Technoleg Iechyd Cymru
Health Technology Wales

Topic Exploration Report

Topic explorations are designed to provide a high-level briefing on new topics submitted for consideration by Health Technology Wales. The main objectives of this report are to:

1. Determine the quantity and quality of evidence available for a technology of interest.
2. Identify any gaps in the evidence/ongoing evidence collection.
3. Inform decisions on topics that warrant fuller assessment by Health Technology Wales.

Topic exploration report number:	TER301
Topic:	Active middle ear hearing implants for complex hearing conditions.
Summary of findings:	Conventional modern-day hearing aids work well for mild-to-moderate sensorineural hearing loss. However, those with complex hearing conditions often experience poor performance. Additionally, some patients may not be able to use conventional hearing aids for medical reasons. Active middle ear implants (MEIs) have been developed as a treatment option for those patients who are either unable to wear or dissatisfied with conventional hearing aids. This topic exploration report identified two health technology assessment (HTA) reports, seven systematic reviews and three primary studies. The most recent HTA report, from the Australian Medical Services Advisory Committee (MSAC 2015), did not support public funding for the use of this device in patients with sensorineural hearing loss (SNHL) due to substantially uncertain cost-effectiveness. Likewise, the Health Technology and Policy Unit (HTPU) in Canada published a report in 2011, stating that 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 bone-anchored hearing aid (BAHA), there were no alternative treatment options at the time. Five out of seven systematic reviews compared active MEIs with conventional hearing aids (comparing pre- and post-operative outcomes) and concluded that active MEI a safe and effective option for patients unable to use conventional hearing aids. However, outcome findings were mixed, suggesting the main advantages of using active MEIs are functional gain, sound quality, and patient satisfaction. Reviews varied in their aim and/or objective and therefore also differed in their inclusion criteria (i.e., different study populations, types of active MEIs, comparisons with other hearing devices, and outcomes). Three studies (Bruchhage et al. 2017; Kliess et al. 2017; Snik et al. 2006) concluded that active MEIs were a cost-effective option. Conversely, however, the advice from MSAC (2015) did not support public funding of

	active MEIs for sensorineural hearing loss due to substantially uncertain cost effectiveness.

Introduction and aims

Implantable middle ear systems have been used for candidates that cannot benefit from conventional external amplification for medical reasons, such as external otitis, external ear aplasia, external ear skin irritations or not enough amplification with conventional hearing aids. Active MEIs are devices which aims to correct hearing loss by stimulating the middle ear. The principle of a MEI is based on the direct drive of the ossicular chain using mechanical vibrations, relayed via an implanted transducer.

Health Technology Wales researchers searched for evidence on the clinical and cost effectiveness of active MEIs for patients with complex hearing conditions.

Evidence overview

Health Technology Assessments (HTA)

We identified two health technology publications. The most recent HTA guideline by the Medical Services Advisory Committee (MSAC) in Australia as of 2015 did not support public funding for the use of this device in patients with SNHL due to substantially uncertain cost-effectiveness. MSAC acknowledged the focussed eligible patient population was better targeted to an unmet clinical need for this device and accepted the clinical effectiveness claim albeit supported by low quality data.

A HTA published in 2011 by the Health Technology and Policy Unit (HTPU) in Canada found that good quality evidence on MEIs was still lacking. In patients medically able to wear conventional hearing aids (CHAs), the evidence indicated that MEIs offers a similar improvement in functional gain to that achieved with CHAs 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 CHA, MEI appears to offer a viable treatment option. This report also stated that 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 at the time.

Systematic Reviews

We identified seven systematic reviews on the effectiveness of active MEIs (Butler et al. 2013, Ernst et al. 2016, Kahue et al. 2014, Klein et al. 2012, Schwab et al. 2020, Tysome et al. 2011; Bruchhage et al. 2017). These reviews varied in their aim/objective and therefore also differed in their inclusion criteria (i.e., different study populations, types of active MEIs, comparisons with other hearing devices, and outcomes). Overall, the systematic reviews concluded that active MEIs are a safe and/or effective treatment option for hearing loss. However, all of the reviews also noted limitations of the available evidence, including variation in the study designs (e.g., retrospective, non-comparative or comparison of pre- and post-MEI), heterogeneity in outcomes reported, and poor/moderate quality of data. Older systematic review findings (Tysome et al. 2011 and Klein et al. 2012) were less certain of outcomes due to the smaller evidence base at that time.

Five of the reviews included comparisons between MEIs and conventional hearing aids; comparisons were made pre- and post-MEI use. No randomised controlled data was identified.

Butler et al. (2013) reviewed the effectiveness of active MEIs in people with sensorineural hearing loss, compared with external hearing aids (14 studies). They concluded that the active MEI appears

to be as effective as external hearing aids in improving hearing outcomes in patients with sensorineural hearing loss. Nine studies reported on the primary outcome of functional gain; One found that the MEI was significantly better than external hearing aids ($p < 0.001$), while another found that external hearing aids were generally significantly better than MEIs ($p < 0.05$). Six of the seven remaining studies found that MEIs were better than external hearing aids, although generally, no clinically significant difference (i.e., ≥10 dB) was seen.

Kahue et al. (2014) reviewed the safety and efficacy of three MEIs approved for use by the Food and Drug Administration in the US, for the rehabilitation of sensorineural hearing loss (17 studies). In their findings, all three types of MEIs provided significant increases in functional gain over unaided hearing. However, only one of 12 studies demonstrated a statistically significant improvement over optimally fitted hearing aids. Similarly, seven of 12 studies revealed no statistically significant advantage of MEIs over optimally fitted hearing aids, whereas four found improvement, and one demonstrated inferior performance. When assessing patient-reported outcomes, most studies demonstrated improvements about sound clarity, occlusion effect, and feedback. Thus, the objective audiometric benefits derived from MEIs are comparable to those received from conventional hearing aids, whereas patient-reported outcomes demonstrate potential advantages.

Klein et al. (2012) conducted a systematic review of the safety and effectiveness of active MEIs (specifically the Carina and Esteem systems; 20 studies). 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 (at the time of publication), these devices seemed to offer a relatively safe and effective treatment option, particularly for patients who are medically unable to wear conventional hearing aids.

Tysome et al. (2011) reviewed the effectiveness of MEIs in comparison to conventional hearing aids in adults with sensorineural hearing loss (17 studies). The evidence supports the use of MEIs because, overall, they do not decrease residual hearing, but result in a functional gain in hearing comparable to conventional hearing aids and may improve perception of speech in noise and sound quality. However, methods of statistical comparison varied. Of the six studies where functional gain of the Vibrant Soundbridge (VSB) was reported, three found the functional gain to be significantly better than conventional hearing aids, and three found it to be the same. This suggests that the VSB has a functional gain at least as good as, if not better than, conventional hearing aids. Of the remaining studies, only the MET fully implantable MEI had a significantly worse functional gain when compared with conventional hearing aids. The studies also indicate that perception of speech in noise may be better with MEIs than conventional hearing aids, and that patient satisfaction with MEIs was better than conventional hearing aids overall. Patients reported better sound quality, less feedback, and occlusion.

Both Ernst et al. 2016 and Bruchhage et al. 2017 assessed the safety and effectiveness of a specific active MEI system (Vibrant Soundbridge).

Ernst et al. (2016) assessed the safety and effectiveness of the Vibrant Soundbridge compared to ear reconstruction surgery plus hearing aids. In general, the VSB proved to be safe and effective when compared to no intervention and bone conduction hearing implants (BCHI) and provided more and consistent hearing gain compared to middle ear surgery plus conventional hearing aids. The study concluded that the VSB as an active device offers an effective alternative for patients with mixed hearing loss and failed previous tympanoplasties when classical ossiculoplasty could not provide enough functional gain. Likewise, Bruchhage et al. 2017 concluded that the VSB is a highly reliable and a safe device which significantly improves perception of speech in noisy situations with a high

sound quality. In addition, the subjective benefit of the VSB was found to be mostly significant in all their studies.

Primary studies

We identified two studies comparing MEIs to conventional hearing aids (pre- and post-operative). McRackan et al. (2018) conducted a review of audiological data from a prospective FDA clinical trial (91 participants). Compared to conventional hearing aids, MEIs resulted in better mean word recognition (77.6% versus 81.8%). However, Uhler et al. 2016 found that there was no difference in performance between an appropriately fit CHA and the MEI at 12 months but indicates MEIs have the potential to help individuals who choose not to use CHAs.

One other study compared the quality of life in patients with bilateral active MEIs to their quality of life when they were unilaterally implanted (Seebacher et al. 2020). In their findings, usage of a second active middle ear implant substantially improved patients' subjective hearing and general quality of life compared with unilateral use. The increase in quality of life may be linked to improved speech understanding due to bilateral use of a middle ear implant.

Economic evidence

Three studies included economic evidence.

In Kliess et al. 2017, a Markov model was developed and analysed as microsimulation to estimate the incremental cost utility ratio of partially implantable active MEIs compared with no (surgical) intervention in individuals with sensorineural hearing loss and an outer ear medical condition in Australia. Compared with baseline strategy, active MEIs yielded an incremental cost of Australian dollars (AUD) 13,339.18, incremental quality adjusted life year (QALY) of 1.35, and an ICUR of AUD 9,913.72/QALY. The study concluded that partially implantable active MEIs offer a safe and cost-effective solution compared with no intervention.

Snik et al. (2006) designed a cost-effectiveness analysis using single-subject repeated measures of quality of life and total cost determinations. Mean health utility gain (individual change mean 95% CI) was 0.046 (0.012 to 0.079 (p = 0.01), measured using the mental component of the SF-36. With a mean profitable time of 19.4 years and an overall cost of euro 14,354, minimal cost-effectiveness of middle-ear implantation was euro 16,085/QALY. Based on the cost per QALY, middle-ear implantation proved to be a cost-effective and justified health care intervention in the Netherlands.

Finally, Kahue et al. (2014) noted that, in terms of cost, as of 2014, the cost of MEIs was approximately three to five times that of hearing aids when totalling audiologic and clinic fees with device and operative costs.

Ongoing research

There is one on-going systematic review related to our inclusion criteria entitled, ‘Quality of life and hearing with the use of middle ear implant: a systematic revision and meta-analysis’. They are yet to have their results published. The actual start date commenced in October 2017 and the anticipated completion date was due in April 2021 (Vasquez and Beto 2017).

Areas of uncertainty

- The current proposed population (complex hearing loss) is a broad condition area that would require refining for appraisal.
- The systematic reviews in this report included different comparators, e.g., conventional hearing aids, ear reconstruction surgery, bone-conduction hearing aids, no aid. If this topic was to proceed to fuller appraisal, consideration would be needed as to what comparators would be appropriate to include. However, refining the population would mean restricting the evidence base, as we identified different evidence for different types of hearing loss.
- A fuller appraisal would be required to ascertain the appropriateness of the evidence as all the reviews noted limitations of the available evidence, including variation in the study designs, and heterogeneity in outcomes reported.

Literature search results

Health Technology Assessments and Guidance

Hearing loss in adults: assessment and management - NICE guideline [NG98] Published: 21 June 2018
Available at: https://www.nice.org.uk/guidance/ng98

Hearing loss in adults (Quality Standard [QS185]: Published 10th July 2019)
Quality Statement 5: Provision of hearing aids
Available at: https://www.nice.org.uk/guidance/qs185

Active middle ear implant for sensorineural hearing loss – Medical Services Advisory Committee, Australia. Published: 2015. Available at: https://database.inahta.org/article/16448

Middle ear implants for the treatment of hearing loss - Health Technology and Policy Unit (HTPU), Canada. Published: 2011. Available at: https://open.alberta.ca/dataset/6c2d9c40-724a-4275-8a02-6a7358bee003/resource/bd8d320c-c804-4c6b-8725-4a152a7dd6c4/download/AHTDP-MEI-UofA-STE.pdf

Evidence reviews and economic evaluations

Butler CL, Thavaneswaran P, Lee IH. (2013). Efficacy of the active middle-ear implant in patients with sensorineural hearing loss. The Journal of laryngology and otology. 127 Suppl 2(S2): S8-16. doi: 10.1017/S0022215113001151. Available at: https://pubmed.ncbi.nlm.nih.gov/23790515/

Ernst A, Todt I, Wagner J. (2016). Safety and effectiveness of the Vibrant Soundbridge in treating conductive and mixed hearing loss: A systematic review. The Laryngoscope. 126(6): 1451-7. doi: 10.1002/lary.25670. Available at: https://pubmed.ncbi.nlm.nih.gov/26468033/

Kahue CN, Carlson ML, Daugherty JA, et al. (2014). Middle ear implants for rehabilitation of sensorineural hearing loss: a systematic review of FDA approved devices. Otology & neurotology : official publication of the American Otological Society, American Neurotology Society [and] European Academy of Otology and Neurotology. 35(7): 1228-37. doi: 10.1097/MAO.0000000000000341. Available at: https://pubmed.ncbi.nlm.nih.gov/24643033/

Klein K, Nardelli A, Stafinski T. (2012). A systematic review of the safety and effectiveness of fully implantable middle ear hearing devices: the carina and esteem systems. Otology & neurotology : official publication of the American Otological Society, American Neurotology Society [and] European Academy of Otology and Neurotology. 33(6): 916-21. doi: 10.1097/MAO.0b013e31825f230d. Available at: https://pubmed.ncbi.nlm.nih.gov/22772013/

Schwab B, Wimmer W, Severens JL, et al. (2020). Adverse events associated with bone-conduction and middle-ear implants: a systematic review. European Archives of Oto-Rhino-Laryngology. 277(2): 423-38. doi: https://dx.doi.org/10.1007/s00405-019-05727-8

Tysome JR, Moorthy R, Lee A, et al. (2011). Systematic review of middle ear implants: do they improve hearing as much as conventional hearing aids? Database of Abstracts of Reviews of Effects (DARE). Otology and Neurotology. 31(9): 1369-1375. Available at: https://pubmed.ncbi.nlm.nih.gov/20479696/

Individual studies

Seebacher J, Weichbold V, Schörg P, et al. (2020). Subjective Hearing Impression and Quality of Life in Patients With Bilateral Active Middle Ear Implants. Otol Neurotol. 41(6): e641-e7. doi: 10.1097/mao.0000000000002630. Available at: https://pubmed.ncbi.nlm.nih.gov/32569243/

Uhler K, Anderson MC, Jenkins HA. (2016). Long-Term Outcome Data in Patients following One Year's Use of a Fully Implantable Active Middle Ear Implant. Audiol Neurootol. 21(2): 105-12. doi: 10.1159/000444243. Available at: https://pubmed.ncbi.nlm.nih.gov/27031589/

McRackan TR, Clinkscales WB, Ahlstrom JB, et al. (2018). Factors associated with benefit of active middle ear implants compared to conventional hearing aids. Laryngoscope. 128(9): 2133-8. doi: 10.1002/lary.27109. Available at: https://pubmed.ncbi.nlm.nih.gov/29481695/

Ongoing research

Vasquez, AN. and Beto, LR. (2017). Quality of life and hearing with the use of middle ear implant: a systematic revision and meta analysis.
https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42017080811

Evidence submitted by topic proposer

Bruchhage KL, Leichtle A, Schönweiler R, Todt I, Baumgartner WD, Frenzel H, Wollenberg B. (2017). Systematic review to evaluate the safety, efficacy and economical outcomes of the Vibrant Soundbridge for the treatment of sensorineural hearing loss. Eur Arch Otorhinolaryngol. Apr;274(4):1797-1806.
Available at: https://pubmed.ncbi.nlm.nih.gov/27796557/

Kosaner Kliess M, Kluibenschaedl M, Zoehrer R, Schlick B, Scandurra F, Urban M. (2017). Cost-utility of partially implantable active middle ear implants for Sensorineural hearing loss: a decision analysis. Value Health. 20(8): 1092- 1099.
Available at: https://www.sciencedirect.com/science/article/pii/S1098301517302206

Snik AF, van Duijnhoven NT, Mylanus EA, Cremers CW. (2006). Estimated cost-effectiveness of active middle-ear implantation in hearing-impaired patients with severe external otitis. Arch Otolaryngol Head Neck Surg. Nov;132(11):1210-5.
Available at: https://jamanetwork.com/journals/jamaotolaryngology/fullarticle/484577

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Concepts used:	Search terms: “middle ear implants” AND complex hearing conditions OR “hearing loss”