# Middle ear implants in people with hearing impairment

## QUESTION(S) TO BE ADDRESSED:

1. Are middle ear implants clinically effective in children and adults with moderate to severe sensori-neural, mixed or conductive hearing loss compared with conventional hearing aids, bone anchored hearing aids or cochlear implants?

2. Are middle ear implants cost effective in children and adults with moderate to severe sensori-neural, mixed or conductive hearing loss compared with conventional hearing aids, bone anchored hearing aids or cochlear implants?

## SUMMARY:


### Background

- Middle ear implants (MEI) are surgically implanted electronic devices which aim to correct hearing loss through stimulation of the ossicular chain or middle ear. MEIs are placed into the middle ear and generally leave the external auditory canal (EAC) open and unobstructed.
- Alternatives include conventional hearing aids of various types, bone-anchored hearing aids, and cochlear implants. A middle ear implant differs from a cochlear implant, in that the latter stimulates the auditory nerve directly.
- The basic components of MEIs are a microphone, an audio processor, a battery, a receptor and a vibration transducer which attaches to the ossicular chain. The transducer may be either piezoelectric or electromagnetic and produces vibrational energy that subsequently vibrates the ossicular chain

### Clinical Effectiveness

- We found five primary studies investigating the effectiveness of MEIs in children, seven primary studies investigating the effectiveness of MEIs in mixed populations of children and adults, four systematic reviews investigating the effectiveness of MEIs in adults (two of which were appraised in an earlier SPH/Bazian evidence review [16]) and fifteen primary studies in adults that were published after the most recent systematic review, of which seven had study populations of fifteen or more.
- Overall, there is a lack of high-level, high quality evidence investigating the effectiveness of middle ear implants in both children and adults. Evidence identified was from the findings of systematic reviews of non-randomised comparative studies and case series (for adults) and from more recently published primary non-randomised comparative studies and case series (both children and adults). No randomised studies were found. There is considerable heterogeneity in available studies regarding patient enrolment, study design, intervention, comparator, length of follow-up and outcome measures. The studies comprise small numbers of patients with a range of severities and types of hearing loss and, in studies of children, a range of underlying causes of hearing loss, which made meaningful reporting of outcomes difficult.

- In children, air conduction thresholds and speech recognition appeared to improve with MEIs compared with the unaided post-operative condition (i.e. with the implant not activated). Some studies reported improvements in functional gain and speech outcomes with MEI compared with the pre-operative condition, but often did not specify whether the pre-operative condition was aided or unaided. Studies of children only did not include patient-reported outcomes.
- Studies of mixed populations of children and adults showed similar results to those in children only. In addition, two studies included patient-reported outcomes. In one study, patients were either broadly satisfied or sometimes satisfied with their MEI; in the other study, a significant improvement was seen between the aided and unaided post-operative condition in ease of communication and listening under reverberant conditions.
- Some studies of children and mixed populations of children and adults included participants with atresia and microtia. The design of the studies, the small sample sizes and the differences in the reporting of outcomes does not allow any general conclusions to be drawn about the outcomes for this group. One study noted that participants with different atresia severities showed similar post-operative outcomes.
- In adults, there was some evidence demonstrating that MEIs appear to be effective in improving hearing from unaided pre-implantation levels in patients with sensori-neural neural hearing loss, mixed hearing loss and conductive hearing loss. Subject to the caveats associated with study design, there was also some evidence demonstrating that MEIs appear to be at least as effective as external hearing aids in patients with sensorial neural hearing loss and mixed hearing loss.
- Speech discrimination in quiet and in noise with the middle ear implant was improved when compared with unaided hearing and at least as good as (and in some studies reported as better than) the external hearing aid.
- Patient satisfaction was greater with the middle ear implant than with the external hearing aid, with improved sound quality, less canal occlusion, less feedback and improved quality of life.

**Cost Effectiveness**

- No studies were found on the cost-effectiveness of MEIs in children.
- No studies were found on the cost-effectiveness of MEIs in adults in the UK. Three economic studies of MEI conducted outside the UK were identified but their findings are not directly applicable to the UK.

**Safety**

- No safety issues were reported in any of the studies of MEIs for hearing loss in children. In studies of adults, the majority of complications reported were rare and of low severity, although the MEI appears to be associated with loss of residual hearing post implantation. Safety, and in particular safety relatively to other therapies, has not been well studied.

**Activity and Cost**

- No information was available at the time of writing this report on cost or activity associated with use of MEIs in England.

**Equity**

- We did not identify any equity issues.

# 1 Context

## 1.1 Introduction

***Hearing*** [1]

The human ear has three main parts:

- the outer ear (which includes the visible, external ear, the auditory canal and the tympanic membrane or eardrum)
- the middle ear (an air-filled space that contains the three small bones of the ossicular chain: the malleus, incus and stapes)
- the inner ear (cochlea, vestibule, and semicircular canals).

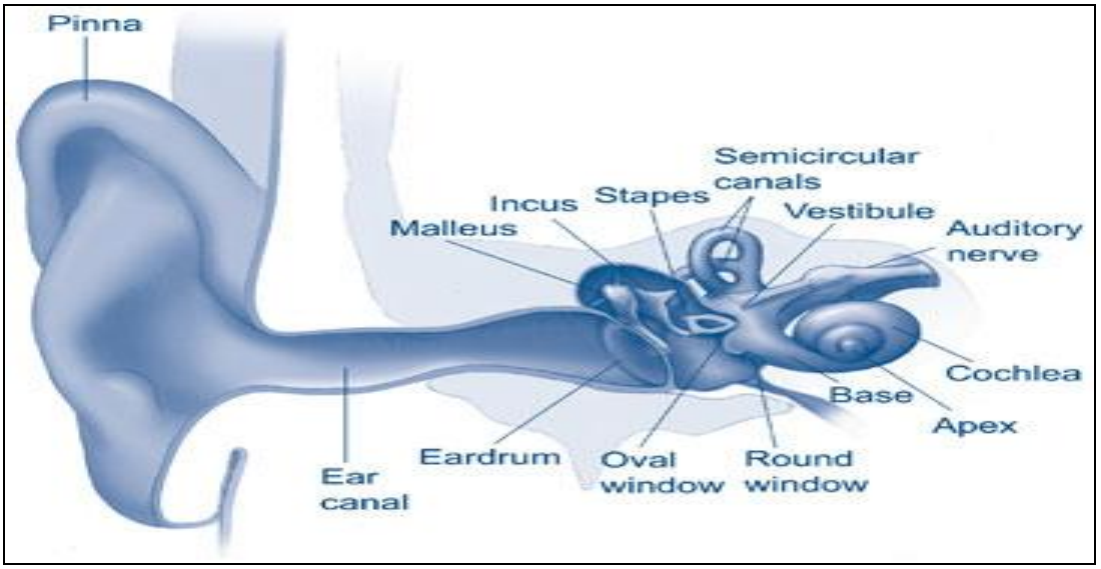


*Figure 1: The sound pathway* [2]

Hearing begins with the outer ear funneling sound waves towards the middle ear. When the sound waves reach the middle ear, they cause vibrations of the bones of the ossicular chain. These vibrations move cochlear fluid and hair cells within the inner ear, generating electrical signals that are transmitted to the brain via the auditory nerve and interpreted as sound [2]. Sound can be transmitted to the cochlea in two ways: by air conduction (through the auditory or ear canal), and by bone conduction (through the mastoid bones of the skull) [3].

Sound can be described in two ways: by pitch, measured by frequency in Hertz (Hz), and by loudness, measured in decibels (dB) [3].

***Hearing loss***

Hearing loss is diagnosed using auditory tests that compare the patient's air conduction and bone conduction hearing levels across different frequencies (high and low pitches) and thresholds (decibels) [1;4]. For people with normal hearing the minimal audible level (threshold) of a tone is less than 20 dB across all frequencies. People with higher thresholds are considered to have hearing loss, which may be classified into mild, moderate, severe and profound hearing loss (Table 1).

**Table 1: Classification of hearing impairment by hearing threshold** [5]

| *Hearing threshold (dB)* | *Level of hearing impairment* |
|---|---|
| 0-15 | Normal hearing (children) |
| 0-25 | Normal hearing (adults) |
| 15-25 | Minimal hearing loss (children) |
| 26-40 | Mild hearing loss |
| 41-55 | Moderate hearing loss |
| 56-70 | Moderate-severe hearing loss |
| 71-90 | Severe hearing loss |
| 91+ | Profound hearing loss |

The main types of hearing loss are:

- Sensori-neural hearing loss (SNHL) is the most common form of hearing loss [6;7]. It occurs where there is damage to the hair cells of the cochlea (sensory) or to the nerve pathway from the inner ear to the brain (neural). SNHL may be congenital (present at birth) or acquired and is usually permanent. SNHL can be caused by damage or malformation of the cochlea and the sensitive hairs, exposure to excessive noise, vestibular schwannomas[a], viral infections, temporal bone fractures, Meniere's disease, ototoxic medications and the ageing process.
- Conductive hearing loss (CHL) occurs when sound is not conducted efficiently from the external auditory canal (EAC) to the middle ear. This is generally caused by a blockage or damage in the outer or middle ear (or both) and may be transient or permanent.
- Mixed hearing loss (MHL) occurs when both sensori-neural and conductive hearing loss are present.
- Central hearing loss is caused by damage to the central nervous system that affects the processing of auditory signals.

Sometimes, hearing loss is categorised by its cause. For example, age-related hearing loss, is usually (in 90% of cases) caused by SNHL due to gradual damage to the hair cells of the inner ear over time [6]. Noise-related hearing loss is the second most common form of SNHL [8]. It is caused by occupational or recreational exposure to noise, such as loud music, motorcycles or the use of firearms.

***Management of hearing loss***

The management of hearing impairment will depend on the underlying cause. Options intended to improve quality of life include sign language, amplification, cochlear implant or auditory brain stem implant [9].

**Hearing aids:** A hearing aid is an electro-acoustic device that typically fits in or behind the wearer's ear, and is designed to amplify and modulate sound for the wearer. More modern devices can fit in the wearer's ear canal and digital technology has enhanced sound processing [10]. Examples are listed below [9]:

- Behind-the-ear: Where the ear mould sits inside the ear, connected to the rest of the hearing aid behind the outer ear
- In-the-ear: Similar to ear mould, though filling the opening of ear canal.
- In-the-canal: These are just visible and fill the outer part of the ear canal.
- Completely in-the-canal: Smaller and less visible than in-the-canal hearing aids.
- Body-worn: A small box containing the microphone, which can be clipped to clothes.

[a] benign primary intracranial tumor of the myelin-forming cells of the vestibulocochlear nerve (8th cranial nerve)

- Bone conduction: Recommended for conductive hearing loss or if the user can't wear a conventional hearing aid, this generates vibrations conducted through the mastoid, but can be painful.
- Bone anchored hearing aid (BAHA): A bone-anchored hearing aid has a titanium plate, which is implanted and anchored to the patient's skull. The hearing aid clips onto the pedestal, which is screwed into the mastoid. Implantation requires surgery under local anaesthesia, which takes approximately 45 minutes [10]. The bone-anchored hearing aid detects sound waves and transforms them into vibratory signals, which are transmitted to the underlying plate and bone, so that bone conduction hearing can then take place. As the bone anchored hearing aid bypasses both the external and the middle ear it can be used in patients with conductive hearing loss. Patients with sensori-neural hearing loss or mixed hearing loss may also be candidates for a bone anchored hearing aid if their bone conduction thresholds do not exceed 45 dB [10].
- Middle ear implants: Surgically implanted devices.

**Cochlear implant:** The cochlear implant bypasses missing or damaged cochlear hair cells and directly stimulates the auditory nerve to provide auditory sensation. The implantation procedure takes approximately two hours and is performed under general anaesthesia. The cochlear implant consists of an external and an implanted component. The external component contains a microphone that detects sound and transforms it from an acoustic signal to an electromagnetic signal. This signal is then sent to the implanted component via communicating magnetic coils. The implanted component (consisting of a receiver and stimulator) is placed within the cranium, behind the auricle, and generates stimulation. A cable delivers this stimulation to the electrodes placed in the scala tympani chamber of the cochlea, which then stimulate the auditory nerve [10]. Indications are listed in the NICE guidance on Cochlear implants for children and adults with severe to profound deafness 2009 [11].

**Middle ear implants (MEI):** Middle ear implants are semi- or fully-implantable devices that increase sound transmission by vibrating and moving the small bones of the middle ear (the ossicular chain), transmitting sound vibrations to the inner ear.

### 1.2 Existing national policies and guidance

In April 2013, the NHS Commissioning Board published a policy statement [12] on active middle ear implants. The policy stated the following as the commissioning position:

> *"Active middle ear implants are not routinely commissioned except under the following circumstances, as no other alternative treatment is available:*
>
> - *Patients with bilateral sensori-neural hearing loss in whom conventional hearing aids have been used and found to be medically unsuitable due to conditions of the external ear.*
> - *Patients with a mixed hearing loss in whom conventional hearing aids have been used and found to be medically unsuitable due to conditions of the external ear [including microtia and other congenital conditions] and in whom a BAHA has been implanted and been associated with medical problems of the soft tissues or loss of fixture on more than one occasion.*
>
> *For all other clinical indications, including all situations where inner ear function is normal, the active middle ear implants will only be used as part of a recognised and structured clinical research project."*

## 2 Epidemiology

It is estimated that there are approximately nine million people in the UK with a hearing impairment [13]. The prevalence of deafness by severity is shown in table 2. The prevalence of deafness varies with the age of the individual. The prevalence of a permanent hearing loss is 1 in 1000 for newborn children, and 2 in 1000 for children aged 9-16 years [13]. The increase in prevalence with age is related to later diagnosis, late onset or progressive hearing loss.

**Table 2: Estimated prevalence of hearing impairment in the UK population** [13]

| Classification | Prevalence in population | Numbers in the UK |
|---|---|---|
| Mild/slight | 16.1% | 7.6 million |
| Moderate | 4.9% | 2.3 million |
| Severe | 1% | 0.5 million |
| Profound | 0.4% | About 200,000 |

The Royal National Institute for the Deaf reported that approximately 2 million people in the UK wear a hearing aid [14].

Deafness may impact on all aspects of an individual's life though reducing their ability to communicate and integrate with family, friends and the broader community. It can effect education, employment and recreational activities [13]. An impact upon mental health is not unusual, with increased prevalence of anxiety and depression in the deaf population. The impact on the individual and their ability to communicate is influenced by many factors including: the age of onset, age of identification of the loss, type of hearing loss, the configuration of the hearing loss, auditory discrimination abilities, environmental factors and the introduction, correct provision and consistent use of aids or cochlear implants [13]. Family support is particularly important.

## 3 The intervention

Middle ear implants (MEI) are surgically implanted electronic devices which aim to correct hearing loss through stimulation of the ossicular chain or middle ear. MEIs are placed into the middle ear and generally leave the external auditory canal (EAC) open and unobstructed. The basic components of MEIs are a microphone, an audio processor, a battery, a receptor and a vibration transducer which attaches to the ossicular chain. The transducer may be either piezoelectric or electromagnetic and produces vibrational energy that subsequently vibrates the ossicular chain [10]. There are a variety of different types:

- Vibrant Soundbridge Middle Ear Implant System by Med-El
- Esteem Implantable Hearing System by Envoy Medical
- Carina Fully Implantable Hearing System by Otologics
- Middle Ear Transducer (MET) Semi-Implantable Hearing System by Otologics
- Soundtec Direct Drive Hearing System by Soundtec (this has been withdrawn from market so is not discussed further)

The Vibrant Soundbridge (VSB) Middle Ear Implant System is a semi-implantable device. The Vibrant Soundbridge consists of three components; an audio processor, a receiver and a magnetic component. The external audio processor is held in place on the scalp behind the ear by a magnet. The audio processor detects and amplifies sound waves and transforms them into electric signals, which are transmitted to the subcutaneous receiver component. The receiver transduces these signals into electromagnetic energy, creating an alternating electromagnetic

field. The magnetic component is coupled to the ossicles of the middle ear, causing them to vibrate [10].

The Esteem Implantable Hearing System is a fully implantable device. The Esteem consists of two components. A piezoelectric transducer, the sensor, is placed at the head of the incus and converts mechanical vibrations detected from the tympanic membrane to an electrical signal that is amplified, filtered, and converted back to a vibratory signal by a second piezoelectric transducer, the driver. The vibrations are transmitted to the stapes [10].

The Carina Fully Implantable Hearing System is a fully implantable device. The implant consists of a microphone, a sound processor and a transducer. The subcutaneous microphone detects sound. This is amplified and converted into an electrical signal, which is transmitted to the piezoelectric transducer. The transducer converts the electrical signal into mechanical movements, which vibrate the ossicles [15].

# 4 Findings

A search was conducted of Medline, Embase, Cochrane and TRIP on 23rd September 2014 using the search terms detailed in section 9. The search for studies in children identified those published from 2004 onwards. The search for studies in adults was limited to those published from 2012 onwards in order to update an earlier SPH/Bazian review of MEI in adults [16]. The search excluded papers on middle ear prostheses and on stapes surgery.

## 4.1 Evidence of effectiveness

Outcomes measured

*Functional gain* (in dB) is a measure of benefit provided by the device and was the primary outcome in most studies. It is calculated by determining the difference between the unaided preoperative and aided postoperative pure-tone average thresholds.

*Speech outcomes* were measured in a variety of standardised ways. For example, a 'speech detection level' is the softest level at which a person detects (rather than understands) speech sounds, whereas 'speech intelligibility in quiet' is determined using monosyllabic words presented at the conversational level (between 40-65 dB SPL). One error is counted each time an element is mispronounced or not repeated.

A variety of *patient related outcome* tools and scales are used. For example a 'Glasgow Benefit Inventory' was developed for otorhinolaryngological interventions and measures a patient's change in health status on an 18-item questionnaire completed by the patient. The Hearing Device Satisfaction Scale, Hough Ear Institute Profile and the Gothenburg Profile were used amongst others.

### 4.1.1 Studies of effectiveness in children

Five studies were found which assessed the effectiveness of MEIs in children (n=74). The studies, all comparative studies investigating the VSB, are summarised in table 3. In four studies, patients were used as their own controls, and in the fifth study, by Colletti [17] a comparison was made between children receiving VSB and others undergoing vestibulotomy with ossiculoplasty (V-OPL).

The studies were retrospective or prospective case series, each enrolling a small numbers of patients (range 5 to 23) with a range in both type (mostly conductive and/or mixed hearing loss)

and severity of hearing loss. Where stated, the underlying causes of hearing loss also varied and included oval window aplasia, osseous atresia and microtia. Although all studies reported functional gain, the comparators varied. Some studies measured pre-operative and post-operative thresholds while some measured post-operative aided and unaided (MEI switched off) thresholds.

*Functional gain*
Generally, there was no change in mean bone conduction (BC) thresholds. Overall, mean air conduction (AC) thresholds appeared better with activated MEIs compared with the unaided post-operative condition. Although some studies reported improvements with activated MEI compared with the pre-operative condition, they did not specify whether the pre-operative condition was aided or unaided.

*Speech outcome*
Speech recognition appeared to improve with activated MEIs compared with the post-operative unaided condition. Two studies reported an improvement between pre-operative and post-operative speech recognition. One of these studies (Mandala 2011) [22] did not specify whether the pre-operative testing was aided or unaided. The other study (Lesinskas 2012) [24], of only three children, reported a significant increase in aided post-operative speech perception in quiet conditions compared to best-aided pre-operative condition.

*Patient-reported outcomes*
No studies reported patient-reported outcomes.

It is to be noted that the evidence does not relate to relative effectiveness compared with other devices.

### 4.1.2 Studies of effectiveness in mixed populations of children and adults

Seven studies (n=121) were identified of MEIs in mixed populations of children and adults. The studies, summarised in table 4, were before and after studies with patients used as their own controls rather than a comparison with other devices. The studies were all retrospective, enrolled small numbers of patients (range 5 to 33) and assessed VSB. The studies reported outcomes for the whole study population and did not report on outcomes separately for children or for adults.

*Functional gain*
When reported, there was no change in mean bone conduction thresholds. For mean air conduction thresholds, four studies reported an improvement from the pre-operative unaided to the post-operative aided condition. In the two studies that reported the results of significance tests [28, 29], this difference was statistically significant. One study [Colleti 2013) [25] reported a significant improvement between the aided and unaided post-operative conditions at 24 and 60 months follow-up.

*Speech outcome*
Five studies reported an improvement in speech recognition between the pre-operative and post-operative aided conditions. When specified, the pre-operative condition was unaided. In the two studies that reported the results of significance tests [25,28], this difference was statistically significant.

It is to be noted that the evidence does not relate to relative effectiveness compared with other devices.

It should also be noted that many of the studies on children and mixed populations of children and adults did not specify whether the results reported for pre-operative testing was aided or unaided. In some studies (e.g. Colletti 2013 [25]), the inclusion criteria specified people with no benefit from and/or no acceptance of conventional air conduction and bone conduction hearing aids or bone-anchored hearing aids.

Some studies of children and children and adults included participants with atresia and microtia. The design of the studies, the small sample sizes and the differences in the reporting of outcomes does not allow any general conclusions to be drawn about the outcomes for this sub-group. One study (McKinnon 2014) [26] noted that participants with different atresia severities showed similar post-operative outcomes.

*Patient-reported outcomes*
Two studies reported patient-reported outcomes. In one study (Lim 2012) [29] patients were reported to be broadly satisfied or sometimes satisfied with their MEI. In the other study (Verhaert 2011) [30] a significant improvement was seen between the aided and unaided post-operative condition in ease of communication and listening under reverberant conditions.

### 4.1.3 Studies of effectiveness in adults

Three systematic reviews (SRs) published since January 2012 were found. Of these, two reviews by Kahue (2014) [18] and by Butler (2013) [19] investigated the effectiveness of a variety of MEIs, including VSB, in adults. A third SR by Klein (2012) [20] investigated only the Envoy Esteem and Carina MEI systems and included studies which were included in the later reviews by Kahue and Butler; it is therefore not considered further in this review. The SRs by Kahue and Butler are summarised in table 5 along with two SRs published in 2010 (by MSAC [10] and by Tysome [14]) and which were covered in an earlier rapid evidence review of MEIs in adults.

Kahue et al [18]
This SR included 17 comparative studies, published between 2001 and 2011, of MEIs in adults with varying degrees of SNHL. The studies investigated VSB (9 studies), Envoy Esteem (5) and Soundtec Direct (3). Although the search date for the SR was not specified, the review appeared to be well conducted. All of the included studies were small non-randomised comparative studies using patients as their own controls and comparing MEI with pre-operative best aided condition (12 studies) and/or pre-operative unaided condition (14 studies). Many reported only observed differences in performance, with no statistical analyses. Due to the study design of the included primary studies, all were subject to bias.

*Functional gain*
Overall, MEI improved performance compared with the pre-operative unaided condition but there was no difference between MEIs and conventional hearing aids.

Speech recognition
In quiet, MEI improved performance compared with pre-operative unaided condition but there was no difference between MEIs and conventional hearing aids. In noise, two studies showed an improvement with MEI compared with the pre-operative unaided condition; only one of these studies still showed improvement compared with the pre-operative aided condition.

*Patient-reported outcomes*
These showed improved ease of communication, improved hearing in background noise and a decrease in averseness to sound for MEIs compared with conventional hearing aids. Additional benefits of MEIs perceived by patients included improved quality of sound, elimination of

occlusive effect, and improved ability to lead an active lifestyle when compared with conventional hearing aid use.

Butler et al [19]
This SR included 14 comparative studies of MEIs in adults with symmetrical SNHL and chronic therapy-resistant external otitis. The review was well conducted. All included studies were small, non-randomised studies using patients as their own controls and comparing MEIs with conventional hearing aids; however, only four studies clearly specified the comparator as optimal best-aided condition. The review did not report on comparisons between MEI and the unaided pre-operative condition. Due to the study design of the included primary studies, all were subject to bias.

Overall, there was no difference in functional gain or speech recognition between MEI and conventional hearing aids. Some studies reported improvements in patient-reported outcomes with MEI. Three studies, reporting on a total of 127 patients, found that patient satisfaction was generally higher with MEI than with a hearing aid, but statistical significance was not reported.

MSAC [10]
This well conducted SR included comparative studies and case series published between 2006 and 2009. There was one comparative study which assessed MEI versus cochlear implants; the other comparative studies assessed MEI versus HAs. The primary studies varied widely in patient enrolment, study design and length of follow-up. They included small numbers of patients with a range of hearing severities and assessed a variety of MEI devices; most studies assessed VSB, but some also assessed devices such as MET and Esteem. 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 types of MEI and also between patients receiving the same MEI. Not all studies reported functional gain, patient-related outcomes or complications and where these were reported, different outcome measures were used. Baseline measurements were taken with either a state-of-the-art digital hearing aid, the patient's own HA or unaided. Due to the study design of the comparative studies and case series, all were subject to bias and confounding.

*Functional gain*
MEIs led to improvements from baseline in patients with SNHL, MHL and CHL. Four studies provided evidence that MEIs appear to be effective in improving hearing from baseline pre-implantation levels in patients with mild to moderate SNHL and a single study suggested that MEIs appear to be effective in improving hearing from baseline pre-implantation levels in patients with severe SNHL. Evidence assessing effectiveness of MEIs compared with external HAs suggested that MEIs were as effective in patients with SNHL. Several case series suggested MEIs improve hearing in patients with mild, moderate or severe MHL. In patients with MHL, the MEI demonstrated a mean functional gain compared with the external HA. Case series appeared to demonstrate improvement in patients with CHL, but only included 12 patients.

*Speech recognition*
Discrimination in quiet and in noise with MEIs was at least as good as or better than external HAs. Whether the comparator was the patient's walk-in hearing aid or a state-of-the-art digital hearing aid impacted on the results. The MEI tended to be better than the patient's walk-in hearing aid but the same as the digital hearing aids.

*Patient-reported outcomes*
Patient satisfaction was greater with MEIs than with external HAs with improved sound quality, canal occlusion, feedback and quality of life.

Tysome et al [14]
This review investigated whether MEIs improve hearing as much as conventional hearing aids (Has). Between 1950 and 2010, 17 relevant studies were identified with a total of 643 patients with 649 MEIs. The review was well conducted, but its conclusions were limited by the overall quality of the studies, which was judged to be poor. The studies identified contained low numbers of patients and were subject to selection bias and confounding. The significant heterogeneity between the intervention, comparators (various conventional hearing aids) and outcome measures (12 tests, 4 languages and 6 patient-related outcome measure [PROM] questionnaires) prevented pooling of results for meta-analysis and analysis for publication bias.

*Functional gain*
Three studies found functional gain of VSB to be statistically significantly better than conventional HAs and three found it to be the same. Only the MET device was found to have significantly worse functional gain when compared with conventional HAs. The review reported that overall, MEIs are as good as conventional HAs. Follow up was less than 1 year in most studies and therefore not long enough to determine long-term reliability.

*Speech recognition*
There were mixed results for speech recognition in quiet conditions, but all studies found speech perception in noise to be at least as good as conventional HAs.

*Patient-reported outcomes*
Overall patient satisfaction with the MEI was better than with the conventional HA. Patients reported better sound quality, less feedback and less occlusion.

Individual studies
In addition to the SRs, fifteen individual studies were found which were published from 2012 onwards and after the search dates (where specified) of the SRs. The study population sizes were small and ranged from 3 to 56. Of these comparative studies, the seven which included at least 15 patients are summarised in table 6; all were studies of VSB (with one study also investigating MET), in patients with CHL or MHL; one study also included patients with SNHL. All studies were subject to selection bias and confounding.

*Functional gain*
Three studies measured functional gain. There was no difference between MEI and pre-operative condition in bone conduction hearing thresholds but some improvements were reported at selected frequencies in air conduction thresholds. In some cases, it was not clear whether the pre-operative results were aided or unaided.

*Speech recognition*
Overall, there was no improvement in speech recognition between MEI and pre-operative aided condition.

*Patient-reported outcomes*
All three studies reporting only patient-reported outcomes showed improved outcomes for MEI compared with conventionally aided hearing.

**Table 3: Summary of evidence of effectiveness in studies of children only**

| Study | Patients | Intervention | Comparator | Outcomes | Comments |
|---|---|---|---|---|---|
| Colletti 2014 [17]<br><br>Retrospective cohort study | Children with hearing loss due to bilateral oval window aplasia (OWA)<br><br>n=23 (but results only reported on 19) | RW vibroplasty with VSB (RWV)<br>n=8 | Vestibulotomy with ossiculoplasty (V-OPL)<br>n=11 | **Functional gain (VSB vs. V-OPL)**<br>Mean bone conduction threshold – no significant difference at 6 months p>0.05<br>Mean air conduction thresholds (dB HL) at 6 months post-op:<br>VSB pre-op 58.3 ± 6.5; post-op 18.8± 9.9; p<0.0001<br>V-OPL pre-op 56.7± 8.4; post-op 38.6 ±17.4 p=0.02<br>p=0.01 between groups in favour of RWV<br><br>Mean air conduction thresholds (dB HL) at 36 months post-op:<br>No significant difference comparing follow-up at 6 and 36 months in RWV group p>0.05<br>Significant deterioration in V-OPL group comparing follow-up at 6 and 36 months p=0.01<br><br>**Speech outcome**<br>Speech discrimination score with VSB (% of bisyllabic words at 65 dB SPL) at 36 months: VSB increased from 12.5% to 87.5%; V-OPL increased from 14.5% to 29.1%; p<0.0001 between groups | |
| Claros 2013 [21]<br><br>Retrospective, single-subjects design | Children & adolescents with C/MHL[b]<br><br>n=22 | RW (n=13) or OW (n=9) implantation with VSB | Pre- and post-operative evaluation | **Functional gain at 3 months, post-op unaided vs. VSB aided**<br>Functional gain of 35, 34, 27dB at 1, 2, 4 kHz respectively; p<0.001<br><br>**Speech outcome, post-op unaided vs. VSB aided**<br>Post-operative word recognition score with VSB at 65 dB SPL: 97% compared to 19% unaided; p<0.001<br><br>No significant difference in unaided pre- and post-operative air conduction and bone conduction thresholds at any frequency | |
| Mandala 2011 [22]<br><br>Retrospective case series | Children with moderate to severe C/MHL<br><br>n=14 | RW implantation with VSB | Pre- and post-operative evaluation | Mean follow-up 41.7± 18.6 months<br><br>**Functional gain**<br>No change in pre-op vs post-op aided mean bone conduction threshold<br>Mean air conduction thresholds: Pre-op 66± 12.9 dB HL, post-op aided 22 ± 9.1 dB HL, p=0.0018 | Not specified if pre-op scores aided or unaided. Since study involves children who are not suited for/ unwilling to accept |

[b] Conductive/ mixed hearing loss

| | | | | | |
|---|---|---|---|---|---|
| | | | | **Speech outcome**<br>Speech understanding scores for bisyllabic words at 65 dB SPL increased from 14% pre-op to 90% post-op<br><br>No significant difference in pre-op vs. post-op BC or unaided AC | conventional HAs, pre-op scores are more likely to be unaided. |
| Roman 2012 [23]<br><br>Retrospective study | Children with C/MHL<br><br>n=10<br><br>(8 patients had microtia associated with CHL) | VSB | Pre- and post-operative evaluation | **Functional gain**<br>Mean bone conduction threshold – no change pre-op to post-op<br><br>Mean air conduction threshold – reduced by 38.02± 9dB HL<br>Pre-op 64.89± 13 dB HL vs. aided post-op 26.87dB HL± 5; p=0.002<br><br>**Speech outcome**<br>Post-op word discrimination thresholds in quiet without and with VSB activated were 50% at 72.08 dB SPL (±9 dB SPL) and 38.33 dB (±9 dB SPL) respectively WDT gain 33.75 dB (±9 dB SPL); p=0.002 | |
| Lesinskas 2012 [24]<br><br>Case series single-subjects design | Children with Treacher Collins syndrome with bilateral osseous atresia with moderate to severe CHL<br><br>n=5 (but results only reported on 3) | VSB | Pre- and post-operative evaluation | **Functional gain**<br>Mean bone conduction threshold – no change pre-op to post-op<br>Pre-op unaided 8.6±12.1 dB HL; post-op aided -11.7± 10.1 dB HL; p>0.05<br><br>Mean air conduction threshold – reduced by 44.4dB HL<br>Pre-op 67.3±8.9 dB HL post-op 22.8±5.5dB HL; p<0.001<br><br>**Speech outcome**<br>Mean word recognition score with VSB (for bisyllabic words at 65 dB SPL) increased from 0 to 97% with VSB activated. Significant improvement in VBS-activated speech perception in quiet conditions compared to pre-op best aided situation; p<0.05 | Paper indicates study population as n=5 but only reports findings for the 3 patients with Treacher Collins syndrome |

**Table 4: Summary of evidence of effectiveness in studies of mixed populations of children and adults**

| Study | Patients | Intervention | Comparator | Outcomes | Comments |
|---|---|---|---|---|---|
| Colletti 2013 [25]<br><br>Retrospective case series | Patients with moderate to severe C/MHL<br><br>n=50 (33 available for analysis) | VSB | Pre- and post-operative evaluation | **Functional gain**<br>Mean bone conduction threshold – no change pre-op to post-op<br>Mean post-op air conduction (AC) threshold without and with VSB activated: at 24 months, 82.1±11.9 dB HL (AC) vs. 30.5±9.8 (VSB-AC); p=0.0008; at 60 months, 82.7±9.7 dB HL (AC) vs. 31.9±8.8 (VSB-AC); p=0.0007<br><br>**Speech outcome**<br>Speech understanding with VSB (for bisyllabic words at 65 dB HL) increased from pre-op values of 8.5% ±5.6% to post-op aided values of 75.7% ±17.4% at 24 months and 72.4% ±15.6% at 60 months p<0.0001 for both follow-up times | No difference in outcomes between children and adults |
| McKinnon 2014 [26]<br><br>Retrospective case series | Patients with congenital aural atresia<br><br>n=28 | VSB | Pre- and post-operative evaluation | **Functional gain**<br>Pre-op bone PTA[c] (dB) = 24± 15<br>Initial aided post-op bone PTA (dB) = 28± 15<br>Long term aided post-op bone PTA (dB) = 26± 15<br><br>**Speech outcome**<br>Initial post-op (mean of 2.4 months) aided word recognition 96%; long-term post-op (mean of 17 months) aided word recognition 94%<br><br>No unaided word recognition values reported | Patients had a wide range of aural atresia severity. All atresia severities showed similar post-operative outcomes.<br><br>No p values reported |
| Zernotti 2013 [27]<br><br>Retrospective case series | Patients with congenital aural atresia<br><br>n=12 | VSB | Pre- and post-operative evaluation | **Functional gain**<br>All patients achieved individual mean functional gain >42dB with VSB at 3 months post-op for all frequencies compared to pre-op<br>General functional gain (pre-op to post-op) was 55 db for all frequencies<br><br>**Speech outcome**<br>Speech discrimination VSB aided scores (word recognition at 65dB SPL) all between 80% and 100%. Pre-op unaided scores all <40% | No p values reported |

[c] Pure tone audiometry

| | | | | | |
|---|---|---|---|---|---|
| Colletti 2011 [28]<br><br>Retrospective case series | Patients with severe MHL due to EAC[d] and middle ear malformations<br><br>n=12 (7 children, 5 adults) | VSB | Pre- and post-operative evaluation | **Functional gain**<br>Mean bone conduction threshold – no change pre-op to post-op<br>Mean air conduction threshold - pre-op unaided 69.78± 8.9 dB HL post-op aided 28. ± 8.8 67dB HL; p=0.009<br><br>**Speech outcome**<br>Speech discrimination VSB aided scores (for bisyllabic words at 65dB SPL) improved from 8.9% pre-op to 89.8% post-op aided; p=0.0095 | |
| Lim 2012 [29]<br><br>Retrospective case series | Patients with SNHL[e], C/MHL<br><br>n=7 (3 children, 4 adults) | VSB | Pre- and post-operative evaluation | **Functional gain**<br>At 12 months follow-up VSB aided thresholds for all patients were better than unaided pre-op thresholds; p=0.003<br><br>**Speech outcome (adults only)**<br>Mean SD scores in quiet –pre-op unaided 60%; 12 months post-op VSB aided 84.5%<br>Mean SD scores in noise - pre-op unaided 46%; 12 months post-op VSB aided 72%<br><br>**Hearing device satisfaction scale (HDSS)[f] (n=5)**<br>Two patients had a score of about 2 (sometimes satisfied/ dissatisfied). Three patients had a score of about 1.5 (between satisfied and sometimes satisfied/ dissatisfied) | Speech outcome tests performed only on 4 adult patients due to autism and language difficulties in the children<br><br>HDSS scores reported graphically |
| Verhaert 2011 [30]<br><br>Retrospective case series | Patients with aural atresia, all associated with a 'certain degree' of microtia<br><br>n=5 (mean age 22.4, range12 to 44 years) | VSB | Pre- and post-operative evaluation | **Functional gain**<br>At 12 months bone conduction mean functional gain (difference between pre-op unaided free-field thresholds and post-op aided) was 18.9 dB HL<br>At 12 months air conduction mean functional gain was 32.5 dB HL<br><br>**Speech outcome**<br>Speech discrimination VSB aided scores (word recognition at 65dB SPL) improved from 52% unaided to 91.4% aided | No p values reported<br><br>A difference of 10% or more on the APHAB was considered a significant difference at the |

[d] External auditory canal

[e] Sensori-neural hearing loss

[f] A 21-item questionnaire assessing the satisfaction level with hearing device in six categories of mold-related issues, sound-related issues, feedback, improvement in quality of life, ease of use and telephone use. Scores range from 0 'very satisfied' to 4 'very dissatisfied.

| | | | | | |
|---|---|---|---|---|---|
| | | | | **Abbreviated profile of hearing aid benefit questionnaires (APHAB)[g] (n=4)**<br>Significant improvement in ease of communication and listening under reverberant conditions for aided vs. unaided scores at 12 months follow-up. No significant difference between aided and unaided conditions in background noise or aversiveness to loud sounds | 95% confidence level |
| Frenzel 2009 [31]<br><br>Prospective case series | Children/young adults (median age 25, range 10 to 25 years) with unilateral microtia and osseous atresia<br><br>n=7 | VSB | Pre- and post-operative evaluation | **Functional gain**<br>Mean functional gain (difference between pre-op unaided free thresholds and post-op VSB activated) was 45.5 dB HL (at 0.5, 1,2, 3kHz warble tones) and 44.6dB HL (at 0.5, 0.75, 1, 1.5, 2, 3, 4, 6 kHz warble tones)<br><br>**Speech outcome**<br>Speech discrimination in quiet with VSB activated at 65 dB SPL was 99%,<br>Initial observation was not reported | No p values reported |

[g] This questionnaire quantifies hearing difficulties in various everyday listening situations and contains 4 subscales on ease of communication, listening to reverberate situations, listening in background noise and aversiveness to sounds. The results are presented as percentages of difficulty with listening in a score of 0% to 100%. Higher scores reflect more problems.

**Table 5: Systematic reviews on effectiveness of MEIs in adults**

| Study | Population | Intervention/s | Comparator | Outcomes | Comments |
|---|---|---|---|---|---|
| Kahue 2014 [18]<br><br>17 comparative studies | n=503<br>Average age 58.2; 57% male. All with varying degrees of SNHL | Soundtec Direct: n=190 (23 to 103)<br><br>Envoy Esteem: n=102 (7 to 57)<br><br>Vibrant Soundbridge: n=211 (6 to 54) | Pre-op performance in best aided condition (12 studies).<br><br>Pre-op unaided performance (14 studies). | Follow up inconsistently reported and highly variable in duration.<br><br>**Audiometric threshold shift after surgery**: No significant loss in AC or BC threshold changes reported after surgery. With exception of one study in which mean decline was 7dB, post-op hearing levels were within 5dB of pre-op values.<br><br>**Functional gain**: All 14 studies comparing pre-op unaided condition with post-op MEI, performance improved with MEI (weighted mean difference 25.2dB; range 15.6dB to 48.2dB). In 9 of 12 studies comparing best aided pre-op condition with post-MEI, change in PTA[h] was <10dB (weighted mean, 8.1 dB improvement; range -8.4 to 13 dB); only 1 study (in VSB) reported statistically significant improvement (8dB) compared with optimally fitted HAs.<br><br>**Speech recognition**: in quiet (12 studies), pre-op unaided vs. MEI showed improvement with MEI (weighted mean difference 44.8%; range 8.8% to 64%, SS). Compared with optimally fitted HAs, MEI showed improvement in 4 of 12 studies (1 Soundtec, 2 Esteem and 1 VSB), with 1 study (in VSB) showing decline in word recognition scores; in noise, 2 of 5 studies (VSB) showed improvement for MEI vs. unaided (13.7%, 64%, SS), 1 study (VSB) also showed improvement for MEI vs. aided (5.5%, SS[i]).<br><br>**Patient-reported outcome measures:**<br>Reported in 12 of 17 studies. APHAB used in 7 studies, of which 4 showed SS improvement in ease of communication, hearing in background noise, hearing in reverberant background and decrease in averseness to sound compared with CHA[j]. 7 studies reported improved patient satisfaction with MEI (SS reported in only 1 study). | Many studies did not include statistical comparisons between pre-operative and post-operative audiometric performance.<br><br>Methods of speech recognition performance testing highly heterogeneous (>12 tests used). |

[h] pure tone average

[i] statistically significant

[j] conventional hearing aid

| | | | | | |
|---|---|---|---|---|---|
| Butler 2013 [19]<br><br>14 comparative studies | n=617<br>(5 to 282, half of studies recruited <20 patients).<br><br>Symmetrical SNHL and chronic therapy-resistant external otitis | Variety of active MEIs including:<br>Envoy Esteem (n=7)<br><br>Otologics Middle Ear Transducer (n=292, 10 to 20)<br><br>Soundtec Direct (n=136, 10 to 103)<br><br>Vibrant Soundbridge (n=95, 6 to 53). | External HAs (all studies).<br><br>Method of comparison not described. | Follow up, where reported (13 studies), varied between 2 months and 1.5 years.<br><br>**Functional gain**: 2 studies (n=53, n=25) found VSB better than HA (one study, mean diff 14.1dB, p<0.001; second study mean diff 8 dB, p value NR); 1 study (n=7) found HAs better than Envoy MEI (mean diff NR, p<0.05); 6 studies found MEIs better than HAs but difference not clinically significant (i.e. <10dB).<br><br>**Speech recognition:**<br>3 (1 VSB, 2 Soundtec) of 9 studies reported improvement (5.3% to 26%) in speech discrimination with MEI compared with HA. No p values indicated.<br><br>Hearing in Noise Test: assessed in only 1 patient in 1 study (Envoy) and no p value indicated.<br><br>Speech Perception in Noise: 2 studies (in VSB, Soundtec) reported no significant improvement after MEI compared with HA.<br><br>**Patient-reported outcome measures:**<br>APHAB: 3 of 4 studies reported SS improvement with MEIs (VSB in 2 studies, Soundtec in 1 study) compared with HAs.<br><br>Hough Ear Institute Profile: 3 studies (n=127) found patient satisfaction higher with Soundtec MEI, no p values.<br><br>Profile of Hearing Aid Performance: in 1 study of 53 patients (VSB), a higher % reported improvement post-MEI vs HA in all 7 sub-scales of the inventory (p=0.001). | Method of data collection only reported in 1 study.<br><br>Only 4 studies clearly stated that they used optimal, best-fit or 'state-of-the-art' HA as comparator. |

| | | | | | |
|---|---|---|---|---|---|
| MSAC [10] 2010<br><br>18 comparative studies | Adults (n=450) with mild to severe SNHL or MHL. | Variety of active MEIs including:<br><br>VSB<br><br>Otologics MET and Esteem<br><br>Rion device<br><br>Soundtec<br><br>TICA | External HA (18 studies)<br><br>Cochlear implant (1 study, n=12) | MEI led to improvements in: mild, moderate and severe SNHL; SNHL of undefined severity; mild, moderate and severe mixed hearing loss; mixed hearing loss of undefined severity; and conductive hearing loss. MEI at least as effective as external HAs in patients with SNHL.<br><br>**Speech recognition:** Discrimination in quiet and in noise with the MEI at least as good or better than external HA. Whether the comparator was the patient's walk-in HA or a state-of-the-art digital HA impacted on the results. MEI tended to be better than the patient's walk-in HA but the same as the digital HAs.<br>**Patient satisfaction***:* Greater with MEI than with external HA with improved sound quality, canal occlusion, feedback and quality of life. | All studies of moderate to poor quality. |
| Tysome 2010 [14]<br><br>17 comparative studies | Adults (n=643) with SNHL or MHL | Variety of MEIs (n=649) including VSB and Otologics MET | Conventional HAs | **Functional gain**: 9 studies reported improvement with MEI. 3 found VSB significantly better than conventional HA, 3 found VSB to be the same, 1 found MET to be significantly worse than conventional HAs.<br><br>**Speech recognition** (12 different tests in 4 languages): 3 studies found speech recognition in quiet significantly better with MEI than conventional HAs and 2 found MEI were significantly worse. All studies reporting speech recognition in noise found MEIs were as good as or better than conventional HAs.<br><br>**Patient reported outcome measures** (6 validated questionnaires used by 10 studies): Overall, better with MEI than HAs. | Because of heterogeneity of outcome measures, comparisons were made by structured review rather than meta-analysis.<br><br>Quality of studies moderate to poor with short follow-up. |

**Table 6: Effectiveness studies of MEI in adults, published since 2012 and with study population of 15 or more**

| Study | Population | Intervention | Comparator | Outcomes | Comments |
|---|---|---|---|---|---|
| Atas 2014 [32]<br><br>Before and after study | 19 adults, mean age 46.6 (20 to 62) years.<br><br>Mild-moderate, moderate, or moderate-profound C/MHL | VSB (with direct placement of FMT against OW[k] (n=14) or RW (n=5)) | Pre-op assessment of conventionally-aided hearing using IOI-HA[l]. | 3 months follow up.<br><br>**Patient-reported outcomes**: Comparison of IOI-HA[e] score after 3 months showed significantly post-op better scores for total score (28.53±3.89 vs. 25.53±3.76, p<0.05) and on the sub-domains of benefit and residual participation restrictions (p<0.05). | Patients used CHAs for at least 3 months before VSB. |
| Edfeldt 2014 [33]<br><br>Before and after study | 25 adults, mean age 53 (18 to 75) years.<br><br>Bilateral hearing loss with SNHL (n=15) or C/MHL (n=10). | VSB (with incus vibroplasty in SNHL patients, RW-applied vibroplasty in C/MHL patients). | Pre-op assessment of conventionally-aided hearing using HUI[m] | **Patient-reported outcomes:** HUI[f] score for the single attribute 'hearing' before and after intervention was 0.58+/-0.29 and 0.73+/-0.08, showing improvement of 0.15 (p<0.05). Mean HUI2 and HUI3 scores also improved post-intervention (from 0.72+/-0.18 to 0.82+/-0.16, p= 0.001 for HUI2; NS change for HUI3).<br><br>Patient satisfaction (measured using GHABP[n]): 24 patients scored between 50 and 100, equivalent to a 'high VSB benefit' score. | |
| Skarzynski 2014 [34]<br><br>Retrospective case series | 21 adults, mean age 48.4 (19 to 62) years.<br><br>CHL (n=10) or MHL (n=11) (unilateral in 6 patients); radical or radical modified mastoidectomy in 1 | VSB in one ear (with direct placement of FMT[p] against RW[q]) | Pre-op assessment of MEI ear and non-MEI (opposite) ear. | 3 year follow up.<br><br>**Functional gain**: Comparison of hearing for BC[r] thresholds before and 36 months after MEI showed no significant differences for all tested frequencies for both operated and non-operated ears.<br>Comparison of AC[s] thresholds in operated ears showed significant differences between thresholds at 250 Hz before and after implantation up to 1 year after MEI and over each interval | Only 'a few' patients used HAs prior to MEI.<br><br>Not clear if non-MEI ear comparator was aided or unaided. |

[k] Oval Window

[l] International Outcome Inventory for Hearing Aids: a 7-item survey assessing daily use, benefit, residual activity limitations, satisfaction, residual participation restrictions, impact on others and quality of life. The maximum score is 35.

[m] Health Utility Index (Marks 2 and 3): a 15-item questionnaire reporting health-related quality of life (HRQL) in relation to different attributes such as hearing, vision, cognition; the single attribute, hearing, can be measured separately. According to Drummond [35] , differences of ≥0.03 in mean HUI HRQL score, and differences of ≥0.05 in a single attribute score, should be considered clinically important.

[n] Glasgow Hearing Aid Benefit Profile

| | | | | | |
|---|---|---|---|---|---|
| | or both ears before selection for MEI[o]. | | | (p=0.05). | |
| Zwartenkot 2013 [36]<br><br>Before and after study | 56 adults, mean age 60 (28 to 76) years, of whom 15 were excluded from long term evaluation.<br><br>Severe therapy-resistant external otitis. | Amongst patients followed up: VSB, n=33 (unilateral (n=29); bilateral (n=4)) MET[t], n=8 | Pre-op assessment of conventionally-aided hearing using the APHAB[g] and NCIQ[u] questionnaires | At least 2 years follow up (mean post-op follow up 7.5 years).<br>**Patient-reported outcomes:** Comparison of APHAB score after at least 2 years showed significantly post-op better scores for total score (55.6±16.6 vs. 63.3±14.8, p<0.05) and the ease of communication subscale (p<0.05).<br>Comparison of NCIQ score after at least 2 years showed significantly post-op better scores for total score (61.1±13.7 vs. 49.7±16.4, p<0.05) and on the general physical and social sub-domains (p<0.05).<br>No difference in subjective outcomes between VSB and MET patients. | 15 of 56 patients excluded from follow up because of complications (4), death (1) or post-op duration <2 years (7). All patients used CHAs before MEI. |
| Marino 2013 [37]<br><br>Before and after study | 18 adults, mean age 52.61 (24.7 to 78.5) years.<br><br>CHL (n=5) or MHL (n=13) | VSB in one ear (against RW) | Pre-op assessment of unaided and conventionally aided hearing conditions | Post-op testing at 1, 3, 6 and 12 months with the most recent result as the post-op score.<br><br>**Functional gain:** Comparison of hearing for BC thresholds at pre-op and post-op showed no statistically significant differences for all tested frequencies.<br><br>**Speech recognition:** in quiet, significant improvement with VSB (83.8%; SD[v] ±24.5%) compared to unaided pre-op testing (7.6%; SD±15.2%) (p<0.05). No significant difference between aided pre-op score (85.3%; SD±11.8%) and VSB (p=0.8).<br>In noise, significant improvement reported in scores with VSB (p<0.05). Mean scores not reported. NB % change plotted for individual scores for HA vs VSB but no summary scores shown. | In patients with bilateral hearing loss, both ears were fitted pre-operatively with CHAs. Results were obtained for patients, including those who could not tolerate consistent use of HAs. |

[p] Floating Mass Transducer
[q] Round Window
[r] Bone conduction
[s] Air conduction
[o] Middle Ear Implant
[t] Semi-Implantable Otologics MET Device (Otologics LLC, Boulder, CO, USA)
[u] Nijmegen Cochlear implant Questionnaire – A questionnaire assessing disease-related quality of life with 3 sub-domains on general physical domain (hearing and speech problems), psychological domain (self-esteem) and social domain (activity limitations and social interactions). The maximum score is 100
[v] Standard deviation

| | | | | | |
|---|---|---|---|---|---|
| Verhaert 2013 [38]<br>Retrospective case series | 16 adults, (mean age for VSB patients not reported).<br>All but 1 of the patients (from the whole study group) had MHL. | VSB against RW (n=13), OW (n=1) or clipped to the stapes (n=2). | Pre-op assessment of conventionally-aided hearing.<br><br>A 'small majority' of the subjects could not be correctly fitted with HAs pre-operatively due to local anatomical conditions | Minimum 6 months follow up.<br><br>**Speech recognition:**<br>For speech perception, with VSB the mean $SD_{65db}$ improved from 1% (SD[v] of 5) to 75% (SD of 28.7). Mean $SD_{80dB}$ improved from 25% unaided (SD 32.7) to 90% with VSB (SD 25.1).<br><br>Significance tests not reported. | The 16 VSB patients were a subgroup in a retrospective study with the primary objective of evaluating efficacy and outcome of subtotal petrosectomy with fatty obliteration before MEI placement in 22 adults. |
| Gunduz 2012 [39]<br>Before and after study | 19 adults, mean age 46.6 (20 to 62) years.<br>Patients had mild, moderate, or moderate to profound CHL or MHL. | VSB against RW (n=14) or OW (n=5) | Pre-op scores with conventional HA | Post-op follow up period not specified.<br>**Functional gain:** comparison of pre-op and post-op scores showed no significant difference in hearing threshold or functional gain[w] in the low frequencies (125 to 500 Hz). Comparison of pre-op and post-op scores showed significant improvement in the hearing threshold and functional gain in the mild and high frequencies (1000 to 8000 Hz) ($p<0.05$).<br><br>**Speech recognition:** in both soundproof and acoustic environments (signal to noise ratio of 5), there was no statistically significant difference between the pre-op conventional HA and post-op VSB scores. | Patients had been using a conventional HA for at least 3 months pre-operatively. |

[w] The functional gain of a hearing aid was defined as the difference between the aided and unaided air conduction thresholds obtained in the free field.

## 4.2 Trials in progress

A search of clinicaltrials.gov in October 2014 did not identify any ongoing trials of MEIs.

## 4.3 Evidence of cost-effectiveness

No studies were found on the cost-effectiveness of MEIs for hearing loss in children.

No studies were found on the cost-effectiveness of MEIs for hearing loss in adults in the UK. Three studies
conducted outside the UK are described here; two of the studies [10][40] were identified in the earlier SPH/Bazian review of MEIs in adults [16].

A multicentre study in Sweden and Norway [33] investigated the cost-utility of middle ear implantation in 24 patients with sensori-neural, conductive and mixed hearing loss implanted with a VSB MEI. All patients had been previously rehabilitated with conventional HAs. Multiple validated quality of life patient questionnaires were used to determine the utility gain and quality adjusted life years (QALYs). Direct treatment costs for the implantation were calculated and related to the utility gain and QALY. The cost per QALY for patients with SNHL was estimated at 7,260 Euros/QALY and for patients with C/MHL at 12,503 Euros/QALY.

MSAC conducted a cost analysis of MEI, bone-anchored HAs and cochlear implants in Australia. The first year and incremental costs (in Australian dollars) from the cost analysis are listed below [10].
1st year cost:

- Middle ear implant $23873
- Bone-anchored hearing aid $15207
- Cochlear implant $34466

Incremental costs:

- MEI rather than bone-anchored hearing aid $8666
- MEI rather than cochlear implant -$10596

A Dutch study assessed QALY gain associated with MEI in patients with severe external otitis [40]. The study concluded that based on the cost per QALY the MEI was a cost-effective and justifiable intervention in the Netherlands.

However, the findings from the three studies described here are not transferable to England due to the differing healthcare systems in the countries in which the studies were conducted.

It is important to note that the MEI is surgically implanted, which will increase the overall cost of the MEI compared with non-surgical therapies [10].

## 4.4 Safety

No safety issues were reported in any of the studies of MEIs for hearing loss in children.

Safety outcomes reported in the systematic reviews of MEIs in adults are presented in table 7. In all of these reviews, the safety of MEIs is described in absolute terms. No evidence was found on the comparative safety of MEIs compared with other therapies.

In the SR by Kahue et al [18], ten studies reported adverse events, the most common of which was device malfunction leading to explantation (11.4% of MEIs). The most commonly reported subjective complaints were pain, vertigo/dizziness and tinnitus. Less than 1% of patients had temporary facial paralysis.

In the Butler SR [19], the most commonly reported adverse events included otitis (28.1%), middle ear effusion (15%) and haematoma of the tympanic membrane or ear canal (10.3%). As with the Kahue review, the most common subjective complaint was pain (28.1%), with tinnitus (2.3%) and vertigo (1.4%) occurring less commonly. Facial palsy occurred in 5.2% of patients and perforated tympanic membrane in 5.6%. In addition to the adverse events shown in the table, individual patients in six studies included in the Butler SR suffered a decline in mean residual hearing after MEI whereas nine studies reported no significant decline in mean residual hearing.

In the MSAC report [10], most adverse events were relatively rare and of low severity and included chorda tympani nerve damage, device malfunction and migration. Serious adverse events were reported rarely and there were no deaths reported. Significant decline in residual hearing after implantation was reported by 13 studies.

Tysome's review [14] concluded that generally complications were poorly reported and only reported by 7 studies. Two studies reported a 15% revision rate. Two studies reported a significant reduction in residual hearing after middle ear implantation. The remainder of the reported complications were minor.

In relation to safety when undergoing MRI scanning, a review by Wagner et al concluded that, although there seems to be no serious risk of harm to the patient or damage to the VSB during MRIs, a dislocation of the floating mass transducer is possible. This depends on transducer position, security of the transducer to the vibratory structure and the coupling mode used [41].

**Table 7: Adverse events reported in systematic reviews of MEIs in adults**

| Study | Population | Adverse events |
|---|---|---|
| Kahue 2014 [18] | 10 (n=353) of 17 studies reported adverse events after MEI surgery | 15 of 132 (11.4%) MEIs experienced device malfunction leading to explantation.<br>4 of 87 (4.6%) Envoy Esteem patients developed wound complications leading to device explantation.<br>4 of 173 (2.3%) Soundtec patients developed tympanic membrane perforation as a result of peritympanic earmould impression fitting, and 12 of 173 (9.9%) had ear canal haematomas.<br>3 of 353 (0.8%) patients had temporary facial paralysis.<br>Most common subjective complaints included pain, dizziness and tinnitus. |
| Butler 2013 [19] | 12 (n=551) of 14 studies reported adverse events.<br>1 of the other two studies (n=28) reported no complications. | No deaths reported.<br>3 of 20 (15%) patients had middle ear effusion and 9 of 32 (28.1%) had otitis.<br>13 of 126 (10.3%) patients reported haematoma of the ear canal or tympanic membrane.<br>7 of 126 (5.6%) patients had a perforated tympanic membrane.<br>7 of 123 (5.7%) MEIs experienced device malfunction. In 3 of 58 (5.2%) MEIs, microphone and wire leads extruded. 6 of 25 (24%) experienced implantation difficulty.<br>1 of 38 (5.2%) patients had facial palsy.<br>1 of 45 (2.2%) patients had device-related wound infection.<br>The most common subjective complaints were pain (9 of 32, 28.1%), tinnitus (3 of 130, 2.3%) and vertigo (2 of 141, 1.4%).<br>Other various adverse events occurred in 27 of 146 (18.5%) patients. |
| MSAC 2010 [10] | 18 studies (n=1222) | No deaths.<br>Serious adverse events occurred rarely and included facial nerve damage.<br>Most adverse events were relatively rare and of low severity – chorda tympani nerve damage (some transient); device malfunction, migration or insufficient gain.<br>Residual hearing loss after implantation reported by most studies.<br>VSB is not MRI safe. |
| Tysome 2010 [14] | Complications poorly reported and only by 7 of 17 studies. | Most complications were minor.<br>2 studies reported 15% revision rate, 14 studies reported change in residual hearing post surgery, with only 2 reporting significant hearing loss. |

## 4.5 Summary of section 4

We found five primary studies investigating the effectiveness of MEIs in children, seven primary studies investigating the effectiveness of MEIs in mixed populations of children and adults, four systematic reviews investigating the effectiveness of MEIs in adults (two of which were appraised in an earlier SPH/Bazian evidence review [16]) and fifteen more recently published primary studies in adults, of which seven had study populations of fifteen or more.

In children, air conduction thresholds and speech recognition appeared to improve with MEIs compared with the unaided post-operative condition (i.e. with the implant not activated). Some studies reported improvements in functional gain and speech outcomes with MEI compared with the pre-operative condition, but did not specify whether the pre-operative condition was aided or unaided. Studies of children only did not include patient-reported outcomes.

Studies of mixed populations of children and adults showed similar results to those in children only. In addition, two studies included patient-reported outcomes. In one study, patients were either broadly satisfied or sometimes satisfied with their MEI; in the other study, a significant improvement was seen between the aided and unaided post-operative condition in ease of communication and listening under reverberant conditions.

Some studies of children and mixed populations of children and adults included participants with atresia and microtia. The design of the studies, the small sample sizes and the differences in the reporting of outcomes does not allow any general conclusions to be drawn about the outcomes for this group. One study noted that participants with different atresia severities showed similar post-operative outcomes.

In adults, there was some evidence demonstrating that MEIs appear to be effective in improving hearing from unaided pre-implantation levels in patients with sensori-neural neural hearing loss, mixed hearing loss and conductive hearing loss. Subject to the caveats associated with study design, there was also some evidence demonstrating that MEIs appear to be at least as effective as external hearing aids in patients with sensorial neural hearing loss and mixed hearing loss.

Speech discrimination in quiet and in noise with the middle ear implant was improved when compared with unaided hearing and at least as good as (and in some studies reported as better than) the external hearing aid.

Patient satisfaction was greater with the middle ear implant than with the external hearing aid with improved sound quality, less canal occlusion, less feedback and improved quality of life.

No studies were found on the cost-effectiveness of MEIs for hearing loss in children.

No studies were found on the cost-effectiveness of MEIs for hearing loss in adults in the UK. Three economic studies of MEI conducted outside the UK were identified but their findings are not directly applicable to the UK.

There is no comparative evidence on the safety of middle ear implants. Safety has not been well studied. Reported complications were rare and mostly of low severity. Some studies reported significant decline in residual hearing after MEI implantation.

## 5 Cost and Activity

No information on costs or activity was available at the time of writing this report.

## 6 Equity issues

We did not identify any equity issues.

# 7 Discussion and conclusions

***1. Are middle ear implants clinically effective in children and adults with moderate to severe sensori-neural, mixed or conductive hearing loss compared with conventional hearing aids, bone anchored hearing aids or cochlear implants?***

Overall, there is a lack of high-level, high quality evidence investigating the effectiveness of middle ear implants in both children and adults. Evidence identified was from the findings of systematic reviews of non-randomised comparative studies and case series (for adults) and from more recently published primary non-randomised comparative studies and case series (both children and adults). No randomised studies were found.

There is considerable heterogeneity in the available studies regarding patient enrolment, study design, intervention, comparator, length of follow-up and outcome measures. The studies comprise small numbers of patients with a range of severities and types of hearing loss, and in studies of children, a range of underlying causes of hearing loss, which made meaningful reporting of outcomes difficult.

In studies of children and mixed populations of children and adults, air conduction thresholds and speech recognition appeared to improve with MEIs compared with the unaided post-operative condition. Some improvements were also reported with MEI compared to pre-operative conditions however it was not always clear whether the pre-operative condition was aided or unaided.

In adults, there was some evidence demonstrating that MEIs appear to be effective in improving hearing and speech discrimination from unaided conditions in patients with sensori-neural neural hearing loss, mixed hearing loss and conductive hearing loss. There was also some evidence that speech discrimination in quiet and in noise was at least as good as the external hearing aid.

Patient-reported outcome were not reported in the studies of children only. In the mixed population studies, patients appeared to be generally satisfied with their MEI and one study reported improvements in ease of communication and listening under reverberant conditions compared to the unaided post-operative condition. In the adult only studies, improved sound quality, canal occlusion, feedback and quality of life were reported compared with an external hearing aid.

The MEI appears to be associated with loss of residual hearing post implantation. The majority of complications reported were rare and of low severity. However, safety and in particular safety relative to other therapies, has not been well studied.

There are a number of factors that determine suitability for middle ear implants. The patient's inner ear must be sufficiently anatomically intact to allow for implantation of the device and the patient must be fit for surgery. Patients must be fully informed of all their options and the potential complications that are associated with each option.

Larger centres would support the development of surgical skill and the opportunity to practice more than one approach to implantation as several are described in the literature. Choice of approach may be influenced by the individual anatomy of the patient

***2. Are middle ear implants cost effective in children and adults with moderate to severe sensori-neural, mixed or conductive hearing loss compared with conventional hearing aids, bone anchored hearing aids or cochlear implants?***

We found insufficient evidence to answer this question.

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## 9 Search Strategy

**Databases searched:** Medline, Embase, Cochrane and TRIP. PubMed for the last three months for any recent e-publications ahead of print publication.

**Search date:** 23 September 2014

**Medline search:**
1. (middle ear* adj5 (implant* or prosthe*)).ti,ab.
2. (middle ear* and (implant* or prosthe*)).ti.
3. ((ossicle* or ossicular or tympanic cavity or cavum tympani or oval window* or malleus or incus or stapes) adj5 (implant or prosthe*)).ti,ab.
4. ((ossicle* or ossicular or tympanic cavity or cavum tympani or oval window* or malleus or incus or stapes) and (implant or prosthe*)).ti,ab.
5. (otologics and (implant or prosthe*)).ti,ab.
6. (envoy and (implant or prosthe*)).ti,ab.
7. (med-el and (implant or prosthe*)).ti,ab.
8. (ototronix and (implant or prosthe*)).ti,ab.
9. totally integrated cochlear amplifier.ti,ab.
10. vibrant soundbridge.ti,ab.
11. esteem implantable hearing system.ti,ab.
12. maxum system.ti,ab.
13. (ossiculoplast* and (implant* or prosthe*)).ti,ab.
14. Ossicular Prosthesis/
15. Ear Ossicles/ and "Prostheses and Implants"/
16. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15
17. limit 16 to (english language and yr="2012 -Current")
18. adolescent/ or exp child/ or exp infant/
19. (child* or adolescen* or teen* or infan* or boy? or girl? or pediatric* or paediatric*).ti,ab.
20. 18 or 19
21. 16 and 20
22. limit 21 to (english language and yr="2004 -Current")

**Inclusion criteria for identification of relevant studies**

| Characteristic | Criteria |
|---|---|
| Publication type | Systematic review, meta-analysis, randomised controlled trials, prospective non-randomised clinical study, other clinical study (any type), Health economic study (any type).<br><br>Abstracts were excluded where no clinical outcomes reported, or where the paper was a non-systematic literature review, editorial, letter, laboratory or animal study.<br>Studies published as abstract only (e.g. conference poster) were excluded. |
| Patients | Children and adults with moderate to severe sensori-neural, mixed or conductive hearing loss<br>Children with congenital ears (microtia) |
| Intervention | Middle ear implant |
| Comparators | No intervention, Any other hearing devices including:<br>• air-conduction hearing aids<br>• bone-anchored hearing aids<br>• cochlear implants |

| | |
|---|---|
| Outcome | Any, including:<br>• Successful implantation<br>• Hearing quality (e.g. hearing threshold, sound localisation, speech recognition)<br>• Quality of life, patient satisfaction<br>• Functional outcomes (e.g. educational/learning outcomes)<br>• Safety/Complications<br>• Survival of device/its components<br><br>Cost/cost-effectiveness |
| Language | English only |