Outcomes of Cochlear Implantation in Patients with Post-Meningitis Deafness: A Systematic Review and Narrative Synthesis

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INTRODUCTION

Background and Epidemiology

Bacterial meningitis (BM) is a leading cause of acquired sensorineural hearing loss worldwide. Approximately 60-90% of BM cases occur in children [1,2]. Permanent and profound hearing loss occurs in up to 35% and 5% of patients with BM respectively [3]. Hearing loss can occur within 48 hours of infection [4,5]. Since the introduction of a vaccination, the number of BM cases due to Haemophilus influenzae Type B has decreased dramatically [6]. Currently, the most prevalent aetiologic agents are Streptococcus pneumoniae and Neisseria meningitidis.

The estimated risk of deafness in meningitis caused by Streptococcus pneumoniae is 22% compared to 8% with Neisseria meningitidis [7,8]. Deafness is caused by the spread of infection from the meninges to the perilymphatic spaces of the inner ear. This occurs primarily via the cochlear aqueduct but can also occur via the internal auditory canal. The resulting labyrinthitis leads to hair cell loss, degeneration of the spiral ganglion cells and bony obliteration of the cochlear lumen [9,10]. The organ of Corti can become damaged in three successive stages: acute inflammation, fibrosis and then ossification. The final stage, labyrinthitis ossificans (LO), is where neo-ossification obliterates the endolymph and perilymph spaces. LO can be found in up to 90% of patients with profound hearing loss secondary to BM [11] and can occur as early as 4 weeks after the onset of meningitis [12]. Deafness in BM can also be caused by auditory nerve damage or a central lesion [13].

Summarise outcomes following cochlear implantation (CI) in patients with post-meningitis deafness. Systematic review and narrative synthesis.

Databases searched: Medline, Pubmed, Embase, Web of Science, Cochrane Collection and ClinicalTrials.gov. No limits placed on language or year of publication. Studies with a minimum of 20 individuals with post-meningitis deafness were included. Review conducted in accordance with the PRISMA statement. Searches identified 906 abstracts and 291 full texts. Of these, 19 studies met the inclusion criteria, reporting outcomes in 610 patients with 650 implants. Audiological outcomes improved across all studies following cochlear implantation. 7 studies demonstrated a statistically significant difference between pre and post-CI outcomes. Patients with no cochlear ossification, full electrode insertion, shorter duration of deafness and no neurological sequelae generally appeared to perform best. A total of 31 minor and 19 major complications were reported, with 15 cases of reimplantation. The methodological quality of the included studies was sufficient, predominantly consisting of cohort studies. 15 studies were OCEBM grade III and 4 studies were OCEBM grade IV. All studies had a minimum of 20 individuals with post-meningitic deafness and used multi-channel cochlear implant devices. Audiological outcomes following cochlear implantation in meningitis are satisfactory, providing functional levels of speech perception and intelligibility. Improvement in hearing is dependent on the amount of cochlear ossification, duration of deafness prior to implantation, electrode insertion depth and presence of neurological sequelae. Cochlear implantation in meningitis patients can be challenging due to the presence of ossification and inaccuracies of pre-operative imaging. Therefore, early and bilateral implantation is recommended in all patients with post-meningitis hearing loss to improve the likelihood of full electrode insertion.

KEYWORDS: Meningitis, cochlear implants, systematic review
Diagnosis
Most authorities recommend early audiological testing in meningitis. For instance, in the UK National Institute for Health and Care Excellence (NICE) guidelines 2010 (14), all children (and adults) with confirmed or suspected bacterial meningitis should be offered a formal audiological test within four weeks of being fit to test and preferably before discharge from hospital. Although it is not routine for children with viral meningitis to be referred for a hearing test, parents should contact their clinician if concerned.

Neurological complications
In addition to hearing loss, BM can cause other neurological sequelae including focal neurological deficits, epilepsy and cognitive impairment. Studies have reported a higher incidence of hearing loss in patients with neurological sequelae following BM. Thus, early recognition of such complications is essential to identify patients who are at high risk of hearing impairment (15). The learning difficulties, lower intelligence quotients (IQs), language deficits and behaviour problems observed in children following BM can also affect their ability to process auditory signals from a cochlear implant and negatively impact their auditory performance and CI use trajectory (16-18).

Ossification During Cochlear Implantation
Ossification is most marked in the scala tympani of the basal turn of the cochlea, which is the standard site of electrode array insertion in cochlear implantation (19). Due to failure of full-length electrode insertion and subsequent poor auditory results, LO was previously considered to be a contraindication to cochlear implantation. However, advances in surgical techniques and development of new electrode designs have made it possible for many centres to routinely attempt implantation in these patients (20-24).

Risks and Complications of Cochlear Implantation
Whilst considered a safe and effective surgical procedure, cochlear implantation poses risks of device failure, infection, facial nerve palsy and cerebrospinal fluid leakage (25, 26). Studies report a higher risk of infectious complications in CI users, including a 30-fold increase in bacterial meningitis, compared to non CI users (27).

MATERIALS AND METHODS

Protocol and Registration
The protocol for this systematic review was registered on the International Prospective Register of Systematic Reviews (188262) and has been created according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines (28).

Eligibility Criteria
Population: The participants of interest were children or adults with post-meningitis deafness. Studies comprising populations of a minimum of 20 individuals with post-meningitis deafness were eligible for inclusion.

Intervention: The intervention was cochlear implantation. Only studies using multi-channel cochlear implant devices were included. No restrictions were placed on the type of insertion. Interventions consisting of cochlear re-implantation were excluded.

Comparator: No formal comparison group since pre-implantation hearing status was expected to remain stable (i.e. very little functional hearing) without implantation.

Outcomes: The primary outcomes consisted of pre- and post-implantation audiological outcomes measured using audiometry and/or speech perception and/or speech production. Where preimplantation outcomes were unavailable, post-implantation outcomes have been evaluated only. The secondary outcomes considered were intra-operative complications, post-operative complications, re-implantation, schooling and quality of life.

Study Design: Case-series, case-control, cohort studies and randomised controlled trials were eligible for inclusion. Studies reporting audiological outcomes at a minimum of three months post-implantation and studies with full-texts available only were included.

Search Strategy
The following electronic databases were searched: MEDLINE, EMBASE, CENTRAL, Web of Science and ClinicalTrials.gov. A search was conducted using text and index terms relating to “cochlear implant” and “meningitis”. The search strategy for the MEDLINE database is presented in Supplementary Material 1; modified versions of this search strategy were used for the other electronic databases. The electronic database search was supplemented by hand-searching the reference lists of included studies and relevant systematic reviews to locate any additional studies that had been missed. A citation search of included studies was further conducted using google scholar. No language or publication date limits were applied.

Study Selection
Electronic database search results were imported into the referencing software, EndNote Web. Titles and abstracts of the studies were screened in duplicate and independently by two reviewers (JS and KS). Full texts of potentially relevant studies were assessed for inclusion in duplicate and independently by two reviewers (JS and KS). Disagreements at the abstract and full-text screening stages were discussed within the author team and consensus was reached in determining eligible studies. The PRISMA flow diagram is shown in Figure 1.

Data Extraction
Data was extracted into an Excel spreadsheet, which had been designed and piloted a priori. The data of interest comprised location, study design, setting, duration, recruitment process, participant characteristics (including ossification, duration of deafness and neurological sequelae), intervention characteristics (including depth of electrode insertion), primary outcome data at baseline and follow-up time points, secondary outcomes and attrition. Data extraction was performed by two reviewers (JS and KS) and verified by the other reviewer (JS or KS). Missing data were sought, where possible, by email

MAIN POINTS
- Cochlear implantation can be an effective treatment for hearing impairment following meningitis.
- Preoperative imaging can be helpful in predicting surgical challenges but is not always accurate.
- Early bilateral implantation is recommended to improve the likelihood of full electrode insertion leading to the greatest chance of good audiometric performance.
A total of 610 meningitis patients underwent 650 cochlear implant procedures. There were 40 reported bilateral cochlear implantations. All studies had an average follow-up length of 12 months. Only 10 studies reported the causative organism; 169 cases of meningitis were caused by Streptococcus pneumoniae, 24 cases were caused by Neisseria meningitidis and 25 cases were caused by Haemophilus influenzae. 91 patients were reported to have neurological sequelae or learning disabilities. Cochlear ossification was reported in at least 200 patients; partial (n=69), total (n=52), unspecified (n=79). Full electrode insertion was reported in at least 288 patients. 11 studies mentioned the use of preoperative imaging to assess cochlea patency. Study characteristics are summarised in Table 1.

Quality of Studies
The methodological quality of included studies was sufficient, predominantly consisting of cohort studies (n=15). 15 studies were OCEBM grade III and 4 studies were OCEBM grade IV. The majority of studies (n=16) were retrospective and all studies had a minimum of 20 individuals with post-meningitic deafness. There were limitations in the reporting of type of meningitis, gender, electrode design, surgical technique, surgical complications and outcomes relating to quality of life and education. Heterogeneity of audiological outcomes precluded a meta-analysis. Quality assessment of studies is summarised in Table 1.

Audiological Outcomes
Audiological outcomes improved across all studies following cochlear implantation. However, reporting was heterogeneous in terms of assessment method and follow-up duration. Only 11 studies reported on pre-implantation hearing status with all cases having severe to profound bilateral hearing loss. Of these, 7 used statistical analysis to demonstrate a significant improvement in audiological outcomes following CI [1, 31-36]. The most commonly used outcome measures were speech perception (word and sentence) scores and Categorised Auditory Performance (CAP). CAP was reported in 5 studies [31, 37-40]. In 3 of the studies (n=88), the mean post CI CAP was greater than 5 [31, 37, 40]. In Parisier et al. (n=20), a mean CAP of 3.9 was reported and a higher CAP was noted in the full insertion group than the partial insertion group, however no statistical testing was used. In Philimon et al. (n=40), only 13 people achieved CAP 3 or 4.

Open-set speech perception was reported in 13 studies [1, 31-35, 40-46]. Significantly fewer patients with cochlear ossification achieved open-set speech perception following CI compared to patients with no cochlear ossification in 2 studies. In Cordero et al, 84% of the patent cochlea group achieved open set speech perception (n=20) compared to 0% in the ossification group (n=8) [40]. In Helmstaedter et al., the mean monosyllabic word understanding was 36% in the ossification group compared to 63% in the patent cochlea group. Likewise, the mean sentence understanding was 8% in the ossification group compared to 26% in the patent cochlea group [46]. Although this trend was also found in Liu et al. [32] and Saldaña et al. [46], the difference in open set speech perception was not reported to be statistically significant.
| Study Reference | Patient Characteristics | Intervention Summary | Outcomes and Quality Assessment |
|-----------------|-------------------------|----------------------|----------------------------------|
| Primary author: Parisier et al. Publication year: 1993 Study setting: USA Study design: case-series (retrospective) | Eligibility criteria: profound deafness Number of meningitis patients: 22 Subgroups: none Prelingual deafness: not specified Causative organism: S. pneumoniae (n=13), H influenzae (n=9) Age group: children Mean age at diagnosis (months): 34.8 Mean duration of deafness (months): 44.4 Mean age at implantation (months): 91.2 Ossification: 19 (partial = 16, total = 3) Number of patients with neurological sequelae or learning disabilities: not specified | Surgical technique: canal wall-up mastoidectomy and facial recess approach Cochlear implant device: Nuclerus-22 channel (n=20), 3M/House (n=2) Speech processing strategy: not specified Mean length of follow-up (months): 24 Full insertion: 17 patients Pre-operative imaging (CT/MRI): yes Insertion method: scala tympani Bilateral implantations: not specified | Primary outcomes: modified CAP Secondary outcomes: none Losses to follow-up: 2 OCEBM grade: 4 Brazzelli risk of bias checklist: low = 8, high = 6, unclear = 2, not applicable = 2 |
| Primary author: Bertram et al. (Associated study: Lenarz et al.) Publication year: 1995 Study setting: Germany Study design: cohort (retrospective) | Eligibility criteria: obliteration of cochlea within first year of meningitis, age <2 years at implantation. Number of meningitis patients: 33 Subgroups: none Prelingual deafness: not specified Causative organism: not specified Age group: children Mean age at diagnosis (months): 9.8 (n=26) Mean duration of deafness (months): not specified Mean age at implantation (months): 17.5 (n=26) Ossification: 26 Number of patients with neurological sequelae or learning disabilities: not specified | Surgical technique: not specified Cochlear implant device: Nucleus mini, Combi, Claricon Double Array Speech processing strategy: not specified Mean length of follow-up (months): 36 months Full insertion: not specified Pre-operative imaging (CT/MRI): yes Insertion method: not specified Bilateral implantations: not specified | Primary outcomes: modified Hannover hearing test (consists of 4 closed-set tests and 3 open-set tests). Secondary outcomes: intra-operative complications; post-operative complications; reimplantation Losses to follow-up: 0 OCEBM grade: 3 Brazzelli risk of bias checklist: low = 9, high = 6, unclear = 3 |
| Primary author: Nikolopoulos et al. Publication year: 1997 Study setting: UK Study design: cohort (retrospective) | Eligibility criteria: Not specified Number of meningitis patients: 47 Subgroups: none Prelingual deafness: 47 Causative organism: not specified Age group: children Mean age at diagnosis (months): 16.8 Mean duration of deafness (months): 42 Mean age at implantation (months): 58.8 Ossification: not specified Number of patients with neurological sequelae or learning disabilities: not specified | Surgical technique: not specified Cochlear implant device: Nucleus-22 channel Speech processing strategy: not specified Mean length of follow-up (months): 12 Full insertion: not specified Pre-operative imaging (CT/MRI): not specified Insertion method: not specified Bilateral implantations: not specified | Primary outcomes: LiP scale Secondary outcomes: none Losses to follow-up: 0 OCEBM grade: 3 Brazzelli risk of bias checklist: low = 9, high = 5, unclear = 4 |
| Primary author: Steenerson et al. Publication year: 1999 Study setting: USA Study design: cohort (retrospective) | Eligibility criteria: profound deafness, received a cochlear implant at the age of 2-17 Number of meningitis patients: 28 Subgroups: group 1 = no ossification (n=6), group 2 = partial ossification (n=16), group 3 = total ossification (n=6) Prelingual deafness: not specified Causative organism: S pneumoniae (n=6), N meningitidis (n=1), H influenzae (n=1), unknown (n=20) Age group: children Mean age at diagnosis (months): 27 Mean duration of deafness (months): not specified (group 1 median = 62, group 2 median = 57, group 3 median = 18) | Surgical technique: Gantz procedure used for patients with total ossification Cochlear implant device: Nucleus 22 Speech processing strategy: Spectra/SPEAK (n=16), MPeak (n=12) Mean length of follow-up (months): not specified (median = 69.96) Full insertion: not specified Pre-operative imaging (CT/MRI): yes Insertion method: not specified Bilateral implantations: not specified | Primary outcomes: open-set speech perception measured using GASP; closed-set speech perception measured using WIP; ESP category Secondary outcomes: re-implantation Losses to follow-up: 0 OCEBM grade: 3 Brazzelli risk of bias checklist: low = 9, high = 5, unclear = 4 |
| Study Reference | Patient Characteristics | Intervention Summary | Outcomes and Quality Assessment |
|-----------------|-------------------------|----------------------|---------------------------------|
| Singhal et al.  | Mean age at implantation (months): not specified (group 1 median = 72, group 2 median = 94, group 3 median = 49) Ossification: 22 (partial = 16, total = 6) Number of patients with neurological sequelae or learning disabilities: not specified | Surgical technique: not specified Cochlear implant device: Nucleus 22 Speech processing strategy: MSP (n=9), Spectra (n=27) Mean length of follow-up (months): group 1 = 52.3, group 2 = 69.0 Full insertion: not specified Pre-operative imaging (CT/MRI): not specified Insertion method: not specified Bilateral implantations: not specified | Primary outcomes: open-set speech perception; speech production performance Secondary outcomes: none Losses to follow-up: 0 OCEBM grade: 3 Brazzelli risk of bias checklist: low = 9, high = 6, unclear = 3 |
| Mitchell et al. | Eligibility criteria: not specified Number of meningitis patients: 36 Subgroups: group 1 = deafened by meningitis before age 2 years (n=22), group 2 = deafened by meningitis after age 2 years (n=14) Prelingual deafness: not specified Causative organism: not specified Age group: children Mean age at diagnosis (months): group 1 = 14.3, group 2 = 48 Mean duration of deafness (months): group 1 = 20.9, group 2 = 17.9 Mean age at implantation (months): not specified Ossification: not specified Number of patients with neurological sequelae or learning disabilities: not specified | Surgical technique: facial recess approach Cochlear implant device: not specified Speech processing strategy: not specified Mean length of follow-up (months): 24 Full insertion: 9 patients (group 1) Pre-operative imaging (CT/MRI): not specified Insertion method: scala tympani (n=9), circumodiolar drill-out (n=7) Bilateral implantations: not specified | Primary outcomes: pure-tone average; SPC; open-set speech perception Secondary outcomes: none Losses to follow-up: 0 OCEBM grade: 3 Brazzelli risk of bias checklist: low = 11, high = 4, unclear = 3 |
| El-Kashlan et al. | Eligibility criteria: perioperative documentation of cochlear ossification, pre-lingual onset of deafness, min. 2 years’ experience with cochlear implant Number of meningitis patients: 21 Subgroups: group 1 = minimal ossification (n=9), group 2 = partial insertion (n=5), group 3 = circumodiolar drill-out (n=7) Prelingual deafness: 21 Causative organism: S pneumoniae Age group: children Mean age at diagnosis (months): group 1 = 15.6, group 2 = 13.2, group 3 = 13.2 Mean duration of deafness (months): 63.6 (group 1 = 56.4, group 2 = 67.2, group 3 = 69.6) Mean age at implantation (months): not specified Ossification: 21 (partial = 8, total = 12) Number of patients with neurological sequelae or learning disabilities: not specified | Surgical technique: not specified Cochlear implant device: ABC clarion discrimination measured using GASP, ABC HiFocus (n=6), Nucleus 24 (n=13), Nucleus 22 (n=9), N meningitidis (n=1) Speech processing strategy: not specified Mean length of follow-up (months): 20.8 Full insertion: 26 patients | Primary outcomes: open-set speech discrimination measured using GASP, PBK and LNT; closed-set speech discrimination measured using WIP, ESP, NU-CHIPS Secondary outcomes: none Losses to follow-up: 0 |
| Study Reference | Patient Characteristics | Intervention Summary | Outcomes and Quality Assessment |
|------------------|-------------------------|----------------------|----------------------------------|
|                  | group B strep (n=1), unknown (n=15) | Pre-operative imaging (CT/MRI): not specified | OCEBM grade: 3 |
|                  | Age group: children | Insertion method: not specified | Brazzelli risk of bias checklist: low = 12, high = 3, unclear = 3 |
|                  | Mean age at diagnosis (months): 16.8 | Bilateral implantations: not specified | |
|                  | Mean duration of deafness (months): 34.8 | | |
|                  | Mean age at implantation (months): 51.6 | | |
|                  | Ossification: 9 | | |
|                  | Number of patients with neurological sequelae or learning disabilities: 14 | | |
|                  | Elastin criteria: not specified | Surgical technique: not specified | Primary outcomes: open-set speech |
|                  | Number of meningitis patients: 44 | Cochlear implant device: not specified | perception measured using ESP and |
|                  | Prelingual deafness: 36 | Speech processing strategy: not specified | IT-MAIS |
|                  | Causative organism: S pneumoniae (n=18), N meningitides (n=16), H influenzae (n=4), unknown (n=6) | Mean length of follow-up (months): 36 | Secondary outcomes: schooling |
|                  | Age group: children | Full insertion: 33 patients (permeable cochlea and partial ossification) | Losses to follow-up: 0 |
|                  | Mean age at diagnosis (months): not specified | Pre-operative imaging (CT/MRI): not specified | OCEBM grade: 3 |
|                  | Mean duration of deafness (months): 55.5 | Insertion method: scala vestibuli (n=2) | Brazzelli risk of bias checklist: low = 9, high = 7, unclear = 2 |
|                  | Mean age at implantation (months): not specified | Bilateral implantations: none | |
|                  | Ossification: 15 (partial = 4, total = 11) | Number of patients with neurological sequelae or learning disabilities: mild = 14, moderate = 6, severe = 8 | |
|                  | Number of patients with neurological sequelae or learning disabilities: | | |

### Table 1. Summary of Study Characteristics(Continued)

| Study Reference | Patient Characteristics | Intervention Summary | Outcomes and Quality Assessment |
|------------------|-------------------------|----------------------|----------------------------------|
| Primary author: Cordero et al. | Eligibility criteria: bilateral profound deafness | Surgical technique: not specified | Primary outcomes: CAP, SIR, mode of communication |
| Publication year: 2004 | Number of meningitis patients: 22 | Cochlear implant device: Nucleus 22 | Secondary outcomes: re-implantation, schooling |
| Study setting: UK | Prelingual deafness: not specified | Speech processing strategy: not specified | Losses to follow-up: 0 |
| Study design: cohort (prospective) | Causative organism: not specified | Mean length of follow-up (months): 360 | OCEBM grade: 3 |
|                  | Age group: children | Full insertion: not specified | Brazzelli risk of bias checklist: low = 12, high = 1, unclear = 3, not applicable = 2 |
|                  | Mean age at diagnosis (months): 20.4 | Pre-operative imaging (CT/MRI): not specified | |
|                  | Mean duration of deafness (months): not specified | Insertion method: not specified | |
|                  | Mean age at implantation (months): 60 | Bilateral implantations: not specified | |
|                  | Ossification: not specified | | |
|                  | Number of patients with neurological sequelae or learning disabilities: 2 | | |
|                  | Primary author: Rotteveel et al. | Surgical technique: cochleostomy | Primary outcomes: open-set speech |
| Publication year: 2005 | Eligibility criteria: age of onset of deafness between 0-3 years of age, hearing thresholds at 1,2 and 4kHz exceeding 95dB HL, no open-set speech discrimination, no additional disabilities, normal verbal intelligence, good motivation and support at home. Number of meningitis patients: 25 | Cochlear implant device: Nucleus 22 or Nucleus 24 | discrimination, overall equivalent hearing loss |
| Study setting: Netherlands | Prelingual deafness: 25 | Speech processing strategy: MPEAK, SPEAK, ACE (n=4) | Secondary outcomes: none |
| Study design: cohort (prospective) | Causative organism: S pneumoniae (n=17), N meningitidis (n=1), H influenzae (n=4), unknown (n=2) | Mean length of follow-up (months): 36 | Losses to follow-up: 0 |
|                  | Age group: none | Full insertion: 18 patients | OCEBM grade: 3 |
|                  | Mean age at diagnosis (months): group 1 = 21.6, group 2 = 19.2 | Pre-operative imaging (CT/MRI): yes | Brazzelli risk of bias checklist: low = 14, high = 1, unclear = 3 |
|                  | Mean duration of deafness (months): group 1 = 44.4, group 2 = 34.8 | Insertion method: scala tympani | |
|                  | Mean age at implantation (months): | Bilateral implantations: not specified | |
### Table 1. Summary of Study Characteristics (Continued)

| Study Reference | Patient Characteristics | Intervention Summary | Outcomes and Quality Assessment |
|-----------------|--------------------------|----------------------|----------------------------------|
| **Primary author:** Nikolopoulos et al. | | | |
| **Publication year:** 2006 | | | |
| **Study setting:** UK, Greece | Eligibility criteria: prelingually deafness (onset < 3 years) bilateral profound deafness, age at implantation <5.6 years, implanted with ≥15 electrodes | Surgical technique: not specified | |
| **Study design:** cohort (prospective) | Number of meningitis patients: 46 | Cochlear implant device: Nucleus | Primary outcomes: CAP score; open-set speech perception measured using CDT; mode of communication |
| | Subgroups: none | Speech processing strategy: not specified | Secondary outcomes: schooling |
| | Prelingual deafness: 46 | Mean length of follow-up (months): 60 | Losses to follow-up: 2 for CAP measurements, 6 for CDT measurements |
| | Causative organism: not specified | Full insertion: not specified | OCEBM grade: 3 |
| | Age group: children | Pre-operative imaging (CT/MRI): yes | | |
| | Mean age at diagnosis (months): not specified (range: 12 – 18) | Insertion method: not specified | Brazzelli risk of bias checklist: low = 12, high = 2, unclear = 4 |
| | Mean duration of deafness (months): not specified | Bilateral implantations: none | |
| | Mean age at implantation (months): 39.6 | | |
| | Ossification: not specified | | |
| | Number of patients with neurological sequelae or learning disabilities: 11 | | |
| **Primary author:** Durisin et al. | | | |
| **Publication year:** 2008 | Eligibility criteria: not specified | Surgical technique: mastoidectomy posterior tympanotomy | |
| **Study setting:** Germany (75 ears) | Number of meningitis patients: 60 | Cochlear implant device: not specified | Primary outcomes: MAIS; MUS; open-set test (common phrases); closed-set test (monosyllable words) |
| **Study design:** cohort study (retrospective) | (75 ears) | Speech processing strategy: MPEAK | Secondary outcomes: none |
| | Subgroups: group 1 = duration of deafness <6 months (n=26), group 2 = duration of deafness >6 months (n=34) | (n=2), ACE (n=3), CIS/SAS (n=22) | Losses to follow-up: 0 |
| | Prelingual deafness: not specified | Mean length of follow-up (months): 36 | OCEBM grade: 3 |
| | Causative organism: not specified | Full insertion: 40 patients (group 1 = 17, group 2 = 23) | Brazzelli risk of bias checklist: low = 11, high = 4, unclear = 3 |
| | Age group: children | Pre-operative imaging (CT/MRI): not specified | |
| | Mean age at diagnosis (months): group 1 = 31.2, group 2 = 9.48 | Insertion method: scala tympani | |
| | Mean duration of deafness (months): group 1 = 2.4, group 2 = 45.6 | Bilateral implantations: 15 (group 1 = 12, group 2 = 3) | |
| | Mean age at implantation (months): not specified | | |
| | Ossification: not specified | | |
| | Number of patients with neurological sequelae or learning disabilities: 22 | | |
| **Primary author:** Philippon et al. | Eligibility criteria: profound bilateral deafness | Surgical technique: not specified | Primary outcomes: open-set speech discrimination measured using CAP score |
| **Publication year:** 2010 | Number of meningitis patients: 40 (42 ears) | Cochlear implant device: not specified | Secondary outcomes: none |
| **Study setting:** Canada | Subgroups: group 1 = children (n=27), group 2 = adults (n=13) | Speech processing strategy: | Losses to follow-up: 0 |
| **Study design:** cohort (retrospective) | Prelingual deafness: not specified | Mean length of follow-up (months): 12 | OCEBM grade: 3 |
| | Causative organism: S pneumoniae (group 1 = 22, group 2 = 2), N meningitidis (group 1 = 3), H influenzae type B (group 1 = 1), M tuberculosis (group 2 = 2), group B strep (group 2 = 2), unknown (group 1 = 1, group 2 = 8) | Full insertion: 31 patients (group 1 = 20, group 2 = 11) | Brazzelli risk of bias checklist: low = 9, high = 5, unclear = 4 |
| | Age group: children and adults | Pre-operative imaging (CT/MRI): yes | | |
| | Mean age at diagnosis (months): not specified | Insertion method: not specified | |
| | Mean duration of deafness (months): group 1 = 25, group 2 = 336 | Bilateral implantations: 2 | |
| Study Reference | Patient Characteristics | Intervention Summary | Outcomes and Quality Assessment |
|-----------------|-------------------------|----------------------|---------------------------------|
| Primary author: Mosnier et al. | Eligibility criteria: not specified Number of meningitis patients: 22 (27 ears) Subgroups: group 1 = implanted between 1995-2001 (n=11 ears), group 2 = implanted between 2002-2008 (n=14 ears) Prelingual deafness: 0 Causative organism: not specified Age group: adults Mean age at diagnosis (months): not specified Mean duration of deafness (months): 180 Mean age at implantation (months): group 1 = 564, group 2 = 492 Ossification: not specified Number of patients with neurological sequelae or learning disabilities: 3 | Surgical technique: not specified Cochlear implant device: Nucleus 24 (n=13), Freedom (n=5), Hires 90K (n=3), Combi 40+ (n=2), Pulsar (n=2) Speech processing strategy: Spectra 22 (n=1), Sprint TM (n=5), ESPrit TM (n=5), ESPrit 3G (n=2), Freedom (n=5), Harmony (n=3), Tempo+ (n=2), Opus 2 (n=2) Mean length of follow-up (months): 42 Full insertion: 20 patients (23 ears) Pre-operative imaging (CT/MRI): yes Insertion method: not specified Bilateral implantations: 5 | Primary outcomes: open-set test of speech comprehension (disyllabic words) Secondary outcomes: re-implantation Losses to follow-up: 0 OCEBM grade: 3 Brazzelli risk of bias checklist: low = 12, high = 3, unclear = 1 |
| Primary author: Bille et al. | Eligibility criteria: children <15 years who underwent CI between December 1996 and January 2012 Number of meningitis patients: 22 (32 ears) Subgroups: none Prelingual deafness: 18 Causative organism: S pneumoniae Age group: children Mean age at diagnosis (months): 15 Mean duration of deafness (months): 32 Mean age at implantation (months): 46.9 Ossification: 8 Number of patients with neurological sequelae or learning disabilities: 7 | Surgical technique: not specified Cochlear implant device: Nucleus CI24RE (n=8), Nucleus C24CA (n=1), Nucleus CI24R (n=6), Nucleus CI512 (n=3), Nucleus CI24m (n=3), CI+11+11+2M (n=1) Speech processing strategy: not specified Mean length of follow-up (months): 41.6 Full insertion: 22 ears Pre-operative imaging (CT/MRI): yes Insertion method: not specified Bilateral implantations: 10 | Primary outcomes: CAP; SIR Secondary outcomes: post-operative complications Losses to follow-up: 0 OCEBM grade: 3 Brazzelli risk of bias checklist: low = 9, high = 7, unclear = 2 |
| Primary author: Liu et al. | Eligibility criteria: deafness secondary to bacterial meningitis Number of meningitis patients: 39 Subgroups: group 1 = ossified cochlea (n=19), group 2 = non-ossified cochlea (n=20) Prelingual deafness: not specified Causative organism: not specified (bacteria) Age group: children Mean age at diagnosis (months): group 1 = 18.54, group 2 = 32.35 Mean duration of deafness (months): group 1 = 20.15, group 2 = 38.92 Mean age at implantation (months): group 1 = 38.64, group 2 = 73.76 Ossification: 19 Number of patients with neurological sequelae or learning disabilities: not specified | Surgical technique: not specified Cochlear implant device: not specified Speech processing strategy: not specified Mean length of follow-up (months): 89.8 Full insertion: 32 patients Pre-operative imaging (CT/MRI): not specified Insertion method: scala tympani (n=34), scala vestibuli (n=1), circumodiolar drill-out (n=4) Bilateral implantations: none | Primary outcomes: SPC; open-set speech perception Secondary outcomes: schooling Losses to follow-up: 3 OCEBM grade: 3 Brazzelli risk of bias checklist: low = 7, high = 7, unclear = 4 |
### Table 1. Summary of Study Characteristics

| Study Reference | Patient Characteristics | Intervention Summary | Outcomes and Quality Assessment |
|-----------------|-------------------------|----------------------|---------------------------------|
| Primary author: Helmstaedter et al.  
Publication year: 2018  
Study setting: Germany  
Study design: case-control (retrospective) | Eligibility criteria: uni- or bilateral deafness secondary to bacterial meningitis, no learning or motor disabilities, no bilateral sequential cochlear implantation, no syndromic conditions  
Number of meningitis patients: 27 (35 ears)  
Subgroups: none  
Prelingual deafness: not specified  
Causative organism: not specified  
Age group: children  
Mean age at diagnosis (months): not specified  
Mean duration of deafness (months): not specified  
Mean age at implantation (months): 103.2  
Ossification: 15 ears  
Number of patients with neurological sequelae or learning disabilities: none | Surgical technique: mastoidectomy with posterior tympanotomy  
Cochlear implant device: CI24M, CI24R, CI24REA  
Speech processing strategy: not specified  
Mean length of follow-up (months): not specified (median = 103.2)  
Full insertion: 27 patients  
Pre-operative imaging (CT/MRI): yes  
Insertion method: not specified  
Bilateral implantations: 8 | Primary outcomes: open-set speech perception measured using Freiburger monosyllabic word test and HSM-sentence test  
Secondary outcomes: none  
Losses to follow-up: 0  
OCEBM grade: 4  
Brazzelli risk of bias checklist: low = 9, high = 4, unclear = 5 |
| Primary author: Saldaña et al.  
Publication year: 2019  
Study setting: Argentina (exclusion criteria: >80% missing data)  
Study design: cohort (retrospective) | Eligibility criteria: severe or profound deafness, follow-up of at least one year  
Number of meningitis patients: 21  
Subgroups: group 1 = ossification (n=11), group 2 = no ossification (n=10)  
Prelingual deafness: not specified  
Causative organism: S pneumoniae (n=18), viral (n=2), unknown (n=1)  
Age group: children  
Mean age at diagnosis (months): not specified (group 1 median = 10, group 2 median = 27)  
Mean duration of deafness (months): not specified (group 1 median = 102, group 2 median = 69)  
Mean age at implantation (months): not specified (group 1 median = 108, group 2 median = 390)  
Ossification: 11 (partial = 11)  
Number of patients with neurological sequelae or learning disabilities: 4 | Surgical technique: promontorial cochleostomy (n=20)  
Cochlear implant device: not specified  
Speech processing strategy: not specified  
Mean length of follow-up (months): 12  
Full insertion: 15 patients  
Pre-operative imaging (CT/MRI): yes  
Insertion method: not specified  
Bilateral implantations: not specified | Primary outcomes: CAP score; Ling + vowel test score; open-set test of word recognition  
Secondary outcomes: post-operative complication, schooling  
Losses to follow-up: 0  
OCEBM grade: 3  
Brazzelli risk of bias checklist: low = 14, high = 3, unclear = 1 |
| Primary author: van den Borne et al.  
Publication year: unknown  
Study setting: USA  
Study design: case series (retrospective) | Eligibility criteria: profound bilateral deafness, no benefit from hearing aids  
Number of meningitis patients: 25  
Subgroups: group 1 = no ossification (n=10), group 2 = partial ossification (n=10), group 3 = total ossification (n=5)  
Prelingual deafness: not specified  
Causative organism: S pneumoniae (n=18), H influenzae type B (n=5), N meningitidis (n=2)  
Age group: children  
Mean age at diagnosis (months): 28.8  
Mean duration of deafness (months): 46.8  
Mean age at implantation (months): 75.6  
Ossification: 15 (partial = 10, total = 5)  
Number of patients with neurological sequelae or learning disabilities: not specified | Surgical technique: canal wall-up mastoidectomy  
Cochlear implant device: Nucleus 22-channel  
Speech processing strategy: not specified  
Mean length of follow-up (months): 36  
Full insertion: 20 patients  
Pre-operative imaging (CT/MRI): yes  
Insertion method: scala tympani  
Bilateral implantations: not specified | Primary outcomes: overall equivalent hearing loss, mode of communication  
Secondary outcomes: middle or inner ear abnormalities, post-operative complications  
Losses to follow-up: 0  
OCEBM grade: 4  
Brazzelli risk of bias checklist: low = 12, high = 3, unclear = 3 |

OCEBM, Oxford Centre for Evidence-Based Medicine; CT, computed tomography; MRI, magnetic resonance imaging; CI, cochlear implantation; CAP, categorized auditory performance; SIR, speech intelligibility rating; ESP, early speech perception; IT-MAIS, infant-toddler meaningful auditory integration scale; MUSS, meaningful use of speech scale; MPEAK, multipeak; SPC, statistical process control; LiP, listening profile; BKB, Bench-Kowal-Bamford; GASP, Glendonald auditory screening procedure; WIPI, word intelligibility by picture identification; NU-CHIPS, Northwestern University Children's Perception of Speech; ACE, Advanced Combined Encoder; CIS, Continuous Interleaved Sampler; SAS, Simultaneous Analogue Stimulation; LNT, Lexical Neighborhood Test; CDT, Connected Discourse Tracking.
Patients with additional handicaps are less likely to achieve open-set speech perception following CI compared to patients with no handicaps. In Francis et al., a comparison of meningitic patients with and without hydrocephalus, found significant worse speech perception performance in the hydrocephalus group. Longitudinal WIPI scores suggested that children with neurological sequelae experience a gain in speech perception that is delayed and more gradual. In Cordero et al., none of the children with severe neurolinguistic handicaps were able to achieve open-set speech recognition. Saldaña et al. were the only ones to disagree with this general finding.

Table 2. Brazzelli Risk of Bias Assessment

| Study                        | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 |
|------------------------------|---|---|---|---|---|---|---|---|---|----|----|----|----|----|----|----|----|----|
| Parise et al. 1993, USA      |   |   |   |   |   |   |   |   |   |    |    |    |    |    |    |    |    |    |
| Bertram et al. 1995, Germany |   |   |   |   |   |   |   |   |   |    |    |    |    |    |    |    |    |    |
| Nikolopoulos et al. 1997, Greece |   |   |   |   |   |   |   |   |   |    |    |    |    |    |    |    |    |    |
| Steenerson et al. 1999, USA  |   |   |   |   |   |   |   |   |   |    |    |    |    |    |    |    |    |    |
| Mitchell et al. 2000, Australia |   |   |   |   |   |   |   |   |   |    |    |    |    |    |    |    |    |    |
| El-Kashlan et al. 2003, USA  |   |   |   |   |   |   |   |   |   |    |    |    |    |    |    |    |    |    |
| Francis et al. 2004, USA     |   |   |   |   |   |   |   |   |   |    |    |    |    |    |    |    |    |    |
| Cordero et al. 2004, Argentina |   |   |   |   |   |   |   |   |   |    |    |    |    |    |    |    |    |    |
| Beadle et al. 2005, UK       |   |   |   |   |   |   |   |   |   |    |    |    |    |    |    |    |    |    |
| Rotteveel et al. 2005, Netherlands |   |   |   |   |   |   |   |   |   |    |    |    |    |    |    |    |    |    |
| Nikolopoulos et al. 2006, UK and Greece |   |   |   |   |   |   |   |   |   |    |    |    |    |    |    |    |    |    |
| Durisin et al. 2008, Germany |   |   |   |   |   |   |   |   |   |    |    |    |    |    |    |    |    |    |
| Phillipon et al. 2010, Canada |   |   |   |   |   |   |   |   |   |    |    |    |    |    |    |    |    |    |
| Mosnier et al. 2012, France  |   |   |   |   |   |   |   |   |   |    |    |    |    |    |    |    |    |    |
| Bille et al. 2014, Denmark   |   |   |   |   |   |   |   |   |   |    |    |    |    |    |    |    |    |    |
| Liu et al. 2015, USA         |   |   |   |   |   |   |   |   |   |    |    |    |    |    |    |    |    |    |
| Helmstaedter et al. 2018, Germany |   |   |   |   |   |   |   |   |   |    |    |    |    |    |    |    |    |    |
| Saldaña et al. 2019, Argentina |   |   |   |   |   |   |   |   |   |    |    |    |    |    |    |    |    |    |
| van den Borne et al. unknown, USA |   |   |   |   |   |   |   |   |   |    |    |    |    |    |    |    |    |    |

1. Were participants a representative sample selected from a relevant patient population?
2. Were the inclusion/exclusion criteria of participants clearly described?
3. Were participants entering the study at a similar point in their disease progression?
4. Was selection of patients consecutive?
5. Was data collection undertaken prospectively?
6. Were the groups comparable on demographic characteristics and clinical features?
7. Was the intervention (and comparison) clearly defined?
8. Was the intervention undertaken by someone experienced at performing the procedure?
9. Were the staff, place and facilities where the patients were treated appropriate for performing the procedure?
10. Were any of the important outcomes considered?
11. Were objective (valid and reliable) outcome measures used, including satisfaction scale?
12. Was the assessment of main outcomes blind?
13. Was follow-up long enough (≥ 1 year) to detect important effects on outcomes of interest?
14. Was information provided on non-respondents, dropouts?
15. Were the characteristics of withdrawals/dropouts similar to those that completed the study?
16. Was length of follow-up similar between comparison groups
17. Were the important prognostic factors identified?
18. Were the analyses adjusted for confounding factors?
| Study Reference                        | Preoperative Data (Mean) | Postoperative Data (Mean)                                                                 |
|---------------------------------------|--------------------------|--------------------------------------------------------------------------------------------|
| Parisier et al., 1993, USA            | None                     | CAP score: 3.9; patients with full insertion: 4.1 (n=15); patients with partial insertion: 2.8 (n=5) |
| Follow-up length of reported outcomes |                          |                                                                                             |
| (months): 24                          |                          |                                                                                             |
| Patients with post-CI outcomes reported: 20 (all nucleus-22 channel) |                          |                                                                                             |
| Subgroups: none                       |                          |                                                                                             |
| Mean duration of deafness (months):   |                          |                                                                                             |
| 44.4                                  |                          |                                                                                             |
| Bertram et al., 1995, Germany         | None                     | Closed-set test of identification of monosyllable words (% pass rate): 55                  |
| Follow-up length of reported outcomes |                          | Closed-set test of identification of two syllable words (% pass rate): 55                 |
| (months): 36                          |                          | Closed-set test of identification of discrimination of phonetics (% pass rate): 30         |
| Patients with post-CI outcomes reported: 33 |                          | Closed-set test of identification of sentences (% pass rate): 19                          |
| Subgroups: none                       |                          | Open-set test of word recognition (% pass rate): 44                                       |
| Mean duration of deafness (months):   |                          | Open-set test of simple sentences recognition (% pass rate): 6                             |
| not specified                         |                          | Open-set test of complex sentences recognition (% pass rate): 0                           |
|                                       |                          | Intra-operative complications: infection of implant (n=1)                                  |
|                                       |                          | Post-operative complications: acute otitis media (n=15), secretory otitis media (n=12), mastoiditis (n=2), cholesteatoma (n=1), stimulation of facial nerve (n=2) |
| Nikolopoulos et al., 1997, UK         | None                     | LiP scale: 36.25                                                                            |
| Follow-up length of reported outcomes |                          |                                                                                             |
| (months): 12                          |                          |                                                                                             |
| Patients with post-CI outcomes reported: 47 |                          |                                                                                             |
| Subgroups: none                       |                          |                                                                                             |
| Mean duration of deafness (months):   |                          |                                                                                             |
| 42                                    |                          |                                                                                             |
| Steenerson et al., 1999, USA          | None                     | Median closed-set speech perception measured by WIPi (% correct items):                      |
| Follow-up length of reported outcomes |                          | group 1: 72 (range: 50 - 93); group 2: 56 (range: 44 - 84)                                  |
| (months): variable (median: 69.96)    |                          | Median open-set speech perception measured using GASP (% correct words or sentences):      |
| Patients with post-CI outcomes reported: 28 |                          | group 1: 67 (range: 33-92); group 2: 46 (range: 14 - 84); group 3: 17                      |
| Subgroups: group 1: no ossification (n=6), group 2: partial ossification (n=16), group 3: total ossification (n=6) |                          | Median ESP category: group 1: 4 (range: 3-4); group 2: 2 (range: 1-4); group 3: 3          |
| Mean duration of deafness (months):   |                          | (range: 2-4)                                                                                |
| not specified (group 1 median: 62, group 2 median: 57, group 3 median: 18) |                          | Re-implantation: 5; group 1: 2 (device failure = 2); group 2: 0; group 3: 3                |
|                                       |                          | (device failure = 2, head trauma = 1)                                                       |
| Mitchell et al., 2000, Australia      | Detection of phenomes:   | Open-set speech perception (no. of patients who achieved): group 1: 11; group 2: 14         |
| Follow-up length of reported outcomes | 1: 36.1% (95% CI: 28.1-44.0); group 2: 48.8% (95% CI: 36.1-61.6) | Good speech production performance at 3-4 years (no. of patients who achieved A or B rating): group 1: 11; group 2: 14 |
| (months): 60-72                       |                          |                                                                                                |
| Patients with post-CI outcomes reported: 36 |                          |                                                                                                |
| Subgroups: group 1: deafened by meningitis before age 2 years (n=22), group 2: deafened by meningitis after age 2 years (n=14) |                          |                                                                                                |
| Mean duration of deafness (months):   |                          |                                                                                                |
| 17.9                                  |                          |                                                                                                |
| El-Kashlan et al., 2003, USA          | SPC category: overall: 0.7; group 1: 0.8; group 2: 0.6; group 3: 0.6                         | SPC category: overall: 3.3; group 1 = 3.6; group 2 = 3.2; group 3 = 3.0                    |
| Follow-up length of reported outcomes (months): 24 |                          | SPC category (long-term follow-up): group 1: 3.8 (follow-up: 7.3 years); group 2 = 3.6 (follow-up: 9.3 years); group 3 = 3.7 (follow-up: 7.1 years) |
| Patients with post-CI outcomes reported: 21 |                          | Open-set speech perception (no. of patients who achieved): 0                                |
| Subgroups: group 1: full insertion (n=9), group 2: partial insertion (n=5), group 3: circumodiolar drill out (n=7) |                          |                                                                                                |
| Mean duration of deafness (months):   | 63.6 (group 1: 56.4, group 2: 67.2, group 3: 69.6)                                           |                                                                                                |

Table 3. Primary Outcomes (Audiometry and/or Speech Perception and/or Speech Production)
Table 3. Primary Outcomes (Audiometry and/or Speech Perception and/or Speech Production)

| Study Reference | Preoperative Data (Mean) | Postoperative Data (Mean) |
|-----------------|--------------------------|---------------------------|
| Francis et al., 2004, USA | Closed-set speech perception (no. of patients who achieved categories 1-4 inclusive): 27 (category 1: 25; category 2: 2; category 3: 0; category 4: 0) | Closed-set speech perception (no. of patients who achieved categories 1-4 inclusive): 16 (category 1: 7; category 2: 0; category 3: 1; category 4: 8). 9 patients (69.2%) have neurological sequelae (n=13) |
| Follow-up length of reported outcomes (months): 12-24 (mean = 20.8) | Open-set speech perception (no. of patients who achieved category 5 or 6): 2 (category 5: 2; category 6: 0) | Open-set speech perception measured using ESP and IT-MAIS (% achieved): full insertion and permeable cochlea: 84 (n=20); partial insertion and totally ossified cochlea: 0 (n=8) |
| Patients with post-CI outcomes reported: 30 | Patients with post-CI outcomes reported: 16 (category 1: 7; category 2: 0; category 3: 1; category 4: 8). 9 patients (69.2%) have neurological sequelae (n=13) | Open-set speech perception measured using ESP and IT-MAIS (% achieved): full insertion and permeable cochlea: 84 (n=20); partial insertion and totally ossified cochlea: 0 (n=8) |
| Subgroups: none | Schooling: special school (n=12), mainstream school (n=16). | Schooling: special school (n=12), mainstream school (n=16). |
| Mean duration of deafness (months): 34.8 | Mean duration of deafness (months): 34.8 |

| Cordero et al., 2004, Argentina | None | Open-set speech perception measured using ESP and IT-MAIS (% achieved): full insertion and permeable cochlea: 84 (n=20); partial insertion and totally ossified cochlea: 0 (n=8) |
| Follow-up length of reported outcomes (months): 36 | Open-set speech perception measured using ESP and IT-MAIS (% achieved): full insertion and permeable cochlea: 84 (n=20); partial insertion and totally ossified cochlea: 0 (n=8) |
| Patients with post-CI outcomes reported: 28 | Schooling: special school (n=12), mainstream school (n=16). |
| Subgroups: none | Schooling: special school (n=12), mainstream school (n=16). |
| Mean duration of deafness (months): 55.5 | Mean duration of deafness (months): 55.5 |

| Beadle et al., 2005, UK | CAP score: 0 | CAP score: 6.1 |
| Follow-up length of reported outcomes (months): 360 | SIR score: 1.2 | SIR score: 3.9 |
| Patients with post-CI outcomes reported: 22 | Mode of communication (no. of patients): oral: 15 |
| Subgroups: none | Re-implantation: 7 (device failure = 7) |
| Mean duration of deafness (months): not specified | Schooling: mainstream school or college: 7, unit or special class within mainstream school: 4, special school or college: 7, university: 2, engineer = 1 |

| Rotteveel et al., 2005, Netherlands | Open-set speech perception (no. of patients who achieved): 0 | Open-set speech perception measured using ESP and IT-MAIS (% achieved): full insertion and permeable cochlea: 84 (n=20); partial insertion and totally ossified cochlea: 0 (n=8) |
| Follow-up length of reported outcomes (months): 36 | Open-set speech perception measured using ESP and IT-MAIS (% achieved): full insertion and permeable cochlea: 84 (n=20); partial insertion and totally ossified cochlea: 0 (n=8) |
| Patients with post-CI outcomes reported: 25 | Schooling: special school (n=12), mainstream school (n=16). |
| Subgroups: group 1: partial insertion (n=7), group 2: full insertion (n=18) | Schooling: special school (n=12), mainstream school (n=16). |
| Mean duration of deafness (months): group 1: 44.4, group 2: 34.8 | Mean duration of deafness (months): group 1: 44.4, group 2: 34.8 |

| Nikolopoulos et al., 2006, UK and Greece | Open-set speech perception measured using CDT (correct words/min): 0 | Open-set speech perception measured using CDT (correct words/min): at 3 years: 22 (n=40) |
| Follow-up length of reported outcomes (months): 60 | CAP score: 0 | CAP score at 5 years: 6 (n=44) |
| Patients with post-CI outcomes reported: 44 | Mode of communication at 5 years (no. of patients): oral communication: 29 (67%); sign communication: 14 (33%) |
| Subgroups: none | Open-set speech perception of patients with neurological sequelae or learning disabilities measured using CDT at 5 years (correct words/min): no neurological sequelae or learning disabilities: 60 (range: 0-91); neurological sequelae or learning disabilities: 38 (range: 0-58) |
| Mean duration of deafness (months): not specified | Schooling: mainstream school: 13, unit or special class within mainstream school: 27, special school: 4 |

| Durisin et al., 2008, Germany | MAIS (% alert to sound): group 1: 1; group 2: 18 | MAIS (% alert to sound): group 1: 70; group 2: 92.5 |
| Follow-up length of reported outcomes (months): 36 | MUSS (% with vocal control): group 1: 17.5; group 2: 25 | MUSS (% with vocal control): group 1: 17.5; group 2: 25 |
| Patients with post-CI outcomes reported: 60 | MUSS (% with vocal control): group 1: 17.5; group 2: 25 | MUSS (% with vocal control): group 1: 17.5; group 2: 25 |
| Subgroups: group 1: duration of deafness <6 months (n=26), group 2: duration of deafness >6 months (n=34) | MUSS (% use of communication strategies): group 1: 17.5; group 2: 25 | MUSS (% use of communication strategies): group 1: 17.5; group 2: 25 |
| Mean duration of deafness (months): group 1: 2.4, group 2: 45.6 | Open-set test of common phrases (% correct): group 1: 0, group 2: 0 | Open-set test of common phrases (% correct): group 1: 40; group 2: 45 |
| MAIS (% alert to sound): group 1: 70; group 2: 92.5 | Open-set test of monosyllable words (% correct): group 1: 0; group 2: 7.5 | Open-set test of monosyllable words (% correct): group 1: 57; group 2: 63 |
| Study Reference | Preoperative Data (Mean) | Postoperative Data (Mean) |
|-----------------|--------------------------|---------------------------|
| Philippon et al., 2010, Canada | None | Open-set speech discrimination (no. of patients who achieved CAP score 3 or 4): group 1: 10 (37%); group 2: 3 (23%) |
| | | CAP score: group 1: 2.26; group 2 = 1.85 |
| Mosnier et al., 2012, France | Open-set test of identification of disyllabic words (% correct): group 1: 2 (SD: 1.7); group 2: 5 (SD: 3.4) | Open-set test of identification of disyllabic words (% correct): group 1: 32; group 2: 70 |
| | | Re-implantation: 1 (device failure = 1) |
| Bille et al., 2014, Denmark | None | CAP score: 5.5 (range: 0-7) |
| | | SIR score: 3.5 (range: 1-5) |
| | | Post-operative complications: haematoma (n=1) |
| Liu et al., 2015, USA | SPC category: overall: 0.82 (n=34); group 1: 0.65 (n=17); group 2: 1.00 (n=17) | SPC category: overall: 4.25; group 1: 3.35; group 2: 5.05 |
| | | Open set speech perception (no. of patients who achieved): 18 group 1: 5, group 2: 13 |
| | | Schooling: group 1: mainstream school: 4, special school: 13; group 2: mainstream school: 12, special school: 6 (n=35) |
| Helmstaedter et al., 2018, Germany | None | Open-set speech perception measured using the Freiburger monosyllabic word test (% correct): overall: 55 (SD: 34); implants in ossified cochlea: 36 (SD: 43, n=15); implants in obliterated cochlea: 56 (SD: 38, n=11); implants in unaltered cochlea: 63 (SD: 19.1, n=9). |
| | | Open-set speech perception measured using the HSM sentence test: (% correct): overall: 24 (SD: 27); implants in ossified cochlea: 8 (SD: 25, n=15); implants in obliterated cochlea: 26 (SD: 30, n=11); implants in unaltered cochlea: 26 (SD: 22, n=9) |
| Saldaña et al., 2019, Argentina | Open-set test of word recognition (% correct): group 1: 0; group 2: 0; CAT score: group 1: 0.36 (SD: 0.5); group 2: 0.60 (SD: 0.52); Ling + vowel test score: group 1: 0.18 (SD: 0.6); group 2: 0.30 (SD: 0.48) | Open-set test of word recognition (% correct): group 1: 27.6 (SD: 36.4); group 2: 52.0 (SD: 31.1) |
| | | CAT score: group 1: 2.73 (SD: 1.62); group 2 = 4.70 (SD = 2.31); p=0.036 |
| | | Ling + vowel test score: group 1: 1.55 (SD: 0.69); group 2: 1.70 (SD: 0.67) |
| | | Post-operative complications: tinnitus (n=1) |
| | | Schooling: special school: 10 (group 1: 8; group 2: 2) |
| van den Borne et al., unknown year of publication, USA | Overall equivalent hearing loss (dB HL): >125 | Overall equivalent hearing loss (dB HL): group 1: 72; group 2: 76; group 3: 121 |
| | | Mode of communication (no. of patients): group 1: oral: 5, total: 5; group 2: oral: 4, total: 6; group 3: oral: 1, total: 4 |
| | | Post-operative complications: wound infection (n=1), acute otitis media (n=1) |
Only three of the included studies accounted for all of these variables [34, 36, 47].

Mosnier et al. [34] investigated the impact of advances in cochlear implant technology by comparing audiological outcomes in patients implanted before and after 2001. A significantly higher magnitude of improvement was found in patients implanted after 2001, who achieved speech scores similar to those of control subjects. Audiological outcomes are summarised in Table 2.

Surgical Complications and Reimplantation

Post-operative complications were documented in 6 studies [36, 40-42, 46, 48, 49]. These were as follows: infection of implant (n=1), stimulation of facial nerve (n=2), acute otitis media (n=16), secretory otitis media (n=12), mastoiditis (n=2), cholesteatoma (n=1), haematoma above insertion site (n=1), wound infection (n=1), tinnitus (n=1). There were 13 cases of device failure and 15 cases of reimplantation (1 due to infection of implant and 2 due to head injury). Surgical outcomes are summarised in Table 3.

Educational and Occupational Outcomes

5 studies reported on educational outcomes following cochlear implantation. These were as follows: mainstream school/college (n=52), special class within mainstream school (n=31), special school/college (n=52), university (n=1), full time job (n=1). The majority of children with cochlear ossification required special schooling whereas those with no ossification were able to attend mainstream school [32, 43, 46]. After 5 years of CI use, approximately 90% of children were placed in mainstream school [31] and after more than 10 years of CI use, several children were able to go onto higher-level education and acquire full-time jobs [40]. Educational outcomes are summarised in Table 2.

DISCUSSION

This systematic review and narrative synthesis reports on outcomes of cochlear implantation in patients with post-meningitis deafness. To the authors’ knowledge, this is the first systematic review on the topic. Improvements in audiology, speech perception and speech production were observed following CI across all studies. Many studies also demonstrated that the audiological outcomes achieved in meningitis patients post-implantation were comparable to those in a wider group of implanted patients, deafened by other causes [31, 35, 37, 41, 48]. It has also been well documented that patients with LO have a poorer prognosis in hearing rehabilitation following CI compared to patients with a patent cochlea, despite advances in surgical techniques [52, 39, 41, 43, 44, 46]. This is in keeping with Nadol et al. [10], who found a strong negative correlation between the degree of cochlear ossification and spiral ganglion cell count. Histopathological studies on human temporal bones in ears deafened by meningitis have demonstrated a huge reduction in spiral ganglion cells [9]; this is thought to contribute to the underlying pathology of deafness in meningitis. Nevertheless, patients with LO still receive significant benefit from CI.

High-resolution CT is used preoperatively to check the patency of the cochlear ducts. However, this mode of imaging has poor sensitivity when detecting the early stages of cochlear ossification, with reported sensitivities of 40-64% [33, 36, 38, 39]. This is thought to be due to the fact that post-inflammatory bone is less dense, more fibrous and contains less calcium [38]. Therefore, in profoundly deaf meningitis children, the otologist should expect to encounter some cochlear ossification even if the CT scan is normal. MRI can detect the presence of early fibrosis and therefore some studies advocate the use of both HRCT and MRI [90, 51]. Most centres have now moved towards primarily using highly T2 weighted MRI imaging sequences in children, in order to show loss of fluid signal in the scala from fibrosis or ossification.

Two methods have been mentioned in the literature for the management of profound deafness in meningitis patients. The conservative “wait and see” approach requires regular hearing evaluation and MRI scans to detect early signs of ossification; this raises questions of feasibility and costs. Furthermore, no improvement is observed in the contralateral ear following unilateral implantation [52]. The interventionist approach, which is supported by many studies [1, 39], recommends early and bilateral implantation in all patients with post-meningitis deafness in order to improve the likelihood of full electrode insertion. This is due to the fact that post-meningitis cochlear ossification can develop as early as 21 days [39] and preoperative imaging can fail to show any sign of ossification at all. However, it should be noted that recovery of hearing can occur after meningitis, and so some degree of waiting is recommended [33-53], but how long is contentious.

In addition to ossification, the presence of neurological sequelae poses significant challenges to the CI rehabilitation process. Patients with additional handicaps experience delayed benefits from the cochlear implant due to slower acquisition of speech perception and additional behavioural or emotional problems which can complicate speech development [35, 36, 57]. Thus, it is important to set realistic expectations with parents and patients prior to implantation. Patients with neurological complications should undergo a full evaluation before and after implantation so that any additional difficulties can be identified and addressed. They also require specialised follow-up care and additional analytical auditory training in order to maximise benefit from the device. Aural rehabilitation, both within the school and at home, should be individualised, intensive, sustained and frequently evaluated to optimise outcomes for all patients [31, 35, 37].

Table 3. Primary Outcomes (Audiometry and/or Speech Perception and/or Speech Production) (Continued)

| Study Reference | Preoperative Data (Mean) | Postoperative Data (Mean) |
|-----------------|--------------------------|--------------------------|
| Patients with post-CI outcomes reported: 25 |
| Subgroups: group 1: no ossification (n=10), group 2: partial ossification (n=10), group 3: total ossification (n=5) |
| Mean duration of deafness (months): 46.8 |
| Cochlear implant failure: 1 (after 12 months) |

CI, cochlear implantation; ESP, early speech perception; IT-MAIS, infant-toddler meaningful auditory integration scale; MUSS, meaningful use of speech scale; SPC, statistical process control; SD, standard deviation; LIP, listening profile; CAP, categorized auditory performance; WIPi, Word Intelligibility by Picture Identification; GASp, Glendonald auditory screening procedure; SIR, speech intelligibility rating; CAT, Calisign Acquisition Test; HSM, Hochmair-Schulz-Moser test; CDT, Connected Discourse Tracking.

Mean duration of deafness (months): 46.8

Group 1: no ossification (n=10), group 2: partial ossification (n=10), group 3: total ossification (n=5)

Patients with post-CI outcomes reported: 25

Educational and Occupational Outcomes

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CONCLUSION
Audiological outcomes following cochlear implantation in meningitis are satisfactory, providing functional levels of speech perception and intelligibility. Improvement in hearing is dependent on the amount of cochlear ossification, duration of deafness prior to implantation, electrode insertion depth and presence of neurological sequelae; patients with patent cochlea, full electrode insertion, shorter duration of deafness and no additional handicaps, appear to perform best. Cochlear implantation in meningitis patients can be challenging due to the presence of ossification and inaccuracies of pre-operative imaging. Therefore, early and bilateral implantation is recommended in all patients with post-meningitis hearing loss to improve the likelihood of full electrode insertion.

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Supplementary Material 1. Search strategy for MEDLINE database

| Field number | Search Terms |
|--------------|--------------|
| 1            | Exp meningitis, Hemophilus/ or exp meningitis, Cryptococcal or exp meningitis, Listeria or exp meningitis, Pneumococcal or exp meningitis, bacterial or exp meningitis, Meningococcal or exp meningitis, Escherichia coli or exp meningitis, aseptic or exp meningitis, viral or exp meningitis, fungal/ |
| 2            | Exp cochlear implants/ |
| 3            | Cochlear implantation |
| 4            | Cochlear implants.mp |
| 5            | Cochlear implant.mp |
| 6            | Cochlea prosthesis |
| 7            | 2 or 3 or 4 or 5 or 6 |
| 8            | 1 and 7 |