shows the partially implantable MEI for SNHL+medical condition (Vibrant Soundbridge) to be non-inferior to/at least as safe and effective as other partially implantable MEI (Maxum). This conclusion is limited to the small number of non-randomised studies available for the comparator, however covering a large number of participants. The decision is also conservative as the number of adverse events is slightly higher and subjective outcomes relatively worse with the comparator.

Using the classification grid a cost-minimization analysis is the most appropriate for this comparison. However, discrepancies in the design of the two MEI systems lead to differences in the surgical procedure, the amount of follow-up required and in the everyday handling and use of the device. It is believed that the differences between the two systems cannot be reduced to a simple comparison of costs. The economic evaluation of choice is a modelled cost-effectiveness (CE) analysis.

## D.2 Population and circumstances of use reflected in the economic evaluation

### D.2.1 Baseline population

The baseline population for both base-case analyses includes adults with sensorineural hearing loss who cannot wear or benefit from hearing aids due to several reasons. Adults are considered being 18 years of age and above. The age and sex distribution of the included studies, when reported, reflect the general population. The study demographics

of each CE model are compared to the target population in Table 30. Values for the target population are those estimated from Wilson et al. (1999) and described previously in section C.1.1.

A start age of 53 was used for both models. This is the mean age at implantation from which health utility values were obtained from. This study was identified in the systematic review carried out for the following section D.3.

## **D.2.2 Circumstances of use**

According to the clinical management algorithm presented in Section A.5, the proposed medical service can be offered as first- or second-line treatment to individuals who have mild-to-severe sensorineural hearing loss and a recurring/persistent medical condition in the outer ear. The line of treatment depends on whether the identified medical condition could be eradicated by conservative interventions and whether a hearing aid could be trialled. Hearing aid use has been proven to exacerbate individuals' conditions. Current treatment options for such patients include no treatment or treatment with an active middle ear implant.

Another partially implantable MEI intended for individuals with sensorineural hearing loss is the Maxum. According to the candidacy criteria, this implant system can only be provided as second-line treatment to those who have trialled a hearing aid but are not satisfied with their experience.

The provision of either MEI is on a one-off basis after assessing individuals against candidacy criteria that are determined by the manufacturer. The criteria for the two AMEI systems can be seen in sections A.2 and A.4 respectively. Candidacy assessment is carried out by audiologists using calibrated diagnostic devices and validated language-specific speech material.

Implantation with either device is carried out by a trained surgeon under local or general anaesthesia. After a healing process of 4-10 weeks patients are invited to the clinic/hospital to activate the device. They are then followed-up on a regular basis to assess device functionality and outcomes. Throughout their lifetime users of partially implantable AMEI are contraindicated to undergo MRI without removing their magnet.

Differences in circumstances of use for each CE model are tabulated against the target population in Table 30.

Table 30 – Comparison of baseline populations and circumstances of use

Population and circumstance	Studies for CE model AMEI vs no treatment	Studies for CE model AMEI vs AMEI	Target	Wider
<b>Medical condition</b>	Mild to severe SNHL with/without outer ear medical condition	Mild to severe SNHL with/without outer ear medical condition	Mild to severe SNHL with outer ear medical condition	Mild to severe SNHL with outer ear medical condition
<b>Age</b>	18-86	18-86	adults and children	adults and children
Comment	Inclusion criteria for the proposed medical service were extended in 2009 to include children. All studies identified were completed before this date and thus children were excluded from data collection.			
<b>Sex</b>	51,8% male	53% male	55% male	55% male
	48,32% female	47% female	45% female	45% female
Comment	The sex composition of the study population may be an underestimate as not all studies reported this information. As for the target population the sex composition is descriptive for individuals with any type of hearing loss. There is no data available for those with only sensorineural hearing loss. Hearing loss may be more common in males, but it does not alter the outcomes of implantation.			
<b>Position in management algorithm</b>	first- or second-line treatment	first- or second-line treatment	first-line treatment	first-line and some second-line treatment
<b>Indication criteria</b>	stable bilateral symmetrical SNHL	stable bilateral symmetrical SNHL	stable bilateral symmetrical SNHL	stable bilateral symmetrical SNHL
	ABG ≤ 10 dB HL	ABG ≤ 10 dB HL	ABG ≤ 10 dB HL	ABG ≤ 10 dB HL
	PTA (,5-1-2-4 kHz) of 25-80 dB HL	PTA (,5-1-2-4 kHz) of 25-80 dB HL	PTA (,5-1-2-4 kHz) of 25-80 dB HL	PTA (,5-1-2-4 kHz) of 25-80 dB HL
	WRS ≥ 65% in the best aided condition	WRS ≥ 60% in the best aided condition	WRS ≥ 65% in the best aided condition	WRS ≥ 65% in the best aided condition
	Unable to wear or benefit from HAs due to medical reasons	Unable to wear or benefit from HAs due to medical reasons; or dissatisfied with HAs	Unable to wear or benefit from HAs due to medical reasons	Unable to wear or benefit from HAs due to medical reasons
	normal middle ear with no previous middle ear surgery	no otitis externa, otitis media, and retrocochlear pathology	normal middle ear with no previous middle ear surgery	normal middle ear with no previous middle ear surgery
	no history of post-adolescent, chronic middle ear infections or inner ear disorders		no history of post-adolescent, chronic middle ear infections or inner ear disorders	no history of post-adolescent, chronic middle ear infections or inner ear disorders

## **D.3 Structure and rationale of the economic evaluations**

### **D.3.1 Systematic literature review**

As part of the systematic review carried out for section B, studies carrying out economic evaluations or assessing costs or quality of life of partially implantable active middle ear implants were also identified. Details of the search strategy and inclusion/exclusion criteria can be found in the respective parts of this section.

Of the 47 studies included in the systematic review, 5 had carried out an economic evaluation. Three of these were health technology assessment reviews, and two were primary research. These studies are described in Table 31.

The HTA reviews identified have been previously described in Section B.2. The analyses carried out in these reports included an economic decision model by Alberta Health and Wellness (2011), a cost analysis by CEDIT (2002) and a cost minimisation analysis by the MSAC (2010). In all of these publications the costs of different MEI were pooled together and consequently could not be used in the current model.

The decision model developed by AHW was developed for the application of MEI in moderate to severe sensorineural, conductive and mixed hearing loss. The application of the proposed medical service (of this submission) in sensorineural hearing loss only covered a small part of the overall decision model and appeared to over-simplify the treatment pathway: Individuals were successful or not successful after determining MEI candidacy, and if not successful required device revision or no further intervention. The decision model was hence not used for informing the cost effectiveness models developed for this submission.

The two primary research papers consisted of a cost-effectiveness analysis of two different types of MEI in individuals with sensorineural hearing loss and severe external otitis (Snik et al. 2006), and a cost-utility analysis of the Vibrant Soundbridge in individuals with sensorineural or conductive/mixed hearing loss (Edfeldt et al. 2014). Both studies had a prospective case series design with data collection before and after implantation.



**Table 31 – Overview of economic evaluations identified in the literature**

Publication	Country	Study design	Intervention	Comparators	Perspective for analysis	Outcome	Comments
Edfeldt et al. 2014	Sweden and Norway	Cost-utility analysis	VSB	None	Hospital	Utility gain: 0,09 Cost/QALY: € 7.260	Utility values obtained before and after implantation rather than from a comparator group.
Snik et al. 2006	The Netherlands	Cost-effectiveness analysis	MEI (VSB, Otologics MET)	None	Healthcare system/payer	Utility gain: 0,05 Cost/QALY: € 16.085	Utility values obtained before and after implantation rather than from a comparator group. Outcomes obtained for each MEI are pooled together.
Alberta Health and Wellness (2011)	Canada	Decision model	MEI (VSB, Esteem, Carina)	HA, BAHA, CI	Healthcare system/payer	Total cost of MEI over 5 years: \$2'677.497	The cost was calculated as an average of the inflated cost (5%) over 5 years.
Medical Services Advisory Committee (2010)	Australia	Cost-minimisation analysis	MEI (VSB, Otologics MET, Esteem, Rion, SOUNDTEC, TICA MEIs)	BAHA, CI	limited societal	Average cost of MEI: \$23.873	All implants deemed as being equally effective on primary outcome.
Comite d'Evaluation et de Diffusion des Innovations Technologiques (2002)	France	Cost analysis per case	MEI (VSB, Otologics MET, SOUNDTEC)	None	Hospital	\$19.173/case	Information based on executive summary, full text not available in English.

The study by Snik et al. evaluated individuals who received a MEI within a 4-year period at a single clinic in Nijmegen, the Netherlands. 13 patients received the Vibrant Soundbridge with the 404 audio processor and 8 patients received the Otologics MET device with the standard button audio processor. Quality of life was measured using the SF-36 prior to middle ear implant (MEI) surgery and 6 and 12 months after device activation. Costs included in analysis were the direct costs related to the selection phase, implantation procedure (ENT specialist, surgical nurse, anaesthesia, surgical assistance), hospital-stay of 2 days, follow-up care (ENT specialist, audiologist, assistant), and consumables (including the device itself). QALYs were calculated by multiplying the health utility gain scores with the number of profitable years a MEI can be worn. Individual profitable usage periods in years were calculated by subtracting the average hearing loss from the maximum hearing loss (3 frequency PTA of 70 dB HL for the Vibrant Soundbridge and 80-dB HL for the Otologics MET) and dividing this by an assumed deterioration of 1 dB per year (average at 0.5, 1.0, and 2.0 kHz). The cost per QALY for MEI was thus calculated to be € 16.085 (AUD 25.647). It was concluded that middle-ear implantation proved to be a cost-effective and justified health care intervention.

Several limitations to this study were noted. Due to the unavailability of other QOL and cost-effectiveness data on middle-ear implantation, comparisons were made with studies on cochlear implants. It must be noted that the target populations for the two hearing devices are not equal: The middle-ear implant is used in subjects with mild-to-severe sensorineural hearing loss, while the cochlear implant is offered to deaf subjects. Next and most importantly, the two different types of MEI devices (Vibrant Soundbridge and Otologics MET) were combined in the analysis because of small patient numbers in each group. No conclusions could, therefore, be drawn about the relative cost-effectiveness of the independent devices. MEI was also not compared to any other treatment modality. Furthermore, the use of a generic (as opposed to disease specific) quality of life instrument in this patient population may not be appropriate. Last but not least, a sensitivity analysis was not performed.

This study provides a lot of information for the target population; however, particularly because of the data from the two devices being pooled together the results could not be used in the current submission.

The second study by Edfeldt et al. evaluated individuals who received a Vibrant Soundbridge over a period of 2.5 years in six different centres in Norway and Sweden. After trialling hearing aids, 24 patients with sensorineural (SNHL), conductive (CHL), or mixed hearing loss (MHL) were implanted due to medical reasons and received the

Amadé audio processor. Quality of life was measured using the mark 2 and 3 of the Health Utilities Index (HUI) prior to middle ear implant (MEI) surgery and 6 months after device activation. Costs included in analysis were the direct costs related to preoperative assessment, implantation procedure (ENT specialist, surgical nurse, anaesthesia, surgical assistance, hospital stay), follow-up care (ENT specialist, three clinical visits), and device costs. QALYs were again calculated by multiplying the health utility gain scores with the number of profitable years. The estimation of profitable years was this time based upon hearing levels at 0.5, 1.0, 2.0 and 4.0 kHz. Using the HUI-3, the cost/QALY for patients with SNHL was estimated at €7'260 (AUD 10.454). An estimation of utility gain with the two versions of the HUI (Mark 2 and 3) can be considered as a sensitivity analysis. The authors concluded that "hearing restoration using an active middle ear implant (AMEI) is a highly cost-effective treatment for a selected group of patients with no other possibilities for auditory rehabilitation".

One of the major limitations of this study is in the collection and utilization of costs data. This information was obtained not at the individual level but from two centres (Uppsala and Oslo) thought to be representative of the respective countries, and then the cheaper costs were entered into analysis. Another limitation is that utility data from individuals with different types of hearing loss were pooled together. This means that both cost and utility data are not representative of the target population.

Considering that this study is the only economic evaluation that has really investigated generic QOL outcomes with the proposed medical service, the authors were contacted to gain access to individual level utility data for use in this submission. Cost data were disregarded and not included in the models.

Overall, there were no studies identified in the literature that could inform the structure of a new cost-effectiveness model; and only one study that could supply the model with QOL data. The CE models for this submission were developed in TreeAge Pro (Williamstown, MA, USA) together with professionals in the field to determine a representative model of implant use and follow-up care.

### **D.3.2 Structure of the economic model and its justification**

A state-transition model was developed to represent the pathways by which a person might or might not receive an active middle ear implant and the clinical events that might occur following their decision. The model was evaluated first to compare partially-implantable middle ear implants (the Vibrant Soundbridge) against no intervention, and

then for comparing different MEI (Vibrant Soundbridge and SOUNDTEC/MAXUM) against each other while omitting the no intervention arm. The clinical events in the model are defined as events that can affect the costs and course of treatment in the short or long-term. Results from the systematic review in Section B highlighted the occurrence of adverse events in the post-operative period, including device failure, which resolved on their own; remained unresolved over time; or required revision surgery, explantation or re-implantation. Therefore, the main economic model included the following main health states:

- Successful
- Successful with complications
- MEI failure

A description of all the health states can be found in Table 32.

**Table 32 – The main Markov states included in the main economic evaluation**

<b>Model state</b>	<b>Definition</b>
<b>Successful</b>	Individuals achieve an audiological and subjective benefit of wearing a MEI without experiencing any complications
<b>Successful with complications</b>	Individuals experience a complication that may resolve on its own or require surgical revision
<b>MEI failure</b>	The occurrence of device failure that requires explantation and possibly re-implantation with a new device
<b>Cease MEI</b>	Individuals voluntarily decide to stop wearing their device at any point during the model
<b>Death</b>	All-cause mortality

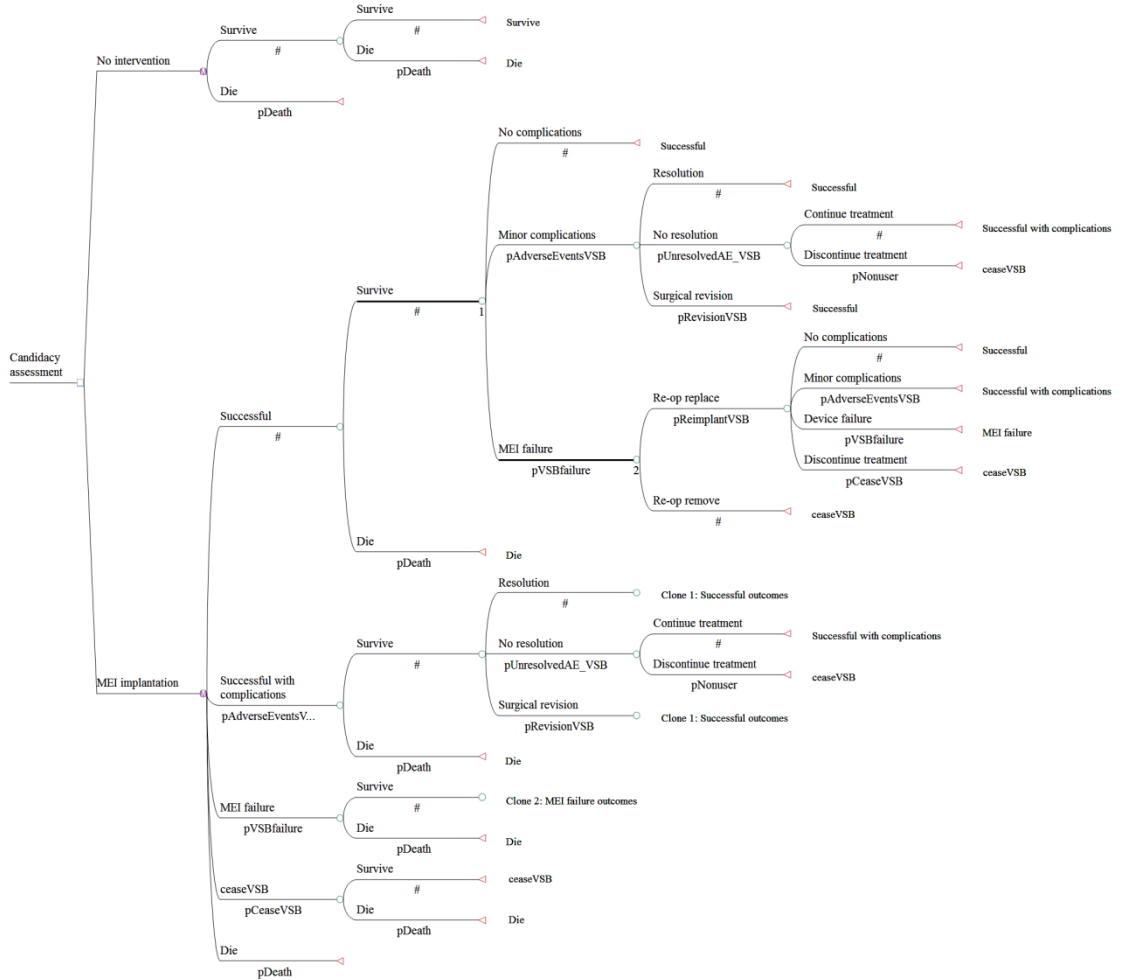
A person in the `successful` state may not experience any adverse events at all and remain successfully aided; they may experience an adverse event and move on to the `successful with complications` state; or experience problems in device function and move on to the `MEI failure` state.

Individuals in the `successful with complications` state may, as a result of their condition resolving on its own or with a surgical revision, move on to the `successful` state; or remain affected over the long-term and decide to keep using their device despite of complications and remain in the `successful with complications` state or stop using their device and move on to the `cease MEI` state.

Individuals in the `MEI failure` state may choose to undergo surgery to remove the

internal components and move into the `cease MEI` state; or choose to undergo implantation to receive a new device, with the possible outcomes of being successful, successful with complications, having a MEI failure or discontinuing treatment.

Individuals enter the model after being screened for implant candidacy by a multidisciplinary team. In the economic model depicted in Fig 11, those who are not candidates or decide against receiving AMEI follow the branch No Intervention and are assigned the costs of candidacy assessment. These individuals are at risk of recurring pathologies that require medical treatment at any point in their life. The probability of recurring pathologies is estimated from the literature. The successful or unsuccessful outcome of such treatments should not affect the quality of life or health state of individuals, but is expected to incur higher costs if unsuccessful and requiring further treatment. Individuals who decide to receive an AMEI follow the branch MEI Implantation and are assigned all the costs related to candidacy assessment, surgery and short-term follow-up. The MEI Implantation node is associated with three main health states (successful, successful with complications, MEI failure) and two absorbing states, cease MEI and death. This does not imply that individuals stop using their implant straight away after device activation, or that MEI implantation leads to death. As there is no evidence of this happening in the literature, the dead state is included to take account for all-cause mortality over time in the population that is being modelled. People undergoing the implantation procedure are allocated to potential short-term outcomes (success, success with complications, MEI failure) on the basis of probabilities calculated from the literature. In each cycle of the model, individuals who are successful after surgery are further at risk of developing adverse events; and those starting off in the `successful with complications` and `MEI failure` states are at risk of encountering another adverse event or failure. The safety outcomes of the systematic review carried out in Section B were used for populating the model and the costs associated with the management of each clinical event was sought from the Australian population. Effectiveness outcomes in the unaided (before implantation) and aided (after implantation) situations were also sought from the literature. All assumptions underlying the model structure are summarized in Table 33.



**Fig 11 – Structure of the economic model**

For evaluating the different middle ear implant systems against each other, the MEI implantation branch of the model was cloned and the Markov states were named according to the respective devices. Individuals with mild-to-severe sensorineural hearing loss enter the model after candidacy assessment and then follow the VSB or MAXUM implantation arm of the model depending on the clinical decision. The new Markov model was populated using data from the literature.

**Table 33 – Base case model assumptions**

<b>Assumption</b>	<b>Comment</b>
Individuals who remain unaided are at constant risk of experiencing a recurring pathology in the same ear.	It is unknown whether repeated treatment decreases the chance of an outer ear pathology to reoccur.
Conservative treatment of recurring pathologies, whether successful or not, does not alter the quality of life of individuals receiving no intervention.	The successful eradication of an outer ear condition may positively affect QOL, however minimum, as the pathology may reoccur.
Individuals who are successfully aided do not cease to use their device.	Studies demonstrate patients to stop using their device after various complications. Unsatisfactory benefit due to decreased gain or hearing loss can also be categorized as an adverse event.
Surgical revision provides a full resolution of adverse events.	This reflects general clinical practice.
Re-implantation with a new implant occurs in the same ear from which a failed device is explanted from.	This reflects general clinical practice.
The rate of device failure and reimplantation does not vary significantly between partially implantable MEI.	Differences in design and surgical application of partially implantable MEI is not large.
Individuals wear their device for at least six months before potentially deciding to stop using their device.	Individuals that do not experience a device failure try out their device for a few months before making a decision to stop using their device.
All-cause mortality in the hearing impaired population is equal to that in the general population.	Hearing loss or implantation with a partially implantable MEI does not impact mortality.

### **D.3.3 Time horizon and outcomes used in the economic evaluation**

The time horizon for the economic models was 10 years. This is shorter than the time horizon proposed in the Decision Analytic Protocol; however, it is long enough for differences between interventions to become apparent and to avoid extrapolating too far beyond the available data. Outcomes with the Maxum/Soundtec were only available at 3 and 12 months of device use.

The cycle length was set to 6 months. In clinical practice, adverse events usually occur immediately or soon after surgery and are resolved at most within a few months. Additionally, in the case of revision surgery or re-implantation, six-months allows for a waiting period and delivery of surgical tools if needed. Hence, a half-cycle correction was not applied.

Outcomes included in the models are the direct costs related to pre-operative assessment, surgery, hospital stay, follow-up and consumables (including battery and device costs). The primary effectiveness outcome is the ICER based upon utility values for the main economic evaluation. For the evaluation comparing different MEI, patient perceived benefit was the preferred outcome as no utility measures were available with Maxum/Soundtec implants.

### **D.3.4 Discounting**

All costs and outcomes were discounted using a 5 % discount rate as recommended by the Medical Services Advisory Committee.

### **D.3.5 Methods used to generate the results**

Cost-effectiveness analyses were carried out using cohort (expected value) analysis using results from the literature. To test the robustness of the results, deterministic sensitivity analyses was carried out on all probability and cost estimates by applying ranges around the point estimates used in the base-case analysis. A Poisson distribution was assigned to all probability estimates except VSB device failure to calculate confidence intervals. For VSB device failure the minimum and maximum values based upon the CSR were used. Cost estimates were varied by  $\pm 25\%$ .



Variables found to be sensitive in DSA were entered into probabilistic sensitivity analysis. Probability distributions were assigned to the point-estimates used in the base-case analyses. Beta distributions were assigned to transition probabilities, Gamma distributions were assigned to cost variables and Gaussian distributions were assigned to utility measures. The variables included in PSA, the sampling distributions and the parameterisations of the sampling distributions are reported in Appendix D.

## **D.4 Variables in the economic evaluation**

### **D.4.1 Transition probabilities**

Most of the transition probabilities were based upon information from studies identified in the literature. As previously reported in Section C.1.3., the studies reported outcomes from differential follow-up periods and only very few provided time-to-event data. In order to be consistent in our methods and for transition probabilities to be comparable, observed event probabilities were transformed into instantaneous 6 month rates using the declining exponential approximation to life expectancy (DEALE) method (Beck et al. 1982), which assumes a constant risk over time. These calculations were based upon the mean duration of follow-up unless the study timeframe was same for all participants. The instantaneous rates were then converted back into 6-month probabilities using the equation  $1-(1-r)^{1/t}$  for obtaining base-case values. The value of instantaneous rates was limited to a maximum of 1 for inclusion in analyses. A summary of all parameters input into economic evaluation are provided in Appendix D.

### **Recurring pathologies**

The three most common outer ear pathologies are otitis externa, EAC exostoses and excessive cerumen. A literature search was carried out to identify studies reporting epidemiological values on these conditions. Only few studies were found that investigated the number of recurring or chronic cases. The observed probability of recurring pathologies in the identified studies was respectively 25 %, 2.4 % and 3.2 %. The high prevalence of otitis externa could be due to the much smaller sample size and much shorter study timeframe. This study is however accepted worldwide as a significant resource.

Table 34 lists the study demographics used for estimating the 6-month probability of each variable. Assuming that individuals are constantly at risk of a recurring pathology, the estimated base-case values were kept constant in the model.

**Table 34 – The estimated rate of recurring pathologies**

Source	Pathology	n	Event count	Time interval	Observed probability	Instantaneous rate
Agius 1992	Otitis externa	48	13	2 w	0,27083	1
House 2008	EAC exostosis	91	8	2 (1-15) yrs	0,08791	0,023
Ahmed 2009	Excessive cerumen	500	16	up to 2 yrs	0,03200	0,0081

### Adverse events

In the scope of the economic evaluation an adverse event refers to minor events that are not related to a device failure and can resolve on their own or with surgical treatment. Of the eight studies identified in Section B.6.2 that reported on safety outcomes with AMEI, four provided sufficient information over a long enough study timeframe for the Vibrant Soundbridge and Maxum/Soundtec. These studies were re-evaluated to obtain values for all possible outcomes of having an adverse event. The study characteristics and derived estimates are given in Table 35. For the VSB the weighted mean (based on sample size) of the instantaneous rates were used to derive the 6-month probability of the respective variables. Considering that individuals are at constant risk at developing an adverse event, estimated probabilities were kept constant in the model.

Table 35 - Estimated rate of adverse events in individual studies

Source	Time interval (months)	All adverse events		Unresolved AE		Surgical revision	
		Event count	instantaneous rate	Event count	instantaneous rate	Event count	instantaneous rate
<b>Vibrant Soundbridge</b>							
Fraysse 2001	11 (6-22)	4 in 25	0,09528	0 in 4	0	0 in 4	0,0000
Schmuziger 2006	42 (26-55)	9 in 20 <sup>a</sup>	0,08540	4 in 9	0,08397	2 in 9	0,0359
Sterkers 2003	17 (2-47)	20 in 95 <sup>b</sup>	0,08353	20 in 59 <sup>b</sup>	0,14785	-	
<b>Maxum/SOUNDTEC</b>							
Hough 2002	12	14 in 103	0,07305	2 in 14	0,07708	1 in 14	0,0371

a: In Section B 10 complications were identified in this study, including one device failure, which is excluded the calculations here.

b: Re-evaluating the study it was found that in addition to the 12 adverse events previously reported there were 11 complaints of aural fullness. All these were reported over a long-term follow-up. In the short-term there was a total of 59 complaints. The 3 instances of limited benefit were excluded from analysis.

## MEI failure

**For the Vibrant Soundbridge.** Information on device failure for the Vibrant Soundbridge system was obtained using the cumulative survival curve calculated over a period of 11.3 years. This is only 9 month shorter than the product life cycle, this data was however not considered due to the reduced number of implants entering the late interval. The CSR (cumulative survival rate) was calculated using life tables based upon the scheme specified by the Pacemaker standard ISO 5841-2:-2014. Only device- and accident-related failures as well as unknown failures were accounted for in the device-related CSRs which are used in the calculation of device failure rate. As the data available was reported in intervals of three months, a six-month failure rate was estimated from the reported cumulative proportion surviving at the end of each 6-month interval using the DEALE method. The estimated device failure rate averaged 0.186 % and at the end of 11.3 years was equal to 0.148 % .

Applying a constant failure rate of 0.186 % (average device failure rate) shows very good agreement between the cumulative survival rate and the line of fit using the DEALE method in the first eight years of device use, but may heavily underestimate the failure rate in the longer term. With a constant failure rate of 0.148 % (based on the cumulative proportion surviving of 0,96582 at 11.3 years), the agreement between the cumulative survival and line of fit is more consistent with the estimated CSRs being nearly always within the 95 % confidence intervals of the original data. This constant rate was preferred in the base-case analysis.

## Figure redacted

### **Fig 12 – Goodness of fit between the true cumulative survival rate and estimated 6-month values (derived using the DEALE method) for the VSB**

The rate of reimplantation following device failure was reported in three studies (Luetje 2010; Mosnier 2008; Schmuziger 2006), however mostly for the previous generation of the Vibrant Soundbridge implant. In a total of 16 device failures 12 were known to be reimplanted, resulting in a probability of 75 %. Assuming that a device-related failure is the only complication in these cases, this rate can be used for the current generation of implants in the economic analysis. The calculated probability can also be applied as a constant value as in clinical practice re-operation always occurs within 6 months after device failure.

**For the Maxum/SOUNDTEC.** In the clinical trial of the SOUNDTEC Direct Drive system there were no reported device failures over a period of 12 months. A rate of 0 events is however not realistic for extrapolating to a 10 year time frame. It can be assumed that the device-related survival is similar to the VSB as both systems employ a transducer coupled to the ossicles and can be damaged for example by trauma to the head. Hence, to provide a comparison of costs, the device failure and explantation rates estimated for the VSB were also applied for the Maxum/Soundtec.

### **Cease MEI**

Two studies in the literature provided information on voluntary non-use of the Vibrant Soundbridge and a third study provided information on the Maxum/Soundtec. Reasons for non-use were various, including explantation of the internal device without re-implantation. The study characteristics and derived estimates are listed in Table 36. For the VSB, the weighted mean (based on sample size) of the instantaneous rates were used to derive the 6-month probability. The rates for ceasing to use either MEI were assumed to remain constant over time and were used directly in base-case analysis.

There was no information in the identified studies on the proportion of people with unresolved adverse events ceasing to use their device, hence it was accepted to be 0 for both MEI. The proportion of non-use in patients who are reimplanted following a device failure is equivalent to the probability of voluntary non-use in the whole population, which is described above.

**Table 36 - Estimated rate of voluntary non-use of the Vibrant Soundbridge**

Source	Time interval	n	Event count	Observed probability	Instantaneous rate
<b>Vibrant Soundbridge</b>					
Mosnier 2008	6 (5-8) yrs	100	15	0,15	0,01354
Luetje 2010	7,3 (1-11) yrs	34	9	0,26471	0,02106
<b>SOUNDTEC</b>					
Silverstein 2005	3 mo	64	4	0,0625	0,129077042

### All-cause mortality

The most recent life tables made available by the Australian Bureau of Statistics (ABS) were used in the model to estimate the number of people dependent on age that dies in each cycle of the model. Gender-dependent mortality rates were combined and linear interpolation was implemented in the TreeAge table to generate values for each cycle.

### D.4.2 Direct health-care resources

The costs associated with the Vibrant Soundbridge implant system were sought directly from the manufacturer (MED-EL Australasia). Costs for the VSB middle ear implant can be divided into the implant and processor costs which sum to AUD 13.970, and the procedural costs which can be further separated into pre-operational, operational and post-operational costs for the Australian population were retrieved mostly from the Medicare Benefits Schedule. All costs and resources are described in detail below.

#### Pre-operational costs

Individuals suspected of having a hearing loss are referred for a full audiometric evaluation of their hearing by an audiologist. This includes an examination of the outer and middle ear (impedance audiometry), determination of the type and degree of hearing loss (pure tone audiometry) and speech perception. There may also be an assessment of potential hearing aid use. The cost of audiological assessment according to the identified MBS items is in total AUD 84,75.

Those found to have a mild-to-severe sensorineural hearing loss and a pathology in the outer ear are referred on to an ENT surgeon for conservative treatment. In the case this

is unsuccessful patients are consulted by the ENT surgeon on surgical options, namely AMEI implantation. The costs for the procedure carried out by the surgeon equal to AUD 256,65.

Candidates are counselled and a mental assessment is made by a clinical psychologist/counsellor to understand the risks of middle ear surgery and establish realistic expectations with the implant system. The cost of AUD 126,75 was obtained from the Department of Veteran Affairs (DVA) fee schedule for allied health practitioners. A good candidate is referred on to an anaesthetist for preparation for surgery at a cost of AUD 43. All pre-operational resources together add up to AUD 511,15.

### **Operational costs**

It is recommended to obtain a CT scan (AUD 290) before surgery to examine patient anatomy and determine the surgical approach; and to carry out facial nerve monitoring (AUD 149,90) throughout the procedure to avoid surgical trauma. The anaesthetics can then be initiated and be monitored by an anaesthetist throughout the surgery. Total costs for this service equals AUD 455,40. The implantation procedure overall incurs a cost of AUD 1.876,95 together with surgical assistance of AUD 375,39. The average per diem cost of AUD 591,00 for hospitalisation was derived from the AR-DRG information for DRG D01Z (version 5.1 round 12 – Private and Public) for CI assuming that a one-night hospital stay would be necessary for the VSB. All operational resources together cost AUD 3.738,64.

### **Post-operational costs**

Upon completion of surgery, auditory brainstem response (ABR) measurement is carried out at a cost of AUD 153,95 to ensure that the middle ear is not damaged. Eight weeks after surgery, the patient returns for medical clearance and initial activation of the Audio Processor. At activation, the audio processor settings are adjusted in accordance with audiometry results and user's perception. This process is repeated at 3 months post-activation to make any necessary changes to AP settings as people adapt to their implant system. Individuals continually wearing their AP will further be required to pay for batteries. Battery life for each of the devices depends on the individual usage. It was assumed that MEI batteries would last for seven days with a price of AUD 1,00 per battery. All post-operational costs occurring within the first cycle of the model are listed in Table 37 alongside the pre-operational and operational costs.

Table 37 - Total costs per patient for successful VSB implantation in the first 6 months

VSB	Source of unit cost	Units	Unit cost	Total
<b>Consumables</b>				
Implant	Manufacturer	1	AUD 7.470,00	AUD 7.470,00
Processor	Manufacturer	1	AUD 6.500,00	AUD 6.500,00
<b>Pre operational</b>				
ENT specialist	MBS item 104	2	AUD 85,55	AUD 171,10
Anaesthesia prep	MBS item 17610	1	AUD 43,00	AUD 43,00
Audiogram (ENT)	MBS item 11315	1	AUD 49,20	AUD 49,20
Impedance audiogram (ENT)	MBS item 11327	1	AUD 19,75	AUD 19,75
Impedance additional to audiogram (Audiologist)	MBS item 82327	1	AUD 15,80	AUD 15,80
Surgery consultation	MSB item 17615	1	AUD 85,55	AUD 85,55
Counselling & mental assessment (US03)	DVA fee schedule item US03	1	AUD 126,75	AUD 126,75
subtotal			AUD 425,60	AUD 511,15
<b>Operational</b>				
CT Scan	MBS item 56016	1	AUD 290,00	AUD 290,00
Facial nerve monitoring	MBS item 11015	1	AUD 149,90	AUD 149,90
Implant procedure (ENT) - proposed service	MBS item 41554	1	AUD 1.876,95	AUD 1.876,95
Assistance	MBS item 51303	1	AUD 375,39	AUD 375,39
Anaesthesia, initiation	MBS item 20225	1	AUD 237,60	AUD 237,60
Anesthesia, time-based attendance	MBS item 23111	1	AUD 217,80	AUD 217,80
Hospital stay	AR-DRG (Vers 5.1 round 12 – Private & Public)	1	AUD 591,00	AUD 591,00
subtotal			AUD 3.738,64	AUD 3.738,64
<b>Post operational</b>				
Brain stem evoked audiometry	MBS item 82300	1	AUD 153,95	AUD 153,95
(ENT/Audiologist) follow up consultation	MBS item 10952	2	AUD 62,25	AUD 124,50
Battery cost	Modeller assumption	26	AUD 1,00	AUD 26,00
ENT specialist	MBS item 104	1	AUD 85,55	AUD 85,55
subtotal			AUD 302,75	AUD 390,00
<b>Total consumables</b>				<b>AUD 13.970,00</b>
<b>Total direct costs</b>				<b>AUD 4.639,79</b>
<b>Total cost of VSB implantation</b>				<b>AUD 18.609,79</b>

MBS: Medical Benefits Schedule. DVA: Department of Veteran Affairs. AR-DRG: Australian Refined Diagnosis Related Group.



After the first cycle of the model, patients are followed up once again in the second cycle and then every year. Throughout this process continuous users will carry on purchasing batteries for their audio processors. In the long-term it is anticipated that for each person who continues to use their implant system the external audio processor will be replaced every 5 years. The cost associated with a new AP is assumed to be the same as the existing one at AUD 6.500. Fitting of a new processor occurs during the regular clinical follow-up visits where a full audiological assessment with the new device is carried out. Long-term costs associated with VSB use are listed in Table 38.

**Table 38 - Long-term costs of VSB use**

<b>Consumables</b>	<b>MBS Item No.</b>	<b>Units</b>	<b>Unit cost</b>	<b>Total</b>
(ENT/Audiologist) follow up consultation	10952	1	AUD 62,25	AUD 62,25
Battery cost		26	AUD 1,00	AUD 26,00
subtotal			AUD 63,25	AUD 88,25

### **Costs of adverse events and device failure**

Studies identified in the literature that reported on safety outcomes with the VSB indicated that for some adverse events it may be required to carry out revision surgery. Surgery may involve correcting the position of the implanted magnet or transducer and is most like a mastoidectomy procedure. The costs associated with revision mastoidectomy was obtained from the MBS and was equal to AUD 1.089,90.

The occurrence of a device failure requires a more difficult procedure where the implanted components need to be removed from the middle ear and in most cases replaced. The explantation procedure was costed as the reference cost for the original operation, excluding surgical consumables, at AUD 3.738,64. The re-implantation procedure was assumed to be equal to the total costs of implantation excluding audio processor costs, that's AUD 12.109,79. The breakdown of costs for treating adverse events and device failure are summarised in Table 39.

**Table 39 - Costs associated with adverse events and device failure for the Vibrant Soundbridge system**

Complication	Procedure	Reference	Total cost
Adverse events	Revision surgery	MBS item 41566	AUD 1.089,90
Device failure	Explantation	Operational costs	AUD 3.738,64
	Re-implantation	Internal device costs	AUD 7.470,00
		Pre-operational costs	AUD 511,15
		Operational costs	AUD 3.738,64
		Post-operational costs	AUD 390,00
		Total cost of re-implantation	AUD 12.109,79

### Costs associated with comparator pathways

**No intervention.** Individuals who have received audiological assessment, ENT consultation and counselling for AMEI may be found not to be a good candidate or the patient themselves may decide against implantation. In either case patients incur all the pre-operational costs described for the VSB except anaesthesia preparation. In addition to this, there is a chance of their existing/treated outer ear pathology to reoccur over time. The interventional costs associated with either type of pathology were sought from the Medicare Benefits Schedule. The total cost for all pathologies together was estimated to be AUD 131,55 as seen in Table 40.

**Table 40 - Total costs per patient associated with recurring outer ear pathologies**

Procedure	MBS Item No.	Units	Unit cost	Total
Ear toilet	41647	1	AUD 109,90	AUD 109,90
Removal of exostoses	41518	1	AUD 928,00	AUD 928,00
Syringing (with GP assistance)	23	1	AUD 37,05	AUD 37,05
Recurring otitis externa		1	AUD 109,90	AUD 109,90
Recurring exostoses		0,023005	AUD 21,35	AUD 21,35
Recurring earwax		0,008131	AUD 0,30	AUD 0,30
<b>Total cost of recurring pathologies</b>			AUD 131,55	AUD 131,55

**MAXUM.** Health care resources required for MAXUM provision were sought from the literature and a further identified publication by Pelosi (2014). The costs of the MAXUM implant system were divided into the implant and processor costs of AUD 6848,44 which was provided by the MSAC; and the procedural costs which can be further separated into pre-operational, operational and post-operational costs. All procedural costs are listed in Table 41.

Pre-operational costs cover the costs of a full audiological assessment (including pure tone and impedance audiometry by an audiologist), surgical consultation with an ENT surgeon including the ear mould impression and counselling by a clinical psychologist/counsellor to understand the risks of middle ear surgery and establish realistic expectations with the implant system. All items except the last were sought from the MBS and the latter was obtained from the Department of Veteran Affairs (DVA) fee schedule for allied health practitioners. A good candidate is then referred on to an anaesthetist for preparation for surgery. All pre-operational costs sum up to a total of AUD 425,60.

Similar to the VSB implantation procedure, it is recommended by Pelosi (2014) to obtain a CT scan before surgery and carry out facial nerve monitoring throughout the procedure. The anaesthetics can then be initiated and be monitored by an anaesthetist throughout the surgery. Together with surgical assistance the implantation procedure incurs a total cost of AUD 2.989,24. No over-night hospitalisation is required after surgery.

About three weeks after surgery, the patient returns for medical clearance and fitting of the integrated processor and coil (PC). During fitting, small adjustments in the shape of the IPC can be undertaken to optimize its alignment with the implanted magnet. A 10-week accommodation period follows the sound processor fitting in which further adjustments of the IPC and sound processor settings may be made. Typically 1-3 postoperative visits are required for this process. Audiological assessment is carried out at the 20 weeks postoperative follow-up. Individuals continually wearing their IPC will further be required to pay for batteries which are expected to last for seven days. All post-operational costs occurring within the first cycle add up to a total of AUD 469,40.

After the first cycle of the model, patients are followed up once again in the second cycle and then every year. Throughout this process continuous users will carry on purchasing batteries for their audio processors. In the long-term it is anticipated that for each person who continues to use their implant system the external IPC will be replaced every 5 years. The cost associated with a new AP is assumed to be the half of the implant system costs which would equal to AUD 3.424,22. Fitting of a new processor occurs during the regular clinical follow-up visits where a full audiological assessment with the new device is carried out.

Table 41 - Total costs per patient for successful MAXUM/Soundtec implantation in the first 6 months

Maxum/Soundtec	Source of unit cost	Units	Unit cost	Total
<b>Consumables</b>				
Implant	MSAC	1	AUD 6.848,44	AUD 6.848,44
Processor	MSAC	1		
<b>Pre operational</b>				
ENT specialist	MBS item 104	1	AUD 85,55	AUD 85,55
Anaesthesia prep	MBS item 17610	1	AUD 43,00	AUD 43,00
Audiogram (ENT)	MBS item 11315	1	AUD 49,20	AUD 49,20
Impedance audiogram (ENT)	MBS item 11327	1	AUD 19,75	AUD 19,75
Impedance additional to audiogram (Audiologis	MBS item 82327	1	AUD 15,80	AUD 15,80
Surgery consultation (pre-OP Ear Canal Impres	MBS item 17615	1	AUD 85,55	AUD 85,55
Counselling & mental assessment (US03)	DVA fee schedule item US03	1	AUD 126,75	AUD 126,75
subtotal			AUD 425,60	AUD 425,60
<b>Operational</b>				
CT Scan	MBS item 56016	1	AUD 290,00	AUD 290,00
Facial stem monitoring	MBS item 11015	1	AUD 149,90	AUD 149,90
Procedure (ENT) - Operating room & recovery f	MBS item 41554	1	AUD 1.876,95	AUD 1.876,95
Assistance (Surgeon fee)	MBS item 51303	1	AUD 375,39	AUD 375,39
Anaesthesia initiation	MBS item 20225	1	AUD 237,60	AUD 237,60
Anesthesia, time-based attendance	MBS item 23033	1	AUD 59,40	AUD 59,40
subtotal			AUD 2.989,24	AUD 2.989,24
<b>Post operational</b>				
(ENT/Audiologist) follow up consultation	MBS item 10952	3	AUD 62,25	AUD 186,75
Battery cost	Modeller assumption	26	AUD 1,00	AUD 26,00
ENT specialist	MBS item 104	3	AUD 85,55	AUD 256,65
subtotal			AUD 148,80	AUD 469,40
<b>Total consumables</b>				<b>AUD 6.848,44</b>
<b>Total direct costs</b>				<b>AUD 3.884,24</b>
<b>Total cost of MAXUM implantation</b>				<b>10732,68</b>

MSAC: Medical Services Advisory Committee. MBS: Medical Benefits Schedule. AR-DRG: Australian Refined Diagnosis Related Group.

Long-term costs associated with MAXUM use are listed in Table 42.

The clinical trial of the SOUNDTEC Direct Drive system indicated the need for revision surgery in a single case. Surgery may involve checking the status of the tympanic membrane or the positioning of the transducer on the stapes bone and is most like a transcanal stapedectomy procedure.

**Table 42 - Long-term costs of Maxum/Soundtec use**

Consumables	MBS Item No.	Units	Unit cost	Total
(ENT/Audiologist) follow up consultation	10952	1	AUD 62,25	AUD 62,25
Battery cost		26	AUD 1,00	AUD 26,00
subtotal			AUD 63,25	AUD 88,25

The costs for stapedectomy obtained from the MBS were AUD 1089.90. In the case of a device failure the implanted components need to be removed from the middle ear and in most cases replaced. The explantation procedure was costed as the reference cost for the original operation, excluding surgical consumables, at AUD 2.989.24. The re-implantation procedure was assumed to be equal to the total costs of implantation excluding the estimated audio processor costs, that's AUD 7.308,46. The breakdown of costs for treating adverse events and device failure are summarised in Table 43.

**Table 43 - Costs associated with adverse events and device failure for the Maxum/Soundtec system.**

Complication	Procedure	Reference	Total cost
Adverse events	Revision surgery	MBS item 41608	AUD 1.089,90
Device failure	Explantation	Opeartional costs	AUD 2.989,24
	Re-implantation	Internal device costs	AUD 3.424,22
		Pre-operational costs	AUD 425,60
		Opeartional costs	AUD 2.989,24
		Post-operational costs	AUD 469,40
		Total cost of re-implantation	AUD 7.308,46

### D.4.3 Health outcomes

#### For the main evaluation

In the main economic evaluation the health outcome of interest was generic quality of life measured with the HUI-3. The HUI-3 has been used in other economic evaluations of hearing implants (Bond 2009; Colquitt 2011) and case series of QOL before and after

hearing implant provision (Bichey 2002; Monksfield 2011). Such data were reported for the Vibrant Soundbridge in the study by Edfeldt (2014) which was identified in the systematic review described in section D.3.1. As part of this study patients responded to the HUI mark 2&3 before implantation and 6 months after AP activation.

Individual-level data which were not reported in the publication was sought through personal communication with the author. The data from 15 patients with sensorineural hearing loss was bootstrapped using 1000 samples. The mean utility weight measured in the unaided situation which is implemented in the No intervention arm of the model is 0,57514, and the mean utility weight measured with the VSB and implemented in the MEI implantation arm of the model is 0,66868. The confidence levels The mean utility weights included in the No intervention and MEI implantation arms of the model are depicted in Table 44.

**Table 44 - Health outcome values used in the main economic evaluation**

<b>Treatment</b>	<b>mean utility</b>	<b>95%CI</b>
No intervention	0,57514	0,46031-0,68997
MEI implantation	0,66868	0,55261-0,78474

As hearing deteriorates with age, it is expected that health utility weights will also decrease. However there were no identified studies that reported quality of life over a long time of device use, or as a measure dependent on age. HUI reference scores from the Australian population were obtained from the HUIInc. website to use as a reference for calculating age-dependent utility values. As the starting age of the economic model was 53, the reference score for the 50-59 age range was accepted as the baseline value. For each age range a scaling factor was calculated using the formula:

$$\text{Scaling factor} = \text{age group utility} / \text{baseline utility}$$

The scaling factor was then multiplied by the mean utility value entered in to the model. The resulting age-dependent utility values for the unaided and aided conditions are given in Table 45. Linear interpolation was enabled in TreeAge tables to enable the calculation of utility values for each cycle.

**Table 45 - Age-dependent values used to model incremental utility in the main economic evaluation.**

Age range								
	15-19	20-29	30-39	40-49	50-59	60-69	70-79	80+
<b>Scaling factor</b>	112,99%	115,58%	112,99%	110,39%	100,00%	100,00%	93,51%	83,12%
<b>Unaided utility</b>	0,64968	0,66461	0,64968	0,63474	0,57514	0,57514	0,53766	0,47792
<b>Aided utility</b>	0,75475	0,77210	0,75475	0,73740	0,66868	0,66868	0,62462	0,55522

### For comparing MEI

When comparing the different partially implantable AMEI against each other, the health outcome of choice was patient perceived benefit. This is due to no utility measures being carried out in the studies investigating outcomes with the SOUNDTEC Direct Drive system. These studies implemented the Abbreviated Profile of Hearing Aid Benefit (APHAB) which is a common measure used in studies of the Vibrant Soundbridge implant system. This questionnaire documents the amount of difficulty experienced by implant users and higher numbers represent poorer outcomes.

Three of the six identified studies on the VSB and one of the two identified studies on the SOUNDTEC reported outcomes on all subscales of the APHAB within the first six months of device use. For the VSB, the weighted mean of the estimated global scores was used as the initial effectiveness reward while single study data for the SOUNDTEC was used directly in the model. None of these studies reported results measured in the unaided situation before implantation. The study by Cox and Alexander (1995) describing the development of the APHAB was used for estimating values in the unaided population. The study demographics and the values entered into the model are described in Table 46.

**Table 46 - Health outcome values used for comparing partially implantable MEI.**

	Source	n	Global score	Sd
<b>Unaided</b>	Cox & Alexander 1995	100	65,7	-
<b>Aided with VSB</b>	Todt 2002	5	20,3	-
	Uziel 2003	5	25,9	10,5
	Saliba 2005	8	42,7	-
	weighted mean	18	31,8	-
<b>Aided with MXM</b>	Hough 2002	93	42,4	19,4

As with utility values, it is expected that patient perceived benefit decreases over time. One of the studies identified in the systematic literature search but not included in

analysis reported long-term outcome on the APHAB with different MEI. The reason for exclusion was due to data from different implant systems being pooled together. This study is still useful to get an impression about how APHAB outcomes vary over time. Looking at the results of this paper it was observed that outcomes at 6 and 12 months were similar (43.6 vs. 46.6), but substantially decreased over a period of 7.5 years (55.6). After the first year of device use, average scores dropped by 9 units over a period of 6.5 years. Assuming a constant decrease over time, a rate of 0.7 dB change every 6 months can be estimated. Incremental effectiveness was thus kept constant in the second cycle and then reduced by 0.7 every cycle.

## D.5 Results of the main economic evaluation

Base-case results produced by the state-transition model for a cohort of individuals with sensorineural hearing loss with/without medical condition entering the model at age 53 are depicted in Table 47 and Table 48. Compared to no intervention, the provision of the Vibrant Soundbridge AMEI results in an improvement of 1,41 QALYs at a cost of AUD 21.927 per patient over a 10 year timeframe.

**Table 47 - Base-case results produced by the state-transition model comparing VSB vs. No intervention.**

Strategy	No intervention	Incremental cost	QALY	Incremental QALY	ICER (\$/QALY)
No intervention	AUD 2.541	AU -	8,86	0,00	-
VSB implantation	AUD 24.468	AUD 21.927	10,27	1,41	AUD 15.575

**Table 48 - Base-case results produced by the state-transition model comparing VSB vs. Maxum/Soundtec intervention.**

Strategy	No intervention	Incremental cost	Effectiveness	Incremental effectiveness	ICER (\$/effectiveness)
MXM implantation	AUD 13.850	-	791,79	-	-
VSB implantation	AUD 24.468	AUD 10.619	592,38	199,41	AUD 53,25



The Vibrant Soundbridge is more costly than the MAXUM implant system with an increment of AUD 10.619 and also proves to be more beneficial for the patient with effectiveness improved by 199.4 units over a 10 year period. This demonstrates that VSB users experience substantially fewer difficulties in hearing than Maxum/Soundtec users.

The costs accumulated over a period of 10 years are shown in Table 49. Here it can be seen that most of the costs are accrued within the first six months due to implantation. Long-term expenses account for up to 24 % of VSB costs and 22.6 % of MAXUM costs, which can be mostly attributed to the renewal of the audio processor in the tenth cycle of the model.

**Table 49 - Costs accumulated over a period of 10 years for all interventions as depicted by the model.**

Model cycle	VSB	No intervention	MAXUM
0	AUD 18.587	AUD 641	AUD 10.723
1	AUD 18.688	AUD 768	AUD 10.808
2	AUD 18.786	AUD 893	AUD 10.890
3	AUD 18.826	AUD 1.013	AUD 10.921
4	AUD 18.918	AUD 1.131	AUD 10.999
5	AUD 18.955	AUD 1.245	AUD 11.028
6	AUD 19.043	AUD 1.356	AUD 11.102
7	AUD 19.078	AUD 1.464	AUD 11.129
8	AUD 19.161	AUD 1.569	AUD 11.198
9	AUD 19.194	AUD 1.671	AUD 11.224
10	AUD 24.071	AUD 1.770	AUD 13.522
11	AUD 24.102	AUD 1.866	AUD 13.546
12	AUD 24.175	AUD 1.959	AUD 13.608
13	AUD 24.205	AUD 2.050	AUD 13.631
14	AUD 24.274	AUD 2.138	AUD 13.689
15	AUD 24.301	AUD 2.224	AUD 13.711
16	AUD 24.367	AUD 2.307	AUD 13.765
17	AUD 24.393	AUD 2.387	AUD 13.786
18	AUD 24.454	AUD 2.465	AUD 13.837
19	AUD 24.468	AUD 2.541	AUD 13.850

It is possible to compare the cost impact of each health state and the respective effectiveness outcomes of the two MEI systems. The outcomes tabulated below in Table 50 demonstrate that individuals in the successful health state contribute the most to the incremental cost and effectiveness. Individuals who are in the `successful with complications` state pose slightly higher costs when using the VSB while demonstrating

similar effectiveness outcomes as Maxum/Soundtec users. Those in the MEI failure state contribute the least to costs and as while they remain unaided cannot benefit. The costs associated with voluntary non-use of middle ear implants are much less in those who were initially implanted with the Vibrant Soundbridge, and the effectiveness outcomes are better too. This could be explained by the lower probability of ceasing VSB use.

All of these results are derived from non-randomised studies and are subject to uncertainty. Randomisation in medical device research is not always plausible due to the invasiveness of interventions. To reduce uncertainty one-way deterministic sensitivity analysis was carried out on all variables in the model. Those variables found to be influential on model outcomes were then entered into probabilistic sensitivity analysis.

Table 50 - List of health states and summary of cost impacts and health outcomes included in the economic evaluation.

Health state	Cost of VSB	Cost of MAXUM	Incremental cost		Effectiveness of VSB	Effectiveness of MAXUM	Incremental effectiveness	
			count	%			count	%
Successful	AUD 22.437	AUD 11.608	AUD 10.830	101,99%	561,3	639,3	78	39,14%
Successful with complications	AUD 1.691	AUD 811	AUD 880	8,29%	10,2	7,1	-3,1	-1,56%
MEI failure	AUD 28	AUD 16	AUD 12	0,11%	0,1	0,1	0	0,00%
Cease MEI	AUD 312	AUD 1.415	-AUD 1.103	-10,39%	20,8	145,2	124,4	62,42%
<b>Total</b>	AUD 24.468	AUD 13.850	AUD 10.619	100,00%	592,4	791,7	199,3	100,00%

## D.6. Sensitivity analysis

### D.6.1. Deterministic sensitivity analysis

A series of one-way deterministic sensitivity analyses were conducted where each parameter was varied one at a time from its base-case value while all other variables were kept the same. This kind of analysis helps to identify and quantify any uncertainty in the cost-effectiveness outcomes. Probability parameters except device failure were varied between their 95% confidence intervals which were estimated using exact confidence intervals for Poisson distributions. The probability of device failure was varied between the minimum and maximum values estimated at each 6 month interval of the cumulative survival curve. In the absence of appropriate measures of variability in the MBS reference costs, cost parameters were varied by 25% above and below the base-case values.

Table 51 reports the results of the DSA for the main economic evaluation. The input parameters for each analysis, the lower and upper limits of variability, are shown in the second column of the table. The results obtained at each limit are summarised in two rows: The first row reports the results at the lower limit and the second row reports those at the upper limit.

The DSA show the probability of exostoses followed and the cost and probability of otitis externa to be the most influential on the costs of receiving no implantation. The cost of candidacy assessment was found to have a smaller but noticeable influence on outcomes. The cost results of middle ear implantation are generally robust to variation in the value of input parameters. The outcomes are most sensitive to the total cost of MEI(VSB) provision, and to a lesser extent to the probability of revision surgery and ceasing to use MEI. Effectiveness outcomes were also impacted: An increased probability of ceasing to use MEI slightly decreased the QALY value. This is an expected outcome as individuals in this state are no longer receiving aided benefit. Changing the input parameters of the utility variables demonstrated that the model is significantly decreasing the outcomes in accordance with the inputted values.

Table 52 reports the results of DSA for the economic evaluation comparing the two partially implantable MEI. The cost and effectiveness results are generally robust to variation in the value of input parameters. The cost outcomes are most sensitive to the costs of VSB and MAXUM provision, and then to a lesser extent to the probability of ceasing to use MAXUM and VSB, and revision surgery following implantation with either

Table 51 – Deterministic sensitivity analysis for the main economic evaluation (all monetary outcomes in AUD)

Variable	Input value	Cost of no intervention	Cost of VSB	Incremental cost	QALY for no intervention	QALY for VSB	Incremental utility
<b>Cost of treating otitis externa</b>	82,43	2116,84	24468,43	22351,60	8,86	10,27	1,41
	137,38	2965,47	24468,43	24502,96	8,86	10,27	1,41
<b>Cost of treating exostosis</b>	696,00	2458,75	24468,43	22009,69	8,86	10,27	1,41
	1160,00	2623,56	24468,43	21844,87	8,86	10,27	1,41
<b>Cost of treating impacted cerumen</b>	27,79	2539,99	24468,43	21928,44	8,86	10,27	1,41
	46,31	2542,32	24468,43	21926,12	8,86	10,27	1,41
<b>Probability of recurring otitis externa</b>	0,73732	2095,32	24468,43	22373,12	8,86	10,27	1,41
	1	2541,16	24468,43	21927,28	8,86	10,27	1,41
<b>Probability of recurring exostosis</b>	0,00266	2249,65	24468,43	22218,79	8,86	10,27	1,41
	0,07939	3349,33	24468,43	21119,11	8,86	10,27	1,41
<b>Probability of recurring cerumen</b>	0,00218	2537,75	24468,43	21930,68	8,86	10,27	1,41
	0,02048	2548,22	24468,43	21920,21	8,86	10,27	1,41
<b>Cost of candidacy assessment</b>	383,36	2413,75	24468,43	22054,68	8,86	10,27	1,41
	638,94	2668,56	24468,43	21799,88	8,86	10,27	1,41
<b>Cost of MEI provision</b>	13957,34	2541,16	19830,04	17288,88	8,86	10,27	1,41
	23262,24	2541,16	29106,83	26565,68	8,86	10,27	1,41
<b>Cost of revision surgery</b>	817,43	2541,16	24458,15	21917,00	8,86	10,27	1,41
	1362,38	2541,16	24478,72	21937,56	8,86	10,27	1,41
<b>Cost of reimplantation</b>	9082,34	2541,16	24416,35	21875,20	8,86	10,27	1,41
	15137,24	2541,16	24520,52	21979,36	8,86	10,27	1,41
<b>Cost of MEI explantation</b>	2803,98	2541,16	24463,07	21921,92	8,86	10,27	1,41
	4673,30	2541,16	24473,79	21932,64	8,86	10,27	1,41
<b>Probability of adverse events</b>	0,4429	2541,16	24448,76	21907,61	8,86	10,27	1,41
	0,14973	2541,16	24498,53	21957,38	8,86	10,27	1,41

<b>Variable</b>	<b>Input value</b>	<b>Cost of no intervention</b>	<b>Cost of VSB</b>	<b>Incremental cost</b>	<b>QALY for no intervention</b>	<b>QALY for VSB</b>	<b>Incremental utility</b>
<b>Probability of device failure</b>	0,00136	2541,16	24451,77	21910,61	8,86	10,27	1,41
	0,00226	2541,16	24576,59	22035,44	8,86	10,27	1,41
<b>Probability of ceasing to use MEI</b>	0,00181	2541,16	24551,39	22010,24	8,86	10,29	1,43
	0,05391	2541,16	24234,65	21693,49	8,86	10,22	1,36
<b>Probability of unresolved adverse events</b>	0,06101	2541,16	24465,96	21924,80	8,86	10,27	1,41
	0,21301	2541,16	24472,68	21931,52	8,86	10,27	1,41
<b>Probability of revision surgery</b>	0,00004	2541,16	24427,37	21886,21	8,86	10,27	1,41
	0,33386	2541,16	24979,69	22438,53	8,86	10,27	1,41
<b>Probability of reimplantation</b>	0,38735	2541,16	24365,72	21824,57	8,86	10,26	1,40
	1	2541,16	24539,77	21998,61	8,86	10,28	1,42
<b>Utility of receiving no intervention</b>	0,55261	2541,16	24468,43	21927,28	8,75	10,27	1,52
	0,78474	2541,16	24468,43	21927,28	8,98	10,27	1,29
<b>Utility after receiving MEI</b>	0,46030	2541,16	24468,43	21927,28	8,86	10,15	1,29
	0,68996	2541,16	24468,43	21927,28	8,86	10,39	1,53

Table 52 – Deterministic sensitivity analysis for comparing partially implantable MEI (all monetary outcomes in AUD)

Variable	Input value	Cost of MAXUM	Cost of VSB	Incremental cost	Effectiveness of MAXUM	Effectiveness of VSB	Incremental effectiveness
Cost of MXM explantation	2196,18	13845,82	25167,89	11322,07	791,80	592,40	199,40
	3536,55	13852,66	25167,89	11315,23	791,80	592,40	199,40
Cost of MXM provision	8049,51	11174,80	25167,89	13993,09	791,80	592,40	199,40
	13415,85	16524,93	25167,89	8642,96	791,80	592,40	199,40
Cost of MXM reimplantation	5481,35	13821,86	25167,89	11346,03	791,80	592,40	199,40
	9135,58	13877,88	25167,89	11290,01	791,80	592,40	199,40
Cost of VSB explantation	2803,98	13849,87	25161,53	11311,66	791,80	592,40	199,40
	4673,30	13849,87	25173,25	11323,38	791,80	592,40	199,40
Cost of VSB provision	13957,34	13849,87	20529,50	6679,63	791,80	592,40	199,40
	23262,24	13849,87	29806,29	15956,42	791,80	592,40	199,40
Cost of VSB reimplantation	8354,84	13849,87	25119,98	11270,11	791,80	592,40	199,40
	13924,74	13849,87	25215,80	11365,93	791,80	592,40	199,40
Cost of revision surgery	817,43	13838,88	25157,61	11318,73	791,80	592,40	199,40
	1362,38	13860,85	25178,18	11317,33	791,80	592,40	199,40
Probability of AE - MXM	0,0304	13824,37	25167,89	11343,52	791,80	592,40	199,40
	0,14656	13893,93	25167,89	11273,96	791,80	592,40	199,40
Probability of ceasing MXM	0,05397	14124,56	25167,89	11043,33	766,20	592,40	173,80
	0,21630	13422,04	25167,89	11745,85	831,60	592,40	239,20
Probability of revision surgery – MXM	0,00003	13805,95	25167,89	11361,94	791,80	592,40	199,40
	0,31160	14175,54	25167,89	10992,35	791,80	592,40	199,40
Probability of unresolved AE – MXM	0,00169	13846,89	25167,89	11321,00	791,80	592,40	199,40
	0,37143	13865,73	25167,89	11302,16	791,80	592,40	199,40
Probability of AE - VSB	0,44290	13849,87	25148,20	11298,33	791,80	592,40	199,40
	0,14973	13849,87	25198,03	11348,16	791,80	592,40	199,40

Variable	Input value	Cost of MAXUM	Cost of VSB	Incremental cost	Effectiveness of MAXUM	Effectiveness of VSB	Incremental effectiveness
Probability of ceasing VSB	0,00181	13849,87	25260,71	11410,84	791,80	585,60	206,20
	0,05391	13849,87	24966,33	11116,46	791,80	611,40	180,40
Probability of revision surgery – VSB	0,00004	13849,87	25126,82	11276,95	791,80	592,40	199,40
	0,33386	13849,87	25679,15	11829,28	791,80	592,40	199,40
Probability of unresolved AE – VSB	0,06101	13849,87	25165,38	11315,51	791,80	592,40	199,40
	0,21301	13849,87	25172,24	11322,37	791,80	592,40	199,40
Probability of device failure	0,00136	13840,95	25152,83	11311,88	791,70	592,20	199,50
	0,00226	13907,66	25265,68	11358,02	792,60	593,40	199,20
Probability of reimplantation	0,38735	13802,31	25069,14	11266,83	793,20	594,90	198,30
	1,00000	13882,84	25236,46	11353,62	790,80	590,60	200,20
APHAB global scores-MXM	38,46	13849,87	25167,89	11318,02	738,5	592,4	146,10
	46,34	13849,87	25167,89	11318,02	845	592,4	252,60
APHAB global scores-VSB	20,30	13849,87	25167,89	11318,02	791,8	418	373,80
	42,70	13849,87	25167,89	11318,02	791,8	757,7	34,10
APHAB global scores-unaided	61,40	13849,87	25167,89	11318,02	783,5	591,2	192,30
	69,90	13849,87	25167,89	11318,02	799,9	593,6	206,30

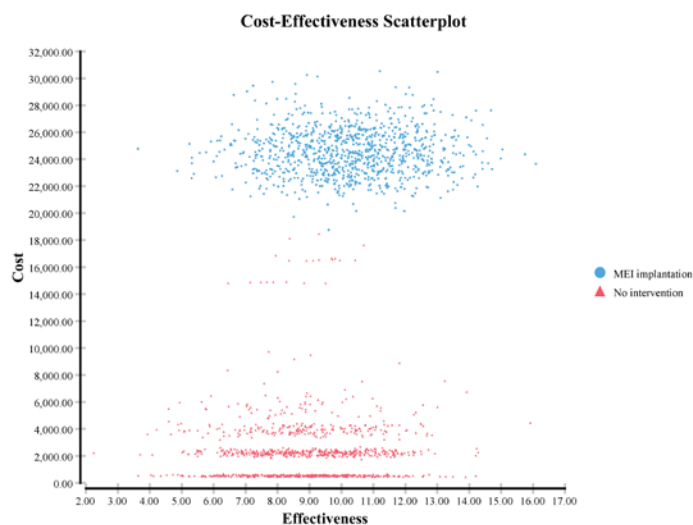


device. The probability of reimplantation plays a smaller role in the model and impacts VSB costs slightly more than MAXUM costs. Effectiveness outcomes were substantially impacted again by the probability of ceasing to use MEI. The probability of device failure and reimplantation varied these outcomes slightly, this is however not significant. Changing the input parameters of the effectiveness variables demonstrated that the model is significantly decreasing the outcomes in accordance with the inputted values.

## D.6.2. Probability sensitivity analysis

The variables found to be effective in DSA were entered into a probabilistic sensitivity analysis. For the main economic evaluation the following variables were sampled probabilistically: the probability of exostosis, the cost and probability of otitis externa, the cost of candidacy; the cost of MEI(VSB) provision, the probabilities of revision surgery and ceasing to use MEI; and the utility of being unaided or aided with MEI. The parameterisation of these variables is described in Appendix E. For the purpose of being able to repeat the outcomes, random number seeding was used with an initial seed set to 1.

The results of PSA tabulated in Table 53 show the cost and effectiveness outcomes to be similar to those reported for the base-case analysis (see Table 47) Providing a partially implantable MEI, namely the Vibrant Soundbridge, is associated with increased QALY ranging from 1,19 to 1,52 but also increased costs ranging from AUD 21.881,48 to AUD 22.265,86, when compared to receiving no intervention. The results are visualized in Figure 13.



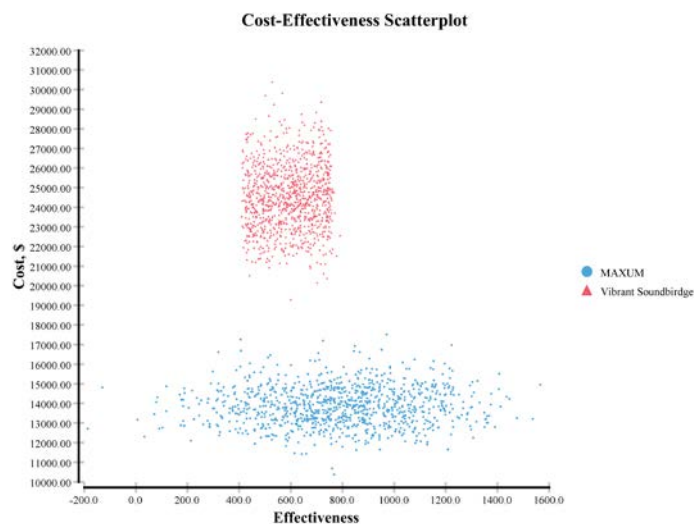
**Fig 13 – Cost-effectiveness scatterplot of the Vibrant Soundbridge against no intervention**

**Table 53 –Probabilistic sensitivity analysis for the main economic evaluation**

Strategy	Cost (95%CI)	Incremental cost	Effectiveness	Incremental effectiveness
No intervention	2469,08 (453,44 to 8339,73)	-	8,9 (5,09 to 12,49)	-
VSB implantation	24542,75 (21545,92 to 28010,05)	22073,67 (21881,48 to 22265,86)	10,26 (6,64 to 13,77)	1,36 (1,19 to 1,52)

A second PSA was carried out for comparing the two partially implantable middle ear implants. The variables sampled probabilistically included the total costs of VSB and MAXUM provision, the probabilities of revision surgery and voluntary non-use for each implant, the probability of reimplantation, the effectiveness variables for each implant system and the unaided situation. The parameterisation of these variables is also described in Appendix E. For the purpose of being able to repeat the outcomes, random number seeding was used with an initial seed set to 1.

Table 54 provides the outcomes for each middle ear implant system. The cost and effectiveness results are found similar to those reported for the base-case analysis (see Table 48) Providing the Vibrant Soundbridge is associated with increased effectiveness ranging from 176 to 211.9 but also increased costs ranging from AUD 10,505.87 to AUD 10,745.28, when compared to receiving the MAXUM. The comparison of the outcomes for the different MEI are visualized in figure 14.

**Fig 14 – Cost-effectiveness scatterplot of the Vibrant Soundbridge against the MAXUM**

**Table 54 – Probabilistic sensitivity analysis for comparing different partially implantable middle ear implants**

Strategy	Cost (95%CI)	Incremental cost	Effectiveness	Incremental effectiveness
<b>MAXUM implantation</b>	13879,8 (12099,7 to 15874)	-	786,6 (235,6 to 1301,5)	-
<b>VSB implantation</b>	24505,5 (21541,2 to 27916,3)	10625,7 (10505,87 to 10745,28)	592,6 (427,6 to 751,6)	194 (176 to 211,9)

### D.6.3. Sensitivity of the results to changes in the modelled economic evaluation

Base-case analysis as well as sensitivity analysis was conducted on an economic model discounted at a 5% rate over a 10 year time period. As a further measure of uncertainty the model was re-evaluated to assess differences in outcomes when both cost and effectiveness measures were undiscounted, and then again with the time horizon extended to 20 years.

Results for the main economic evaluation shown in Table 55 and Table 56 indicate that discounting over a 10-year time period does not influence incremental costs too much while effectiveness outcomes are significantly decreased. Comparing the discounted costs at the 10 and 20 year periods show marked differences between the costs of interventions and in the effectiveness outcomes. The incremental QALY outcomes are substantially better with the VSB over the longer time horizon.

A similar trend was observed in the cost effectiveness outcomes of the model comparing different MEI. The results summarized in Table 57 and Table 58 show not too much of a difference in costs while incremental effectiveness is significantly reduced when discounted. Over a 20-year time horizon differences in the cost and effectiveness of the two interventions become more apparent with incremental effectiveness (patient perceived difficulty) being substantially better for the Vibrant Soundbridge middle ear implant system.

Table 55 – The effect of different discount rates on the main economic model

Strategy	Cost	Incremental cost	QALY	Incremental QALY	ICER (\$/QALY)
<b>10 year undiscounted</b>					
No intervention	AUD 3.036,76	-	11,02	-	-
VSB implantation	AUD 26.059,55	AUD 23.022,79	12,77	1,75	13160,06
<b>10 year discounted</b>					
No intervention	AUD 2.541,16	-	8,86	-	-
VSB implantation	AUD 24.468,43	AUD 21.927,28	10,27	1,41	15.575,26

Table 56 – The effect of different time horizons on the main economic model

Strategy	Cost	Incremental cost	QALY	Incremental QALY	ICER (\$/QALY)
<b>10 year discounted</b>					
No intervention	AUD 2.541,16	-	8,86	-	-
VSB implantation	AUD 24.468,43	AUD 21.927,28	10,27	1,41	15.575,26
<b>20 year discounted</b>					
No intervention	AUD 3.626,74	-	13,38	-	-
VSB implantation	AUD 31.149,79	AUD 27.523,06	15,50	2,12	12986,73

Table 57 – The effect of different discount rates on the model comparing partially implantable MEI

Strategy	Cost	Incremental cost	Effective-ness	Incremental effectiveness	ICER
<b>10 year undiscounted</b>					
MXM implantation	AUD 14.685,71	-	996,78	-	-
VSB implantation	AUD 26.059,55	AUD 11.373,84	748,17	248,61	45,75
<b>10-year discounted</b>					
MXM implantation	AUD 13.849,87	-	791,79	-	-
VSB implantation	AUD 24.468,43	AUD 10.618,57	592,38	199,41	53,25

**Table 58 –The effect of different time horizons on the model comparing partially implantable MEI**

<b>Strategy</b>	<b>Cost</b>	<b>Incremental cost</b>	<b>Effective-ness</b>	<b>Incremental effectiveness</b>	<b>ICER</b>
<b>10-year discounted</b>					
MXM implantation	AUD 13.849,87	-	791,79	-	-
VSB implantation	AUD 24.468,43	AUD 10.618,57	592,38	199,41	53,25
<b>20 year discounted</b>					
MXM implantation	AUD 17.168,10	-	1332,85	-	-
VSB implantation	AUD 31.149,79	AUD 13.981,69	1026,00	306,85	45,57

## **E. Estimated extent of use and financial implications**

The purpose of this section is to generate the most likely utilisation and financial estimates by requesting a set of budget impact analyses. These analyses will inform the deliberations of MSAC about its recommendation to the Australian Government concerning the outcome of the application. A budget impact analysis (BIA) is an economic assessment that estimates the financial consequences of adopting a new intervention for local, regional and national budgets. A BIA is performed in addition to a cost-effectiveness analysis in order to provide a comprehensive economic assessment of a new health care intervention. The BIA is assessed from the payer's perspective, and uses a short-term time horizon, therefore does not use discounting or long term modeling.

A BIA identifies the size of the population affected by the intervention, and the effect of implementation on costs over the short-term. The BIA focuses is on the direct costs of specific resources needed to put the intervention into effect.

The suggested impacts presented below assume change to the ENT treatment options. These comments are presented to illustrate the potential impact of MBS listing of insertion of a partially implantable Middle Ear Implant under current conditions whilst recognising that DoHA decision making will ultimately determine the extent of use and hence financial impact.

The proposed listing will offer an additional treatment to the MBS listing. This means that given the cost-effectiveness benefit amount requested for implantation of a partially implantable Middle Ear Implant in this submission, any use of the new treatment on the MBS will be accompanied by substitution effect of opportunity costs to the society as a whole, thereby generating cost savings to the MBS on the long term and thus offsetting the costs of insertion of a partially implantable Middle Ear Implant.

Given the data in Section B, an epidemiological approach is considered to inform decision making rather than a market share approach. When compared with No treatment, implantation of a partially implantable active middle ear implant has been shown to improve the quality of life of the patient derived by QALY measures, enhancement of functional gain, speech perception in quiet and in noise and subjective benefits for the patients. This means that a specific niche population of patients that is currently left untreated can be provided with a solution to restore their hearing to a close to a normal level. The costs associated with an implant life span of approximately 20

years are also considered in this analysis.

Section E.1 describes data sources that are selected to inform the current analysis. Section E.2 estimates the likely extent of use for insertion of a partially implantable active middle ear implant over the next five years. The projected use of implantation of a partially implantable active middle ear implant is determined on the basis of the estimated Australian population growth of 1.7 % per year (available online: [http://www.ausstats.abs.gov.au/ausstats/subscriber.nsf/0/13D196FB0DBECC3BCA257C2E00173FAD/\\$File/32220\\_2012%20\(base\)%20to%202101.pdf](http://www.ausstats.abs.gov.au/ausstats/subscriber.nsf/0/13D196FB0DBECC3BCA257C2E00173FAD/$File/32220_2012%20(base)%20to%202101.pdf); downloaded 2015-09-23), which will influence the increase of number of patients per year. Besides the overall usage the financial implications associated with the expected usage are quantified. Section E.3 provides an estimation of changes in use and cost of other medical services. Section E.4 determines the estimated net financial implications of the proposed treatment for the MBS in each year over the next five years. Section E5 provides a detailed sensitivity analysis of the parameters used in the economic model addressing possible sources of uncertainty. An electronic spread sheet with calculations contained in section E is provided in Attachment F.

## **E.1 Justification of the selection of sources of data**

A literature search, though not systematic, was carried out using the search terms “incidence OR prevalence OR epidemiology” together with common outer ear pathology terms “otitis externa OR (ear) exostosis OR earwax OR cerumen” to identify epidemiological research. The best available evidence was used to conduct the estimation of the use of the proposed listing.

### **E.1.1 Prevalence of hearing loss in Australia according to DAP**

According to the decision analytical protocol provided by PASC, in Australia SNHL is the most common form of hearing loss. The overall prevalence of hearing loss  $\geq 25$  dBHTL<sup>2</sup> in adults is 20.2 % for SNHL, 0.4 % for CHL and 1.6 % for MHL (Table 59). In adults, SNHL is largely caused by ageing, with most people aged over 50 years. Sensorineural hearing loss may also be caused by congenital malformation and exposure to noise or ototoxic substances. There are more adult males with hearing loss than females (26.3 %

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<sup>2</sup> BHTL = decibels hearing threshold level.

males vs. 17.1 % females). In adults, 66 % have mild hearing loss; 23 % have moderate hearing loss and 11 % have severe to profound hearing loss.

**Table 59 - Overall prevalence of hearing impairment, South Australian population**

Age yr	≥ 25dBHTL			≥ 21dBHTL		
	SNHL	CHL	MHL	SNHL	CHL	MHL
15-50	4.0 (0.0-8.3)	0.5 (0.2-0.7)	0.8 (0.0-2.0)	5.5 (0.9-10.2)	1.0 (0.0-3.2)	0.8 (0.1-1.5)
51-60	25.5 (10.8-40.3)	0.4 (0.0-1.1)	2.4 (0.6-4.1)	28.5 (13.6-43.4)	0.4 (0.0-1.1)	1.6 (0.2-3.0)
61-70	55.5 (37.4-73.6)	0.5 (0.0-1.2)	2.7 (1.2-4.3)	64.2 (45.7-82.7)	0.5 (0.0-1.2)	3.6 (1.9-5.3)
>70	68.5 (41.3-95.7)	0.0	5.0 (0.0-11.8)	77.7 (51.4-100.0)	4.8 (0.0-11.5)	4.1 (0.0-10.6)
<b>Total</b>	<b>20.2 (14.9-25.4)</b>	<b>0.4 (0.1-0.7)</b>	<b>1.6 (0.7-2.5)</b>	<b>23.6 (18.3-29.0)</b>	<b>1.3 (0.0-2.9)</b>	<b>1.5 (0.9-2.1)</b>

Data deriving from (Wilson et al., 1999)

The overall prevalence of hearing loss in children (<15 years) is 2.5 in 1,000. Of these, it is estimated that 36.7 % have mild hearing loss; 38.3 % have moderate hearing loss, 13.3 % have severe hearing loss and 11.7 % have profound hearing loss. Sensorineural hearing loss in children may be caused by genetics, maternal infection, birthing issues or childhood infections such as meningitis. Certain population groups such as communities of Aboriginal or Torres Strait Islander people have a significantly higher prevalence of ear disease and hearing loss. For example, the rate of hearing loss in Aboriginal children is estimated at between 10 % and 41 %.

In Table 60 all data sources used for the financial estimations are summarized.



**Table 60 - Data sources used for the financial estimates**

Data retrieved	Source of data	Justification
Australian adult population	ABS	Used as the basis for the Australian epidemiological estimates.
Proportion of Australian adults with SNHL: 20.2%	Wilson et al (1999)	Used to estimate the number of eligible patients for insertion of partially implantable MEIs. Used in the Protocol provided by PASC.
Proportion of SNHL patients that would be possible candidates for MEI based on audiograms: 0.76%	Junker et al (2002)	Used to estimate the number of eligible patients for insertion of partially implantable MEIs. As stated in Section C1.1, a quite good overlap of the population cited in Junker et al. and the Australian population is given: <ul style="list-style-type: none"> <li>• Age range between 18 and 70 years.</li> <li>• No history of chronic otitis, Menière's disease, otosclerosis, central or retrocochlear lesions, systemic disease, psychiatric problems, or malignant tumors.</li> <li>• Symmetrical SNHL..</li> </ul>
Proportion of the Australian population affected by outer ear pathology (chronic otitis externa, ear canal stenosis/exostosis, excessive cerumen): 2.95%	Combined estimate, based on Agius et al (1992), DiBartolomeo et al (1979), Karlsmose et al (2001) and Ahmed et al (2009)	Used to estimate the number of eligible patients for insertion of partially implantable MEIs under the proposed MBS listing.
Proposed MBS item Schedule fee	Section A.2	As per proposed MBS item descriptor and fee in Section A.2. Used in the economic evaluation. The Assessment Report did not disaggregate the total cost of the procedure in the financial estimates. The Critique shows the breakdown of costs to the MBS.
Associated MBS items for service	Section D.4	Used in the economic evaluation
Associated non-MBS items for service	Section D.4.1 and Section D.4.2	Used in the economic evaluation. The societal costs were revised during the Critique.

### E.1.2 Prevalence of hearing loss according to the application

Prevalence of hearing loss in the better ear (Hearing thresholds  $\geq 25$  dB) in Australia was reported in a study of Wilson (Wilson et al., 1999) to be on the overall population 22.2 %. The prevalence of SNHL was increasing with age. No evidence indicating a considerable patient demand for MEI was identified in the published literature. The authors also observed that their patients' main concerns were audiological, rather than cosmetic or financial (Junker et al., 2002).

Using the prevalence data reported in Appendix F, sheet 'prevalence of pathologies' we conservatively estimate that up to 2,95 % of the Australian population (687'922) could be affected by an outer ear pathology. We would like to point out there may be an overlap between ear pathologies and that this number is conservative. The probability of a person having both a sensorineural hearing loss within our candidacy criteria, and having an outer ear pathology can thus be calculated using basic probability functions. With the numbers given above, it is estimated that 4.4 in 10'000 ( $2.95/100 \times 0.15/100$ ) may be

affected. This would estimate 1`032 potential candidates in Australia. This number is a projection of how many could be implanted over a 10-15 year period. This would provide an **average of 69-103 cases per year**.

Alternatively in 2012 according to the German OPS codes used in the G-DRG system (available from [http://www.g-drg.de/cms/Datenveroeffentlichung\\_gem. 21 KHEntgG](http://www.g-drg.de/cms/Datenveroeffentlichung_gem.21_KHEntgG)), 0.57 % of the ENT population (approx. 75`454) received a partially implantable active MEI, for sensorineural or conductive/mixed hearing loss. This equals to 431 cases of implantation. Considering that Germany has a population of approximately 82`000`000, the prevalence to the whole population would be 0.052 in 10`000. According to these estimations, 121 cases per year of implantation for either type of hearing loss can be estimated for Australia. In Germany, 27.3 % of all cases can be assigned to SNHL, 41 % to MHL and 27 % to CHL indications. Approximately 4 % of the cases cannot be assigned based on the ICD-10 codes. Applying this information to Australia it can be estimated that **33 cases** of insertion of a partially implantable Middle Ear Implant are to be expected **per year** immediately after introduction of the procedure.

The use of the insertion of partially implantable Middle Ear Implants over the next five years to 2021 is estimated based on a combination of these information. This is shown in Section E.2.1.

## **E.2 Estimation of use and costs of the proposed listing**

### **E.2.1 Historical and projected use of insertion of a partially implantable MEI**

The service numbers associated with the insertion of partially implantable Middle Ear Implants in 2017–2021 are estimated. Taking prevalence data from German data sources into account, the numbers of possible usage of the procedure can be estimated. As the proposed service is new to the MBS listing no historical data can be presented.

Based on the prevalence data provided in Section E.1, Table 61 presents the method for determining the patient population eligible to receive the proposed intervention over the first five years of an MBS listing and the maximum, minimum and average number of procedures to be expected in each year. The insertion of partially implantable MEI is likely to take place in both the private and public setting, although the extent to which procedures will be done in public hospitals is unknown so far. Table 61 accounts for a

population growth of about 1.7 % per year starting in 2016, as the listing is expected for 2016 this year is chosen as the base year.

In addition, it can be assumed that in addition to the estimated number of patients eligible for implantation in the first year, new patients with SNHL and external ear pathology will enter the pool of candidates each year. No increase in the rate of SNHL over time is taken into account.

**Table 61.- Estimated eligible population of patients <sup>3</sup>**

	Description	Method	current (2016)	2017	2018	2019	2020	2021
<b>A</b>	Australian population	ABS	24359761	24781121	25201317	25619895	26037356	26479991
<b>B</b>	Number of Australian adults	ABS	18871777	19201809	19529153	19853831	20173593	20516544
<b>C</b>	Prevalence of SNHL in the adult population (%)	Wilson et al., (1999)	20,20%	20,20%	20,20%	20,20%	20,20%	20,20%
<b>D</b>	Estimated number of Australian adults with SNHL	B x C	3812099	3878765	3944889	4010474	4075066	4144342
<b>E</b>	Proportion of patients as possible candidate for a MEI	Junker et al., (2002)	0,76%	0,76%	0,76%	0,76%	0,76%	0,76%
<b>F</b>	Number of Australian adults with SNHL and candidates of a MEI	D x E	28972	29479	29981	30480	30970	31497
<b>G</b>	Prevalence of external ear pathology in the Australian population (%)	see Table 34	2,95%	2,95%	2,95%	2,95%	2,95%	2,95%
<b>H</b>	Estimated number of Australian adults eligible for implantation	F x G	855	870	884	899	914	929
<b>I</b>	Minimum number of services per year	H / 15	57	58	59	60	61	62
<b>J</b>	Maximum number of services per year	H / 10	85	87	88	90	91	93
<b>K</b>	Mean number of services per year	Average of I & J	<b>71</b>	<b>72</b>	<b>74</b>	<b>75</b>	<b>76</b>	<b>77</b>

As stated in the critique of the assessment report, still the calculation of number of

<sup>3</sup> Reproduced from the critique of the assessment report

services each year is based on the assumption that the existing pool of eligible patients could be implanted over a 10 to 15 year period, with 10 years representing a minimum and 15 years representing a maximum number of services per year. Of course this assumption may be influenced by patients' preferences, their willingness to undergo a surgical procedure and their ability to pay out-of-pocket for additional services or non-covered device costs. "Therefore, assuming that the eligibility criteria in the proposed MBS item descriptor are adhered to, there is a potential for the number of services to be less than the estimate" given in Table 61.

Taking into consideration that patients with the medical condition (i.e., candidates for the insertion of partially implantable Middle Ear Implant) are properly examined before the implantation the number of patients that are eligible for the requested intervention equals the number of patients who are candidates not taking service restrictions into account (e.g., hospitals/surgeons are not trained to offer the service).

## E.2.2 Estimated costs of insertion of partially implantable MEIs on the MBS

Table 62 presents the estimated budget impact to the MBS. Costs for the proposed MBS fee for the insertion of partially implantable MEIs are taken from section A.2. Costs from section D.4. will be used to determine the financial implications of the service for the first five years of MBS listing. Again, these cost estimates reflect a full uptake assumption, thereby offering a conservative estimate from the perspective of the MBS. Cost offsets associated with substitution effects are determined in Section E.3.

**Table 62 - Estimated cost of proposed MBS item**

	<b>Description</b>	<b>Method</b>	<b>current (2016)</b>	<b>2017</b>	<b>2018</b>	<b>2019</b>	<b>2020</b>	<b>2021</b>
<b>L</b>	Estimated number of services per year	Table 61, row K	71	72	74	75	76	77
<b>M</b>	Cost to MBS of the proposed item	L x AUD 1,876.95	AUD 133.263	AUD 135.140	AUD 138.894	AUD 140.771	AUD 142.648	AUD 144.525

### **E.3 Estimation of changes in use and cost of other medical services**

Other MBS-funded medical services that are likely to be affected by listing the proposed medical service could not be identified. The devices are mutually exclusive to the CI and the BAHA, as was identified by the PASC committee. The proposed listing is an extension of the current treatment options for patients who suffer from a SNHL plus medical condition, as defined in Section A.

Other MBS costs associated with the insertion of the VSB include the cost of a CT scan, assistance with surgery, and anaesthetist services (pre-anaesthesia consultation, anaesthesia initiation, anaesthetist attendance for 2-2.5 hours). In addition, there are pre-operational and post-operational MBS items associated with the procedure (accounted for in details in Table 63 to Table 65. Issues relating to the cost of the implantation procedure are addressed in relation to Section D.4 Unit costs for Maxum/Soundtec were derived from appropriate MBS unit costs.

Table 63 presents the cost of other MBS items co-administered with the proposed MBS service, over the first five years of the proposed listing. Other costs associated with the implantation procedure (theatre/admission, equipment, hospital stay) are largely worn by hospital budgets, private health fund ex-gratia payments, and occasionally self-funded by patients. Although the Maxum/Soundtec system is not indicated in patients with external ear pathology (see Section A.4), the costs associated with the insertion of the Maxum/Soundtec are shown in Table 63 for comparison.

Costs of MBS items of pre-operational services are shown in Table 64 again for the first 5 years of listing.

Table 65 presents the cost of MBS items associated with post-operational services, over the first five years of the proposed listing.

In Table 66 cost to the MBS of re-implantation over the first five years of listing are presented. As discussed in Section A.2, the protocol proposed a separate MBS item for explantation or revision surgery for the MEIs. Data for revision surgery were already provided in Table 26 und Table 27 for VSB and Maxum/Soundtec, respectively, and account for 2.72 % for VSB and 1 % for Maxum/Soundtec. These percentages were used in the estimation of re-implantations costs to the MBS in the first five years of listing.

Table 67 presents the total cost of associated items to the MBS for both devices.

Table 63 - Estimated cost to the MBS of co-administered items

	Description	Method	current (2016)	2017	2018	2019	2020	2021
	<b>VSB</b>							
<b>N</b>	Cost of CT scan	Table 61, row K x AUD 290,00	AUD 20.590	AUD 20.880	AUD 21.460	AUD 21.750	AUD 22.040	AUD 22.330
<b>O</b>	Cost of anaesthesia (initiation & perfusion; MBS items 20225 & 23101)	Table 61, row K x AUD 435,60	AUD 30.928	AUD 31.363	AUD 32.234	AUD 32.670	AUD 33.106	AUD 33.541
<b>P</b>	Cost of assistance	Table 61, row K x AUD 375,39	AUD 26.653	AUD 27.028	AUD 27.779	AUD 28.154	AUD 28.530	AUD 28.905
<b>Q</b>	Total cost to MBS of associated items	N + O + P	AUD 78.170	AUD 79.271	AUD 81.473	AUD 82.574	AUD 83.675	AUD 84.776
	<b>Maxum/Soundtec</b>							
<b>R</b>	Cost of anaesthesia (initiation & perfusion; MBS items 20225 & 23032)	Table 61, row K x AUD 297,00	AUD 21.087	AUD 21.384	AUD 21.978	AUD 22.275	AUD 22.572	AUD 22.869
<b>S</b>	Cost of assistance	Table 61, row K x AUD 375,39	AUD 26.653	AUD 27.028	AUD 27.779	AUD 28.154	AUD 28.530	AUD 28.905
<b>T</b>	Cost to MBS of the proposed item	R + S	AUD 47.740	AUD 48.412	AUD 49.757	AUD 50.429	AUD 51.102	AUD 51.774

Table 64 – Estimated cost to the MBS of associated pre-operational items

	Description	Method	current (2016)	2017	2018	2019	2020	2021
<b>VSB</b>								
<b>U</b>	Cost of ENT specialist (2 visits)	Table 61, row K x AUD 85,55 x 2	AUD 12.148	AUD 12.319	AUD 12.661	AUD 12.833	AUD 13.004	AUD 13.175
<b>V</b>	Cost of facial stem monitoring	Table 61, row K x AUD 149,90	AUD 10.643	AUD 10.793	AUD 11.093	AUD 11.243	AUD 11.392	AUD 11.542
<b>W</b>	Cost of pre-anaesthesia consult	Table 61, row K x AUD 43	AUD 3.053	AUD 3.096	AUD 3.182	AUD 3.225	AUD 3.268	AUD 3.311
<b>X</b>	Cost of audiogram	Table 61, row K x AUD 49,20	AUD 3.493	AUD 3.542	AUD 3.641	AUD 3.690	AUD 3.739	AUD 3.788
<b>Y</b>	Cost of impedance audiogram	Table 61, row K x AUD 19,75	AUD 1.402	AUD 1.422	AUD 1.462	AUD 1.481	AUD 1.501	AUD 1.521
<b>Z</b>	Cost of impedance additional to audiogram	Table 61, row K x AUD 15,80	AUD 1.122	AUD 1.138	AUD 1.169	AUD 1.185	AUD 1.201	AUD 1.217
<b>AA</b>	Cost of surgery consultation	Table 61, row K x AUD 85,55	AUD 6.074	AUD 6.160	AUD 6.331	AUD 6.416	AUD 6.502	AUD 6.587
<b>AB</b>	Total cost to MBS of associated items	U + V + W + X + Y + Z + AA + AB	AUD 37.935	AUD 38.470	AUD 39.538	AUD 40.073	AUD 40.607	AUD 41.141
<b>Maxum/Soundtec</b>								
<b>AC</b>	Cost of ENT specialist	Table 61, row K x AUD 85,55	AUD 6.074	AUD 6.160	AUD 6.331	AUD 6.416	AUD 6.502	AUD 6.587
<b>AD</b>	Cost of audiogram	Table 61, row K x AUD 49,20	AUD 3.493	AUD 3.542	AUD 3.641	AUD 3.690	AUD 3.739	AUD 3.788
<b>AE</b>	Cost of surgery consultation	Table 61, row K x AUD 85,55	AUD 6.074	AUD 6.160	AUD 6.331	AUD 6.416	AUD 6.502	AUD 6.587
<b>AF</b>	Total cost to MBS of associated items	AC + AD + AE	AUD 15.641	AUD 15.862	AUD 16.302	AUD 16.523	AUD 16.743	AUD 16.963

Table 65 – Estimated cost to the MBS of associated post-operational services

	Description	Method	current (2016)	2017	2018	2019	2020	2021
<b>VSB</b>								
<b>AG</b>	Cost of brain stem evoked audiometry	Table 61, row K x AUD 153,95	AUD 10.930	AUD 11.084	AUD 11.392	AUD 11.546	AUD 11.700	AUD 11.854
<b>AH</b>	Cost of follow-up consultation (ENT/audiologist)	Table 61, row K x AUD 62,25	AUD 4.420	AUD 4.482	AUD 4.607	AUD 4.669	AUD 4.731	AUD 4.793
<b>AI</b>	Cost of ENT specialist	Table 61, row K x AUD 85,55	AUD 6.074	AUD 6.160	AUD 6.331	AUD 6.416	AUD 6.502	AUD 6.587
<b>AJ</b>	Total cost to MBS of associated items	AG + AH + AI	AUD 21.424	AUD 21.726	AUD 22.330	AUD 22.631	AUD 22.933	AUD 23.235
<b>Maxum/Soundtec</b>								
<b>AK</b>	Cost of ENT specialist (6 visits)	Table 61, row K x AUD 85,55 * 6	AUD 36.444	AUD 36.958	AUD 37.984	AUD 38.498	AUD 39.011	AUD 39.524
<b>AL</b>	Cost of follow-up consultation (ENT/audiologist; 3 visits)	Table 61, row K x AUD 62,25 * 3	AUD 13.259	AUD 13.446	AUD 13.820	AUD 14.006	AUD 14.193	AUD 14.380
<b>AM</b>	Total cost to MBS of associated items	AC + AD + AE	AUD 49.704	AUD 50.404	AUD 51.804	AUD 52.504	AUD 53.204	AUD 53.904



Table 66 – Estimated cost to the MBS of re-implantation

	Description	Method	current (2016)	2017	2018	2019	2020	2021
	<b>VSB</b>							
<b>AN</b>	Cost to MBS of re-implantation	Table 62, row M *0,0272	AUD 3.625	AUD 3.676	AUD 3.778	AUD 3.829	AUD 3.880	AUD 3.931
<b>AO</b>	Operational	Table 63, row Q x 0,0272	AUD 2.126	AUD 2.156	AUD 2.216	AUD 2.246	AUD 2.276	AUD 2.306
<b>AP</b>	Pre-operational	Table 64, row AB x 0,0272	AUD 1.032	AUD 1.046	AUD 1.075	AUD 1.090	AUD 1.105	AUD 1.119
<b>AQ</b>	Post-operational	Table 65, row AJ x 0,0272	AUD 583	AUD 591	AUD 607	AUD 616	AUD 624	AUD 632
<b>AR</b>	Total cost to MBS of re-implantation	AN + AO + AP + AQ	AUD 7.366	AUD 7.469	AUD 7.677	AUD 7.781	AUD 7.884	AUD 7.988
	<b>Maxum/Soundtec</b>							
<b>AS</b>	Cost to MBS of re-implantation	Table 62, row M x 0,01	AUD 1.333	AUD 1.351	AUD 1.389	AUD 1.408	AUD 1.426	AUD 1.445
<b>AT</b>	Operational	Table 63, row T x 0,01	AUD 477	AUD 484	AUD 498	AUD 504	AUD 511	AUD 518
<b>AU</b>	Pre-operational	Table 64, row AF x 0,01	AUD 156	AUD 159	AUD 163	AUD 165	AUD 167	AUD 170
<b>AV</b>	Post-operational	Table 65, row AM x 0,01	AUD 497	AUD 504	AUD 518	AUD 525	AUD 532	AUD 539
<b>AW</b>	Total cost to MBS of re-implantation	AS + AT + AU + AV	AUD 2.463	AUD 2.498	AUD 2.568	AUD 2.602	AUD 2.637	AUD 2.672

Table 67 – Estimated total cost of associated items to the MBS

	Description	Method	current (2016)	2017	2018	2019	2020	2021
	<b>VSB</b>							
<b>AX</b>	Total cost to MBS of associated items	Table 63, row Q + Table 64, row AB + Table 65, row AJ + Table 66, row AR	AUD 144.895	AUD 146.936	AUD 151.018	AUD 153.059	AUD 155.099	AUD 157.140
	<b>Maxum/Soundtec</b>							
<b>AY</b>	Total cost to MBS of associated items	Table 63, row T + Table 64, row AF + Table 65, row AM + Table 66, row AW	AUD 115.548	AUD 117.175	AUD 120.430	AUD 122.058	AUD 123.685	AUD 125.313

## **E.4 Net financial implications to the MBS**

Total non-MBS cost associated with the proposed intervention are calculated using the costs for hospital stay, counselling, batteries as well as the implant and processor, although these may be covered by the patient itself or private insurances. Table 68 gives an overview for the VSB and the Maxum/Soundtec over the first 5 years of listing.

The estimated overall net financial impact to the MBS of the proposed listing, including associated items, is shown in Table 69 for both devices.

Table 68 – Estimated total non- MBS costs for both devices

	Description	Method	current (2016)	2017	2018	2019	2020	2021	
	<b>VSB</b>								
<b>AZ</b>	Cost of hospital stay	Table 62, row L x AUD 591,00	AUD 41.961	AUD 42.552	AUD 43.734	AUD 44.325	AUD 44.916	AUD 45.507	
<b>BA</b>	Cost of counselling	Table 62, row L x AUD 126,75	AUD 8.999	AUD 9.126	AUD 9.380	AUD 9.506	AUD 9.633	AUD 9.760	
<b>BB</b>	Cost of batteries	Table 62, row L x AUD 52	AUD 3.692	AUD 3.744	AUD 3.848	AUD 3.900	AUD 3.952	AUD 4.004	
<b>BC</b>	Cost of re-implantation - other services	(AZ + BA + BB)*0,0272	AUD 1.487	AUD 1.507	AUD 1.549	AUD 1.570	AUD 1.591	AUD 1.612	
<b>BD</b>	Cost of VSB	Table 62, row L x AUD 13970	AUD 991.870	AUD 1.005.840	AUD 1.033.780	AUD 1.047.750	AUD 1.061.720	AUD 1.075.690	
<b>BE</b>	Cost of VSB – reimplantation	(BD - Table 62, row L x AP cost AUD 6500) x 0,0272	AUD 14.426	AUD 14.629	AUD 15.036	AUD 15.239	AUD 15.442	AUD 15.645	
<b>BF</b>	Total cost of non-MBS services	AZ + BA + BB + BC + BD + BE	AUD 1.062.435	AUD 1.077.399	AUD 1.107.326	AUD 1.122.290	AUD 1.137.254	AUD 1.152.218	
	<b>Maxum/Soundtec</b>								
<b>BG</b>	Cost of batteries	Table 62, row L x AUD 43	AUD 3.692	AUD 3.744	AUD 3.848	AUD 3.900	AUD 3.952	AUD 4.004	
<b>BH</b>	Cost of re-implantation - other services	BG x 0,01	AUD 37	AUD 37	AUD 38	AUD 39	AUD 40	AUD 40	
<b>BI</b>	Cost of Maxum/Soundtec	Table 62, row L x AUD 6848,44	AUD 486.239	AUD 493.088	AUD 506.785	AUD 513.633	AUD 520.481	AUD 527.330	
<b>BJ</b>	Cost of MAXUM – reimplantation	BI x 0,01	AUD 4.862	AUD 4.931	AUD 5.068	AUD 5.136	AUD 5.205	AUD 5.273	
<b>BK</b>	Total cost of non-MBS services	BG + BH + BI + BJ	AUD 494.831	AUD 501.800	AUD 515.739	AUD 522.708	AUD 529.678	AUD 536.647	

Table 69 – Estimated total costs for both devices to the MBS

	Description	Method	current (2016)	2017	2018	2019	2020	2021	
	<b>VSB</b>								
<b>BL</b>	Cost to MBS of the proposed item <sup>a</sup>	Table 62, row M	AUD 133.263	AUD 135.140	AUD 138.894	AUD 140.771	AUD 142.648	AUD 144.525	
<b>BM</b>	Cost to the MBS of associated items <sup>b</sup>	Table 67, row AX	AUD 144.895	AUD 146.936	AUD 151.018	AUD 153.059	AUD 155.099	AUD 157.140	
<b>BO</b>	<b>Total costs to the MBS</b>	BL + BM	<b>AUD 278.159</b>	<b>AUD 282.077</b>	<b>AUD 289.912</b>	<b>AUD 293.830</b>	<b>AUD 297.748</b>	<b>AUD 301.665</b>	
<b>BP</b>	Total non-MBS costs	Table 68, row BF	AUD 1.062.435	AUD 1.077.399	AUD 1.107.326	AUD 1.122.290	AUD 1.137.254	AUD 1.152.218	
<b>BQ</b>	<b>Overall total costs of the proposed intervention</b>	BL + BM	<b>AUD 1.340.594</b>	<b>AUD 1.359.475</b>	<b>AUD 1.397.239</b>	<b>AUD 1.416.120</b>	<b>AUD 1.435.002</b>	<b>AUD 1.453.883</b>	
	<b>Maxum/Soundtec</b>								
<b>BR</b>	Cost to MBS of the proposed item	Table 62, row M	AUD 133.263	AUD 135.140	AUD 138.894	AUD 140.771	AUD 142.648	AUD 144.525	
<b>BS</b>	Cost to the MBS of associated items	Table 67, row AY	AUD 115.548	AUD 117.175	AUD 120.430	AUD 122.058	AUD 123.685	AUD 125.313	
<b>BT</b>	<b>Total costs to the MBS</b>	BR + BS	<b>AUD 248.811</b>	<b>AUD 252.316</b>	<b>AUD 259.325</b>	<b>AUD 262.829</b>	<b>AUD 266.333</b>	<b>AUD 269.838</b>	
<b>BU</b>	Total non-MBS costs	Table 68, row BK	AUD 494.831	AUD 501.800	AUD 515.739	AUD 522.708	AUD 529.678	AUD 536.647	
<b>BV</b>	<b>Overall total costs of the proposed intervention</b>	BU + BT	<b>AUD 743.642</b>	<b>AUD 754.116</b>	<b>AUD 775.064</b>	<b>AUD 785.537</b>	<b>AUD 796.011</b>	<b>AUD 806.485</b>	

Source: Calculated by MSAC during the Critique based largely on the approach used in the Assessment Report, including corrections.

a: Includes co-administered services, pre-operational services, post-operational services, and MBS costs associated with re-implantation (assuming that 2.72% of implants will require re-implantation).

b: Includes cost of the VSB implant, processor, batteries, counselling, hospital stay, and non-MBS costs associated with re-implantation, which are met by hospital budgets, private health funds and patient self-pay.

## **E.5 Identification, estimation and reduction of uncertainty**

As demonstrated in Section D and E.2, the proposed listing of insertion of a partially implantable Middle Ear Implant can only be achieved with additional costs to the MBS.

The current analysis conservatively assumed a mean number of procedures based on epidemiological data from Australia, best available evidence research on outer ear pathologies and comparable, highly developed health care markets like Germany. As a form of sensitivity analysis, alternative scenarios (minimum and maximum numbers of procedures) were also explored.

As stated before, the estimated number of individuals affected by an outer ear pathology in the Australian population is conservative. The calculations do not account for an overlap of the medical conditions and hence may represent an underestimate of the real number of affected individuals. It is expected that the occurrence of overlapping medical conditions is rare and the impact on BIA would be minimal.

Another uncertainty is whether the recent observations regarding the German market reflect the fundamental changes to the utilisation of the MBS items. The maximum expected usage may differ from expectations but experience from countries where the service is started shows that especially during the first years the maximum number of procedures done is far beyond the estimations (overestimation of usage). The reasons for that are market development (surgeons and audiologists that have to be trained, clinics have to be convinced of the procedure, awareness has to be intensified) and especially patient awareness and knowledge has to be built up.

In general, the extent of partially implantable middle ear implant use in the target population is expected to be a good estimate. The uptake of such devices is controlled by health care practitioners and individuals need to match the candidacy criteria to receive a middle ear implant. It might happen that individuals diagnosed with mild to severe SNHL but without an outer ear medical condition are interested in receiving the proposed medical service. The provision of the service would depend on clinical opinion and individuals' willingness to fund themselves. Taking this into consideration, the derived estimates of VSB implantation may be an underestimate however the potential impact on the MBS is anticipated to be minimal.

To assess whether the above specified factors affect the budget impact analysis outcomes, deterministic sensitivity analysis was carried out. The number of candidates determined by Junker (2002) for the German market was varied from its base-case value

between its 95% lower and upper confidence intervals. Secondly, the probability of overlapping outer ear pathologies was identified from the literature and added on to the previous estimate. Based on the estimated number of affected people, the 95% lower and upper confidence intervals were calculated. All confidence intervals were calculated by applying exact binomial confidence intervals. The procedure taken is summarized in Table 70.

**Table 70.- Calculated confidence intervals for the deterministic sensitivity analysis**

		Probability	CI* lower	CI upper	Description	Source/Method
<b>Step 1</b>	<b>a</b>	0,0076	0,0069	0,0085	VSB candidates depending on their audiogram	Junker 2002
<b>Step 2</b>	<b>b</b>	0,0060	0,0050	0,0080	Individuals in the general population who have exostosis	DiBartolomeo 1979
	<b>c</b>	0,4190	0,3649	0,4745	Individuals with exostosis who also have otorrhea	House 2008
	<b>d</b>	0,0025	0,0018	0,0038	Individuals in the general population who have exostoses and otorrhea	Step 2 b x Step 2 c
	<b>e</b>	0,0320	0,0300	0,0341	Individuals with an outer ear pathology in the general population (including overlap in conditions)	CI levels calculated depending on the estimated number of affected people in Australia

\*CIs calculated as exact binomial CI

### **E.5.1 Deterministic Sensitivity Analysis on the proportion of candidates**

As the proposed service is new to the MBS listing no historical data can be presented. Instead, epidemiological data from Germany was used to calculate the estimated use of the proposed medical service in Australia.

Based on the prevalence data provided in Section E.1 and Table 70, Table 71 to Table 74 present the the patient population eligible for receiving the proposed intervention over the first five years of an MBS listing and the minimum and maximum number of procedures to be expected in each year. As described in the previous sections, the population growth is held constant at 1.7 % starting from the base year of 2016. No increase in the rate of SNHL over time is taken into account.

**Table 71.- Estimated minimum number of MEI candidates based on lower CI of proportion of candidates according to Junker et al, 2002**

Description	Method	current (2016)	2017	2018	2019	2020	2021
Australian population	ABS	24359761	24781121	25201317	25619895	26037356	26479991
Number of Australian adults	ABS	18871777	19201809	19529153	19853831	20173593	20516544
Prevalence of SNHL in the adult population (%)	Wilson et al., (1999)	20,20%	20,20%	20,20%	20,20%	20,20%	20,20%
Estimated number of Australian adults with SNHL	B x C	3812099	3878765	3944889	4010474	4075066	4144342
Minimum Proportion of patients as possible candidate for a MEI	Junker et al., (2002)	0,69%	0,69%	0,69%	0,69%	0,69%	0,69%
Number of Australian adults with SNHL and candidates of a MEI	D x E	26303	26763	27220	27672	28118	28596
Prevalence of external ear pathology in the Australian population (%)	see Table 34	2,95%	2,95%	2,95%	2,95%	2,95%	2,95%
Estimated number of Australian adults eligible for implantation	F x G	776	790	803	816	829	844
Minimum number of services per year	H / 15	52	53	54	54	55	56
Maximum number of services per year	H / 10	78	79	80	82	83	84
Mean number of services per year	Average of I & J	<b>65</b>	<b>66</b>	<b>67</b>	<b>68</b>	<b>69</b>	<b>70</b>

The estimated difference in the mean number of services per year will affect the overall costs for the proposed intervention as can be seen from the calculations in Appendix G, and Table 72.



Table 72.- Overall total costs of the intervention based on estimated minimum number of MEI candidates (lower CI of possible candidates)

	Description	Method	current (2016)	2017	2018	2019	2020	2021	
	<b>VSB</b>								
<b>BL</b>	Cost to MBS of the proposed item	Row M	AUD 121.369	AUD 123.491	AUD 125.596	AUD 127.685	AUD 129.741	AUD 131.947	
<b>BM</b>	Cost to the MBS of associated items	Row AX	AUD 131.962	AUD 134.270	AUD 136.559	AUD 138.830	AUD 141.065	AUD 143.464	
<b>BO</b>	<b>Total costs to the MBS</b>	BL + BM	<b>AUD 253.331</b>	<b>AUD 257.761</b>	<b>AUD 262.156</b>	<b>AUD 266.514</b>	<b>AUD 270.806</b>	<b>AUD 275.410</b>	
<b>BP</b>	Total non-MBS costs	Row BF	AUD 967.605	AUD 984.526	AUD 1.001.310	AUD 1.017.957	AUD 1.034.352	AUD 1.051.936	
<b>BQ</b>	<b>Overall total costs of the proposed intervention</b>	BL + BM	<b>AUD 1.220.936</b>	<b>AUD 1.242.288</b>	<b>AUD 1.263.466</b>	<b>AUD 1.284.471</b>	<b>AUD 1.305.159</b>	<b>AUD 1.327.346</b>	
	<b>Maxum/Soundtec</b>								
<b>BR</b>	Cost to MBS of the proposed item	Row M	AUD 121.369	AUD 123.491	AUD 125.596	AUD 127.685	AUD 129.741	AUD 131.947	
<b>BS</b>	Cost to the MBS of associated items	Row AY	AUD 105.235	AUD 107.075	AUD 108.900	AUD 110.711	AUD 112.494	AUD 114.406	
<b>BT</b>	<b>Total costs to the MBS</b>	BR + BS	<b>AUD 226.603</b>	<b>AUD 230.566</b>	<b>AUD 234.497</b>	<b>AUD 238.395</b>	<b>AUD 242.235</b>	<b>AUD 246.353</b>	
<b>BU</b>	Total non-MBS costs	Row BK	AUD 450.663	AUD 458.545	AUD 466.362	AUD 474.115	AUD 481.751	AUD 489.941	
<b>BV</b>	<b>Overall total costs of the proposed intervention</b>	BU + BT	<b>AUD 677.267</b>	<b>AUD 689.111</b>	<b>AUD 700.858</b>	<b>AUD 712.510</b>	<b>AUD 723.986</b>	<b>AUD 736.294</b>	

Table 73 describes the changes to the number of procedures per year taking into account the higher CI calculated for Junker et al, 2002.

**Table 73.- Estimated maximum number of MEI candidates based on lower CI of proportion of candidates according to Junker et al, 2002**

Description	Method	current (2016)	2017	2018	2019	2020	2021
Australian population	ABS	24359761	24781121	25201317	25619895	26037356	26479991
Number of Australian adults	ABS	18871777	19201809	19529153	19853831	20173593	20516544
Prevalence of SNHL in the adult population (%)	Wilson et al., (1999)	20,20%	20,20%	20,20%	20,20%	20,20%	20,20%
Estimated number of Australian adults with SNHL	B x C	3812099	3878765	3944889	4010474	4075066	4144342
Maximum Proportion of patients as possible candidate for a MEI	Junker et al., (2002)	0,85%	0,85%	0,85%	0,85%	0,85%	0,85%
Number of Australian adults with SNHL and candidates of a MEI	D x E	32403	32970	33532	34089	34638	35227
Prevalence of external ear pathology in the Australian population (%)	see Table 34	2,95%	2,95%	2,95%	2,95%	2,95%	2,95%
Estimated number of Australian adults eligible for implantation	F x G	956	973	989	1006	1022	1039
Minimum number of services per year	H / 15	64	65	66	67	68	69
Maximum number of services per year	H / 10	96	97	99	101	102	104
Mean number of services per year	Average of I & J	<b>80</b>	<b>81</b>	<b>82</b>	<b>84</b>	<b>85</b>	<b>87</b>

The estimated difference in the mean number of services per year will affect the overall costs for the proposed intervention as can be seen from the calculations in Appendix G, and Table 74.

Table 74.- Overall total costs of the intervention based on estimated maximum number of MEI candidates (higher CI of possible candidates)

	Description	Method	current (2016)	2017	2018	2019	2020	2021	
	<b>VSB</b>								
<b>BL</b>	Cost to MBS of the proposed item	Row M	AUD 149.512	AUD 152.127	AUD 154.720	AUD 157.293	AUD 159.826	AUD 162.543	
<b>BM</b>	Cost to the MBS of associated items	Row AX	AUD 162.562	AUD 165.405	AUD 168.225	AUD 171.022	AUD 173.776	AUD 176.731	
<b>BO</b>	<b>Total costs to the MBS</b>	BL + BM	<b>AUD 312.075</b>	<b>AUD 317.532</b>	<b>AUD 322.945</b>	<b>AUD 328.314</b>	<b>AUD 333.602</b>	<b>AUD 339.273</b>	
<b>BP</b>	Total non-MBS costs	Row BF	AUD 1.191.977	AUD 1.212.822	AUD 1.233.498	AUD 1.254.005	AUD 1.274.202	AUD 1.295.863	
<b>BQ</b>	<b>Overall total costs of the proposed intervention</b>	BL + BM	<b>AUD 1.504.051</b>	<b>AUD 1.530.354</b>	<b>AUD 1.556.443</b>	<b>AUD 1.582.320</b>	<b>AUD 1.607.804</b>	<b>AUD 1.635.137</b>	
	<b>Maxum/Soundtec</b>								
<b>BR</b>	Cost to MBS of the proposed item	Row M	AUD 149.512	AUD 152.127	AUD 154.720	AUD 157.293	AUD 159.826	AUD 162.543	
<b>BS</b>	Cost to the MBS of associated items	Row AY	AUD 129.637	AUD 131.904	AUD 134.152	AUD 136.383	AUD 138.579	AUD 140.935	
<b>BT</b>	<b>Total costs to the MBS</b>	BR + BS	<b>AUD 279.149</b>	<b>AUD 284.031</b>	<b>AUD 288.873</b>	<b>AUD 293.675</b>	<b>AUD 298.405</b>	<b>AUD 303.478</b>	
<b>BU</b>	Total non-MBS costs	Row BK	AUD 555.165	AUD 564.874	AUD 574.503	AUD 584.055	AUD 593.461	AUD 603.550	
<b>BV</b>	<b>Overall total costs of the proposed intervention</b>	BU + BT	<b>AUD 834.314</b>	<b>AUD 848.904</b>	<b>AUD 863.376</b>	<b>AUD 877.730</b>	<b>AUD 891.867</b>	<b>AUD 907.028</b>	

## E.5.2 Deterministic Sensitivity Analysis on external ear pathologies

A second deterministic analysis was calculated by varying the prevalence of external ear pathologies (EEP) in the Australian population. An estimate of the overlap between the medical conditions was included in the analysis and confidence intervals were applied to this estimate (see Table 70 for details). Table 75 and Table 76 report the results applying the lower CI; and Table 77 and Table 78 report the results applying the upper CI.

**Table 75.- Estimated minimum number of MEI candidates based on lower CI of external ear pathologies**

Description	Method	current (2016)	2017	2018	2019	2020	2021
Australian population	ABS	24359761	24781121	25201317	25619895	26037356	26479991
Number of Australian adults	ABS	18871777	19201809	19529153	19853831	20173593	20516544
Prevalence of SNHL in the adult population (%)	Wilson et al., (1999)	20,20%	20,20%	20,20%	20,20%	20,20%	20,20%
Estimated number of Australian adults with SNHL	B x C	3812099	3878765	3944889	4010474	4075066	4144342
Minimum Proportion of patients as possible candidate for a MEI	Junker et al., (2002)	0,76%	0,76%	0,76%	0,76%	0,76%	0,76%
Number of Australian adults with SNHL and candidates of a MEI	D x E	28972	29479	29981	30480	30970	31497
Prevalence of external ear pathology in the Australian population (%)	Calculated Minimum	3,00%	3,00%	3,00%	3,00%	3,00%	3,00%
Estimated number of Australian adults eligible for implantation	F x G	869	884	899	914	929	945
Minimum number of services per year	H / 15	58	59	60	61	62	63
Maximum number of services per year	H / 10	87	88	90	91	93	94
Mean number of services per year	Average of I & J	<b>72</b>	<b>74</b>	<b>75</b>	<b>76</b>	<b>77</b>	<b>79</b>

The estimated difference in the mean number of services per year will affect the overall costs for the proposed intervention as can be seen from the calculations in Appendix G, and Table 76.

Table 76.- Overall total costs of the intervention based on estimated minimum prevalence (lower CI of EEP)

	Description	Method	current (2016)	2017	2018	2019	2020	2021
<b>VSB</b>								
<b>BL</b>	Cost to MBS of the proposed item	Row M	AUD 135.947	AUD 138.325	AUD 140.683	AUD 143.022	AUD 145.325	AUD 147.796
<b>BM</b>	Cost to the MBS of associated items	Row AX	AUD 147.813	AUD 150.398	AUD 152.962	AUD 155.505	AUD 158.010	AUD 160.696
<b>BO</b>	<b>Total costs to the MBS</b>	BL + BM	<b>AUD 283.761</b>	<b>AUD 288.723</b>	<b>AUD 293.645</b>	<b>AUD 298.527</b>	<b>AUD 303.335</b>	<b>AUD 308.492</b>
<b>BP</b>	Total non-MBS costs	Row BF	AUD 1.083.831	AUD 1.102.786	AUD 1.121.585	AUD 1.140.232	AUD 1.158.596	AUD 1.178.293
<b>BQ</b>	<b>Overall total costs of the proposed intervention</b>	BL + BM	<b>AUD 1.367.592</b>	<b>AUD 1.391.509</b>	<b>AUD 1.415.231</b>	<b>AUD 1.438.759</b>	<b>AUD 1.461.932</b>	<b>AUD 1.486.784</b>
<b>Maxum/Soundtec</b>								
<b>BR</b>	Cost to MBS of the proposed item	Row M	AUD 135.947	AUD 138.325	AUD 140.683	AUD 143.022	AUD 145.325	AUD 147.796
<b>BS</b>	Cost to the MBS of associated items	Row AY	AUD 117.875	AUD 119.936	AUD 121.981	AUD 124.009	AUD 126.006	AUD 128.148
<b>BT</b>	<b>Total costs to the MBS</b>	BR + BS	<b>AUD 253.822</b>	<b>AUD 258.261</b>	<b>AUD 262.664</b>	<b>AUD 267.031</b>	<b>AUD 271.332</b>	<b>AUD 275.944</b>
<b>BU</b>	Total non-MBS costs	Row BK	AUD 504.796	AUD 513.624	AUD 522.380	AUD 531.065	AUD 539.618	AUD 548.791
<b>BV</b>	<b>Overall total costs of the proposed intervention</b>	BU + BT	<b>AUD 758.618</b>	<b>AUD 771.885</b>	<b>AUD 785.044</b>	<b>AUD 798.096</b>	<b>AUD 810.949</b>	<b>AUD 824.736</b>

Table 77 indicates the number of procedures to be expected applying the higher CI value of external ear pathologies.

**Table 77.- Estimated minimum number of MEI candidates based on higher CI of external ear pathologies**

Description	Method	current (2016)	2017	2018	2019	2020	2021
Australian population	ABS	24359761	24781121	25201317	25619895	26037356	26479991
Number of Australian adults	ABS	18871777	19201809	19529153	19853831	20173593	20516544
Prevalence of SNHL in the adult population (%)	Wilson et al., (1999)	20,20%	20,20%	20,20%	20,20%	20,20%	20,20%
Estimated number of Australian adults with SNHL	B x C	3812099	3878765	3944889	4010474	4075066	4144342
Minimum Proportion of patients as possible candidate for a MEI	Junker et al., (2002)	0,76%	0,76%	0,76%	0,76%	0,76%	0,76%
Number of Australian adults with SNHL and candidates of a MEI	D x E	28972	29479	29981	30480	30970	31497
Prevalence of external ear pathology in the Australian population (%)	Calculated Maximum	3,41%	3,41%	3,41%	3,41%	3,41%	3,41%
Estimated number of Australian adults eligible for implantation	F x G	988	1005	1022	1039	1056	1074
Minimum number of services per year	H / 15	66	67	68	69	70	72
Maximum number of services per year	H / 10	99	101	102	104	106	107
Mean number of services per year	Average of I & J	<b>82</b>	<b>84</b>	<b>85</b>	<b>87</b>	<b>88</b>	<b>90</b>

The estimated difference in the mean number of services per year will again affect the overall costs for the proposed intervention as can be seen from the calculations in Appendix G, and Table 78. Results of the deterministic sensitivity analysis for the base year of 2016 are summarized in Table 79.

Table 78.- Overall total costs of the intervention based on estimated minimum prevalence (lower CI of EEP)

	Description	Method	current (2016)	2017	2018	2019	2020	2021
<b>VSB</b>								
<b>BL</b>	Cost to MBS of the proposed item	Row M	AUD 154.527	AUD 157.229	AUD 159.909	AUD 162.568	AUD 165.186	AUD 167.994
<b>BM</b>	Cost to the MBS of associated items	Row AX	AUD 168.015	AUD 170.953	AUD 173.867	AUD 176.758	AUD 179.605	AUD 182.658
<b>BO</b>	<b>Total costs to the MBS</b>	BL + BM	<b>AUD 322.541</b>	<b>AUD 328.182</b>	<b>AUD 333.777</b>	<b>AUD 339.326</b>	<b>AUD 344.791</b>	<b>AUD 350.652</b>
<b>BP</b>	Total non-MBS costs	Row BF	AUD 1.231.955	AUD 1.253.500	AUD 1.274.869	AUD 1.296.064	AUD 1.316.938	AUD 1.339.326
<b>BQ</b>	<b>Overall total costs of the proposed intervention</b>	BL + BM	<b>AUD 1.554.496</b>	<b>AUD 1.581.682</b>	<b>AUD 1.608.645</b>	<b>AUD 1.635.390</b>	<b>AUD 1.661.729</b>	<b>AUD 1.689.978</b>
<b>Maxum/Soundtec</b>								
<b>BR</b>	Cost to MBS of the proposed item	Row M	AUD 154.527	AUD 157.229	AUD 159.909	AUD 162.568	AUD 165.186	AUD 167.994
<b>BS</b>	Cost to the MBS of associated items	Row AY	AUD 133.985	AUD 136.328	AUD 138.652	AUD 140.957	AUD 143.227	AUD 145.662
<b>BT</b>	<b>Total costs to the MBS</b>	BR + BS	<b>AUD 288.511</b>	<b>AUD 293.557</b>	<b>AUD 298.561</b>	<b>AUD 303.525</b>	<b>AUD 308.414</b>	<b>AUD 313.657</b>
<b>BU</b>	Total non-MBS costs	Row BK	AUD 573.785	AUD 583.819	AUD 593.772	AUD 603.644	AUD 613.366	AUD 623.793
<b>BV</b>	<b>Overall total costs of the proposed intervention</b>	BU + BT	<b>AUD 862.296</b>	<b>AUD 877.376</b>	<b>AUD 892.333</b>	<b>AUD 907.169</b>	<b>AUD 921.779</b>	<b>AUD 937.449</b>



**Table 79.- Summary of the deterministic sensitivity analysis of the BIA**

<b>Variable</b>	<b>Input value</b>	<b>Number of Australian adults with SNHL and candidates of a MEI</b>	<b>Prevalence of external ear pathology in the Australian population (%)</b>	<b>Estimated number of Australian adults eligible for implantation</b>	<b>Minimum number of services per year</b>	<b>Maximum number of services per year</b>	<b>Total costs to the MBS</b>	<b>Overall total costs of the proposed intervention</b>
<b>Proportion of patients</b>	0,69%	26303	2,95%	776	52	78	AUD 253.331	<b>AUD 1.220.936</b>
	0,85%	32403	2,95%	956	64	96	AUD 312.075	<b>AUD 1.504.051</b>
<b>Prevalence of external ear pathology</b>	3,00%	-	-	869	58	87	AUD 283.761	<b>AUD 1.367.592</b>
	3,41%	-	-	988	66	99	AUD 322.541	<b>AUD 1.554.496</b>

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