Technology Assessment

Technology Assessment Program

Effectiveness of Cochlear Implants in Adults with Sensorineural Hearing Loss

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The technical consultant, Marilyn W. Neault, PhD, CCC-A discloses her affiliation as an Audiology Advisor on the Advisory Panel of Cochlear™ Americas. Her role in this report was limited to educating the Tufts-EPC on cochlear implantation and speech perception tests.

All other investigators do not have any affiliation or financial involvement related to the material presented in this report.

Peer Reviewers

We wish to acknowledge individuals listed below for their review of this report. This report has been reviewed in draft form by individuals chosen for their expertise and diverse perspectives. The purpose of the review was to provide candid, objective, and critical comments for consideration by the EPC in preparation of the final report. Synthesis of the scientific literature presented here does not necessarily represent the views of individual reviewers.

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Table of Contents

List of Tables

Abbreviations

APHAB	Abbreviated Profile of Hearing Aid Benefit
ADIDS	Adapted Deaf Identity Developmental Scale
AQoL	Assessment quality-of-life
AzBio	AzBio sentence test
BKB	Bamford-Kowal-Bench speech perception test
BKB-SIN	Bamford-Kowal-Bench Speech-in-Noise Test
CID	Central Institute for the Deaf sentences
CNC	Consonant-Nucleus-Consonant words
CPA	Centro de Pesquisas Audiológicas sentence recognition test
CUNY	City University of New York tests
CVC	Consonant-Vocal-Consonant
dB HL	Decibel Hearing Level
EQ-5D	EuroQoL 5 dimensions
FDA	Food and Drug Administration
GBI	Glasgow Benefit Inventory
GHSI	Glasgow Health Status Inventory
HHIA	Hearing Handicap Inventory for Adults
HHIE	Hearing Handicap Inventory for the Elderly
HHQ	Hearing Handicap Questionnaire
HINT	Hearing in Noise Test
HINT-Q	HINT sentences/speech in quiet
HPS	Hearing Participation Scale
HRQoL	Health-related quality-of-life
HSM	Hochmair, Schultz and Moser sentence test
HUI-2	Health Utilities Index Mark II
HUI-3	Health Utilities Index Mark III
Hz	Hertz
KQ	Key Question
MCM	FDA product code for “implant, cochlear”
NCIQ	Nijmegen Cochlear Implant Questionnaire
NICE	National Institute for Clinical Excellence (UK)
OLSA	Oldenburg sentence test
SF-36	The Short Form (36) Health Survey
SNR	Signal to noise ratio
SPL	Sound pressure level
SRT	Speech recognition threshold
TAP	Technology Assessment Program
UKCISG	UK Cochlear Implant Study Group
VAS	Visual Analogue Scale

Detailed descriptions of abbreviations and relevant terms are listed in Appendix A.

Executive Summary

Background

Sensorineural hearing loss is the third leading cause of disability during the adult years, according to the World Health Organization. This type of hearing loss is usually permanent, most commonly occurs gradually, and becomes worse with increasing age with clinical manifestations typically appearing during the fifth and sixth decades. In recent years, cochlear implants have been used in adults with sensorineural hearing loss. Cochlear implants replace the function of hair cells that are no longer able to generate electrical impulses in response to sound. Therefore, these devices may provide a viable alternative to hearing aids among older adults with sensorineural hearing loss as they bypass damaged hair cells by directly transmitting the electrical impulses to the acoustic nerve. Currently, most patients are fitted unilaterally, with some receiving contralateral assistance with a hearing aid when residual low-frequency hearing exists. In recent years, the number of people implanted bilaterally has continued to increase. Therefore, the Centers for Medicare and Medicaid Services (CMS) is interested in an evaluation of recent published literature on the effectiveness of cochlear implantation. After consultation with the Agency for Healthcare Research and Quality (AHRQ) and CMS, this technology assessment has been commissioned specifically to evaluate the clinical effectiveness of unilateral cochlear implants and bilateral cochlear implants in adult patients (≥ 18 years of age) with sensorineural hearing loss. The key questions were formulated in consultation with CMS and AHRQ.

Methods

This report addresses the following key questions:

1. What current cochlear implantation devices are approved by the FDA for individuals ≥ 18 years of age? What are the indications for their use?

2. What are the communication-related health outcomes as well as the quality-of-life outcomes that are achieved in the population of adults (≥ 18 years old) who undergo unilateral cochlear implantation? How is a "successful" implantation defined?

2a. For those individuals ≥ 18 years of age with sensorineural hearing loss, what are the preoperative patient characteristics associated with the successful attainment of the aforementioned improved communication-related health outcomes as well as quality-of-life outcomes in those who undergo unilateral cochlear implantation?
At a minimum, the evidence surrounding the following will be discussed:

1. Speech recognition/word understanding
2. Auditory sensitivity/audibility
3. Duration of impaired hearing
4. Associated ear or bone disease
5. Pre vs. postlinguistic deafness

6. Presence of other disabilities (e.g. visual impairment, impending or current)
7. Age at implantation
8. Degree of preimplant residual hearing
9. Choice of implanted ear
10. Site or center (expertise) of cochlear implant team
11. Implanted device

2b. For studies included in key question 2 and 2a, report the available evidence separately for those individuals with sensorineural hearing loss as demonstrated by preimplantation test scores of > 40 percent and ≤ 50 percent, as well as those with test scores > 50 percent and ≤ 60 percent (best aided listening on tape or otherwise recorded tests of open-set sentence recognition).

3. For those individuals ≥ 18 years of age, what are the additional communication-related health outcomes as well as quality-of-life outcomes (as compared with those achieved in question 2) that are gained from the use of bilateral cochlear implants over a unilateral cochlear implant? How is a "successful" bilateral cochlear implant defined?

3a. What are the preoperative patient characteristics associated with the successful attainment of the communication-related health outcomes as well as quality-of-life outcomes in questions 2 or 3 in individuals ≥ 18 years of age who undergo simultaneous bilateral cochlear implantation?

3b. What are the preoperative patient characteristics associated with the successful attainment of the communication-related health outcomes as well as quality-of-life outcomes in questions 2 or 3 in individuals ≥ 18 years of age who undergo sequential bilateral cochlear implantation?

At a minimum, the evidence surrounding the following will be discussed:

1. Speech recognition/word understanding
2. Auditory sensitivity/audibility
3. Duration of impaired hearing
4. Associated ear or bone disease
5. Pre vs. postlinguistic deafness
6. Presence of other disabilities (e.g. visual impairment, impending or current)
7. Age at implantation
8. Degree of preimplant residual hearing
9. Choice of implanted ear
10. Site or center (expertise) of cochlear implant team
11. Implanted device

3c. For studies included in key question 3, 3a and 3b, report the available evidence separately for those individuals with sensorineural hearing loss as demonstrated by preimplantation test scores of ≤ 40 percent, > 40 percent and ≤ 50 percent, as well as those with test scores between > 50 percent and ≤ 60 percent (best aided listening on tape or otherwise recorded tests of open-set sentence recognition).

For Key Question 1, we searched the Food and Drug Administration (FDA) database, Devices@FDA, the database of cleared and approved devices, for the term *cochlear*. We also searched for the term *MCM* (the specific product code for "implant, cochlear") in the Premarket Approval database of the FDA. In ClinicalTrials.gov, we searched the term *cochlear*. For key questions 2 and 3, we searched MEDLINE®, the Cochrane Central Register of Controlled Trials, and Scopus (which includes articles indexed in Embase since 1997) from January, 2004 through February, 2011 for published studies of adult human subjects to identify articles relevant to each key question. Primary interventions of interest were both unilateral and bilateral cochlear implantation; also included were both sequential and simultaneous bilateral cochlear implantation as well as studies of patients who used both cochlear implants and hearing aids. Eligible devices included one or two multichannel cochlear implants using whole-speech processing coding strategies. We also included studies that compared preoperative and postoperative cochlear implantation, evaluating outcomes of interest. Comparisons of bilateral cochlear implantation with unilateral cochlear implantation with or without hearing aids, and with cochlear implantation left ear or right ear unilaterally were included. Outcomes of interest involved sound localization, speech perception outcomes (open-set sentences, two syllable or multi-syllable words), derived measures of binaural processing outcomes (head shadow, squelch, and summation) and health-related quality-of-life.

Items extracted included relevant study characteristics and population characteristics. Preoperative patient characteristics associated with communication-related health outcomes and health-related quality-of-life included speech recognition/word understanding, duration of impaired hearing, associated ear or bone disease, pre versus postlinguistic deafness, other disabilities (e.g., visual impairment, impending or current), age, degree of preimplant residual hearing, choice of implanted ear, site or center (expertise) of cochlear implant team, and implanted device. Outcomes were categorized according to open-set speech test, two syllable or multi-syllable test, health-related quality-of-life measures, and communication-related adverse events. We used a 3-grade (A, B, C) rating system to rate the quality of each individual study. We also used a 3-category rating system (high, moderate, insufficient) to assess the overall strength of evidence for the outcomes reported in each of the comparisons.

Results and Strength of Evidence

We searched for articles on cochlear implants in adults published between January 2004 and February 2011 in the MEDLINE®, Scopus, and Cochrane Central databases and found 56 out of 1,908 articles that met our inclusion criteria.

Key Question 1: FDA-approved cochlear implant devices

Our search of the FDA Web site found three cochlear implant devices currently approved for use in the U.S.: the Nucleus® 5 (Cochlear™), the Harmony™ HiRes 90K® (Advanced Bionics®), and the MAESTRO™ Cochlear Implant System [either $SONATA_{TI}^{100}$ or $PULSAR_{CI}^{100}$ implants] (MED-EL). Criteria for cochlear implant candidacy are variable across devices and individual to each. Based on the safety and efficacy information provided to the FDA by each device manufacturer, likely candidates could have percent correct scores on the Hearing in Noise Test (HINT) or open–set sentence recognition tests ranging from ≤ 40 to ≤ 60 percent (depending on the device as described in Table 1).

Key Question 2: Effectiveness of unilateral cochlear implants

Evidence was rated as moderate based on nine quality-B studies (total of 22 studies), where postimplantation speech perception among adult subjects was greater compared with preimplantation speech perception as assessed with multi-syllable tests and open-set sentences tests, with or without hearing aids. Benefits were similarly shown in speech perception with unilateral cochlear implantation compared with hearing aids in one study. When health-related quality-of-life was evaluated with generic measures, unilateral cochlear implantation showed significant benefit on overall health-related quality-of-life and social domains compared with preimplantation measures. In addition, using disease-specific instruments of health-related quality-of-life measures, unilateral cochlear implantation showed benefits compared with preimplantation measures in these studies.

Key Question 2a: Preoperative patient characteristics associated with post implant improvement in communication and health outcomes

Evidence was rated low for eight quality-B studies (total of 21 studies), due to methodological deficiencies, that assessed preoperative patient characteristics as potential modifying factors of speech and/or quality-of-life outcomes including: duration of impaired hearing, age of implantation, older (≥ 65 years old) versus younger age (< 65 years old), type of implanted device, preoperative speech recognition or word understanding, degree of preimplant residual hearing, associated ear or bone disease, pre versus postlinguistic deafness, age of onset of hearing loss, and choice of implanted ear. No studies evaluated implant center/expertise of cochlear implant teams or other patient-related disabilities as potential modifying factors of outcomes. Overall, there was a low level of evidence regarding the association between preoperative patient characteristics (such as shorter duration of impaired hearing and better preoperative HINT score) and better postoperative speech outcomes. In addition, the studies provided insufficient evidence to draw a conclusion about the relationships between preoperative patient characteristics and postoperative health-related quality-of-life outcomes.

Key Question 2b: Effectiveness of unilateral cochlear implants by their preimplantation open-set sentence test scores of > 40 percent and ≤ 50 percent, and > 50 percent and ≤ 60 percent

Evidence was rated insufficient based on lack of data to address this question. Of the 22 studies that evaluated Key Question 2, there were no studies that used the results of open-set sentence tests for cochlear implantation indication. Of the 21 qualifying studies that evaluated Key Question 2a, only two (one quality-B; one quality-C) provided relevant data for this question. The quality-B study was a retrospective cohort of elderly (≥ 70 years old). Elderly with preimplantation HINT-Q scores below 20 percent, 20 to 40 percent, and > 40 percent were analyzed with respect to 1 year postimplant HINT-Q scores. The results indicated that better preimplant HINT-Q scores showed significant association with higher postimplant HINT-Q (r=0.44, P=0.02), and HINT-N (r=0.43, P=0.04) scores regardless of age. Only adults implanted with either the Clarion device or Nucleus device between 1991 and 2002 were included in the analyses. The criteria for cochlear implantation included severe-to-profound hearing loss in both ears (mean 70 dB) and a score of less than 50 percent on an open-set sentence test using conventional hearing aid(s). The proportion of patients between the scores of > 40 percent and ≤ 50 percent was unclear. Sixty-five elderly adults (≥ 70 years old) were compared with 101 younger adults (< 70 years old) for speech outcomes. The study found that both elderly and younger adults had significant improvements in HINT and CID scores after implantation.

However, there were no significant differences between groups (P=0.07). This analysis was not adjusted for potential confounding factors.

Key Question 3: Effectiveness of bilateral cochlear implants, sequential and simultaneous

Evidence was rated moderate to low based on data from nine quality-B studies assessing subjects with simultaneous or sequential bilateral cochlear implantation. Overall, 16 studies published since 2004 evaluated subjects with bilateral cochlear implants that met our eligibility criteria. Studies evaluating speech perception in noise conditions found significant gains with bilateral simultaneous cochlear implants compared with a unilateral cochlear implant. One cross-sectional study showed no benefit and another study did not evaluate speech outcomes. The results of speech perception in quiet and health-related quality-of-life were mixed across studies. Only three of 16 studies assessed health-related quality-of-life in subjects with bilateral implants. While subjects with bilateral cochlear implants showed significant gains in some disease-specific instruments of health-related quality-of-life subscales, others found no difference between the two groups. In a randomized controlled trial evaluating sequential bilateral cochlear implants, the second ear implant resulted in negative or non-significant results for quality-of-life after the first ear implant.

Key Question 3a, 3b: Preoperative patient characteristics associated with post implant improvement in communication and health outcomes among bilateral implants

Evidence was rated low based on two quality-B rated studies reporting data on age at implantation as a predictor of postoperative outcomes. The first study reported that preoperative characteristic such as age at implantation (≤ 59 years of age) was predictive of different postoperative outcomes evaluated in this study among simultaneous bilateral implants. The second study did not find an association between age at second implant and postoperative outcomes among sequential bilateral implants. Duration of hearing loss before implant (two quality-B studies) and implant device characteristics (one quality-B study) did not predict postoperative outcomes in bilateral implants.

Key Question 3c: Effectiveness of bilateral cochlear implants by their preimplantation test scores test scores of ≤ 40 percent, > 40 percent and ≤ 50 percent, and > 50 percent and ≤ 60 percent

Overall, evidence was rated low for the effectiveness of simultaneous bilateral implantation by their preimplantation open-set sentence test scores of ≤ 40 percent, which was evaluated in three quality-B studies that showed improved speech perception, and sound localization, but inconsistent gains in terms of hearing-specific quality-of-life in one study. Evidence was rated moderate for the effectiveness of simultaneous bilateral implantation by their preimplantation open-set sentence test scores of ≤ 40 percent, which was evaluated in three quality-B studies that showed improved speech perception, sound localization, and binaural processing. Evidence was rated insufficient for the outcome of hearing-specific quality-of-life in one study that evaluated this outcome. Although two studies of simultaneous bilateral implants conducted in the U.S. reported the requirement of an open-set sentence score of ≤ 50 percent in the best-aided condition as an indication for bilateral cochlear implantation, the evidence was rated insufficient because of lack of information on the percentage of subjects with preimplantation scores of > 40 percent and ≤ 50 percent. No studies reported data on the preimplantation scores of > 50 percent and ≤ 60 percent among bilateral implants.

Evidence was rated insufficient for the effectiveness of sequential bilateral implantation by the preimplantation test scores of ≤ 40 percent, which was evaluated in one quality-B study that showed improved speech perception in noise, and sound localization. This study included subjects who had a preoperative open-set sentence score of minimum 30 percent (after first ear implant) in the best-aided condition as an indication for bilateral cochlear implantation. This study reported that no significant advantage after the second ear implant over the first (unilateral) ear with the CUNY test in quiet at 3 and 9 months of followup. The second ear implant also resulted in negative results or non-significant changes in health-related quality-of-life after the first ear implant.

Discontinuation of use

Of the 56 articles included in this report, four studies reported adverse events of total hearing loss or permanent discontinuation of use as a result of hearing-related complications. Twenty out of 495 distinct subjects within these studies permanently discontinued use of their cochlear implant(s) after experiencing an adverse event.

ES Table 1. Strength of Evidence for Effectiveness of Cochlear Implants in Adults with Sensorineural Hearing Loss

	High	Moderate	Low	Insufficient
KQ1. Current cochlear implantation devices that are approved by the FDA in adults	--	--	--	--
KQ2. Effectiveness of unilateral cochlear implants				
Speech perception using open-set sentences tests; multi-syllable tests		X		
Generic or disease-specific HRQoL outcomes		X		
2a. Association between preoperative patient characteristics and postoperative outcomes after unilateral cochlear implants				
Speech perception using open-set sentences tests				
Duration of impaired hearing		X		
Age at implantation			X	
Type of implanted device			X	
Older age (≥65 yr) versus younger age, preoperative speech perception scores, degree of preimplant residual hearing, associated ear or bone disease, post versus prelinguistic deafness, age of hearing loss onset, or choice of implanted ear				X
Implant center or expertise of cochlear implant team or other patient-related disabilities				X[a]
Generic or disease-specific HRQoL outcomes				
Duration of impaired hearing, age at implantation, older age (≥65 yr) versus younger age, preoperative speech perception scores, or degree of preimplant residual hearing				X
Type of implanted device, associated ear or bone disease, post versus prelinguistic deafness, age of hearing loss onset, choice of implanted ear, implant center or expertise of cochlear implant team or other patient-related disabilities				X[a]
2b. Data for individuals with specific indications for unilateral cochlear implants[b]				X
KQ3. Effectiveness of bilateral versus unilateral cochlear implants				
3. Bilateral simultaneous cochlear implants				
Speech perception using open-set sentences tests; multi-syllable tests		X		
Sound localization		X		
Generic or disease-specific HRQoL outcomes			X	
3. Bilateral sequential cochlear implants				
Speech perception using open-set sentences tests; multi-syllable tests		X		
Sound localization		X		
Generic or disease-specific HRQoL outcomes			X	

Continued

ES Table 1. (continued)

	High	Moderate	Low	Insufficient
3a, b. Association between preoperative patient characteristics and postoperative outcomes after bilateral cochlear implants				
Age at implantation			X	
Duration of impaired hearing			X	
Type of implanted device				X
Degree of preimplant residual hearing, associated ear or bone disease, post versus prelinguistic deafness, age of hearing loss onset, or choice of implanted ear, implant center or expertise of cochlear implant team or other patient-related disabilities				X[a]
3c. Data for individuals with specific indications for bilateral cochlear implants[b]				X
Bilateral simultaneous cochlear implants			X	
preimplantation open-set sentence test scores of ≤ 40 percent and outcome speech perception		X		
preimplantation open-set sentence test scores of ≤ 40 percent and outcome quality-of-life				X
Bilateral sequential cochlear implants				
preimplantation open-set sentence test scores of ≤ 40 percent				X

HRQoL = health-related quality-of-life
[a:] No study available
[b:] Individuals with sensorineural hearing loss as demonstrated by test scores of > 40 percent and ≤ 50 percent, as well as those with test scores > 50 percent and ≤ 60 percent

Discussion

Our review indicates that unilateral cochlear implantation is an effective method of hearing assistance that provides significant gains in speech perception and health-related quality-of-life in adults with sensorineural hearing loss. Adults showed significant benefit in postimplantation speech perception scores (both multi-syllable tests and open-set sentences tests) over preimplantation scores, which were consistent across studies whether they did or did not utilize bimodal hearing (unilateral cochlear implantation with additional use of hearing aids). In general, unilateral cochlear implantation showed benefits in both generic and disease-specific health-related quality-of-life measures compared with preimplantation results. Studies of unilateral implants provided low to insufficient level evidence regarding relationships between preoperative patient characteristics and postoperative health-related quality-of-life outcomes, making it difficult to render any conclusions. There was insufficient evidence to address the effectiveness of unilateral cochlear implants by their preimplantation open-set sentence test scores of > 40 percent and ≤ 50 percent, and > 50 percent and ≤ 60 percent. Reviewed studies from current literature were rated moderate or poor quality due to incomplete reporting of information including study selection criteria, recruitment of study subjects and year of recruitment, center characteristics, and reasons for loss to followup.

Results from recently published studies of bilateral cochlear implantation imply greater benefit in speech perception test scores among adults compared with unilateral cochlear implantation with or without hearing aids, particularly in noise conditions. There is a demonstrated advantage in speech perception discrimination in noise with bilateral hearing, apparently with intact ears or with cochlear implants. However, benefit under quiet conditions was unclear suggesting that in such quiet conditions, the first ear implant may likely to be "ceiling out" the effects of the second ear's implant under such listening conditions. Results from a series of studies indicated significant binaural head-shadow benefit, in bilateral listening conditions over unilateral listening conditions, suggesting that subjects with bilateral cochlear implants could perform better in real world conditions. In the reviewed literature, one study found a small binaural squelch effect after 1 year of bilateral implantation, while four studies found small or non-significant squelch effects. The results of this review document an increase in benefit following long-term experience with bilateral implants, thus emphasizing a need for long-term followup studies. Estimates of binaural summation were slightly better in bilateral listening condition but were statistically non-significant compared with the unilateral listening conditions in two studies. These study results were in contrast and summation values were smaller than the effects reported in one study. Given the small number of subjects with bilateral cochlear implants included in these studies, cautious interpretation of these results is needed to draw definitive conclusions. Although evidence was rated moderate for the effectiveness of simultaneous bilateral implantation by their preimplantation open-set sentence test scores of ≤ 40 percent, there was insufficient data for the outcome of hearing-specific quality-of-life as only one study evaluated this outcome. The evidence was rated insufficient because of lack of information on the percentage of subjects with bilateral implants who had preimplantation scores of > 40 percent and ≤ 50 percent. No studies reported data on the preimplantation scores of > 50 percent and ≤ 60 percent among bilateral implants. Lack of information on candidacy criteria in evaluated studies emphasizes the need for additional research to address health policy needs.

Although published studies revealed significant gains in terms of speech perception outcomes, this did not translate to consistent gains in the perceived performance as assessed through a variety of health-related quality-of-life measures in three studies of bilateral cochlear implantation. Sparse data and inconsistent benefits in terms of health-related quality-of-life outcomes preclude any definitive conclusions with regard to benefits in quality-of-life outcomes in subjects with bilateral cochlear implantation. In general, cochlear implantation is safe and provides benefit to patients. Similar to any surgical procedure, complications can occur. A second ear implant brings additional risk in terms of additional surgery and an increase in operating time. Further studies with longer followup duration are needed to assess the benefits and potential risks of bilateral cochlear implantation.

Conclusion

In summary, unilateral cochlear implantation with or without additional use of hearing aids has been an effective method of hearing assistance. Published studies show improved speech perception and health-related quality-of-life in adults with sensorineural hearing loss. Bilateral cochlear implantation provides added improvements in speech perception outcomes in noisy environments over unilateral cochlear implantation. With future improvements in implant device technology and implant programming, the number of patients implanted bilaterally will continue to increase. Further studies with longer followup duration are needed to assess the additional benefits in terms of improved health-related quality-of-life and potential risks of bilateral cochlear implantation compared with unilateral implantation. Additionally, none of the studies have been able to quantify the sensation described by patients of fusion of bilateral sound into a stereo perception within one's head. There is a need to develop better measures of performance and disease-specific quality-of-life instruments that may reflect the significance of these subjective benefits.

Introduction

Background

Hearing loss is the third most common chronic condition among the elderly in the United States, affecting about one-third of adults over 65 years of age and half in their 80s.[1] The three types of hearing loss are conductive, sensorineural, and central. Of these, sensorineural is most prevalent among older adults, and is the third leading cause of disability during the adult years, according to the World Health Organization.[1] Sensorineural hearing loss most commonly occurs gradually and becomes worse with age, with clinical manifestations typically appearing during the fifth and sixth decades. Sensorineural hearing loss is also usually permanent.

Sensorineural hearing loss is characterized by the gradual attenuation of the intensity of sound. For a pure attenuation loss, acoustic amplification, such as that with a hearing aid, is an excellent option. With increased levels of sensorineural hearing loss, there also comes loss of frequency selectivity and other forms of distortion within the inner ear. These effects cannot be addressed with hearing aids. The result is significant speech perception difficulties, particularly during conversations. This occurs both during one-on-one and group conversations (especially in the presence of ambient noise in a public setting), and while listening to speech conveyed via transmitting equipment (e.g. telephone, fast-food drive-through, etc.). Untreated hearing loss among adults may contribute to the overall decline of health during aging and leads to depression, social withdrawal, underemployment, diminished quality-of-life secondary to communication problems, and may be a factor in dementia.[1, 2]

Presbycusis is the most common type of sensorineural hearing loss among elderly in the United States. In adults (≥ 18 years of age), causes of sensorineural hearing loss can include ototoxicity, otosclerosis, trauma, autoimmune diseases, and others. Among the elderly, chronic systemic conditions including heart disease, high blood pressure, diabetes, and other circulatory problems are common and may exacerbate hearing loss.[2, 3] In addition, some commonly prescribed medications regularly used by adults including some antibiotics, loop diuretics, and anti-inflammatory agents have ototoxic side effects.[2]

Most cases of hearing loss are treated using a number of electronic-acoustic devices such as hearing aids, personal listening systems, bone-anchored hearing aids, and cochlear implants. Of these devices, hearing aids and cochlear implants are the most commonly used devices in the treatment of sensorineural hearing loss.[1] Traditional hearing aids may improve hearing function by amplifying sound, but are often ineffective in people with severe (between 70-94 decibels [dB]) to profound (≥ 95 dB) sensorineural hearing loss. The clarity and comprehension of speech is measured by word recognition (formerly called speech discrimination) with scores in persons with unimpaired hearing typically > 90 percent. In recent years, cochlear implants have been used in older adults.[3] Cochlear implantation is not a treatment option for people with conductive or central deafness.

Cochlear Implantation

Cochlear implants replace the function of sensory hair cells in the cochlea that are no longer able to generate electrical impulses in response to sound. Therefore, cochlear implants may provide a viable alternative to hearing aids among adults with profound sensorineural hearing loss as they bypass the damaged hair cells by directly transmitting electrical impulses to the

acoustic nerve. These devices consist of external components positioned to rest on the head just behind the ear, and internal components that are placed beneath the skin. The external components consist of a microphone; a speech processor, which analyzes and codes the sounds received by the microphone; and a transmitter coil. An internal receiver/stimulator converts signals received from the speech processor into electrical impulses. The impulses are passed into a series of wires that comprise an electrode array, a group of electrodes that are positioned within the cochlea to collect the impulses from the stimulator into the cochlea where they will pass to the acoustic nerve.

Food and Drug Administration Labeled Use

Cochlear implants can improve the user's ability to distinguish speech and hear conversations amid noisy conditions,[3] hear and speak on the phone, and listen to music and the television at more adequate levels than before.[1] Currently, patients are fitted with unilateral cochlear implants, with some receiving contralateral assistance from a hearing aid when residual hearing is present but insufficient. The Food and Drug Administration (FDA) recommended the use of cochlear implants only in adults with profound hearing loss as early as the 1970s,[4] and first approved the use of multichannel cochlear implant devices in 1985 for adults aged 18 and older who are postlinguistically deaf with bilateral, profound sensorineural hearing loss and score 0 percent on aided speech recognition tests, indicating little to no open-set sentence discrimination. As advances were made in cochlear implant technology, these criteria for adults were expanded to include those with residual hearing who are either prelinguistically or postlinguistically deaf with moderate-to-profound sensorineural hearing loss in the low frequencies or profound loss in the mid-to-high frequencies (Table 1 in the Results section lists the current FDA-approved devices).[5]

Social Security Administration Guidelines

Patients fitted with cochlear implants are eligible for disability status. Recent guidelines from the Social Security Administration cite the following hearing loss criteria: adults with implants qualify for disability one year after initial implantation or, if after one year, achieve a speech recognition score of < 60 percent on the Hearing in Noise Test (HINT) as administered in quiet conditions.[6]

Recent Health Technology Assessment

The UK-based National Institute for Health and Clinical Excellence (NICE) guidance document for hearing loss is based on a technology assessment by the NICE Appraisal Committee, which reviewed English-language literature published through 2007 on multichannel cochlear implants using whole-speech processing coding strategies.[7] The findings for adults from the systematic review were as follows: unilateral cochlear implantation benefitted adults who had postlinguistic hearing loss, as compared with those with prelinguistic hearing loss, and reported statistically significant improvement in quality-of-life outcomes following unilateral implantation. For comparisons of bilateral implantation versus unilateral implantation, statistically significant acoustic benefit and speech perception occurred among subjects with bilateral implantation, but mixed results were found for quality-of-life outcomes. The guidelines included an additional cost-effective analysis. Unilateral implantation was recommended as a treatment option for adults with profound deafness as it is highly likely to be cost-effective. In addition, the NICE guidelines included recommendations for bilateral simultaneous cochlear implantation for adults with disabilities, such as blindness, who may rely primarily on their

auditory senses. Although NICE does not recommend bilateral implantation for the treatment of severe-to-profound hearing impairment, it does defer to the clinician's decision regarding individual benefit after informed discussion with potential patients. NICE also recommends that candidacy be determined by a multidisciplinary team that considers each individual's level of disability (physical and cognitive as well as linguistic), and suggests that care be taken to administer speech assessment tests in language familiar to patients. The guideline suggests bilateral implants in adults are likely to provide added benefits for communication in social situations.

As additional studies on adults with cochlear implantation have been published since the recent systematic review,[3] the Centers for Medicare and Medicaid Services (CMS) is interested in a review of current literature on cochlear implantation in adults with prelinguistic or postlinguistic sensorineural hearing loss. The Coverage and Analysis Group at CMS requested this report from The Technology Assessment Program (TAP) at the Agency for Healthcare Research and Quality (AHRQ). AHRQ assigned this report to the following Evidence-based Practice Center: Tufts Evidence Practice Center (Tufts-EPC) (Contract Number: 290 2007 10055 I).

Key Questions

Our objective was to answer the following key questions on the use of cochlear implantation in adults with sensorineural hearing loss and evaluate their applicability in a subset of Medicare populations (65 years of age or older). The key questions were formulated in consultation with CMS and AHRQ.

1. What current cochlear implantation devices are approved by the FDA for individuals ≥ 18 years of age? What are the indications for their use?

2. What are the communication-related health outcomes as well as the quality-of-life outcomes that are achieved in the population of adults (≥ 18 years old) who undergo unilateral cochlear implantation? How is a "successful" implantation defined?

2a. For those individuals ≥ 18 years of age with sensorineural hearing loss, what are the preoperative patient characteristics associated with the successful attainment of the aforementioned improved communication-related health outcomes as well as quality-of-life outcomes in those who undergo unilateral cochlear implantation? At a minimum, the evidence surrounding the following will be discussed:

1. Speech recognition/word understanding
2. Auditory sensitivity/audibility
3. Duration of impaired hearing
4. Associated ear or bone disease
5. Pre vs. postlinguistic deafness
6. Presence of other disabilities (e.g. visual impairment, impending or current)
7. Age at implantation
8. Degree of preimplant residual hearing

9. Choice of implanted ear
10. Site or center (expertise) of cochlear implant team
11. Implanted device

2b. For studies included in key question 2 and 2a, report the available evidence separately for those individuals with sensorineural hearing loss as demonstrated by preimplantation test scores of > 40 percent and ≤ 50 percent, as well as those with test scores > 50 percent and ≤ 60 percent (best aided listening on tape or otherwise recorded tests of open-set sentence recognition).

3. For those individuals ≥ 18 years of age, what are the additional communication-related health outcomes as well as quality-of-life outcomes (as compared with those achieved in question 2) that are gained from the use of bilateral cochlear implants over a unilateral cochlear implant? How is a "successful" bilateral cochlear implant defined?

3a. What are the preoperative patient characteristics associated with the successful attainment of the communication-related health outcomes as well as quality-of-life outcomes in questions 2 or 3 in individuals who are ≥ 18 years of age who undergo simultaneous bilateral cochlear implantation?

3b. What are the preoperative patient characteristics associated with the successful attainment of the communication-related health outcomes as well as quality-of-life outcomes in questions 2 or 3 in individuals who are ≥ 18 years of age who undergo sequential bilateral cochlear implantation?
At a minimum, the evidence surrounding the following will be discussed:
1. Speech recognition/word understanding
2. Auditory sensitivity/audibility
3. Duration of impaired hearing
4. Associated ear or bone disease
5. Pre vs. postlinguistic deafness
6. Presence of other disabilities (e.g. visual impairment, impending or current)
7. Age at implantation
8. Degree of preimplant residual hearing
9. Choice of implanted ear
10. Site or center (expertise) of cochlear implant team
11. Implanted device

3c. For studies included in key question 3, 3a, and 3b, report the available evidence separately for those individuals with sensorineural hearing loss as demonstrated by preimplantation test scores of > 40 percent and ≤ 50 percent, as well as those with test scores between > 50 percent and ≤ 60 percent (best aided listening on tape or otherwise recorded tests of open set sentence recognition).

Methods

The objective of this technology assessment report is to conduct a systematic review of the clinical effectiveness of unilateral and bilateral cochlear implants in adult patients with sensorineural hearing loss. The methods for this technology assessment largely follow those outlined in the AHRQ *Methods Guide for Comparative Effectiveness Reviews*, available at: http://effectivehealthcare.ahrq.gov/healthInfo.cfm?infotype=rr&ProcessID=60.

Technical Experts

The Tufts-EPC collaborated with a physician with expertise in adult cochlear implantation from the Department of Otology and Laryngology, Harvard Medical School, who provided input to the Tufts EPC project team regarding the population, clinical conditions, and the interventions of interest with respect to the key questions of interest, and participated in the review and revisions of the report. An audiologist from the audiology program at the Children's Hospital, Boston conducted an educational seminar on cochlear implantation and speech perception outcomes, but did not participate in conducting the review or in preparation or approval of the report.

Search Strategy

A comprehensive search of the scientific literature was conducted to identify relevant studies addressing the key questions. For Key Question 1, we searched the FDA database, Devices@FDA, the database of cleared and approved devices, for the term *cochlear*. We also searched for the term *MCM* (the specific product code for "implant, cochlear") in the Premarket Approvals database of the FDA. In ClinicalTrials.gov, we searched the term *cochlear*. For Key Questions 2 and 3, we searched MEDLINE®, the Cochrane Central Register of Controlled Trials, and Scopus (which includes articles indexed in Embase since 1997) from January 2004 through February 2011 for published studies of adult human subjects to identify articles relevant to each key question. We also reviewed reference lists of related systematic reviews and selected narrative reviews, and primary articles. In electronic searches, we combined terms for unilateral and bilateral cochlear implantation and sensorineural hearing loss, and limited search terms to adult humans (see Appendix A for complete search strategy). We invited technical consultants and peer and public reviewers to provide additional citations. We did not use any language restriction.

Study Selection

We assessed titles and/or abstracts of citations identified from literature searches for inclusion, using the criteria described below. Full-text articles of potentially relevant abstracts were retrieved, and a second review for inclusion was conducted by reapplying the inclusion criteria.

Population and Condition of Interest

We focused on studies of patients with sensorineural hearing loss, and exclusively on studies of adults (≥ 18 years) with cochlear implantation for sensorineural hearing loss. Studies that included subjects with a cochlear implant ≥ 60 years were considered generalizable to the subset

of Medicare population. We thus excluded studies of conductive deafness, studies evaluating children-only populations or studies with data not separately available for children and adults, and reviews without primary data.

Interventions of Interest

The primary interventions of interest were both unilateral and bilateral cochlear implantation. Eligible cochlear implantation included one or two multichannel cochlear implants using whole-speech processing coding strategies. We included both sequential and simultaneous bilateral cochlear implantation. Also included were studies with patients who used both cochlear implants and hearing aids. We limited data to recent cochlear implant devices that use whole-speech processing strategies by restricting our searches to studies published since 2004. We excluded studies of brain stem implants, middle ear implants, and bone-anchored hearing aids used for conductive and mixed hearing loss.

Comparators of Interest

We considered the following comparisons of interest: unilateral cochlear implantation compared with hearing aids in one ear or both ears, and bilateral cochlear implantation. We also included studies that compared preoperative and postoperative cochlear implantation for clinical outcomes of interest. Bilateral cochlear implantation was compared with unilateral cochlear implantation with or without hearing aids from an external cohort, and with either ear implant unilaterally (i.e., cross-over design within subjects).

Outcomes of Interest

Outcomes of interest involved speech perception outcomes (open-set sentences, two syllable or multi-syllable words) and health-related quality-of-life. A speech perception test is considered to be "open-set" if the listener is required to recognize words or sentences without the presence of response alternatives (a free recall response). Listeners must identify what they heard by repeating or writing down the words or sentences. Two-syllable or multi-syllable words are words that may or may not have equal emphasis on all syllables (see Appendix A1 for term definitions). Health-related quality-of-life outcomes included generic or hearing-specific quality-of-life measures (see Appendix A2 for term definitions). For bilateral cochlear implantation, sound localization and derived measures of binaural processing capabilities such as, head shadow, squelch, and summation were also assessed (see Appendix A3 for term definitions). We included data on device non-use and hearing loss after cochlear implantation. We excluded studies with music tests as the only outcomes and studies of surgical or implant techniques without data on outcomes of interest. Studies with available evidence were evaluated separately for those individuals with sensorineural hearing loss as demonstrated by preimplantation test scores between 40 and 50 percent, as well as those with test scores between 50 and 60 percent (best aided listening on tape or otherwise recorded tests of open-set sentence recognition).

Study designs and sample size

We included studies of any design to address Key Questions 2 and 3. For Key Question 2, we included studies with at least 30 subjects with cochlear implants. Sample size thresholds were chosen based primarily on practical consideration of available resources and time balanced with the likely amount of available literature. For Key Question 3, we included studies with at least 10

subjects with cochlear implants per study. This cut-off was based on a small number of studies evaluating bilateral cochlear implantation.

Predictors of Interest

The predictors of interest were defined a priori during key question development, and included: speech recognition/word understanding, auditory sensitivity/audibility, duration of impaired hearing, associated ear or bone disease, pre versus postlinguistic deafness, presence of other disabilities (e.g. visual impairment, impending or current), age (i.e., age at implantation, or older vs. younger age at baseline), degree of preimplant residual hearing, choice of implanted ear, site or center (expertise) of cochlear implant team, and implanted device.

Data Extraction

For study characteristics, we extracted the following items: the first author's name, year, PubMed ID, study design, country/setting, recruitment dates, funding source, inclusion and exclusion criteria, interventions, comparators, concurrent treatment, outcome assessor, and duration of followup. For population characteristics, the items extracted were: the number of patients enrolled and completed, age, percentage of male patients, degree and duration of deafness, device coding strategy, and time between deafness and cochlear implantation.

We also extracted the following preoperative patient characteristics that might be associated with communication-related health outcomes as well as health-related quality-of-life: speech recognition/word understanding, duration of impaired hearing, associated ear or bone disease, pre versus postlinguistic deafness, other disabilities (e.g., visual impairment, impending or current), age, degree of preimplant residual hearing, choice of implanted ear, site or center (expertise) of cochlear implant team, and implanted device (see Appendix B for the data extraction forms).

For outcomes, we categorized them into speech test, two syllable/multi-syllable test, health-related quality-of-life measures, and communication-related adverse events. We briefly described each outcome measure and summarized the relevant data from the primary studies. We conducted a systematic review without performing any meta-analysis due to heterogeneity in methodologies including duration of deafness, implanted devices, speech coding strategies, and outcome tests. In summary tables, we indicated the direction of outcomes using dark up arrows (benefit with statistical significance), white up arrows (benefit but no statistical significance), dark down arrows (worse and statistical significance), white down arrows (worse but no statistical significance), and white side arrows (no difference between comparison groups).

Quality Assessment

We employed a three-grade classification (A, B, or C) using the AHRQ Methods Guide for Effectiveness and Comparative Effectiveness Reviews (available at: http://effectivehealthcare.ahrq.gov/healthInfo.cfm?infotype=rr&ProcessID=60). We used a quality assessment method that produces a generic grading scale that is applicable to various study designs including randomized controlled trials and cohort studies. We specifically noted study characteristics, such as study design (i.e., prospective, case control, retrospective, and cross-sectional), selection bias, recall bias, the appropriate selection of a representative population sample, attrition bias, and identification for the potential confounders.

"A" quality studies. Quality-A studies are considered good quality studies, which have the least bias and their conclusions are considered valid. Good quality studies generally meet the following criteria: clear description of eligibility criteria, unbiased selection of subjects, drop-rates less than 20 percent, assessment of blinding, adjustments for confounding factors and the use of random sampling.

"B" quality studies. Quality-B studies are considered fair or moderate quality studies that are susceptible to some bias, but it is not sufficient to invalidate the results. Quality-B studies do not meet all the criteria listed for Quality-A studies nor provide complete information. However, none of them introduce a significant bias.

"C" quality studies. Quality-C studies are considered poor quality studies that have significant flaws that imply biases of various types that may invalidate the study results. These studies introduce major errors in methods, analysis or discrepancies in reporting results.

Grading a Body of Evidence

We graded the strength of the body of evidence for each analysis within each key question as per the AHRQ methods guide, with modifications as described below. Risk of bias was defined as low, medium, or high based on the study design and methodological quality. We assessed the consistency of the data as either "no inconsistency" or "inconsistency present" (or "not applicable" if only one study). The direction, magnitude, and statistical significance of all studies were evaluated in assessing consistency, and logical explanations were provided in the presence of equivocal results. We also assessed the relevance of evidence and the precision of the evidence based on the degree of certainty surrounding an effect estimate. A precise estimate was considered an estimate that would allow a clinically useful conclusion. An imprecise estimate was one for which the confidence interval was wide enough to preclude a conclusion.

Based on individual studies rated quality-A or -B, we rated the strength of evidence with one of the following four strengths (as per the AHRQ methods guide): High, Moderate, Low, and Insufficient. Ratings were assigned based on our level of confidence that the evidence reflected the true effect for the major comparisons of interest. Ratings were defined as follows:

High. There is a high level of assurance that the findings of the literature are valid with respect to the relevant comparison. No important scientific disagreement exists across studies. At least two quality-A studies are required for this rating. In addition, there must be evidence regarding important clinical outcomes. Further research is very unlikely to change our confidence in the estimate of effect.

Moderate. There is a moderate level of assurance that the findings of the literature are valid with respect to the relevant comparison. Little disagreement exists across studies. Moderately-rated bodies of evidence contain fewer than two quality-A or-B studies or such studies lack long-term outcomes of relevant populations. Further research may change our confidence in the estimates of effect and may change the estimate.

Low. There is a low level of assurance that the findings of the literature are valid with respect to the relevant comparison. Underlying studies may report conflicting results. Further research is likely to change our confidence in the estimate of effect and may change the estimate for this outcome.

Insufficient. Evidence is either unavailable or does not permit estimation of an effect due to a lack of or sparse data. In general, when only one study has been published, the evidence was considered insufficient, unless the study was particularly large, robust, and of good quality.

Results

Our search of the FDA Web site found three cochlear implant devices currently approved for use in the U.S. We searched for articles on cochlear implants in adults published between January 2004 and February 2011 in the MEDLINE®, Scopus (which includes articles indexed in Embase since 1997) and Cochrane Central databases and found 56 out of 1,908 articles that met our inclusion criteria (Appendix C). Detailed descriptions of individual studies are provided in summary tables available in Appendix D.

Key Question 1

What current cochlear implantation devices are approved by the FDA for individuals ≥ 18 years of age? What are the indications for their use?

In the 1970s, the FDA recommended implantation for adults only with profound hearing loss[4], and in 1985 approved the use of multi-channel cochlear implant devices for adults aged 18 and older, postlinguistically deaf with bilateral profound sensorineural hearing loss, and an aided speech recognition score of 0 percent, indicating little or no open-set sentence discrimination. Our search of the FDA Web site found three cochlear implant systems (comprised of the implant itself along with the external microphone, sound processor, and transmitter system) that currently have market approval. These three devices are respectively produced by three manufacturers: Cochlear™ Americas (Australia; Centennial, CO, USA), Advanced Bionics® (Valencia, CA, USA), and MED-EL (Austria; Durham, NC, USA). Their indications and contraindications for adult use are described by the FDA, or when not available, directly by the manufacturer; these are summarized in Table 1. A fourth company—Racer Technology PTE LTD (Singapore)—was also listed as a currently registered manufacturer, but with no further details. The search in ClinicalTrials.gov revealed no new or emerging devices or manufacturers.

Candidates for Cochlear Implants

Initial use of cochlear implants was restricted to adults who were postlinguistically deaf with profound hearing loss. Over the past few decades these criteria have been gradually expanded to include adults with residual hearing who are either prelinguistically or postlinguistically deaf with moderate-to-profound loss in the low frequencies or profound loss in the mid-to-high frequencies of sound. Candidates for cochlear implants include adult subjects with severe-to-profound, pre or postlinguistic (sensorineural) hearing loss defined as a hearing threshold of pure-tone average of 70 dB (decibels) hearing loss or greater at 500 hertz (Hz), 100 Hz, and 2000 Hz, and have shown limited or no benefit from hearing aids. Criteria for cochlear implant candidacy are variable across devices and individual to each. Based on the safety and efficacy information provided to the FDA by each device manufacturer, likely candidates could have percent correct scores on the Hearing in Noise Test (HINT) or open–set sentence recognition tests ranging from ≤ 40 to ≤ 60 percent (depending on the device as described in Table 1). There is no upper age limit for candidacy.[5]

Recalls

A grey literature search identified three recalls of cochlear implants; each recall was that of an Advanced Bionics device. It should be noted here, however, that data regarding any import bans of devices manufactured outside of the U.S. due to malfunction or potential malfunction—

which are in essence equivalent to recalls—were not found in our search and might not be readily available in a grey literature search; therefore, recall results summarized here could be biased. The first was a voluntary recall in 2004 of unimplanted Clarion and HiResolution cochlear implants because of a potential for malfunction due to moisture within the receiver-stimulator. In 2006, a similar recall was undertaken for unimplanted HiRes 90K® devices that were manufactured by a particular supplier to Advanced Bionics, again because of a potential for device failure due to elevated moisture levels. In both recalls, patients and practitioners were advised to monitor already-implanted patients for intermittent function, complete loss of sound, sudden discomfort, pain, noise, or popping; explantation was not recommended for non-failed devices.

In November 2010, Advanced Bionics issued a voluntary recall of implanted HiRes 90K® devices (though the device maker noted that the risk of significant adverse events is currently remote) and is retrieving all unimplanted devices in response to two instances out of 28,000 devices where the product experienced a malfunction requiring explantation within 8-10 days of device activation.

Table 1. Cochlear Implantation devices currently approved by the FDA

Device \ Usage	Indications	Contraindications
Cochlear™ Nucleus® cochlear implants	• ≥ 18 years old • Bilateral sensorineural hearing loss • Pre, peri, or postlinguistic onset • Moderate to profound loss in low speech frequencies and profound (≥90dB) in mid to high frequencies • ≤ 60% correct on open set sentence recognition tests with hearing aid	• Deafness due to lesions of the acoustic nerve or central auditory pathway • Active middle ear infections • Absence of cochlear development • Tympanic membrane perforation in the presence of active middle ear disease
Advanced Bionics® HiRes 90K® Implant	• ≥ 18 years old • Bilateral sensorineural hearing loss • Postlinguistic onset • Severe to profound (≥ 70dB) loss • ≤ 50% correct HINT sentences with hearing aid	• Deafness due to lesions of the acoustic nerve or central auditory pathway • Active external or middle ear infections • Absence of cochlear development • Tympanic membrane perforations associated with recurrent middle ear infections • Cochlear ossification that prevents insertion
MED-EL MAESTRO™ Cochlear Implant System (either SONATA$_{TI}^{100}$ or PULSAR$_{CI}^{100}$ implants)	• ≥ 18 years old • Bilateral sensorineural hearing loss • Severe to profound loss (≥70 dB) in mid to high speech frequencies • ≤ 40% correct HINT sentences with hearing aid	• [None found in search]

HINT = Hearing in Noise Test, dB = decibels.

Key Question 2

What are the communication-related health outcomes as well as the quality-of-life outcomes that are achieved in the population of adults (≥ 18 years old) who undergo unilateral cochlear implantation? How is a "successful" implantation defined?

Study Characteristics

A total of 22 studies each with ≥ 30 subjects with unilateral cochlear implants met our inclusion criteria and addressed the effectiveness of unilateral cochlear implantation. Of these, six were prospective studies, 10 retrospective studies, and five cross-sectional studies. The baseline characteristics of these studies are presented in Table 2. Among the studies, the number of subjects varied from 30 to 864, and the mean baseline age ranged from 37 to 74 years. The studies were mainly conducted in the U.S. (six studies), followed by the Netherlands and UK (three studies in each country). The quality of the studies was graded fair (nine quality-B studies) to poor (13 quality-C studies), due to limitations in study design and reporting of baseline characteristics.

Table 2. Summary of baseline characteristics of the included studies for KQ2

Number of studies	22[8-29 a]
Study design	Prospective, 6;[8, 10, 13, 14, 21, 24] Retrospective, 10;[9, 12, 15, 17-20, 22, 27-29] Cross-sectional, 5.[11, 16, 23, 25, 26]
Followup duration	Prospective followup: 6 mo - 7.8yr Retrospective followup: 1 mo – 3yr
Country	Australia & New Zealand, 2;[13, 28] Belgium, 1;[25] China, 1;[16] Denmark, 1;[27] France, 1; [29] Germany, 1;[15] Israel, 1;[19] Netherlands, 3;[10, 14, 26] Spain, 1;[21] UK, 3;[8, 17, 20, 24 a] U.S., 6.[9, 11, 12, 18, 22, 23]
Number of patients	30 - 864
Mean age of patients	37 – 74yr
Severity of deafness	Severe to profound
Duration of deafness	9 - 32yr
Time (range) between deafness and implant	0 – 16yr
Cochlear implant indication	Severe or profound sensorineural hearing loss
Device characteristics	Advanced Bionics (HiRes 90K™, CLARION CII HiFocus, CLARION 1.2), Cochlear UK (Nucleus® 24R, Nucleus® 24 Contour, Nucleus® 24, Nucleus® 22, Nucleus® Freedom), MED-EL (COMBI 40+), Digisonic® (SP; Convex)
Study quality	9 B studies;[8, 10, 13, 14, 18, 19, 21, 22, 24] 13 C studies.[9, 11, 12, 15-17, 20, 23, 25-29]

mo = month, yr = year
[a] Two publications from the same study (Mawmen 2004 and Orabi 2006)

Study Results

Speech perception measures

Open-set sentences tests

The overall evidence for the effectiveness of unilateral cochlear implants on speech perception using open-set sentences tests was rated moderate because the results were consistent across the five quality-B studies. Twelve studies assessed speech perception employing six open-set sentences tests (Table 3): AzBio sentences in one study;[11] Bamford Kowal Bench (BKB) sentences in three studies;[8, 17, 24] Central Institute for the Deaf (CID) sentences in one study;[21] City University of New York (CUNY) test in four studies;[9, 18, 20, 24] Hearing in Noise Test (HINT) in seven studies;[9, 11, 12, 18, 22, 23, 28] and Hochmair-Schultz-Moser (HSM) test in one study.[15] One study did not specify the "open-set sentences" test used to measure speech perception.[29]

Pre versus postunilateral cochlear implants

Thirteen studies (14 publications) used participants as their own control to compare post with preimplantation speech perception.[8, 9, 11, 12, 15, 17, 18, 20-24, 28, 29] All or most of the quality-B studies that compared unilateral cochlear implantation with preimplantation showed a significant clinical benefit and most of the quality-C studies showed a statistically non-significant but clinical benefit after unilateral cochlear implantation.

The UK Cochlear Implant Study Group [UKCISG] (n=316) study, rated quality-B, evaluated the effectiveness of unilateral cochlear implants on speech perception.[24] They used two open-set sentences tests (i.e., the BKB sentence test and the audiovisual gain for CUNY sentence test) and calculated the standardized response mean difference between pre and postimplantation at 9 months. Both speech perception measures showed large effects at post compared with precochlear implantation: effect size (ES) = 1.50 for BKB, and ES = 1.78 for CUNY.

One quality-B study found that postimplantation percent scores of two syllable tests were significantly increased to 52 percent, 62 percent, and 54 percent at 1, 2, and 3 years of followup, respectively, compared with preimplantation scores of 20 percent.[21]

Table 3a. Summary results of speech perception measures in unilateral cochlear implants (quality-B studies)

Outcome category	Specific outcome	Study [subjects]	Comparison groups	Results	Study quality
BKB	% correct	Bai 2005[8] [47]	Post vs. preimplant	⬆ 5.5 mo	B (prospective; no adj.)
BKB	% correct	UK CI Study Group 2004[24] [316]	Post vs. preimplant	⬆ 9 mo (ES=1.5)	B (prospective; mostly qualitative interpretations)
CID	% correct	Rama-Lopez 2006[21] [30]	Post vs. preimplant	⬆ 1, 2, 3yr	B (prospective; poor reporting)
CUNY-Q	% correct	Morris 2007[18] [101]	Post vs. preimplant	⬆ 1yr	B (retrospective; good analyses)
CUNY-N	% correct		Post vs. preimplant	⬆ 1yr	
HINT-Q	% correct	Morris 2007[18] [101]	Post vs. preimplant	⬆ 1yr	B (retrospective; good analyses)
HINT-Q	% correct	Roditi 2009[22] [55]	Post vs. preimplant	⬆ 28mo[a]	B (retrospective; some information could not be used because of eligibility criteria)
HINT-N	% correct		Post vs. preimplant	⬆ 28mo[a]	
2-syllable words	% correct	Rama-Lopez 2006[21] [30]	Post vs. preimplant	⬆ 1, 2, 3yr	B (prospective; unclear description of sampling method)

Adj = adjustment, BKB = Bamford-Kowal-Bench, CID = Central Institute for the Deaf, CUNY = City University of New York, HINT = Hearing in Noise test, Q = quiet, N = Noise, ES = effect size, mo = month, yr = year, ⬆ = benefit with statistical significance, ⇧ = benefit but no statistical significance.

[a] Original study did not perform statistical significance testing but the results were judged statistically significant based on non-overlapping confidence intervals

Unilateral cochlear implants versus hearing aids

There was only one cross-sectional study of quality-C (that met the inclusion criteria) that compared unilateral cochlear implant users with hearing aid users.[11] Gifford 2008 conducted cross-sectional analysis of retrospectively collected data. The study included 143 unilateral implants, 13 bilateral implants, as well as 50 hearing aid users; results of bilateral implants from this study are discussed under Key Question 3. All speech perception tests were presented at the 60 dB SPL. The group means for HINT sentences in quiet were significantly higher in unilateral implants (84.8 percent) and bimodals (94.1 percent) versus hearing aid users (73.1 percent). Similarly for the AzBio sentence recognition, the performance was significantly higher in unilateral implants (72.1 percent) and bimodals (83.5 percent) versus hearing aid users (47.3 percent). The scores among hearing aid users (15.2 dB) were poorer in BKB-SIN test compared with unilateral implants (11.4 dB) and bimodals (8.7 dB).

Table 3b. Summary results of speech perception measures in unilateral cochlear implants (quality-C studies)

Outcome category	Specific outcome	Study [subjects]	Comparison groups	Results	Study quality
AzBio-Q	% correct	Gifford 2008[11] [156]	Unilateral implant vs. HA	⬆	C (cross-sectional)
BKB	% correct	Mawman 2004[17] [214]	Post vs. preimplant	⇧ 9, >18mo	C (retrospective; missing data)
CUNY	% correct	Orabi 2006[20] [34]	Post vs. preimplant	⬆ 9, 21 mo	C (retrospective; no adj.)
CUNY-Q	% correct	Bassim 2005[9] [87]	Post vs. preimplant	⇧ 1, 2, 3yr	C (retrospective; poor reporting, no adj.)
HINT-Q	% correct	Bassim 2005[9] [87]	Post vs. preimplant	⇧ 1, 2, 3yr	C (retrospective; poor reporting, no adj.)
HINT +10dB SNR	% correct		Post vs. preimplant	⇧ 1, 2, 3yr	
HINT-Q	% correct	Hay-McCutcheon 2005[12] [34]	Post vs. preimplant	⬆ 1yr	C (retrospective; poor reporting; no adj.)
HINT +10dB SNR	% correct		Post vs. preimplant	⇧ 1yr	
HINT 0 audiovisual	% correct	Bradley 2010[28] [53]	Post vs. preimplant	⇧ 3, 6, 9mo	C (missing data; poor reporting; no adj.)
HINT-Q	% correct	Firszt 2004[23] [78]	70 vs. 60dB	⇔	C (cross-sectional; poor reporting)
HINT-Q	% correct		70 vs. 50dB	⬆	
HINT-Q	% correct		60 vs. 50dB	⬆	
HINT-Q/N	% correct		70dB Q vs. 60dB N	⬆	
HINT-Q/N	% correct		60dB Q vs. 60dB N	⬆	
HINT-Q/N	% correct		50dB Q vs. 60dB N	⬆	
HINT-Q	% correct	Gifford 2008[11] [156]	Unilateral implant vs. hearing aid	⬆	C (cross-sectional)
HSM-N 10dB	% correct	Krueger 2008 [864]	Post vs. preimplant	⇧	C (retrospective)
"Speech perception sentences in open set" (not defined)	% correct	Lazard 2010[29] [45]	Post vs. preimplant	⬆ 3, 12mo	C (no adj.; selection bias)

Adj = adjustment, BKB = Bamford-Kowal-Bench, BKB-SIN = Bamford-Kowal-Bench speech in noise, CID = Central Institute for the Deaf, CUNY = City University of New York, HA = hearing aid , HINT = Hearing in Noise test, N = noise, , mo = month, Q = quiet , SNR = signal to noise ratio, yr = year, ⬆ = benefit with statistical significance, ⇧ = benefit but no statistical significance, ⇔ = no difference between comparison groups.

Generic quality-of-life measures

The overall evidence for the effectiveness of unilateral cochlear implants on quality-of-life using generic measures was rated moderate because the results were consistent across the six quality-B studies. In general, there were significant effects from the use of unilateral cochlear implants on overall health-related quality-of-life and social domains in quality-B studies; the one quality-B study and most of the quality-C studies did not show significant effect on physical, cognitive, and emotional domains (Table 4).

Pre versus postunilateral cochlear implants

Ten studies evaluated health-related quality-of-life using generic measures, mainly the Glasgow Benefit Inventory (GBI), Glasgow Health Status Inventory (GHSI), Health Utilities Index (HUI), and Short-Form (SF)-36 (Table 4).[8, 10, 13, 14, 16, 19, 20, 24, 25, 27]

Damen 2007 conducted a long-term (up to 6 years) followup study to examine health-related quality-of-life by comparing pre and postimplantation using the two generic health-related quality-of-life instruments (i.e., SF-36 and HUI-3).[10] A group of 22 shorter term cochlear implant users (< 6 years) showed significant benefits on hearing, emotion, and HUI-3 utility for HUI-3 results; and mental health and mental summary score for Short Form (36) Health Survey (SF-36) results. The other group of 37 longer term cochlear implant users (≥ 6 years) showed a slight decrease in HUI and SF-36 over time.

The UKCISG examined the effectiveness of unilateral cochlear implants for generic health-related quality-of-life. Nine-month postimplantation showed large benefits on GHSI (ES=1.22) and HUI3 (ES=1.05) as compared with preimplantation.[24]

In one cross-sectional study, postimplantation also showed significant benefits on all SF-36 subdomains (i.e., energy, social function, psychological well-being) compared with preimplantation.[27]

Table 4a. Summary results of health-related quality-of-life (generic) in unilateral cochlear implants (quality-B studies)

Outcome category	Specific outcome	Study [subjects]	Comparison groups	Results	Study quality
AQoL	Mean score	Hawthorne 2004[13] [34]	Post vs. preimplant	⬆ (total)	B (prospective; not account for all participants)
GHSI	% score	UK CI Study Group 2004[24] [316]	Post vs. preimplant	⬆ (total: large effect, ES=1.22)	B (prospective; mostly qualitative interpretations)
HUI2	Mean score	Klop 2008[14] [44]	Post vs. preimplant	⬆ (sensation, pain)	B (prospective; no adj.)
HUI3	% score	Damen 2007[10] [59]	Post vs. preimplant	⬆ (hearing, emotion, HUI3 utility)	B (prospective; not representative sample)
HUI3	% score	UK CI Study Group 2004[24] [316]	Post vs. preimplant	⬆ (total: large effect, ES=1.05)	B (prospective; mostly qualitative interpretations.)
Loneliness	Mean score	Most 2010[19] [38]	Post vs. preimplant	⬆ (loneliness)	B (retrospective; no adj.)
SF-36	Mean score % score	Damen 2007[10] [59]	Post vs. preimplant	⬆ (mental health, mental summary score) ⇔ (physical, social, and role (physical & emotional))	B (prospective; not representative sample)
Quality-of-life	% score	Bai 2005[8] [47]	Post vs. preimplant	⇧ (total)	B (prospective; no adj.)
Self-esteem	Mean score	Most 2010[19] [38]	Post vs. preimplant	⇔ (self-esteem)	B (retrospective; no adj.)

Adj = adjustment, AQoL =Assessment quality-of-life, GHSI = Glasgow Health Status Inventory, HUI-2 = Health Utilities Index Mark II, HUI-3 = Health Utilities Index Mark III, SF-36 = The Short Form (36) Health Survey, CI = cochlear implant, ES = effect size, ⬆ = benefit with statistical significance, ⇧ = benefit but no statistical significance, ⇔ = no difference between comparison groups

Table 4b. Summary results of health-related quality-of-life (generic) in unilateral cochlear implants (quality-C studies)

Outcome category	Specific outcome	Study [subjects]	Comparison groups	Results	Study quality
GBI	Benefit score	Orabi 2006[20] [34]	Post vs. preimplant	⬆ (overall QoL, general health, social aspects, complete satisfaction) ⇔ (health state)	C (retrospective; no adjusted analysis)
GBI	Mean score	Vermeire 2005[25] [89]	Post vs. preimplant	⬆ (total, general, social) ⇔ (physical)	C (cross-sectional; poor reporting)
GHSI	State score	Orabi 2006[20] [34]	Post vs. preimplant	⬆ (overall quality-of-life, general health subscale) ⇔ (social support, physical health scores) ⇔ (mobility, emotion, cognition) ⇔ (vision, speech, ambulation, dexterity, cognition, pain)	C (retrospective; no adjusted analysis)
NCIQ (Self-confidence and social interaction)	% score	Liu 2008[16] [32]	Post vs. preimplant	⇧ (self-confidence, social interaction)	C (cross-sectional; poor reporting)
SF-36	Mean score	Wanscher 2006[27] [46]	Post vs. preimplant	⬆ (energy, social function, psychological well-being)	C (cross-sectional;, potential recall bias)

GBI = Glasgow Benefit Inventory, GHSI = Glasgow Health Status Inventory, SF-36 = Short Form (36) Health Survey. ⬆ = benefit with statistical significance, ⇧ = benefit but no statistical significance, ⇔ = no difference between comparison groups

Disease specific quality-of-life measures

The overall evidence for the effectiveness of unilateral cochlear implants on health-related quality-of-life using disease-specific measures was rated moderate because the results were consistent across the four quality-B studies.

Six studies assessed quality-of-life employing the following disease-specific assessments (Table 5): Adapted Deaf Identity Developmental Scale for one study;[19] Hearing Handicap Inventory for Adults (HHIA) for two studies;[25, 26] Hearing Participation Scale (HPS) for one study;[13] and Nijmegen Cochlear Implant Questionnaire (NCIQ) for two studies.[10, 14]

Pre versus postunilateral cochlear implants

Five studies with disease specific measures (HHIA, HPS, and NCIQ) showed significant benefits on health-related quality-of-life from unilateral cochlear implants compared with preimplantation measures.[10, 13, 14, 19, 25, 26] However, one study that used the Adapted Deaf Identity Developmental Scale found no statistical difference in family relations between post and preimplantation. This study did show significant effects on communication, social skills, academic and work performance, and general satisfaction with unilateral cochlear implants.[19]

Table 5. Summary results of health-related quality-of-life (disease-specific) in unilateral cochlear implants

Outcome category	Specific outcome	Study [subjects]	Comparison groups	Results	Study quality
Adapted Deaf Identity Developmental Scale	Mean score	Most 2010[19] [38]	Post vs. preimplant	⬆ (communication, social skills, academic and work performance, general satisfaction) ⇔ (family climate)	B (retrospective; no adjusted analysis)
HPS	Mean score	Hawthorne 2004[13] [34]	Post vs. preimplant	⬆ (total)	B (prospective; missing data)
NCIQ	Mean score	Damen 2007[10] [59]	Post vs. preimplant	⬆ (sound perception, sound perception advanced, speech production, self-esteem, activity, social interactions)	B (prospective; not representative sample)
NCIQ	Mean score	Klop 2008[14] [44]	Post vs. preimplant	⬆ (sound perception, basic & advanced; speech production; self-esteem; activity; social interactions)	B (prospective; no adjusted analysis)
HHIA	Mean score	Vermeire 2005[25] [89]	Post vs. preimplant	⬆ (total, emotional, situational)	C (cross-sectional; poor reporting)
HHIA	Mean score	Vermeire 2006[26] [50]	Post vs. preimplant	⬆ (total)	C (cross-sectional; huge drop out)

HHIA = Hearing Handicap Inventory for Adults, HPS = Hearing Participation Scale, NCIQ = Nijmegen Cochlear Implant Questionnaire.
⬆ = benefit with statistical significance, ⇔ = no difference between comparison groups

Key Question 2a

For adult individuals (≥ 18 years of age) with sensorineural hearing loss, what are the preoperative patient characteristics associated with the successful attainment of the above improved communication-related health outcomes as well as quality-of-life outcomes in those who undergo unilateral cochlear implantation?

The overall evidence for the duration of impaired hearing, age at implantation, and type of implanted devices as preoperative predictors of postoperative speech outcomes after unilateral cochlear implants was rated moderate, low, and low, respectively, based on consistent results among quality-B studies. The overall evidence for other preoperative predictors, including older age (≥65 years old), preoperative speech perception scores was rated insufficient.

Study Characteristics

Twenty one studies analyzed preoperative patient characteristics as potential modifying factors of postoperative speech perception outcomes (open-set sentences, two syllable words) and/or health-related quality-of-life outcomes.[9, 12-14, 18, 20, 24, 25, 28-40] Of these, 4 were prospective cohort studies;[13, 14, 24, 38] 13 were retrospective cohort studies (in 14 publications);[9, 12, 18, 20, 28-30, 32-35, 37, 39, 40] one was a case-control study;[30] and 3 were cross-sectional studies.[25, 31, 36] Followup durations ranged from 6 months to 1 year for prospective studies, and 1 to 12 years for retrospective studies. All four prospective studies were of quality-B; four retrospective studies were of quality-B, and the remaining 10 were quality-C; all cross-sectional studies were of quality-C. None of the C-quality studies (neither retrospective nor cross sectional) accounted for potential confounding factors in their analyses. Other common methodological deficiencies included missing data and poor reporting of patient characteristics.

The studies were generally small in sample size, ranging from 22 to 316 patients with cochlear implants. Mean age of patients ranged from 37 to 74 years. Of the 21 studies, eight reported the baseline severity of deafness of enrolled patients, ranging from severe-to-profound hearing loss. Average duration of deafness ranged from 13 to 16 years among patients in the prospective cohort studies (reported in 3 studies), from 8 to 32 years among patients in the retrospective studies (reported in 7 studies), and from 6 to 13 years among patients in the cross-sectional studies (reported in 2 studies). Time between onset of deafness and cochlear implantation or indication for cochlear implant were poorly reported (i.e., only 5 studies reported relevant information). Table 6 summarizes the baseline characteristics of the 21 studies.

Potential preoperative patient characteristics that were examined in the 21 studies included: duration of impaired hearing (7 studies), age of implantation (7 studies), older [≥ 65 years old] versus younger age [< 65 years old] (7 studies), type of implanted device (7 studies), preoperative speech recognition or word understanding (5 studies), degree of preimplant residual hearing (4 studies), associated ear or bone diseases (2 studies), pre versus postlinguistic deafness (2 studies), age at onset of hearing loss (2 studies), and choice of implanted ear (1 study). We found no studies that examined implant center/expertise of cochlear implant teams or other patient-related disabilities as potential modifying factors of speech and/or health-related quality-of-life outcomes. Table 7 shows summary findings tabulated by potential preoperative modifying factors and postoperative outcomes.

Study Results

Duration of impaired hearing

Seven studies (5 quality-B,[13, 14, 24, 35, 39] 2 quality-C[12, 37]) with a total of 627 patients with a cochlear implant examined the duration of preoperative impaired hearing as a potential modifying factor of postoperative speech perception or health-related quality-of-life outcomes.

Five studies (3 quality-B, 2 quality-C) reported speech outcomes. Of these, three quality-B studies found that longer duration of preoperative impaired hearing was significantly correlated with poorer speech outcomes as measured by CUNY and/or BKB scores.[24, 35, 39] Another study (quality-C) reported that, among the younger adults (< 65 years old), longer duration of hearing loss before cochlear implantation was associated with better speech reading skill as measured by HINT (r= 0.86; P= 0.003), but this association was not significant among older adults (≥ 65 years old).[13] The last study (quality-C) found no significant differences in the duration of impaired hearing between patients who had high postoperative speech performance (BKB score > 47 percent) and those who had low postoperative speech performance (BKB score ≤ 47 percent).[37] This definition of high speech performance, a BKB score > 47 percent was based on the 25th percentile of the BKB data among study participants whose score was 47 or more percent correct.

Two studies (both quality-B) reported health-related quality-of-life outcomes. In one study, longer duration of preoperative impaired hearing was significantly correlated with better postoperative (general and hearing-specific) quality-of-life after controlling for other potential confounders.[14] However, another study found that duration of preoperative impaired hearing was not significantly associated with postoperative (general and hearing-specific) quality-of-life.[13]

Age at implantation

Seven studies (3 quality-B,[14, 35, 39] 4 quality-C[12, 28, 30, 32]) with a total of 593 patients with a cochlear implant examined age at implantation as a potential modifying factor of postoperative speech perception or health-related quality-of-life outcomes.

Six studies (2 quality-B, 4 quality-C) reported speech outcomes. Overall, in none of the studies was there a significant correlation between age at implantation and postoperative speech outcomes as measured by HINT, CUNY, or BKB. One quality-C study of only older adults (≥ 65 years old) reported that although the age at implantation was not associated with postoperative HINT scores in a quiet environment, older age at implantation was marginally correlated with better HINT scores under noise conditions (r=0.40; P=0.05).[30]

One quality-B study reported health-related quality-of-life outcomes. This study showed that younger age at implantation was associated with better hearing-specific quality-of-life outcomes.[14]

Older age (≥ 65 years old)

Seven quality-C studies[12, 20, 25, 30, 31, 33, 40] with a total of 807 patients with a cochlear implant examined whether older age (≥ 65 years) versus younger age (< 65 years) is a potential modifying factor of postoperative speech perception or health-related quality-of-life outcomes.

Six quality-C studies reported speech outcomes. Overall, most of the studies found significant differences in postoperative speech perception outcomes as measured by HINT, CUNY, BKB and/or speech perception between older (≥ 65 years old) and younger (< 65 years old) patients. One study found that older patients had a significantly lower postoperative HINT score in quiet conditions than younger patients (70 percent vs. 83 percent, respectively;

P=0.02).[30] However there was no significant difference in HINT score in noise conditions between the two groups. Another study showed that older (≥ 80 years old) patients had a significantly higher postoperative AzBio sentence recognition score than younger (< 80 years old) patients.[40] However, there was no significant difference in BKB scores in noise conditions between the two groups.

One quality-C study reported health-related quality-of-life outcomes. This study found no significant differences in general or hearing-specific quality-of-life outcomes between young (≤ 55 years old), middle (56 to 69 years olds), and geriatric (≥ 70 years old) patients.[25]

Implanted device

Seven studies (2 quality-B,[35, 38] 5 quality-C[28, 29, 32, 36, 37]) with a total of 625 patients with a cochlear implant examined type of implant device as a potential modifying factor of postoperative speech perception outcomes. Five of the seven studies did not find significant differences in postoperative speech perception outcomes as measured by HINT, CUNY, BKB and/or CPA recognition tests (Centro de Pesquisas Audiológicas recognition test at different noise ratios) among patients who received different cochlear implant devices. One quality-B study showed that, although there was no significant differences in CUNY and BKB scores, patients who received an Advance Bionics CII implant had significantly higher AzBio sentence scores than patients who received a Nucleus 3G implant (75 vs. 61%, P=0.01).[38] One quality-C study found that patients with a new model of cochlear implant (Nucleus® Freedom™) had higher HINT auditory scores in noisy conditions than patients with older models (Nucleus® 22 or 24) (89 vs. 73%, P=0.01).[28] Another quality-C study showed similar findings comparing another new model of cochlear implant (Digisonic® SP) with its older model (Digisonic® Convex), but did not report what "open set sentences" test was used to measure the speech perception outcomes.[29] Neither of these two models (Digisonic® SP or Digisonic® Convex) have been approved by the FDA and thus are not available in the United States.

Preoperative speech perception scores

Five studies (2 quality-B,[14, 30] 3 quality-C[28, 30, 40]) with a total of 468 patients with a cochlear implant examined preoperative speech perception as a potential modifying factor of postoperative speech perception or health-related quality-of-life outcomes.

Four studies (1 quality-B, 3 quality-C published in three publications) reported speech perception outcomes. Results were mixed. Two studies (1 quality-B; 1 quality-C) found that a better preoperative HINT score was significantly associated with a better postoperative HINT score (cohort study: r= 0.44; P=0.02; case-control study: r=0.31; P=0.02).[30] The other two quality-C studies did not find significant relationships between preoperative and postoperative speech recognition scores as measured by HINT auditory and audiovisual or AzBio sentences tests.[28, 40]

One quality-B study reported health-related quality-of-life outcomes. This study showed that better preoperative CVC (consonant-voice-consonant word list) score was significantly associated with better postoperative general quality-of-life score (multivariate regression beta coefficient= 0.0003; P=0.02).[14]

Degree of preimplant residual hearing as defined by pure tone thresholds

Four studies (2 quality-B,[13, 35] 2 quality-C[34, 40]) with a total of 423 patients with a cochlear implant examined degree of preimplant residual hearing as a potential modifying factor of postoperative speech perception or health-related quality-of-life outcomes.

Three studies (1 quality-B, 2 quality-C) reported speech outcomes. None found a significant association between degree of preimplant residual hearing and postoperative speech perception outcomes as measured by HINT, BKB, or AzBio sentences.[34, 35, 40]

One quality-B study reported health-related quality-of-life outcomes. This study found that postoperative general quality-of-life improved more among patients who had "profound deafness" than those who had "severe-moderate deafness" [Note: severity of deafness was not defined in the original article] (P=0.08).[13] However, there were no significant differences in hearing-specific quality-of-life outcomes between the two groups of patients.

Associated ear or bone diseases

Two quality-C studies[32, 37] with a total of 62 patients with a cochlear implant examined associated ear or bone disease as a potential predictor of postoperative speech perception outcomes. One study found no significant difference in the proportion of patients with varying clinical types of otosclerosis (types 1 to 3) when comparing patients with high postoperative speech performance (BKB score > 47 percent) and those with low postoperative speech performance (BKB score ≤ 47 percent).[37] This definition of high speech performance, a BKB score > 47 percent was based on the 25th percentile of the BKB data among study participants whose score was 47 percent correct. Another study also found no difference in the percentage of patients with normal temporal bone when comparing patients with excellent or poor postoperative speech performance.[32] Poor performers were defined as patients who realized a worsening, no improvement, or an improvement of less than 10 percent in their audiologic scores.

Post versus prelinguistic deafness

Two quality-C studies[9, 32] with a total of 339 patients with a cochlear implant examined whether postlinguistic deafness (versus prelinguistic deafness) was a potential modifying factor of postoperative speech perception outcomes. Both studies found that postlinguistic deafness was significantly associated with better postoperative speech outcomes as measured by HINT, CUNY, or BKB, when compared with prelinguistic deafness.

Age at onset of hearing loss

Two quality-C studies[12, 37] with a total of 62 patients with a cochlear implant examined the age at onset of hearing loss as a potential modifying factor of postoperative speech perception outcomes. One study found no significant relationship between age of hearing loss onset and postoperative BKB score.[37] The other study found that, among the younger adults (< 65 years old), earlier age of hearing loss onset was significantly associated with poorer speech reading skill as measured by HINT, but this association was not significant among older adults (≥ 65 years old).[13]

Choice of implanted ear

One quality-B study[18] with 101 patients with a cochlear implant examined the choice of implanted ear as a potential modifying factor of postoperative speech outcomes. This study did not find significant association between right- and left-ear implant and postoperative speech outcomes as measured by HINT and CUNY.

Key Question 2b

Of studies included for Key Question 2 and Key Question 2a, are there data available separately for those individuals with sensorineural hearing loss as demonstrated by test scores of > 40 percent and ≤ 50 percent, as well as those with test scores > 50 percent and ≤ 60 percent (best aided listening on tape or otherwise recorded tests of open-set sentence recognition)?

Of the 22 studies that evaluated key question 2, there were no studies that used the results of open-set sentence tests for cochlear implantation indication.

Of the 21 qualifying studies that evaluated key question 2a, only two (one quality-B; one quality-C) provided relevant data for this question.[30, 33] The quality-B study analyzed a retrospective cohort of 78 elderly (≥ 70 years old) patients for the associations between preimplant HINT scores (≤20%, 21-40%, ≥40%), and 1-year postimplant HINT scores. Elderly with preimplantation HINT-Q scores below 20 percent, of 20 through 40 percent, and to 41 percent or greater were analyzed with respect to 1-year postimplant HINT-Q scores. The results indicated that better preimplant HINT-Q scores showed significant association with higher postimplant HINT-Q (r=0.44, P=0.02), and HINT-N (r=0.43, P=0.04) scores regardless of age.

The quality-C study was based on a retrospective chart review. Only adults implanted with either the Clarion device or Nucleus device between 1991 and 2002 were included in the analyses. The criteria for cochlear implantation included severe to profound hearing loss in both ears (mean 70 dB) and a score of less than 50 percent on an open-set sentence test using conventional hearing aid(s). Sixty-five elderly adults (≥ 70 years old) were compared with 101 younger adults (< 70 years old) for speech outcomes. The study found that both elderly and younger adults had significant improvements in HINT and CID scores after implantation. However, there were no significant differences between groups (P=0.07). This analysis was not adjusted for potential confounding factors.

Two studies reported information on the indication of cochlear implantation for study participants, although these studies did not use the term ‘indications’ as specified in the key question. The criteria for cochlear implantation used in these studies include pure-tone threshold > 90 dB hearing loss or phoneme recognition of < 40 percent,[14] and monosyllabic word recognition of < 30 percent (open-set; 70 dB).[31] For these two studies, Table 7 shows summary findings tabulated by potential preoperative modifying factors and postoperative outcomes. The first study showed that younger age at implantation was associated with better hearing-specific quality-of-life outcomes.[14] The second study found significant differences in postoperative speech perception outcomes between older (≥ 65 years old) and younger (< 65 years old) patients.[31]

Table 6. Summary of baseline characteristics of the included studies for KQ 2a

Number of studies	21 studies[9, 12-14, 18, 20, 24, 25, 30-39]**
Study design	Prospective: 4 studies[13, 14, 24, 38] Retrospective: 11 studies[9, 12, 18, 20, 28-30, 32-35, 37, 39, 40] Cross-sectional: 3 studies[25, 31, 36]
Followup duration	Prospective followup: 6 mo to 1 yr Retrospective followup: 1 to 12 yr
Country	U.S., 7;[9, 12, 18, 30, 33, 34, 40] UK, 5;[20, 24, 35, 37, 38] Australia and New Zealand, 3;[13, 28, 39] Netherlands, 1;[14] Germany, 1;[31] Belgium, 1;[25] Canada, 1;[32] France, 1;[29] and Brazil.[36]
Number of patients	Prospective: 424 (ranged from 30 to 316) Retrospective: 1576 (ranged from 22 to 252) Cross-sectional: 202 (ranged from 40 to 89)
Mean Age of patients	Prospective: 49 to 55 yr Retrospective: 46 to 74 yr Cross-sectional: 37 to 69 yr
Severity of deafness	Prospective: 83 to 140 dB[14, 24, 38] or "profound or severe-moderate" deafness[13] Retrospective: 77 to 109 dB[34], "profound",[37] or severe-profound (mean 70 dB)[33] Cross-sectional: mean 101 dB[38]
Duration of deafness	Prospective: mean 13 to 16 yr[14, 24, 38] Retrospective: mean 8 to 32 yr[13, 18, 20, 28, 30, 34, 35, 39] Cross-sectional: mean 6 to 13 yr[31, 36]
Time between deafness and implant	Prospective: mean 1.7 y[38] Retrospective: mean 6 to 23 yr[33, 39] Cross-sectional: mean 1 to 2 yr[31, 36]
Cochlear implant indication	Prospective: Pure-tone threshold >90 dB hearing loss, phoneme recognition of <40%[14] or severe or profound sensorineural hearing loss[24] Retrospective: Severe-profound hearing loss in both ears;[33, 39] ≥50% on open-set sentence test using hearing aid[33] Cross-sectional: Monosyllabic word recognition of <30% (open-set; 70 dB)[31]
Device characteristics	Brand: Nucleus 24, Nucleus 22, Nucleus Freedom, Clarion, MedEL Combi-40+, Advanced Bionics Clarion (Hifocus CII, HiRes 90K, MPEAK, SPEAK ACE, CIS), Digisonic (SP; Convex); Laura Coding strategy: Multi-peak, spectral peak, continuous interleaved sampling, and advanced combination encoders, hi-resolution sound processing strategy, MPIS coding strategy
Study quality	Prospective: 4 B Retrospective: 4 B; 10 C Cross-sectional: 3 C

dB = decibel, mo = month, yr = year

* 10 studies[9, 12-14, 18, 20, 24, 25, 30, 31] also reported data on key question 2. Of which, one publication[30] reported two separate studies (one cohort and one case-control design).

** Patients in two publications[20, 35] were from the same population (thus counting only 1 study). Different analyses were performed in these two publications therefore both were included in our report.

Table 7. Results from studies evaluating the association between preoperative characteristics and outcomes

Potential modifying factor	Number of studies, Total patients (range), Quality	Speech perception outcomes		Health-related quality-of-life outcomes	
Longer duration of impaired hearing	7, 627(28 to 311) 5 B; [13, 14, 24, 35, 39] 2 C[12, 37]	CUNY	Worse[24, 39]	General	Better;[14] NS[13]
		HINT	Better (< 65 yr); NS (≥ 65 yr)[12]	Hearing specific	Better;[14] NS[13]
		BKB	Worse;[35]		
		High performer (BKB score > 47%) vs. low performer (BKB score ≤ 47%)	NS[37]		
Younger age at implantation	7 593 (29 to 252), 3 B;[14, 35, 39] 4 C[12, 28, 30, 32]	CUNY	NS[39]	Hearing specific	Better[14]
		HINT	NS[12, 28, 30]		
		BKB	NS[35]		
		Poor performers vs. excellent performers[b]	NS[32]		
Older age (≥65 yr) vs. younger age (<65 yr)	7, 807 (34 to 232), 7 C[12, 20, 25, 30, 31, 33, 40]	CUNY	NS[20]	General	NS[25]
		HINT	NS[12, 25, 30, 33]	Hearing specific	NS[25]
		BKB	NS[20, 40]		
		CID	NS[33]		
		Speech perception	NS[31]		
		AzBio sentences	Better (≥ 80 yr)[40]		
Type of implanted device	7, 625 (28 to 252), 2 B;[35, 38] 5 C[28, 29, 32, 36, 37]	CUNY	NS[38]		
		HINT	NS[38]		
			Better (Nucleus® Freedom™ vs. Nucleus® 22&24)		
		BKB	NS[35, 37]		
		Poor performers vs. excellent performers[b]	NS[32]		
		CPA recognition test	NS[36]		
		AzBio sentences	Better (Digisonic® SP vs. Digisonic® Convex)[29]		
			Better (Advance Bionics CII vs. Nucleus 3G)[38]		

Potential modifying factor	Number of studies, Total patients (range), Quality	Speech perception outcomes		Health-related quality-of-life outcomes	
Preoperative speech recognition or word understanding	5,[a] 468 (44 to 232), 2 B;[14, 30] 3 C[28, 30, 40]	HINT	Better preoperative HINT score was sig. associated with better postoperative HINT score (reported in 2 studies in 1 publication)[30] NS[28]	General	Better preoperative CVC score was sig. associated with better postoperative general QoL score[14]
		BKB	NS[28]		
		AzBio sentences	NS[40]		
Degree of preimplant residual hearing as defined by pure tone	4, 423 (34 to 232), 2 B;[13, 35] 2 C[34, 40]	HINT	NS[34]	General	Better among patients who had "profound deafness" than those who had "severe-moderate deafness"[13]
		BKB	NS[35, 40]	Hearing specific	NS[13]
		AzBio sentences	NS[40]		
Associated ear or bone diseases	2, 280 (28 to 252), 2 C[32, 37]	BKB	Extent of otosclerosis: NS[37]		
		Poor performers vs. excellent performers[b]	Normal temporal bone: NS[32]		
Post vs. prelinguistic deafness	2, 339 (87 to 252), 2 C[9, 32]	CUNY	Better[9]		
		HINT	Better[9]		
		Poor performers vs. excellent performers[b]	Better[32]		
Earlier age at onset of hearing loss	2, 62 (28 to 34), 2 C[12, 37]	HINT	Worse (< 65 yr); NS (≥ 65 yr)[12]		
		BKB	NS[37]		

Potential modifying factor	Number of studies, Total patients (range), Quality	Speech perception outcomes		Health-related quality-of-life outcomes
Choice of implanted ear	1, 101, 1 B[18]	CUNY	NS[18]	
		HINT	NS[18]	

NS = not statistically significant, CPA = Centro de Pesquisas Audiológicas recognition test at different noise ratios; CVC = consonant-voice-consonant word list, QoL = quality-of-life, CID, Central Institute for the Deaf sentences, yr = year

[a] There are two studies (case-control and cohort study) included in Friedland, 2010[30] publication

[b] Poor performers were patients who realized a worsening, no improvement, or an improvement of <10% in their audiologic scores. Excellent performers were patients who scored between 91 and 100% postimplantation

Key Question 3

For those individuals ≥ 18 years of age, what are the additional communication-related health outcomes as well as quality-of-life outcomes (as compared to those achieved in Key Question 2) that are gained from the use of bilateral cochlear implants over a unilateral cochlear implant? How is a "successful" bilateral cochlear implant defined?

Evidence was rated moderate to low based on data from nine studies assessing subjects with simultaneous or sequential bilateral cochlear implantation that were graded a methodological quality of B. Overall, 16 studies published since 2004 evaluated subjects with bilateral cochlear implants that met our eligibility criteria. Summary of baseline characteristics is provided in Table 8. Studies evaluating speech perception in noise conditions found significant gains with bilateral simultaneous cochlear implants compared with a unilateral cochlear implant. One cross-sectional study showed no benefit and another study did not evaluate speech outcomes. The results of speech perception in quiet and health-related quality-of-life were mixed across studies. Only three of nine studies assessed health-related quality-of-life in subjects with bilateral implants. While subjects with bilateral cochlear implants showed significant gains in some health-related quality-of-life subscales, others found no difference between the two groups. In a randomized controlled trial evaluating sequential bilateral cochlear implants, the second ear implant resulted in negative or non-significant results for quality-of-life after the first ear implant.

Simultaneous Bilateral Cochlear Implantation

Evidence was rated moderate to low based on data from seven studies that were graded a methodological quality-B. In total, nine studies assessed subjects with simultaneous bilateral cochlear implantation that were graded a methodological quality of B or C. Of these eight studies evaluating speech perception using open-set sentences or multi-syllable tests found gains with bilateral simultaneous cochlear implants compared with a unilateral cochlear implant or unilateral listening condition. All five studies evaluating sound localization reported significant bilateral benefit over unilateral listening condition. However, only two studies assessed disease specific health-related quality-of-life. While subjects with bilateral cochlear implants showed significant gains in some health-related quality-of-life subscales such as lower social restriction, no difference between the two groups was reported in other subscales.

Study Characteristics

Nine studies of quality-B or -C (a total of 451 subjects) in ten publications compared simultaneous bilateral cochlear implants with unilateral cochlear implantation.[41-50] Six were prospective studies with followup durations of 3 months to 1 year,[43, 44, 46, 48-50] and the remaining three were cross-sectional design studies.[11, 41, 42, 45] All studies were conducted in the U.S. except for one study that was conducted in France.[50] The mean or the median age of included subjects at cochlear implantation ranged from 46 to 64 years. The proportion of males included in studies ranged from 31 and 47 percent. Studies recruited subjects with severe to profound hearing loss for a mean duration of 3.5 to 15 years. Only two of the six studies reported that subjects were required to have an open-set sentence score of ≤ 50 percent in the best-aided condition as an indication for cochlear implantation.[43, 44] Bilateral simultaneous cochlear implantation was compared with either ear unilaterally within subjects, [41, 43, 44, 46, 48-50] or was compared with

different subjects with unilateral cochlear implantation (with or without hearing aid use).[42, 45] There could be considerable overlap of subjects in the two studies.[41, 45] Seven studies were graded quality-B, (moderate) [42-44, 46, 48-50] and the remaining two studies were graded quality-C (poor).[41, 45] In general, the studies lacked reporting of baseline characteristics, and had considerable differences in methodologies including duration of deafness, implanted devices, speech coding strategies, and tests for evaluation (Appendix Table D8 – D9).

Study Results

Speech perception with open-set sentences tests

Seven studies evaluated open-set sentences tests including, BKB-SIN (speech in quiet or in noise), CUNY sentences in noise, and HINT (speech in quiet or in noise).[41, 43, 44, 46, 48-50] Of these, three studies examined BKB-SIN test; one study tested in nine test conditions, which included three listening conditions and three noise locations[44] or as speech in babble task.[48, 49] In Litovsky 2006, a bilateral listening condition was better than either ear unilaterally at 3 and 6 month intervals. In Litovsky 2009, bilateral listening with both ears benefitted most as compared with one ear, when the target and interfering speech-in-babble task was spatially separated and 82 percent of subjects had bilateral benefit for correct hemi field identification. When target speech and babble were collocated at 0^o azimuth, 60 percent of subjects benefitted at 3 months and 53 percent at 6 months of postbilateral activation. In Litovsky 2004, bilateral benefit against poorer ear was significant, while bilateral benefit against better ear was minimal. All three studies that tested HINT sentences in quiet,[41, 43, 44] reported that bilateral cochlear implants scored statistically significantly better than the unilateral cochlear implants (Table 9). Buss 2009 reported bilateral listening was significantly better than unilateral listening during 1 year followup. While SNR values decreased between an interval of 3 months to 6 months, this did not reach statistical significance; of note, SNR values decreased significantly during an interval of followup between 6 months and 1 year.

Speech perception with multi-syllable tests

Two studies evaluated speech perception using a multiple-jammers test or disyllabic words.[42, 50] One study (60 subjects) conducted a multiple-jammers test using the target spondee words and sentences as combinations of randomly selected male and female sentences (jammers) that were presented simultaneously from one of the two speakers placed at $\pm 8^o$ from 0^o azimuth. On the multiple-jammers tests, the bilateral cochlear implant group performed statistically significantly better than the unilateral cochlear implant group (Table 9).[42] The bilateral cochlear implant group listened better against significantly higher noise levels (9 dB more) to identify words 50 percent of the time compared with the unilateral cochlear implant group. This study also showed that the bilateral cochlear implant group scored significantly better at processing speech by 11 dB SNR while attending to other simultaneous activities as identified by their scores in the Cognitive load test. The second study (Mosnier 2009) evaluated 27 subjects for speech performance using disyllabic words in both quiet and noise conditions.[50] Bilateral listening versus the better ear (unilateral condition) was better in both quiet and noise conditions at 12 months postactivation, while magnitude of improvement was higher when tested in quiet and was slightly lower when tested in noise. This study reported that at 6 months, subjects were able to identify words at low SNR of +5dB in bilateral listening condition, and had benefit over unilateral condition. However, the bilateral benefit at 12 months was largely similar at +5 dB and at +15 dB.

Additional outcomes of binaural processing

Litovsky 2006 reported that between 3 and 6 months, an overall improvement in BKB-SIN test performance occurred under most of the listening conditions as well as most of the noise locations, suggesting that bilateral implantation aided participants to overcome the "head shadow effect" when in noise. The "head shadow effect" refers to the "shadow" or partial blockage of sound created when the head and shoulders are interposed between a sound source and the opposite sided implant (or hearing ear). The reduction of speech perception by the "head shadow effect" is amplified in the presence of background noise. However, noise from the frontal location (0^o azimuth) resulted in a significantly poorer performance than when the noise was from either side of the head. For the noise from the front, there was no difference between the right and left ear. Buss 2009 reported binaural benefits in derived measures of head shadow effect, squelch, and summation during 1 year followup.

Sound Localization

All studies tested sound localization in quiet and one study in noise with the use of speakers in varying numbers located in a frontal plane, as well as different types of sound stimuli. Although there was an overall improvement in sound localization ability in bilateral listening compared with unilateral listening conditions, there was considerable inter-subject variability in at least three studies. Grantham 2007 reported that subjects with both ear implants localized speech signal better than noise signal.[47] Mosnier 2009 additionally tested speech localization in the presence of five noise sources that was similar to a cocktail party setting and reported large individual differences among 44 percent of a total of 27 subjects.[50] While 82 percent of a total of 17 subjects demonstrated bilateral benefit when right or left discrimination was evaluated at 3 months of postactivation in Litovsky 2009, only 47 percent subjects had bilateral benefit when sound localization was tested.[49]

Health-related quality-of-life

Two studies evaluated three different disease-specific instruments.[44, 45] One study used four subscales of the Abbreviated Profile of Hearing Aid Benefit (APHAB) to assess the perceived performance of each subject's real world listening experiences.[44] Compared with the best unilateral implant, the quality-of-life with bilateral cochlear implants was significantly better ($P<0.0001$) in three of four subscales including the ease of communication, listening in reverberant conditions, and background noise (Table 10). No significant difference between the two groups was reported for the subscale of aversiveness to sound. The second study examined two different disease-specific quality-of-life measures using the Hearing Handicap Inventory for the Elderly (HHIE) and the Hearing Handicap Questionnaire (HHQ).[45] For both HHIE and HHQ measures, subjects with bilateral cochlear implants had significantly lower social restriction scores compared with those with unilateral cochlear implant (Table 10). However, for the scores of emotional distress, there was no difference between the two groups. None of the studies reported any generic measures of health-related quality-of-life.

Table 8. Summary of baseline characteristics of the included studies for bilateral simultaneous and sequential cochlear implant

Number of studies	Simultaneous Bilateral implant: 9 studies (10 publications)[41-50] Sequential Bilateral implant: 5 studies (8 publications) .[11, 51-57] Both: 2 studies[58, 59]
Study design	Simultaneous Bilateral implant: 6 prospective cohort;[43, 44, 46, 48-50] 3 cross-sectional Sequential Bilateral implant: 1 RCT (also examined as 2 prospective cohorts)[51, 52, 56]; 3 cross-sectional[11, 53, 54]; 1 retrospective[57] Both: 1 prospective cohort;[58] 1 cross-sectional[59]
Followup duration	0.5 yr (3 studies); 0.75 (1 study); NA (5 cross-sectional studies)
Country	Simultaneous Bilateral implant: U.S; France. Sequential Bilateral implant: UK, U.S., Austria; Switzerland Both: Switzerland
Number of patients	Simultaneous Bilateral implant: 451 Sequential Bilateral implant: 239 Both: 63
Mean Age of patients	Simultaneous Bilateral implant: 46 – 64 yr Sequential Bilateral implant: 46 – 60 yr Both: 46 yr; 56 yr
Severity of deafness	Bilateral, severe to profound hearing loss: 10 studies
Duration of deafness	3 – 11yr
Time between deafness and implant	0 – 17yr
Cochlear implant indication	Open-set sentence scores ≤50% in the best-aided condition: 2 studies Open-set recognition with HINT in quiet ≤40%: 1 study Open set recognition with BKB in quiet 30%: 1 study
Study quality	Simultaneous Bilateral implant: 7 B; 2 C Sequential Bilateral implant: 2 B; 2 C Both: 2 C

BKB = Bamford-Kowal-Bench, HINT = Hearing in Noise Test, RCT = randomized controlled trial; yr = year.

Table 9. Open-set sentences and multi-syllable tests in subjects with bilateral simultaneous cochlear implant

Outcome category	Specific outcome	Study [N subjects]	Comparison groups	Results	Study quality
Speech perception test					
BKB-SIN	SNR-50 mean scores	Litovsky 2006 [37]	Bilateral implant vs. either ear unilaterally (within subject comparisons)	⬆	B (prospective; some patients not accounted)
HINT	Subjects with higher scores			⬆*	
BKB-SIN speech in babble task	% scores and correct hemifield identification	Litovsky 2009 [17]	Bilateral implant vs. either ear unilaterally (within subject comparisons)	⇧	B (prospective; selection process unclear)
BKB-SIN speech in babble task	% scores	Litovsky 2004 [17]	Bilateral implant vs. either ear unilaterally (within subject comparisons)	⬆ (poorer ear) ⇧ (better ear)	B (prospective; selection bias cannot be ruled out)
CUNY in noise	SNR	Buss 2008 [29]	Bilateral implant vs. either ear unilaterally (within subject comparisons)	⇧ (6, 12 mo)	B (prospective; unclear selection process, 10% excluded from analysis)
	Derived measures of binaural processing			⬆	
HINT-Q	Subjects with higher scores	Koch 2009 [15]	Bilateral implant vs. either ear unilaterally (within subject comparisons)	⬆	B (prospective; unclear selection process)
HINT-Q	Mean scores	Dunn 2008 [66]	Bilateral implant vs. unilateral implant	⬆	C (cross-sectional; without matching)
			Bilateral implant vs. either ear unilaterally (within subject comparisons)	⬆	
Multisyllable words					
Disyllabic words in noise and quiet	SNR scores	Mosnier 2009 [27]	Bilateral implant vs. either ear unilaterally (within subject comparisons)	⬆	B (prospective; unclear if consecutive patients were enrolled)
Speech test - Multiple-jammers	SNR scores	Dunn 2010 [60]	Bilateral implant vs. unilateral implant	⬆	B (cross-sectional; matched for age at implant, duration and preoperative hearing loss)

⬆ : bilateral cochlear implant is better ($p<0.05$) versus comparator; ⇧ bilateral better but no statistical significance or it was not reported

BKB-SIN = Bamford-Kowal-Bench speech in noise, HINT = Hearing in Noise test, SNR = signal-to-noise ratio

* Significant at all times except for 3 mo postimplant.

Table 10. Disease-specific health-related quality-of-life in subjects with bilateral simultaneous cochlear implant

Outcome category	Specific outcome	Study [N subjects]	Comparison groups	Results	Study quality
APHAB Subscale EC	Tied ranks	Litovsky 2006 [37]	Bilateral implant vs. either ear unilaterally (within subject comparisons)	⬆ (ease of communication)	B (prospective; some patients not accounted)
APHAB subscale RV				⬆ (reverberant listening conditions)	
APHAB subscale BN				⬆ (background noise)	
APHAB subscale AV				⇔ (aversion to sound)	
HHIE Emotional Distress	Mean scores	Noble 2008 [183]	Bilateral implant vs. unilateral implant	⇔ (emotional)	C (cross-sectional)
HHQ - Emotional Distress				⇔ (emotional)	
HHIE – Social restriction				⬆ (social)	
HHQ – Social restriction				⬆ (social)	

APHAB = Abbreviated Profile of Hearing Aid Benefit, EC = ease of communication, RV = reverberant listening conditions, BN = background noise; AV = aversiveness to sounds, HHIE = Hearing Handicap Inventory for the Elderly, HHQ = Hearing Handicap Questionnaire, ⬆ = benefit with statistical significance, ⇔ = no difference between comparison groups

Sequential Bilateral versus Unilateral Cochlear Implantation

Evidence was rated low based on data from two studies in four publications that were graded methodological quality-B. While a randomized controlled trial and a cross-sectional study showed benefit in speech perception in noise from sequential bilateral cochlear implants, a cross-sectional study did not find similar benefit in speech perception tests, both in noise and quiet conditions. In a randomized controlled trial evaluating sequential bilateral cochlear implants, the second ear implant resulted in negative results or non-significant changes in health-related quality-of-life after the first ear implant.

Study Characteristics

Five studies reported in eight publications (~ 208 subjects) compared sequential bilateral implantation with unilateral implantation.[11, 51-53] One study conducted in the UK generated three reports, which had considerable overlap of participants. [51, 52] Another study conducted in Austria generated two reports with considerable overlap of subjects.[53, 55] In the UK study, subjects were randomized to receive either immediate sequential second ear implant (1 month after first ear implant), or delayed second ear implant (9 months after first ear implant) with a prospective followup of 9 months.[51, 52] The remaining studies were cross-sectional or retrospective in design and were conducted in the U.S.,[11, 57] Switzerland,[54] and in Austria.[53] The U.S. study compared a small sample size of 13 subjects with bilateral sequential cochlear implants with subjects with unilateral cochlear implant (with or without hearing aid).[11] The second U.S. study compared 22 subjects with bilateral implants to first ear implant. The Switzerland study compared 29 subjects with bilateral implants to either ear unilaterally. The Austrian study compared 18 subjects with bilateral cochlear implants with the unilateral implant use (right and left ear unilaterally).[53] The mean age of included subjects with cochlear implant ranged from 46 to 60 years. The proportion of males included was 46 and 52 percent in three studies.[11, 53, 57] Studies recruited subjects with severe to profound hearing loss for a mean duration of 6 to 32 years. Only one study reported the indication for cochlear implant; the subjects were required to have scores ≤ 30 percent open-set sentence recognition with BKB-SIN in quiet.[52] The cochlear implants used were Nucleus® CI-24 implant system,[51, 52] MED-EL COMBI 40/40+,[53] and Advanced Bionics.[57] Studies were graded quality-B [51, 52, 57] or were graded quality-C.[11, 53, 54] In general, the studies of sequential bilateral cochlear implants had considerable differences in methodologies including duration of deafness, implanted devices, speech coding strategies, and tests for evaluation (Appendix Table D8 – D9).

Study Results

Speech perception with open-set sentences tests

In the Ramsden 2005 study of subjects with sequential bilateral cochlear implants, no significant advantage over the first (unilateral) ear was observed with the CUNY test in quiet at 3 and 9 months of followup.[52] However, speech perception was better with CUNY test in noise for bilateral cochlear implants, and their scores were better than the first ear scores both at 3 and 9 months of followup. In one cross-sectional study (Gifford 2008) that compared bilateral sequential cochlear implants with unilateral or bimodal cochlear implant, group means of both BKB-SIN in noise and AzBio sentence recognition in quiet were not significantly different.[11] However, in contrast to the BKB-SIN sentence recognition in noise results, the HINT sentences in quiet showed significant benefits with bilateral cochlear implants, where 28 percent of the

subjects achieved 100 percent correct (P<0.001) HINT scores. This study did not report testing of HINT sentences in noise conditions. Schleich 2004 evaluated the SRT in 18 of 21 enrolled subjects with sequential bilateral cochlear implants using an adaptive signal to noise ratio (SNR) to minimize floor and ceiling effects with Oldenburg (OLSA) sentence test.

Additional outcomes of binaural processing

In Schleich 2004, comparing bilateral implants with each ear implant unilaterally, when averaged across listening conditions and noise conditions, there was a statistically significant head shadow effect of 6.6 dB, binaural squelch effect of 1.1 dB, and binaural summation of 1 dB.[53] However, the binaural squelch effect was not significant for the comparisons of bilateral implant versus right ear unilaterally. Laske 2009 reported a statistically significant benefit for the head shadow effect when the sound source was from the activated side. For the OLSA test in quiet, the speech perception performance at 65 dB SPL was better by 18 percent in bilateral versus unilateral listening conditions. While for squelch and summation effects, results for the bilateral listening conditions were better for comparison with the unilateral better ear, but were not statistically significant.

Sound localization

Substantial significant benefits for bilateral implants versus unilateral listening conditions were reported in three studies.[54-56] Two studies reported greater difference between bilateral and unilateral conditions, with a unilateral localization accuracy in the range of 50 to 67 degrees versus bilateral accuracy of 24 to 29 degrees.[55, 56] One study reported that the bilateral implants had a mean deviation from the actual sound source of 57 degrees.[54]

Health-related quality-of-life

Five different instruments were used to assess the generic quality-of-life in a randomized controlled trial (Summerfield 2006) of 28 subjects with a unilateral cochlear implant;[51] these included the Glasgow Health Status Inventory (GHSI), Health Utilities Index Mark III (HUI3), Visual Analogue Scale (VAS), EQ5D™ self-reported questionnaire, and tinnitus questionnaire (Table 12). Results from the first (unilateral) ear cochlear implant were compared with results following bilateral sequential cochlear implants at 3 and 9 months. In addition, these subjects (postsecond cochlear implant) were compared with unilateral cochlear implant recipients from the UKCISG. Significant gains were noted in the bilateral cochlear implant group compared with first (unilateral) ear cochlear implant group at 9 months in the GHSI quality-of-life measure. The HUI3 measure showed no change, the VAS showed non-significant but a negative change, and EQ5D showed significant negative changes following bilateral cochlear implant. However, in multivariate analysis negative scores after a second cochlear implant were associated with worsening of tinnitus, while positive changes in health-related quality-of-life were associated with improvement in hearing. To evaluate the issue of worsening of tinnitus, bilateral cochlear implants were compared with unilateral implant from the UKCISG (a cohort recruited for another study) and this comparison resulted in inconclusive results. The authors concluded that a second cochlear implant resulted in non-significant changes in measures of health-related quality-of-life.

Bilateral cochlear (both sequential and simultaneous) versus Unilateral Cochlear Implantation

One study published from Switzerland included 37 subjects with bilateral simultaneous cochlear implant (N = 22) or bilateral sequential cochlear implant (N = 15).[58] All subjects had progressive hearing loss with a mean duration of 11 years; mean age at bilateral cochlear implantation was 46 years. All subjects underwent Nucleus® 24 cochlear implantation. Speech perception was tested using two open-set sentences in quiet and noise – Hochmair-Schulz-Moser (HSM) sentences and the OLSA sentence test. Based on their performance at 3 and 6 months, either ear was classified as poorer or better performing at the 3 month test interval. Bilateral cochlear implants were compared with poorer or better performing ears again at 6 months. There was a significant bilateral benefit with significant mean improvement in performance in noise conditions for both HSM and OLSA, a further indication that there was the bilateral head-shadow benefit. When tested in noise conditions for OLSA, bilateral cochlear implant benefit was significantly greater when the better ear was closest to the source of speech (-11.4 dB) than when the poorer ear was closest to the source of speech (-10 dB). However, in quiet conditions bilateral cochlear implants showed benefit over the poorer ear only. While binaural squelch effect was marginally significant with HSM sentences (speech scores had significant improvement of 8% relative to the better ear alone, P = 0.02), binaural squelch effect was not significant for OLSA sentences in noise. Only a subgroup of 16 subjects had sound localization data assessed that showed binaural localization was significantly better compared with monoaural localization (each ear unilaterally). Bilateral implants had a 50 degree mean error compared with a mean of 90 degrees using unilateral implant only. This study did not evaluate health-related quality-of-life. The second study Cullington 2010 evaluated bilateral implantation with bimodal group. The results are further discussed in that section.[60]

Table 11. Open-set sentences tests in subjects with bilateral sequential cochlear implant

Outcome category	Specific outcome	Study [N subjects]	Comparison groups	Results	Study quality
CUNY in quiet	Mean scores	Ramsden 2005 [31]	Bilateral implant vs. first ear implant	⇔	B (Prospective, no multivariate analysis)
CUNY in noise				⇑	
HINT-Q	% correct	Zeitler 2008 [22]	Bilateral implant vs. first ear implant	⇑	B (Retrospective; unclear selection process; 15 percent attrition)
BKB-SIN	% correct			⇑	
OLSA in quiet	% correct	Laske 2009 [29]	Bilateral implant vs. best ear unilateral	⇔	C (Cross-sectional; well conducted; matched for some outcomes)
			Bilateral implant vs. poorer ear unilateral	⇑	
AzBio	Mean scores	Gifford 2008 [156]	Bilateral implant vs. unilateral or bimodal implant	⇔	C (Cross-sectional)
BKB-SIN				⇔	
OLSA	Change in SRT	Schleich 2004 [18]	Bilateral implant vs. best ear unilateral	⇑	C (Cross-sectional)

BKB-SIN = Bamford-Kowal-Bench speech in noise, CUNY = City University of New York, OLSA = Oldenburg sentence test.

Table 12. Health-related quality-of-life in subjects with bilateral sequential cochlear implant

Outcome category	Specific outcome	Study [N subjects]	Comparison groups	Results	Study quality
GHSI	Mean difference	Summerfield 2006 [28]	Bilateral immediate implant vs. Bilateral delayed implant	⬆ (social, emotional, and psychological)	B (allocation concealment not clearly reported)
HUI3				⇔ (combination of 8 levels of function)	
VAS				⇩ (overall quality-of-life)	
EQ-5D				⬇ (five levels of function)	

GHSI = Glasgow Health Status Inventory, HUI3 = Health Utilities Index Mark III, VAS = Visual Analogue Scale, EQ-5D = EuroQoL 5 dimensions.

Bilateral Cochlear Implantation versus Bimodal (unilateral cochlear implant and an acoustic hearing aid)

Speech perception measures

Three quality-C studies (total of 119 subjects) evaluated bilateral cochlear implants compared with bimodal groups. Of these, two studies reported no difference between the two groups for speech perception measures of HINT sentences in noise and quiet, AzBio, and BKB-SIN.[11, 59] One study noted significant differences in health-related quality-of-life of HHIE and HHQ in the bilateral group versus bimodal group.[45]

Key Question 3a and 3b

3a. What are the preoperative patient characteristics associated with the successful attainment of the communication-related health outcomes as well as quality-of-life outcomes in questions 2 or 3 in individuals ≥ 18 years of age who undergo simultaneous bilateral cochlear implantation?

3b. What are the preoperative patient characteristics associated with the successful attainment of the communication-related health outcomes as well as quality-of-life outcomes in questions 2 or 3 in individuals ≥ 18 years of age who undergo sequential bilateral cochlear implantation?

At a minimum, the evidence surrounding the following will be discussed:

1. Speech recognition/word understanding

2. Auditory sensitivity/audibility

3. Duration of impaired hearing

4. Associated ear or bone diseases

5. Pre vs. postlinguistic deafness

6. Presence of other disabilities (e.g. visual impairment, impending or current)

7. Age at implantation

8. Degree of preimplant residual hearing

9. Choice of implanted ear

10. Site (expertise) of cochlear implant team

11. Implanted device

Preimplantation Characteristics as Predictors of Postimplantation Outcomes

Evidence was rated low based on two quality-B rated studies reporting data on age at implantation as predictor of postoperative outcomes. The first study reported that a preoperative characteristic such as age at implantation (≤ 59 years of age) was predictive of different postoperative outcomes evaluated in these studies. The second study did not find an association between age at second implant and postoperative outcomes. Duration of hearing loss before implantation (two quality-B studies) and implant device characteristics (one quality-B study) did not predict postoperative outcomes.

Age at implantation

One quality-B study evaluated the association of adult implant age on sound localization and quality-of-life measures using the HHIE, and HHQ.[60] The study was conducted as both prospective and retrospective. This study excluded implants followed retrospectively for >100 months, as these subjects had lower disability and handicap scores. The study participants overlapped with one study included under the section of bilateral simultaneous cochlear implantation.[45] The study compared younger and older cohorts in the unilateral implants, bilateral implants, and bimodal groups. There were no significant differences between the two age groups among the unilateral implants, bilateral implants, and bimodal groups for the outcomes of sound localization and quality-of-life measures. However, differences in scores of quality-of-life measures using the preimplant to postimplant change were correlated with chronological age, younger adults (≤ 59 years of age) with bilateral implants had significant increases in both performance and self-rated abilities than the older adults with bilateral implants. In the unilateral implant group, there were no significant correlations between chronological age and preimplant to postimplant change quality-of-life measures. In both bilateral and unilateral groups there were no significant correlations between chronological age and preimplant to postimplant change sound localization. Another quality-B study (Zeitler 2008) did not find any relationship between subject error patterns in sound localization and age at second implant.[57]

Implanted device

One quality-B study evaluated the role of implanted device on speech perception measure of HINT.[42] Twenty bilateral cochlear implants with an average use of 71 months were matched to 20 unilateral cochlear implants with an average use of 128 months on the following variables: age at implantation, duration of deafness, and type of internal device. The study reported that the bilateral implant group performed better compared to the unilateral group, indicating that implanted hardware had no role in the difference between the study groups.

Duration of impaired hearing

Two quality-B studies reported that there was no association between the duration of impaired hearing in the preoperative period with the postoperative performance in bilateral implant users.[50, 57]

Other Predictors

Laske 2009 reported that a short interval between implantations yielded better results for the second implant with an improved performance in the Oldenburger test in quiet.[54] In addition Litovsky 2009 found that better sound localization was associated with binaural advantage in speech performance measures.[49]

Key Question 3c

Report the available evidence separately for those individuals with sensorineural hearing loss as demonstrated by test scores of > 40 percent and ≤ 50 percent, as well as those with test scores between > 50 percent and ≤ 60 percent (best aided listening on tape or otherwise recorded tests of open-set sentence recognition).

Overall, evidence was rated low for the effectiveness of simultaneous bilateral implantation by their preimplantation open-set sentence test scores of ≤ 40 percent, which was evaluated in three quality-B studies that showed improved speech perception and sound localization, but inconsistent gains in terms of hearing-specific quality-of-life in one study. There was lack of information on the percentage of subjects with preimplantation scores of > 40 percent and ≤ 50 percent. No studies reported data on the preimplantation scores of > 50 percent and ≤ 60 percent among bilateral implants. Evidence was rated insufficient for the effectiveness of sequential bilateral implantation by the preimplantation test scores of ≤ 40 percent, which was evaluated in one quality-B study that showed improved speech perception in noise, and sound localization.

Two studies of simultaneous bilateral implants conducted in the U.S. reported the requirement of an open-set sentence score of ≤ 50 percent in the best-aided condition as an indication for bilateral cochlear implantation.[43, 44] Koch 2009 reported that the bilateral scores for the HINT in quiet was greater than the left ear alone (between 3 and 8 months, $P < 0.05$) and greater than the right ear alone (between 6 and 8 months, $P < 0.05$).[41] All subjects in this study localized sounds better with two implants compared with either implant unilaterally, and had a head shadow advantage for all test conditions. However, the binaural squelch effect was small with only 7 of the 15 subjects showing a squelch effect for at least one of the noise-right or noise-left conditions. The second study (Litovsky 2006) examined BKB-SIN test results in nine test conditions, which included three listening conditions and three noise locations.[44] A bilateral listening condition was better than either ear unilaterally at 3 and 6 month intervals. Between 3 and 6 months, an overall improvement in BKB-SIN test performance occurred under most of the listening conditions as well as most of the noise locations, suggesting that bilateral implantation aided participants to overcome the "head shadow effect" when in noise. The reduction of speech perception by the "head shadow effect" is amplified in the presence of background noise. However in this study, noise from the frontal location (0^o azimuth) resulted in a significantly poorer performance than when the noise was from either side of the head.

Two additional studies included subjects who had a preoperative open-set sentence score of minimum 30 or ≤ 40 percent in the best-aided condition as an indication for bilateral cochlear implantations.[46, 52] Buss 2009 reported binaural benefits in derived measures of head shadow effect, squelch, and summation during 1 year followup. While SNR values decreased between an

interval of 3 months to 6 months, this did not reach statistical significance; of note, SNR values decreased significantly between an interval of 6 months and 1 year.[46] In the Ramsden 2005 subjects with a minimum 30 percent open-set speech recognition in the first ear underwent sequential second ear implant. This study reported that no significant advantage over the first (unilateral) ear was observed with the CUNY test in quiet at 3 and 9 months of followup.[52] However, speech perception was better with CUNY test in noise for bilateral cochlear implants, and their scores were better than the first ear scores both at 3 and 9 months of followup. In this cohort of subjects, published in a different study, the second ear implant resulted in negative results or non-significant changes in health-related quality-of-life after the first ear implant.

Discontinued use of Cochlear Implant

In total, 20 subjects across all groups were reported in four studies to have adverse events and details of these events are summarized in the Appendix Table.D5. In summary, where adverse event data were available, 20 out of 495 subjects (4.0 percent) discontinued use of their cochlear implant(s) after hearing-related complications.

Nine (4.2 percent) patients implanted in the series became permanent non-users: three due to exacerbation of co-existing illness, and two due to a worsening of their tinnitus postimplantation; one patient declined preimplantation following a device failure and one patient who initially had a successful implant outcome has been advised against reimplantation following device extrusion in a previously irradiated temporal bone; two patients elected not to use their device with the reason given being disappointment with the outcome from their implantation.[17] One out of 34 subjects had a cerebrovascular accident 5 years postimplantation that caused sudden and permanent inability to hear with implantation.[20] One bilaterally-implanted patient out of 30 discontinued use of a single implant after inability to integrate separate signals from each ear.[52] Three adult patients out of 251 became non-users with reasons listed including depression, tinnitus, concomitant neurological problems, and non-auditory stimulation.[61]

New Technologies: Hybrid implantation

We identified one prospective clinical trial of 87 subjects implanted unilaterally with Nucleus® hybrid devices.[62] This study was rated quality-C. The study tested a **s**ubgroup of 27 subjects with Hybrid implantation using spondee recognition in multitalker babble for speech reception threshold values, which were plotted as a function of their pure tone acoustic thresholds of 125, 250, and 500 Hz.[62] Subjects displayed speech recognition in noise when residual hearing was preserved to levels no worse than severe hearing loss and when there was preservation of low frequency acoustic hearing in the postimplantation period.

This study reported two subjects with total hearing loss within the first month of cochlear implantation. In this study**,** the indication for cochlear implantation was the Consonant-Nucleus-Consonant word scores of 10 to 60 percent in the preimplant ear and up to 80 percent in the contralateral ear.[62] The study did not assess any predictors of postoperative outcomes of open-set sentences or multi-syllable tests. This study did not evaluate quality-of-life outcomes.

Discussion

Our review found that in adults with sensorineural hearing loss, unilateral cochlear implantation is an effective method of hearing assistance that provides significant gains in speech perception and health-related quality-of-life. Adults showed significant benefit in postimplantation speech perception scores (both multi-syllable tests and open-set sentences tests) over preimplantation scores, which were consistent across 11 studies whether they did or did not utilize bimodal hearing (unilateral cochlear implantation with additional use of hearing aids). In general, unilateral cochlear implantation showed benefits in both generic and disease-specific health-related quality-of-life measures compared with preimplantation results. However, in certain subscales, such as social domains of overall health-related quality-of-life, subjects with unilateral implants failed to show significant benefits in physical, cognitive, and emotional measures. Additionally, studies of unilateral implants provided insufficient evidence to draw a conclusion about the relationships between preoperative patient characteristics and postoperative health-related quality-of-life outcomes. There was insufficient evidence to address the effectiveness of unilateral cochlear implants by their preimplantation open-set sentence test scores of > 40 percent and ≤ 50 percent, and > 50 percent and ≤ 60 percent. Overall, there was low level of evidence regarding the association between preoperative patient characteristics (such as shorter duration of impaired hearing, better preoperative HINT score, and postlinguistic deafness) and better postoperative speech outcomes. In addition, the studies provided insufficient evidence to draw a conclusion about the relationships between preoperative patient characteristics and postoperative health-related quality-of-life outcomes. Largely due to small sample sizes, the studies mostly had imprecise estimates of the comparative effects. Small studies reported an association between preoperative patient characteristics, such as shorter duration of impaired hearing, better preoperative HINT score, and postlinguistic deafness and better postoperative speech outcomes. We found no studies that examined side of implantation or expertise of cochlear implant teams or other patient-related disabilities as potential modifying factors of speech perception and/or health-related quality-of-life outcomes. The device non-use rate secondary to hearing-related complications was 4.0 percent among subjects with cochlear implants.

Recently published studies of bilateral simultaneous cochlear implantation show greater benefit in speech perception and localization among adults compared with unilateral cochlear implantation with or without hearing aids, particularly in noise conditions. However, benefit under quiet conditions was unclear among those who had bilateral sequential cochlear implantation. This result is to be expected as it is generally not a test that is usually administered. In such quiet conditions, the first ear implant is likely to be "ceiling out" the effects of the second ear's implant under such listening conditions. Studies showed significant gains in the binaural processing measure of head-shadow benefit with an average 38 to 55 percent improvement over unilateral listening conditions, suggesting that subjects with bilateral cochlear implants may perform better in real world conditions. One study found a small binaural squelch effect after 1 year of bilateral implantation,[46] while others found small or non-significant squelch effects.[44, 48, 53, 54] In addition, a small sample size study of nine subjects followed over a period of 4 years has shown consistent benefit in binaural squelch over longer duration of followup.[63] This results of this study documents an increase in benefit following long-term experience with bilateral implants, thus emphasizing a need for long-term followup studies. Estimates of binaural summation were slightly better in bilateral listening condition but were statistically non-

significant compared with the unilateral listening conditions in two studies.[46, 54] These study results were in contrast and summation values were smaller than the effects reported in one study.[53] Given the small number of subjects with short duration of followup in bilateral cochlear implants included in these studies, cautious interpretation of these results is needed to draw definitive conclusions regarding speech perception outcomes. Small benefits in summation and squelch effects suggest that subjects with bilateral implants may be able to neurally integrate inputs over time. Further continued assessments are needed to know which of these perceptual abilities translate into clinically measurable benefit in real-world performance thereby improving health-related quality-of-life outcomes.

Although there were significant gains in terms of speech perception outcomes, in published studies this did not translate to consistent gains in the perceived performance as assessed through a variety of health-related quality-of-life measures in three studies that reported these outcomes. Sparse data and inconsistent benefits in terms of health-related quality-of-life outcomes preclude any definitive conclusions regarding improved quality-of-life in subjects with bilateral cochlear implantation. Inconsistent benefits may also indicate a lack of better measures of performance and a need to develop quality-of-life instruments specifically designed for people with severe-to-profound hearing loss, which can be used to assess health-related quality-of-life outcomes in subjects with bilateral cochlear implantation. Results from a small number of subjects in a randomized controlled trial reported that the positive binaural benefit may have been offset by the worsening of tinnitus after the second implant.[51] However, observational studies have also shown improvement in tinnitus with bilateral cochlear implantation. In general, cochlear implantation is safe and provides benefit to patients. Similar to any surgical procedure, complications can occur. A second ear implant brings additional risk in terms of additional surgery and an increase in operating time. Of note, only one bilateral cochlear implantation reported adverse events in a small sample with 6 months of followup.[52] It is important to assess long-term outcomes from bilateral implantation because of its irreversible changes to the cochlea, without preserving one ear for future medical intervention. Further studies with longer followup duration are needed to assess health-related quality-of-life outcomes in bilateral cochlear implantation.

Overall, evidence was rated low for the effectiveness of simultaneous bilateral implantation by their preimplantation open-set sentence test scores of ≤ 40 percent, which was evaluated in three quality-B studies that showed improved speech perception, and sound localization, but inconsistent gains in terms of hearing-specific quality-of-life in one study. Although evidence was rated moderate for the effectiveness of simultaneous bilateral implantation by their preimplantation open-set sentence test scores of ≤ 40 percent, there was insufficient data for the outcome of hearing-specific quality-of-life as only one study evaluated this outcome. The evidence was rated insufficient because of lack of information on the percentage of subjects with bilateral implants who had preimplantation scores of > 40 percent and ≤ 50 percent. No studies reported data on the preimplantation scores of > 50 percent and ≤ 60 percent among bilateral implants. Lack of information on candidacy criteria in evaluated studies emphasizes that additional research should be conducted to address health policy needs.

Potential limitations of our review directly reflect the limitations of recently published studies of unilateral and bilateral cochlear implantation. Although unilateral cochlear implantation is a well-established intervention, good-quality studies are still needed to yield stronger evidence of their effectiveness for speech-perception and health-related quality-of-life outcomes. Reviewed studies from current literature were rated moderate or poor quality due to

incomplete reporting of information including study selection criteria, recruitment of study subjects and year of recruitment, center characteristics, adjustment for potential confounders, and reasons for loss to followup. Additionally, more studies with longer duration are suggested to examine change in effectiveness of bilateral cochlear implants especially for health-related quality-of-life using disease specific instruments. Studies that analyzed preoperative patient characteristics as potential predictors of postoperative speech perception outcomes (open-set sentences, two syllable words) and/or health-related quality-of-life outcomes did not account for potential confounding factors in their analyses. Number of subjects needed in a multivariate analysis is typically larger than a univariate analysis (which does not account for potential confounding). There are some guidelines regarding the number of candidate predictors that can reliably be studied in relation to the size of the data set. A well-known rule of thumb is the 1 in 10 rule.[64] That is, for linear regression models, one candidate predictor can be studied for every 10 patients. Thus, most of the included studies did not have sufficient number of subjects for multivariate analysis of more than two candidate predictors. Existing studies do not allow accurate conclusions to be drawn. All except for one study tested sound localization in quiet, with no background noise among bilateral cochlear implant users, thus failing to evaluate in realistic listening environments. Furthermore, use of cross-over study design to evaluate performance of bilateral implants for outcomes of localization and speech perception outcomes may have precluded evaluation of health-related quality-of-life outcomes, which may require use of alternative study designs.

Conclusion

In summary, unilateral cochlear implantation with or without additional use of hearing aids has been an effective method for improving speech perception and health-related quality-of-life in adults with severe to profound sensorineural hearing loss. Bilateral cochlear implantation provides added improvements in speech perception outcomes in noisy environments over unilateral cochlear implantation. Bilateral cochlear implants show significant binaural head-shadow benefit, small benefits in binaural summation, binaural squelch effects, and better sound localization. Although the magnitude of the benefits in noise appears modest, they translate to significant and important differences as reported anecdotally by patients. Additionally, none of the studies have been able to quantify the sensation described by patients of fusion of bilateral sound into a stereo perception within one's head. There is a need to develop better measures of performance and disease-specific quality-of-life instruments that may reflect the significance of these subjective benefits. Further studies with longer followup duration are needed to assess the additional benefits in terms of improved health-related quality-of-life and potential risks of bilateral cochlear implantation compared with unilateral implantation.

Future research needs

- Good quality studies in terms of clear reporting selection criteria, center characteristics, recruitment dates, and reasons for loss to followup are needed on the effectiveness of unilateral cochlear implants for speech perception and health-related quality-of-life outcomes.
- Studies that explore potential modifiers of cochlear implant outcomes need to carefully consider confounders, perform appropriate adjustments, and include sufficient numbers of subjects.
- Large databases or registries of patients who received cochlear implants with long-term followup data on patient outcomes are needed to properly explore potential modifiers of cochlear implant outcomes using multivariate analyses.
- Future research should focus on the association between expanding the candidacy profile of cochlear implants (e.g., degree of hearing loss, speech perception ability) and assessing consequent outcomes.
- Long-term studies are needed to assess health-related quality-of-life outcomes (both generic and disease-specific) in subjects with bilateral cochlear implantation.
- Long-term studies are needed to assess the complications and risks of bilateral cochlear implantation.
- Further research is needed to develop speech perception tests that mimic real-world listening conditions in order to assess the practical benefits associated with unilateral and bilateral cochlear implantation.
- Future research should focus on developing quality-of-life instruments specifically designed for people with severe-to-profound hearing impairment, so that patient-reported outcomes associated with unilateral and bilateral cochlear implantation can be assessed quantitatively.
- Future research is needed to identify a time period needed for the sound localization, improved speech perception, and improved health-related quality-of-life after bilateral implantation.
- Improved measures are needed to more accurately report outcomes in noise and 3D binaural fusion of perception of sound. There is a need to develop better measures of performance and disease-specific quality-of-life instruments that may reflect the significance of these important, but currently subjective benefits.
- There will be increasing demand for hybrid devices in the future with the improvements in technology and increasing elderly population. Studies should be designed to carefully assess baseline (including potentially outcome predictive) characteristics and performance measures to be compared with same subject performances postimplantation.

References

(1) Sprinzl GM, Riechelmann H. Current trends in treating hearing loss in elderly people: a review of the technology and treatment options - a mini-review. *Gerontology* 2010;56(3):351-8.

(2) Gates GA, Rees TS. Hear ye? Hear ye! Successful auditory aging. *West J Med* 1997 October;167(4):247-52.

(3) Bond M, Mealing S, Anderson R et al. The effectiveness and cost-effectiveness of cochlear implants for severe to profound deafness in children and adults: a systematic review and economic model. *Health Technol Assess* 2009 September;13(44):1-330.

(4) Isaacson B, Lee KH, Kutz JW, Roland PS, Sargent EW. Cochlear Implants, Indications. *emedicine medscape com* 2010 June 25;Available at: URL: http://emedicine.medscape.com/article/857164-print.

(5) Huart SA. Unidentified and Underserved: Cochlear Implant Candidates in the Hearing Aid Dispensing Practice. *www audiology online* 2009 August 17;Available at: URL: www.audiologyonline.com/articles/pf_article_detail.asp?article_id=2272. Accessed September 20, 2010.

(6) Disability Programs. *www socialsecurity gov* 2010 August;Available at: URL: http://www.ssa.gov/disability/professionals/bluebook/2.00-SpecialSensesandSpeech-Adult.htm#2_10.

(7) NICE. Cochlear implants for children and adults with severe to profound deafness. *National Institute for Health and Clinical Excellence* 2009 January 28;Available at: URL: http://www.nice.org.uk/TA166.

(8) Bai Z, Stephens D. Subjective outcome measures after cochlear implantation: Overall measures. *Audiological Medicine* 2005;3(4):212-9.

(9) Bassim MK, Buss E, Clark MS et al. MED-EL Combi40+ cochlear implantation in adults. *Laryngoscope* 2005;115(9):1568-73.

(10) Damen GWJA, Beynon AJ, Krabbe PFM, Mulder JJS, Mylanus EAM. Cochlear implantation and quality of life in postlingually deaf adults: Long-term follow-up. *Otolaryngology - Head and Neck Surgery* 2007;136(4):597-604.

(11) Gifford RH, Shallop JK, Peterson AM. Speech recognition materials and ceiling effects: considerations for cochlear implant programs. *Audiol Neurootol* 2008;13(3):193-205.

(12) Hay-McCutcheon MJ, Pisoni DB, Kirk KI. Audiovisual speech perception in elderly cochlear implant recipients. *The Laryngoscope* 2005;115(10):1887-94.

(13) Hawthorne G, Hogan A, Giles E et al. Evaluating the health-related quality of life effects of cochlear implants: a prospective study of an adult cochlear implant program. *Int J Audiol* 2004;43(4):183-92.

(14) Klop WMC, Boermans PPBM, Ferrier MB, Van Den Hout WB, Stiggelbout AM, Frijns JHM. Clinical relevance of quality of life outcome in cochlear implantation in postlingually deafened adults. *Otology and Neurotology* 2008;29(5):615-21.

(15) Krueger B, Joseph G, Rost U, StrauÃŸ-Schier A, Lenarz T, Buechner A. Performance groups in adult cochlear implant users: Speech perception results from 1984 until today. *Otology and Neurotology* 2008;29(4):509-12.

(16) Liu B, Chen XQ, Kong Y et al. Quality of life after cochlear implantation in postlingually deaf adults. *National Medical Journal of China* 2008;88(22):1550-2.

(17) Mawman DJ, Bhatt YM, Green KMJ, O'Driscoll MP, Saeed SR, Ramsden RT. Trends and outcomes in the Manchester adult cochlear implant series. *Clinical Otolaryngology and Allied Sciences* 2004;29(4):331-9.

(18) Morris LG, Mallur PS, Roland J, Waltzman SB, Lalwani AK. Implication of central asymmetry in speech processing on selecting the ear for cochlear implantation. *Otology and Neurotology* 2007;28(1):25-30.

(19) Most T, Shrem H, Duvdevani I. Cochlear implantation in late-implanted adults with prelingual deafness. *Am J Otolaryngol* 2010 November;31(6):418-23.

(20) Orabi AA, Mawman D, Al-Zoubi F, Saeed SR, Ramsden RT. Cochlear implant outcomes and quality of life in the elderly: Manchester experience over 13 years. *Clinical Otolaryngology* 2006;31(2):116-22.

(21) Rama-Lopez J, Cervera-Paz FJ, Manrique M. Cochlear implantation of patients with far-advanced otosclerosis. *Otology and Neurotology* 2006;27(2):153-8.

(22) Roditi RE, Poissant SF, Bero EM, Lee DJ. A predictive model of cochlear implant performance in postlingually deafened adults. *Otology and Neurotology* 2009;30(4):449-54.

(23) Firszt JB, Holden LK, Skinner MW et al. Recognition of speech presented at soft to loud levels by adult cochlear implant recipients of three cochlear implant systems. *Ear Hear* 2004;25(4):375-87.

(24) UK Cochlear Implant Study Group. Criteria of candidacy for unilateral cochlear implantation in postlingually deafened adults III: prospective evaluation of an actuarial approach to defining a criterion. *Ear Hear* 2004;25(4):361-74.

(25) Vermeire K, Brokx JPL, Wuyts FL, Cochet E, Hofkens A, Van De Heyning PH. Quality-of-life benefit from cochlear implantation in the elderly. *Otology and Neurotology* 2005;26(2):188-95.

(26) Vermeire K, Brokx JPL, Wuyts FL et al. Good speech recognition and quality-of-life scores after cochlear implantation in patients with DFNA9. *Otology and Neurotology* 2006;27(1):44-9.

(27) Wanscher JH, Faber CE, Grontved AM. Effect on quality of life of cochlear implantation in deaf adults. *Ugeskr Laeger* 2006;168(33):2656-9.

(28) Bradley J, Bird P, Monteath P, Wells JE. Improved speech discrimination after cochlear implantation in the Southern Cochlear Implant Adult Programme. *New Zealand Medical Journal* 2010;123(1321):34-44.

(29) Lazard DS, Bordure P, Lina-Granade G et al. Speech perception performance for 100 post-lingually deaf adults fitted with Neurelec cochlear implants: Comparison between Digisonic(R) Convex and Digisonic(R) SP devices after a 1-year follow-up. *Acta Otolaryngol* 2010 November;130(11):1267-73.

(30) Friedland DR, Runge-Samuelson C, Baig H, Jensen J. Case-control analysis of cochlear implant performance in elderly patients. *Archives of Otolaryngology - Head and Neck Surgery* 2010;136(5):432-8.

(31) Haensel J, Ilgner J, Chen YS, Thuermer C, Westhofen M. Speech perception in elderly patients following cochlear implantation. *Acta Otolaryngol (Stockh)* 2005;125(12):1272-6.

(32) Bodmer D, Shipp DB, Ostroff JM et al. A comparison of postcochlear implantation speech scores in an adult population. *Laryngoscope* 2007;117(8):1408-11.

(33) Chatelin V, Kim EJ, Driscoll C et al. Cochlear implant outcomes in the elderly. *Otology and Neurotology* 2004;25(3):298-301.

(34) Francis HW, Yeagle JD, Brightwell T, Venick H. Central effects of residual hearing: Implications for choice of ear for cochlear implantation. *Laryngoscope* 2004;114(10 I):1747-52.

(35) Green KMJ, Bhatt YM, Mawman DJ et al. Predictors of audiological outcome following cochlear implantation in adults. *Cochlear implants int* 2007;8(1):1-11.

(36) Nascimento LTd, Bevilacqua MC. Evaluation of speech perception in noise in cochlear implanted adults. *Rev Bras Otorrinolaringol (Engl Ed)* 2005;71(4):432-8.

(37) Rotteveel LJC, Snik AFM, Cooper H, Mawman DJ, Van Olphen AF, Mylanus EAM. Speech perception after cochlear implantation in 53 patients with otosclerosis: Multicentre results. *Audiology and Neurotology* 2010;15(2):128-36.

(38) Spahr AJ, Dorman MF. Performance of Subjects Fit with the Advanced Bionics CII and Nucleus 3G Cochlear Implant Devices. *Archives of Otolaryngology - Head and Neck Surgery* 2004;130(5):624-8.

(39) Matterson AG, O'Leary S, Pinder D, Freidman L, Dowell R, Briggs R. Otosclerosis: Selection of ear for cochlear implantation. *Otology and Neurotology* 2007;28(4):438-46.

(40) Carlson ML, Breen JT, Gifford RH et al. Cochlear implantation in the octogenarian and nonagenarian. *Otology and Neurotology* 2010 October;31(8):1343-9.

(41) Dunn CC, Tyler RS, Oakley S, Gantz BJ, Noble W. Comparison of speech recognition and localization performance in bilateral and unilateral cochlear implant users matched on duration of deafness and age at implantation. *Ear Hear* 2008;29(3):352-9.

(42) Dunn CC, Noble W, Tyler RS, Kordus M, Gantz BJ, Ji H. Bilateral and unilateral cochlear implant users compared on speech perception in noise. *Ear Hear* 2010;31(2):296-8.

(43) Koch DB, Soli SD, Downing M, Osberger MJ. Simultaneous bilateral cochlear implantation: Prospective study in adults. *Cochlear Implants Int* 2009;11(2):84-99.

(44) Litovsky R, Parkinson A, Arcaroli J, Sammeth C. Simultaneous bilateral cochlear implantation in adults: a multicenter clinical study. *Ear Hear* 2006;27(6):714-31.

(45) Noble W, Tyler R, Dunn C, Bhullar N. Hearing handicap ratings among different profiles of adult cochlear implant users. *Ear Hear* 2008;29(1):112-20.

(46) Buss E, Pillsbury HC, Buchman CA et al. Multicenter U.S. bilateral MED-EL cochlear implantation study: Speech perception over the first year of use. *Ear Hear* 2008;29(1):20-32.

(47) Grantham DW, Ashmead DH, Ricketts TA, Labadie RF, Haynes DS. Horizontal-plane localization of noise and speech signals by postlingually deafened adults fitted with bilateral cochlear implants. *Ear Hear* 2007;28(4):524-541.

(48) Litovsky RY, Parkinson A, Arcaroli J et al. Bilateral Cochlear Implants in Adults and Children. *Archives of Otolaryngology - Head and Neck Surgery* 2004;130(5):648-55.

(49) Litovsky RY, Parkinson A, Arcaroli J. Spatial hearing and speech intelligibility in bilateral cochlear implant users. *Ear Hear* 2009;30(4):419-431.

(50) Mosnier I, Sterkers O, Bebear JP et al. Speech performance and sound localization in a complex noisy environment in bilaterally implanted adult patients. *Audiol Neurootol* 2009;14(2):106-14.

(51) Quentin Summerfield A, Barton GR, Toner J et al. Self-reported benefits from successive bilateral cochlear implantation in post-lingually deafened adults: randomised controlled trial. *Int J Audiol* 2006;45 Suppl 1:S99-107.

(52) Ramsden R, Greenham P, O'Driscoll M et al. Evaluation of bilaterally implanted adult subjects with the nucleus 24 cochlear implant system. *Otology and Neurotology* 2005;26(5):988-98.

(53) Schleich P, Nopp P, D'Haese P. Head shadow, squelch, and summation effects in bilateral users of the MED-EL COMBI 40/40+ cochlear implant. *Ear Hear* 2004;25(3):197-204.

(54) Laske RD, Veraguth D, Dillier N, Binkert A, Holzmann D, Huber AM. Subjective and objective results after bilateral cochlear implantation in adults. *Otology and Neurotology* 2009;30(3):313-8.

(55) Nopp P, Schleich P, D'Haese P. Sound localization in bilateral users of MED-EL COMBI 40/40+ cochlear implants. *Ear Hear* 2004;25(3):205-14.

(56) Verschuur CA, Lutman ME, Ramsden R, Greenham P, O'Driscoll M. Auditory localization abilities in bilateral cochlear implant recipients. *Otology and Neurotology* 2005;26(5):965-71.

(57) Zeitler DM, Kessler MA, Terushkin V et al. Speech perception benefits of sequential bilateral cochlear implantation in children and adults: A retrospective analysis. *Otology and Neurotology* 2008;29(3):314-25.

(58) Laszig R, Aschendorff A, Stecker M et al. Benefits of bilateral electrical stimulation with the nucleus cochlear implant in adults: 6-Month postoperative results. *Otology and Neurotology* 2004;25(6):958-68.

(59) Cullington HE, Zeng Fg. Bimodal hearing benefit for speech recognition with competing voice in cochlear implant subject with normal hearing in contralateral ear. *Ear Hear* 2010;31(1):70-73.

(60) Noble W, Tyler RS, Dunn CC, Bhullar N. Younger- and older-age adults with unilateral and bilateral cochlear implants: speech and spatial hearing self-ratings and performance. *Otol Neurotol* 2009;30(7):921-929.

(61) Ray J, Wright T, Fielden C, Cooper H, Donaldson I, Proops DW. Non-users and limited users of cochlear implants. *Cochlear implants int* 2006;7(1):49-58.

(62) Gantz BJ, Hansen MR, Turner CW, Oleson JJ, Reiss LA, Parkinson AJ. Hybrid 10 clinical trial: preliminary results. *Audiol Neurootol* 2009;14 Suppl 1:8-13.

(63) Eapen RJ, Buss E, Adunka MC, Pillsbury HC, Buchman CA. Hearing-in-noise benefits after bilateral simultaneous cochlear implantation continue to improve 4 years after implantation. *Otol Neurotol* 2009;30(2):153-159.

(64) Harrell FE, Jr., Lee KL, Califf RM, Pryor DB, Rosati RA. Regression modelling strategies for improved prognostic prediction. *Stat Med* 1984 April;3(2):143-52.

Appendix A. Description of abbreviations and relevant terms

Table A 1. Description of abbreviations of speech perception outcomes

Name	Outcome category	Description	Score range
AzBio Sentences	Speech perception in quiet	The AzBio sentences include variable number of sentences (20-40) presented from the multiple-talker (both male and female). The score range from 1 to 100 percent based on the percent of words correctly identified.	0-100% (Best score:100)
Bamford-Kowal-Bench (BKB) / BKB-speech in noise (BKB-SIN) sentence test	Speech perception in noise	The BKB Standard Sentence Lists comprise 21 lists, each having 16 sentences and 50 keywords (3 or 4 per sentence). Although designed for testing children, the sentences have also proved useful and appropriate in testing adults. The evaluated studies used variable number of sentence lists. The score range from 1 to 100 percent based on the percent of words correctly identified. The BKB-speech in noise (SIN) presents BKB sentences in high- and low-level sentences to listeners.	0-100% (Best score:100)
Central Institute for the Deaf sentences (CID)	Speech perception in quiet or noise	The CID sentences test involves presenting 10 lists of sentences with 50 keywords per list. The score range from 1 to 100 percent based on the percent of keywords correctly identified.	0-100% (Best score:100)
Centro de Pesquisas Audiologicas (CPA) sentence recognition test	Speech perception in quiet or noise	The CPA sentences are presented in quiet and in competition with noise. Listeners are scored using sentence recognition index.	Sentence recognition index
City University of New York Sentences (CUNY)	Speech perception in quiet or noise	The CUNY Sentences are topic-related sentences consisting of 6 lists of 12 sentences each. The evaluated studies used variable number of sentence lists. Performance is scored for keywords correct per list.	0-100% (Best score:100)
Hearing In Noise Test (HINT)	Speech perception in quiet or noise	The HINT test assesses a listener's recognition of everyday sentences in quiet and noise. The test involves 25 lists per listening condition; 10 sentences / list and is scored for percent of key words correctly identified.	0-100% (Best score:100)
Hochmair-Schulz-Moser (HSM)	Speech perception in quiet or noise	The HSM sentences are presented in quiet and in competition with noise. Listeners are scored based on correctly repeating 50 percent of the sentences.	Poor, medium, and good performers
Multiple-jammers test	Speech perception in quiet or noise	A multiple-jammers test uses the target spondee words and sentences as combinations of randomly selected male and female sentences (jammers) that were presented	0-100% (Best score:100)

Name	Outcome category	Description	Score range
		simultaneously from one of the two speakers placed at two different azimuth.	
Open-set sentences test	Speech perception in quiet or noise	A speech perception test is considered to be "open-set" if the listener is required to recognize words or sentences without the presence of response alternatives (a free recall response). Listeners must identify what they heard by repeating or writing the words or sentences down.	0-100% (Best score:100)
Oldenburg sentence test (OLSA)	Speech perception in noise	The OLSA test consists of 40 lists of 30 sentences each. Each sentence consists of 5 words and is generated by permutations of 50 words.	0-100% (Best score:100)
Spondee recognition test	Speech perception in quiet	This is an open-set test in which the subject is asked to repeat each of 25 spondaic words. The spondee words spoken by a female or male talker and presented in a two-talker background. Scored for percent of words correctly identified.	0-100% (Best score:100)
Spondees or spondaic words	Speech perception in quiet	Spondee words have two-syllables with emphasis on both of them, for example, "base-ball" and "sidewalk." Half credit is given when one of the two syllables are correct.	0-100% (Best score:100)

Table A 2. Description of abbreviations of health-related quality-of-life outcomes

Name	Outcome category	Description	Score range
Abbreviated Profile of Hearing Aid Benefit (APHAB)	Disease specific health-related quality-of-life	The APHAB consists of four subscales: ease of communication (EC), reverberant listening conditions (RV), background noise (BN), and aversiveness to sounds (AV).	Tied Ranks based on the average score for each subscale
Adapted Deaf Identity Developmental Scale (ADIDS)	Disease specific health-related quality-of-life	The ADIDS is 29-item self- assessment in 5 areas: communication, family climate, social skills, academic and work performance, and general satisfaction.	1 (Totally disagree) to 6 (Totally agree)
Assessment of Quality of Life (AQoL)	Generic and disease health-related quality-of-life	The AQoL consists of (generic, with 2 questions hearing-specific) with 15-items and is a multi-attribute utility instrument. It comprises of five dimensions self-assessment measuring illness, independent living, social relationships, physical senses, and psychological well-being.	–0.04 (worst) to 0.00 (death) to 1.00 (best)
EuroQol 5 dimensions (EQ-5D)	Generic measure of health-related quality-of-life	The EQ-5D measures 5 dimensions: mobility, self-care, usual activities, pain and discomfort, and anxiety and depression	0 (death)-1 (full health
Glasgow Benefit Inventory	Generic measure of	The Glasgow Benefit Inventory Questionnaire measures	-100 (maximal worsening)

Name	Outcome category	Description	Score range
(GBI)	health-related quality-of-life	psychological, social and emotional aspects of quality-of-life. The GBI is maximally sensitive to a change in health status brought about by the cochlear implant	to +100 (maximal improvement)
Glasgow Health Status Inventory (GHSI)	Generic measure of health-related quality-of-life	The Glasgow Health Status Inventory Questionnaire measures effect of a hearing problem on the quality-of-life. Measures overall life, general, physical health, and social support	0 (worst) – 100 (best)
Hearing Handicap Inventory for Adults	Disease specific health-related quality-of-life	The HHIA is a test of hearing handicap in adult populations. It is 25 items, hearing-specific, quality-of-life scale with two sub-scales (emotional and situational impact of hearing loss)	0 (best) – 100 (worst with maximum handicap)
Hearing handicap Inventory for the Elderly (HHIE)	Disease-specific health-related quality-of-life	The HHIE comprises 25 item in two subscales, assessing social and emotional handicap. Self-administered using a three point scale (yes, sometimes, no)	Range of scores not documented. Higher scores associated with greater handicap
Hearing Handicap Questionnaire (HHQ)	Disease-specific health-related quality-of-life	The HHQ comprises of 12 item administered questionnaire using a 5 point scale and higher scores indicate greater handicap. The questionnaire has two parts related to emotional distress and social restriction.	Range of scores not documented. Higher scores associated with greater handicap
Hearing Participation Scale (HPS)	Disease-specific health-related quality-of-life	The HPS is a shortened form of the GHSI comprising of 11-item self-assessment measuring self-esteem and level of social interaction related to hearing, and hearing handicap. The scores range between 0 and 1, where a lower score corresponds to profound effects due to hearing loss.	0.00 (worst) -1.00 (best) (0.00 - low score indicates profound effects due to deafness)
Health Utilities Index 2 (HUI-2) or Health Utilities Index 3 (HUI-3)	Generic measure of health-related quality-of-life	The HUI-2 or HUI-3 establishes the respondent's level of function with regard to 8 attributes: hearing, vision, the capacity to be understood when speaking, mobility, dexterity, cognition, feelings, and pain. The quality-of-life scores range from 0 to 1, where 0 corresponds to death and 1 corresponds to full health.	0 (death)-1 (full health)
Index of Self-Esteem	Disease-specific health-related quality-of-life	The Index of Self-Esteem consists of 25 items, which rates how positive a person feels about him or herself. The scores range from 1 to 5, where a higher score corresponds to a higher sense of self-esteem.	1 (worse) – 5 (higher sense of self-esteem)
Loneliness Scale	Disease-specific health-related quality-of-life	The University of California, Los Angeles (UCLA), Loneliness Scale involves 20-item self-assessment rating how frequently a person experiences the feeling of loneliness described in each question. The Loneliness Scale score ranges from 1 (never) to 4 (frequently or higher	1 (never) -4 (frequently or higher sense of loneliness)

Name	Outcome category	Description	Score range
		sense of loneliness).	
Nijmegen Cochlear Implant Questionnaire (NCIQ)	Disease-specific health-related quality-of-life	The NCIQ is specially developed to evaluate how cochlear implantation affects health status. The general physical domain consists of 3 subdomains (basic and advanced sound perception and speech production) and mainly focuses on communication (referred to as NCIQ communication). The psychological domain (NCIQ psychological) contains mainly self-esteem questions, while the social domain (NCIQ social) addresses activity limitations and social interactions. Each subdomain includes 10 items	0 (worse) -100 (best)
Short- Form 36 (SF-36)	Generic measure of health-related quality-of-life	The SF-36 is a multidimensional outcome instrument to measure QOL. It has been designed to prospectively monitor patient outcomes in medical and clinical research settings. It includes 36 items and assesses 8 different health concepts: Physical functioning, role functioning due to physical health or emotional problems, bodily pain, vitality, social functioning, mental health, and general health perceptions	0 (worse) -100 (best)
Overall Quality of Life (VAS)	Generic measure of health-related quality-of-life	The VAS is an unconstrained measure by asking participants about their general well-being, enjoyment of life, independence and ability to take care of themselves, ability to take care of others, feeling about themselves, ability to get around and communicate, ability to socialize and get things done at work or at home	0 (worst) -100 (best)

Table A 3. Description of sound location and other terms

Name	Description
Azimuth	Azimuth refers to the spatial dimensions of the source of sound that relates to the direction from the listener in the horizontal plane.
Binaural Squelch	Binaural squelch refers to the mechanism by which the auditory system potentially can combine the information from the ears to form a better central representation
Binaural Summation or redundancy	Binaural summation or redundancy can occur when speech and noise originate from the same location. It indicates the auditory system's ability to combine duplicate signals (from the ears) in the brain.
dB SPL	Decibel (dB): dB = 10*log10(I/Iref), where I refers to sound intensity, p is sound pressure, ref is a referent intensity or pressure, and log10 is the logarithm to the base 10. SPL is a logarithmic measure of the sound pressure relative to a reference value. It is measured in dB above a standard reference level.

Name	Description
Head Shadow effect	The “head shadow effect” refers to the “shadow” or partial blockage of sound created when the head and shoulders are interposed between a sound source and the opposite sided implant (or hearing ear). The reduction of speech perception by the “head shadow effect” is amplified in the presence of background noise.
Hertz (Hz)	Hertz is the measure of vibratory frequency in which “n” cycles per second of periodic oscillation is “n” Hz.
Signal-to-Noise Ratio (SNR)	The objective is to find the SNR (also known as signal-to-babble ratio) needed for the subject to correctly repeat 50 percent of the items on the speech test presented against a background of noise or speech babble. For example, the background noise is presented at a fixed level of 60 or 70 dB HL and then the level of the sentences are raised or lowered until the level where the subject correctly repeats 50 percent of the items. A lower SNR indicates better speech perception in noise, and a higher SNR means poorer speech perception in noise.
Sound Localization	When sound is presented in the horizontal plane (at ear level), subjects with normal hearing are able to tell where sound is coming from with an accuracy of ±14 degrees. The brain uses differences in intensity and time between the two ears to locate a sound source. To localize sound in a vertical plane (up and down), or when time and intensity cues between the two ears are ambiguous, spectral (pitch) information is important.
Speech recognition threshold (SRT)	The speech recognition threshold (SRT): The SRT is the minimum hearing level of a speech signal at which a listener correctly repeats 50 percent of the spoken message

Appendix B. Data Extraction Forms

Study characteristics

Author		Yr		PMID		Extractor	

Key questions addressed

Study design (prospective/retrospective/cross-sectional)
Recruitment dates

Country/Setting

Funding

Participants (N enrolled)
Inclusion criteria

Participants (N completed)
Exclusion criteria

Intervention
Concurrent treatment

Comparator
Comments

Primary outcome
Outcome assessor

Secondary outcome
Duration of followup

Baseline characteristics of predictors

Description of (Sub-) Groups	N	Mean	SE/SD	(unit) r=	*p*
Speech recognition/word understanding					
Duration of impaired hearing					
Associated ear or bone disease					
Pre vs. postlingual deafness					
Other disabilities*					
Age					
Degree of preimplant residual hearing					
Choice of implanted ear					
Site or center (expertise) of cochlear implant team					
Implanted device					

* Visual impairment, impending or current

Summary of general study characteristics

Author Year Country	Study design Followup (yr)	Population(N) [Cochlear implant]	Mean age	Male (%)	Degree of deafness	Duration of deafness	Mean time (range) between deafness and implantation	Device Coding strategy	Study quality (comments)

Summary of study results

Author Year Country	Outcome category	Specific outcome	Intervention group (n/N) mean (95% CI)	Control group (n/N) mean (95% CI)	p-value	Descriptive analysis
	Speech test					
	Two syllable test					
	HRqol					
	Adverse events					

Definition of specific outcomes

Author Year Country	Outcome category	Specific outcome	Description	Score range	Notes
	Speech test				
	Two syllable test				
	HRqol*				
	Adverse events				

*****Please specify generic or disease-specific health related quality-of-life

Comments

Study quality indicators

Quality criteria	Y/N/NA/NR	Comments
Was the study prospective?		
Selection bias		
Eligibility criteria stated?		

Appropriate?	
Were the participants representative of the population?	
Were potential confounders reported?	
Were they accounted for in the design or analysis?	
Assessment bias	
Were the outcome measures relevant to the research question?	
Independent blind assessment?	
Objective?	
Attrition bias	
Was attrition reported?	
Were all participants accounted for?	
Were missing data accounted for?	
Protocol violations specified?	
Power and analysis	
Data analysis	
Was the analysis appropriate?	
Was there a power calculation?	
Other	
Generalizability? (Yes, if patients ≥ 60 years old)	

Y, yes; N, no; NA, not applicable; NR, not reported.

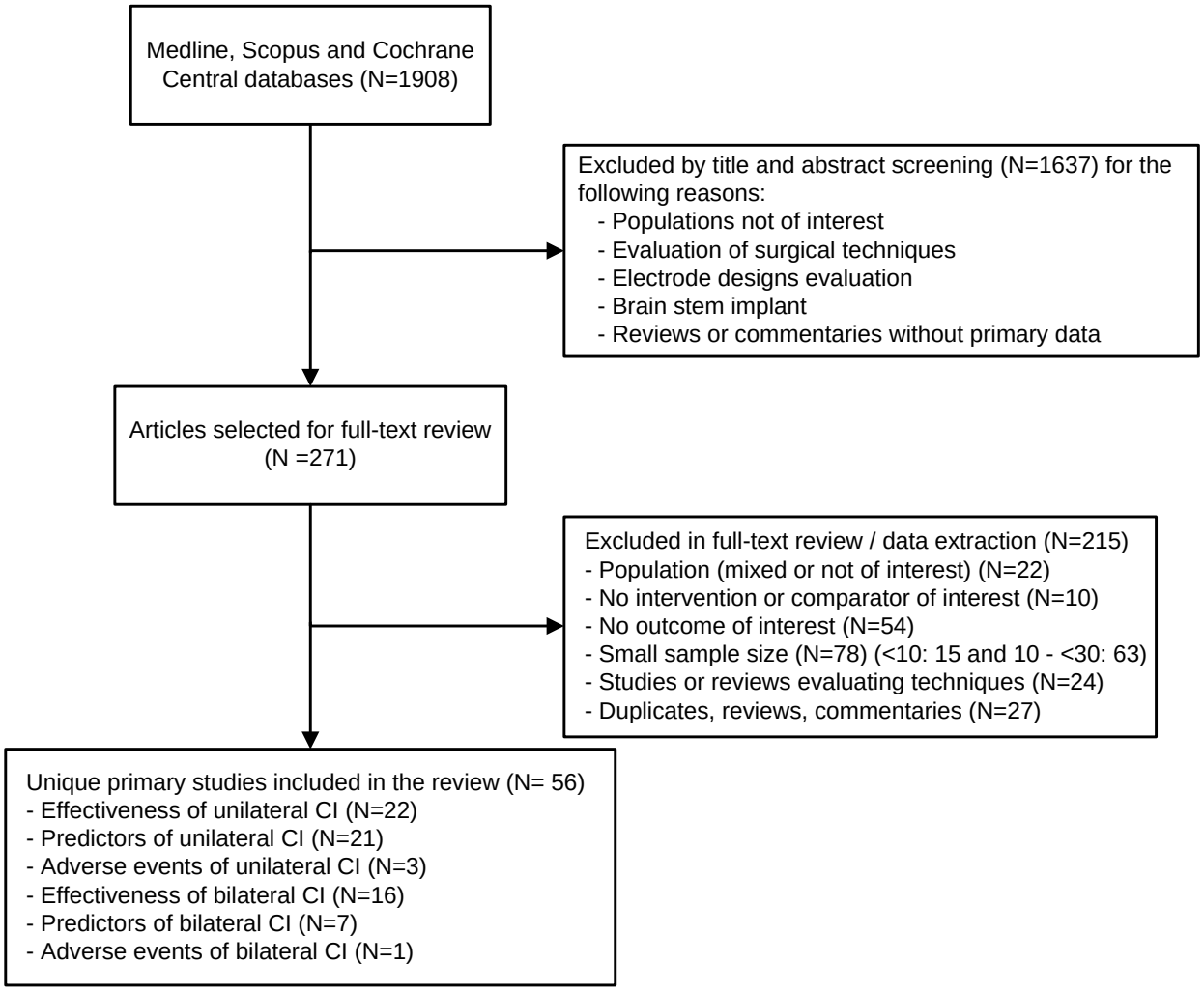
Appendix C. Search Strategy

#	Searches.Cochlear Implant 8-5-10	Results
1	exp hearing loss/	21068
2	exp hearing loss, sensorineural/	8711
3	Hearing Loss, Bilateral/	751
4	exp deafness/	6961
5	severe to profound deafness.mp.	30
6	(severe adj4 deaf$).mp.	222
7	(profound adj4 deaf$).mp.	405
8	Hearing Loss, Unilateral.mp. [mp=ti, ot, ab, nm, hw, ui, sh, kw]	194
9	exp Hearing Disorders/	25838
10	deaf$.ti,ab.	11670
11	or/1-10	30915
12	exp ear, middle/ or exp ear, inner/	19780
13	11 or 12	45309
14	Cochlear Implants/	3141
15	Cochlear Diseases/	383
16	Cochlear Implantation/	2200
17	(cochlear adj5 implant$).mp.	5586
18	(cochlear adj5 device$).mp.	229
19	or/14-18	5921
20	13 and 19	4485
21	limit 20 to yr="2004-Current"	2363
22	animals/ not (animals/ and humans/)	1353004
23	21 not 22	2214
24	(meta-analysis or review).pt.	1020124
25	23 not 24	1985
26	limit 25 to "all child (0 to 18 years)" [Limit not valid in CCTR; records were retained]	1038

27 25 not 26	947
28 remove duplicates from 27	947

Additional searches in the Scopus database yielded 863 abstracts, which were screened separately from the initial yield of 947 abstracts that were identified through Medline and Cochrane databases
Updated search in March 2011 yielded 98 additional citations published between July 2010 through February 2011.

Figure 1. Study Flow



Appendix D. Summary Tables

Table D.1 Effectiveness of cochlear implants: summary of general study characteristics

Study	Study design, followup (yr)	Cochlear implant (N)	Mean age	Male (%)	Degree of deafness	Duration of deafness	Mean time (range) between deafness and implant	Implant indication	Device (coding strategy)	Study quality (comments)
Bai 2005 UK	Prospective cohort 7.8yr	47	52yr	32	Profound deafness 100%	nd	nd	nd	C40+, PRO+, 3G, Espirit 22 (nd)	B (no adj.)
Damen 2007 Netherlands	Prospective cohort 6yr	59	58yr	54	nd	Long-term followup: 24yr; short-term followup: 14yr	Long-term: 14.4yr; short-term: 9.4yr	Postlinguistically deaf adults (without any functional residual hearing)	Long-term: Clarion C1, Laura, Nucleus 22M, Nucleus 24M (nd) Short-term: Clarion C1, Nucleus 24M devices (nd)	B (not representative sample)
Hawthorne 2004 Australia & New Zealand	Prospective cohort 0.5yr	34	49yr	47	Profound deafness 75%, Severe-moderate 22%	nd	nd	nd	Nucleus 24 (nd)	B (did not account for all participants)
Klop 2008 Netherlands	Prospective cohort 1 yr	44	55yr	34	113 dB (83-130 dB)	15yr	nd	Pure-tone threshold >90dB hearing loss, phoneme recognition of less than 40%	CII Hifocus 1 (with/without positioner), HiRes 90K (nd)	B (no adj.)
Rama-Lopez 2006 Spain	Prospective cohort 5.8yr	30	51yr	20	117 dB	nd	nd	Profound bilateral sensorineural hypoacusis	Nucleus 22, Nucleus 24 M, Nucleus Contour (SPEAK/ACE/CIS)	B (unclear description of sampling method)
UK CI Study Group 2004 UK	Prospective cohort 9 mo	316	51yr	49	115 dB HL (85 - 140 dB HL)	13yr	nd	Severe or profound sensorineural hearing loss	Nucleus CI24, Clarion implant, Med-El Combi-40+ (nd)	B (mostly qualitative interpretations)

Study	Study design, followup (yr)	Cochlear implant (N)	Mean age	Male (%)	Degree of deafness	Duration of deafness	Mean time (range) between deafness and implant	Implant indication	Device (coding strategy)	Study quality (comments)
Bassim 2005 U.S.	Retrospective cohort 3 yr	87	54yr	nd	nd	nd	nd	nd	MED-EL Combi40+ (nd)	C (poor reporting, no adj.)
Bradley 2010 New Zealand	Retrospective cohort 9 to 18 mo	113 (55 to 58[1])[2]	50yr	nd	nd	30yr	nd (note: 64% lifetime deafness)	nd	Nucleus Freedom, Nucleus 22 and Nucleus 24	C (missing data; poor reporting; no adj.)
Hay-McCutcheon 2005 U.S.	Retrospective cohort 2 yr	34	Younger: 46yr Older: 74yr	nd	nd	Younger: 2-41yr Older: 9-26yr	nd	nd	Clarion, MedEL C40+ CI24M, CI24R, HiFocus CII (nd)	C (poor reporting; no adj.)
Krueger 2008 Germany	Retrospective cohort (~20 years max.)	864	49yr at implantation	nd	nd	9 yr	nd	nd	Varies	C (retrospective)
Lazard 2010 France	Retrospective cohort 1 yr	100	52yr	nd	nd	nd	nd	nd	Digisonic SP; Digisonic Convex (MPIS coding strategy) (Note: not FDA approved)	C (no adj.; selection bias)
Mawman 2004 UK	Retrospective cohort >18 mo	214[3]	50yr	nd	nd	16 y (2 mo-53 yr)	nd	nd	Nucleus, MedEl, Clarion (PEAK, ACE, CIS,MPS)	C (missing data)
Orabi 2006 UK	Retrospective cohort ~2y	34(~22[4])	70yr	59	nd	11yr	nd	nd	Nucleus C124, Nucleus C122 (ND)	C (no adj.)
Most 2010 Israel	Retrospective cohort 1 mo	38	37yr	32	"Severe-profound"	nd	nd	nd	nd	B (no adj.)

[1] Number analyzed
[2] Baseline characteristics are only available for the entire cohort.
[3] Baseline characteristics are only available for the entire cohort.
[4] Number analyzed

Study	Study design, followup (yr)	Cochlear implant (N)	Mean age	Male (%)	Degree of deafness	Duration of deafness	Mean time (range) between deafness and implant	Implant indication	Device (coding strategy)	Study quality (comments)
Morris 2007 U.S.	Retrospective cohort 12.1 mo	101	53yr	39	nd	32y (0.2-75)	nd	nd	Nucleus 24	B (good analyses)
Roditi 2009 U.S.	Retrospective cohort 2.4 yr	55	62yr	40	94 dB	nd	nd	nd	Cochlear Corporation Advance bionics Med-El (nd)	B (some information could not be used because of eligibility criteria)
Firszt 2004 U.S.	Cross-sectional	78	57yr	nd	Postlinguistic hearing loss	nd	nd	nd	Clarion HiFocus I or II, Med-El Combi 40+, or Nucleus 24M or 24R (SAS, CIS, MPS, SPEAK, ACE)	C (poor reporting)
Gifford 2008 US	Retrospective, cross-sectional	156	60yr	~46	nd	nd	0 to 190 mo	nd	CII, C124RCS, C124RE, C124RCA, HR90K, C122M, C124M, HiFocus C1.2 (SPEAK/ACE/CIS/ HiRes/HiRes120)	C (cross-sectional)
Liu 2008 China	Cross-sectional	32	32yr	60	“severe”	nd	16% <1 yr, 19% 2 yr, 22% 3 yr, 13% 4 yr, 16% 5 yr; 16% >5 yr	nd	nd	C (poor reporting)
Vermeire 2005 Belgium	Cross-sectional	89	58yr	nd	Pure tone average: Young,118 dB;Middle, 115dB; Geriatric 108 dB	nd	nd	nd	Laura, Nucleus 24, Med-El Combi 40+ (SPEAK/ACE/CIS/ CIS+)	C (poor reporting)
Vermeire 2006 Netherlands	Cross-sectional	50	63yr	nd	nd	~20yr	3-10yr	nd	Nucleus 24M/RCS or Med-El Combi 40+ (SPEAK, ACE, CIS+)	C (large drop out)

Study	Study design, followup (yr)	Cochlear implant (N)	Mean age	Male (%)	Degree of deafness	Duration of deafness	Mean time (range) between deafness and implant	Implant indication	Device (coding strategy)	Study quality (comments)
Wanscher 2006 Denmark	Cross-sectional	46	58yr	34	nd	nd	11.9 (13.5)	nd	Nucleus (nd)	C (potential recall bias)

Adj = adjustment, CI = confidence interval, CNC = Consonant-nucleus-consonant words, dB = decibels, nd = no data.

Table D.2 Effectiveness of cochlear implants: summary results of studies with multi-syllable tests

Study	Outcome category	Specific outcome	Preimplantation group (n/N) mean (95% CI)	Postimplantation group (n/N) mean (95% CI)	p-value	Descriptive analysis
Preimplant vs. Postimplant						
Rama-Lopez 2006 Spain	Speech perception	Two-syllable words % correct response	20% (pre)	54% (at 3yr)	p value cut-off 0.05	Significant improvement, post vs. preimplant

Adj = adjustment, CI = confidence interval, CNC = Consonant-nucleus-consonant words, dB = decibels, nd = no data..

Table D.3 Effectiveness cochlear implants: summary results of studies with open-set sentences tests

Study	Outcome category	Specific outcome	Preimplant group (n/N) mean (95% CI)	Postimplant group (n/N) mean (95% CI)	p-value	Descriptive analysis
Preimplant vs. Postimplant						
Bai 2005 UK	Speech perception	BKB % correct	3.4%	Postimplant (5.5 mo), 59.8% Postimplant (13.7 to 39.9 mo)	p<0.01 NS	Significant improvement, post vs. preimplantation Not significantly different postimplantation (13.7 to 39.9 months)
UK CI Study Group 2004 UK	Speech perception	BKB % correct	nd	nd	nd	All patients (n=311): Large effect (standardized effect size=1.50), comparing 9-mo postoperative to baseline session.
Mawman 2004 UK	Speech perception	BKB % correct	(n=91): 1.3% (4.83)	9 mo (n=63): 59.26% (34.52) >18 mo (n=43): 62.27% (34.32)	nd	The mean scores after postimplantation improved compared with preimplantation.
Rama-Lopez 2006 Spain	Speech perception	CID % correct	32% (pre)	72% (at 3yrs)	p value cut-off 0.05	Significant improvement, post vs. preimplant
Bassim 2005 U.S.	Speech perception	CUNY % correct	(n=68) Mean= 12 (nd)	12 mo (n=45) Mean= 96 (nd) 24 mo (n=28) Mean= 94 (nd) 36 mo (n=11) Mean=93 (nd)	nd	The mean scores after postimplant improved compared with preimplant.
UK CI Study Group 2004 UK	Speech perception	Index of audiovisual gain	nd	nd	nd	Large effect (ES=1.78), comparing 9-mo postoperative to baseline session.
Morris 2007 U.S.	Speech perception	CUNY noise % correct	(n=101)	Mean improvement = +59.5 (median 68.8)	<0.05	Significant improvement, post vs. preimplantation
Morris 2007 U.S.	Speech perception	CUNY quiet % correct	(n=101)	Mean improvement = +56.1 (median 63.5)	<0.05	Significant improvement, post vs. preimplantation
Orabi 2006 UK	Speech perception	CUNY % correct	17/34 % Correct 4%[5] % Correct 29%[6]	10/34 % correct 94.5%[7] % Correct 95.5%	<0.01	Highly significant difference ($p < 0.01$) from pre to postimplantation. There was no statistically significant difference between 9 and 12 months.
Morris 2007 U.S.	Speech perception	HINT-Q % correct	101 patients with Nucleus 24	Mean improvement = +53.8 (median 54,	nd	Improvement, post vs. preimplant

[5] Lip reading alone
[6] Lip reading and hearing aid
[7] Percent correct at 9 mo

Study	Outcome category	Specific outcome	Preimplant group (n/N) mean (95% CI)	Postimplant group (n/N) mean (95% CI)	p-value	Descriptive analysis
			implant	ranged 0-100) after implantations		
Bassim 2005 U.S.	Speech perception	HINT-Q % correct	Preoperative (n=70) Mean= 4 (nd)	12 mo (n=45) Mean= 87 (nd) 24 mo (n=26) Mean= 92 (nd) 36 mo (n=11) Mean=91 (nd)	nd	Improvement, post vs. preimplantation
Roditi 2009 U.S.	Speech perception	HINT-Q % correct	(n=55) Mean score: 21.3% (SD 22.7)	55/55 Mean score: 85.9% (SD 18.8)	nd	The mean scores after postimplantation improved compared to preimplantation.
Hay-McCutcheon 2005	Speech perception	HINT-Q & HINT + 10 dB SNR % correct	(n=34) total mean scores ND		<0.001	Both groups had a significant difference from the pre to 12 month postimplantation. No differences were observed between the two age groups.
Bassim 2005 U.S.	Speech perception	HINT + 10 dB % correct	Preoperative (n=0)	12 mo (n=44): 64 (nd) 24 mo (n=26): 70 (nd) 36 mo (n=10): 69 (nd)	nd	Improvement, post vs. preimplantation
Krueger 2008 Germany	Speech perception	HSM	nd	Nd	nd	No performance data are explicitly given. All groups improved slightly and plateau or decreased with time.
Bradley 2010 New Zealand	Speech perception	HINT – audiovisual % correct	(n=53) 66 (SD 24)	3 mo (n=53): 96 (SD 9) 6 mo (n=53): 96 (SD 6) 9 mo (n=53): 98 (SD 4)	nd	Improvement, post vs. preimplantation
Lazard 2010 France	Speech perception	"Speech perception sentences in open set" % correct	Digisonic® Convex implant (n=45) 23% (nd)	3 mo: 39% 12 mo: 49%	<0.0001	Patients received Digisonic® Convex implant between 1999 and 2004 in one medical center had significantly improvements, post vs. preimplantation
Lazard 2010 France	Speech perception	"Speech perception sentences in open set" % correct	Digisonic® SP implant (n=55) 10% (nd)	3 mo: 58% 12 mo: 75%	<0.0001	Patients received Digisonic® SP implant between 2004 and 2006 in 4 different medical centers had significantly improvements, post vs. preimplantation
Preimplant vs. postimplant + hearing aids or unilateral implant vs. hearing aids						
Gifford 2008 US	Speech perception	AzBio sentences	nd	nd	<0.05	Significant improvement, Unilateral implants vs. hearing aids.
Comparison of three stimulus presentation levels (70, 60, and 50 dB SPL), cross-sectional						
Firszt 2004 US	Speech perception	HINT quiet % correct 70 dB vs. 50 dB	70 dB SPL 72% (SD 25)	50 dB SPL 57% (SD 30)	<0.001	The scores at 70 and 60 dB SPL are nearly the same. Performance at 50dB SPL is significantly different. Ability to understand HINT sentences were poorer when listening in soft conversational

Study	Outcome category	Specific outcome	Preimplant group (n/N) mean (95% CI)	Postimplant group (n/N) mean (95% CI)	p-value	Descriptive analysis
						level in quiet.
Firszt 2004 US	Speech perception	HINT quiet % correct 60 dB vs. 50 dB	60 dB SPL 73% (SD 26)	50 dB SPL 57% (SD 30)	<0.001	Ability to understand HINT sentences were poorer listening in soft conversational level in quiet.
Firszt 2004 US	Speech perception	HINT % correct 50dB Q vs. 60dB N	50 dB SPL 57% (SD 30)	60 dB N 48% (SD 29)	<0.05	Ability to understand HINT sentences were poorer when listening in noise compared with listening in soft conversational level in quiet.
Firszt 2004 US	Speech perception	HINT % correct 70dB Q vs. 60dB N 60dB Q vs. 60dB N	70 dB SPL 72% (SD 25) 60 dB SPL 73% (SD 26)	60 dB N 48% (SD 29)	Both <0.001	60 dB SPL in noise represented the most difficult listening condition for the subjects. Ability to understand sentences were poorer when listening in noise compared to listening in quiet.

Adj = adjustment, BKB = Bamford-Kowal-Bench speech perception test, CID = Central Institute for the Deaf sentences, CI = confidence interval, CNC = Consonant-nucleus-consonant words, CUNY = City University of New York tests, dB = decibels, HINT = Hearing in Noise Test (Q = in quiet, N = in noise), nd = no data, SPL = sound pressure level.

Table D.4 Effectiveness cochlear implants: summary results of studies with health-related quality-of-life measures

Study	Outcome category	Specific outcome	Preimplant group (n/N) mean (95% CI)	Postimplant group (n/N) mean (95% CI)	p-value	Descriptive analysis
Preimplantation vs. postimplantation						
Bai 2005 UK	Generic HRQoL	Quality-of-life % score	**nd**	**nd**	**<.05**	Unilateral implants markedly improved quality-of-life (post vs. preimplantation).
Hawthorne 2004 Australia	Generic HRQoL	AQoL mean score	(31) 0.36 SD 0.23	(31) 0.64 SD 0.28	< 0.01	Significantly improved quality-of-life (post vs. preimplantation).
Hawthorne 2004 Australia	Disease-specific HRQoL	HPS mean score	(34) 0.48 SD 0.15	(34) 0.68 SD 0.18	< 0.01	Significantly improved hearing-related quality-of-life (post vs. preimplantation).
Klop 2008 Netherlands	Disease specific HRQoL	NCIQ[8] mean score	(43/44) Mean 70.3 (SD 10.0)[9]	(35/44) Mean 73.1 (SD 10.0)	<0.11[10]	All domains of NCIQ except speech production showed large ES. Effect size = avg change/SD at baseline >0.8 = (a large effect).
Klop 2008	Generic	HUI2[11] mean	(35/44)	(35/44)	0.35[12]	Only HU12 sensation domain showed large ES.

[8] Nijmegen Cochlear Implant Questionnaire
[9] Comparison to change at 4 mo
[10] Change to 4 mo

Study	Outcome category	Specific outcome	Preimplant group (n/N) mean (95% CI)	Postimplant group (n/N) mean (95% CI)	p-value	Descriptive analysis
Netherlands	HRQoL	score	Mean 0.83 (0.12)	Mean 0.84 (0.10)		Effect size = avg change/SD at baseline >0.8 = (a large effect).
Most 2010 Israel	Disease specific HRQoL	Adapted Deaf Identity Developmental Scale mean score	(38) Data for test sub-categories only is given	(38) Data for test sub-categories only is given	<.001	Significantly improved quality-of-life (post vs. preimplantation).[13]
Most 2010 Israel	Generic HRQoL	Loneliness mean score	(38) 1.81 (0.45 SD)	(38) 2.05 (0.51 SD)	<.001	Significantly improved quality-of-life (post vs. preimplantation).
Most 2010 Israel	Generic HRQoL	Self-esteem mean score	(38) 3.83 (0.48 SD)	(38) 3.69 (0.61 SD)	NS	Non-significantly improved quality-of-life (post vs. preimplantation).
Orabi 2006 UK	Generic HRQoL	VAS scores	21/34 80 or more expectation score	19/34 ND	<0.05[14] <0.01[15] <0.001[16] 0.5[17]	Patients felt hearing has improved by ~50% after implantation.
Orabi 2006 UK	Generic HRQoL	GHSI score	Median 44 (24 – 68)	Median 60 (52 – 88)	<0.001[18] NS[19]	Statistically significant difference in 2 scores and no difference in other 2 scores.
Orabi 2006 UK	Generic HRQoL	GBI score	ND	ND	<0.05[20] NS	Patients gained significant overall benefit to overall QoL, general health and social aspect, and complete satisfaction. The health state score was not significant.
UK CI Study Group 2004 UK	Generic HRQoL	GHSI % score	All patients (n=311): 1.22	nd	nd	Large effect, comparing 9-mo postoperative to baseline session.
UK CI Study Group 2004 UK	Generic HRQoL	HUI3 % score	All patients (n=311): 1.05	nd	nd	Large effect, comparing 9-mo postoperative to baseline session.

[11] Ontario Health Utilities Index
[12] Change to 4 mo
[13] After implantation, 51% of subjects reported “great satisfaction”, 40% reported “partial satisfaction”, and 2% reported disappointment; 7% did not respond.
[14] Ability to hear sounds that allow lip reading easily
[15] Understand family and friends without lip reading
[16] For the question, what score would you expect to give yourself if 0: no hearing and 100 perfect hearing
[17] No difference in understanding strangers on phone
[18] Statistically significant difference in overall quality-of-life and general health subscale
[19] For social support and physical health scores
[20] Overall QoL, general health and social aspect, and complete satisfaction

Study	Outcome category	Specific outcome	Preimplant group (n/N) mean (95% CI)	Postimplant group (n/N) mean (95% CI)	p-value	Descriptive analysis
Vermeire 2005 Belgium	Disease specific HRQoL	HHIA mean score	Total score (SD): 69 (0.69) Emotional: 57 (25.49) Situational: 78 (21.96)	Total score (SD): 48 (25.28) Emotional: 39 (26.56) Situational: 58 (27.00)	Total (p<0.001) emotional (p=0.003) Situational (p<0.001)	Significant improvement: Total, emotional. situational
Vermeire 2005 Belgium	Generic HRQoL	GBI score		GBI Total: 35.16 (19.61) General: 46.91 (26.41) Physical: 3.10 (22.25) Social: 19.96 (24.64)	Total: p <0.001 General: p <0.001 Physical p = 0.12 Social: p <0.001	Significant improvement: Total, general, social
Vermeire 2006 Netherlands	Disease specific HRQoL	HHIA mean score	23/50[21] Mean score 72.67 (ND)	23/50 Mean score 56.33 (ND)	0.027	The improvement in QoL was significant post implantation
Liu 2008 China	Generic HRQoL	Self-confidence and social interaction % score	nd	Cochlear implant (n=32): Self-confidence: 82% Social interaction: 77%	nd	Adult implant patients had large improvements in self-confidence and social interaction
Long-term & short-term implant users						
Damen 2007 Netherlands	Disease specific HRQoL	NCIQ mean score	nd	nd	(see descriptive analysis)	Long-term implant use: little change over time, statistically significant decrease in social interactions. Short-term implant use: Significant improvement in all the domains (i.e., sound perception basic, sound perception advanced, speech-production, self-esteem, activity, social interactions)
Damen 2007 Netherlands	Generic HRQoL	HUI % score	nd	nd	(see descriptive analysis)	Long-term implant use: a slight significant decrease in pain, no significant change in the other domains Short-term implant use: Significant improvements in hearing, emotion, emotion, HUI 3 utility.

[21] Only 23 patients had pre and postimplant HHIA questionnaire

Study	Outcome category	Specific outcome	Preimplant group (n/N) mean (95% CI)	Postimplant group (n/N) mean (95% CI)	p-value	Descriptive analysis
Damen 2007 Netherlands	Generic HRQoL	SF36 mean score	nd	nd	(see descriptive analysis)	Long-term implant use: a significant decrease in physical functioning, social functioning, mental health, vitality, general health perception, physical summary score, mental summary score. Short-term implant use: Significant improvements in mental health, mental summary score.

AQoL = assessment quality-of-life, GBI = Glasgow Benefit Inventory, GHSI = Glasgow Health Status Inventory, HHIA = Hearing Handicap Inventory for Adults, HPS = Hearing Participation Scale, HRQoL = health-related quality-of-life, HUI2 = Health Utilities Index Mark II, NCIQ = Nijmegen Cochlear Implant Questionnaire, SF-36= The Short Form (36) Health Survey.

Table D.5 Discontinuation of device use

Study	Outcome category	Specific outcome	Descriptive analysis
Mawman 2004 UK	Adverse events	Device non-use	9 (4.2%) of the patients implanted in the series have become permanent non-users: 3 due to exacerbation of co-existing illness, and 2 due to a worsening of their tinnitus postimplantation; 1 patient declined preimplantation following a device failure and 1 patient who initially had a successful implant outcome has been advised against re-implantation following device extrusion in a previously irradiated temporal bone; 2 patients elected not to use their device with the reason given being disappointment with the outcome from their implantation.
Orabi 2006 UK	Adverse events	Device non-use	1/34 had a cerebrovascular accident 5 years postimplantation that caused sudden and permanent inability to hear with implant
Ramsden 2005 UK	Adverse events	Non-use of a single implant	One bilaterally-implanted patient out of 30 discontinued use of a single implant after inability to integrate separate signals from each ear.
Ray 2006 UK	Adverse events	Device non-use	Three adult patients out of 251 became non-users with reasons listed including depression, tinnitus, concomitant neurological problems, and non-auditory stimulation.

Table D.6 Preoperative patient characteristics associated with postimplant improvement in communication and health outcomes: summary of general study characteristics

Study	Study design, followup (y)	Cochlear implant (N)	Mean age	Male (%)	Degree of deafness	Duration of deafness	Mean time (range) between deafness and implant	Implant indication	Device coding strategy	Study quality (comments)
Rotteveel 2010 UK[22]	Retrospective ~11.7	53 (28 analyzed)	nd	nd	Profound	nd	nd	nd (only patients with otosclerosis analyzed)	Nucleus 22, 24 Med-EL 40+	C; poor reporting of baseline characteristics; only selected patients analyzed.
Chatelin 2004 U.S.	Retrospective 1	166 (65 elderly; 101 younger patients)	59.0y	40.5	Severe-profound (mean 70 dB)	nd	Elderly: 6 (1-62) yr Young: nd	Severe-profound hearing loss in both ears; ≥ 50% on open-set sentence test using conventional hearing aid(s)	nd	C; no adjustment for confounders.
Francis 2004 U.S.	Retrospective 1	23 severe-profound HL patients	57.2	nd	severe-profound (103.5 and 77.2 dB)	20.7 yr	nd	nd	Advanced Bionics: 56.5%, Nucleus 22: 8.7%; Nucleus 24: 34.8%	C; large missing data at 6 mo and 1 yr followup.
		20 bilateral severe HL patients	56.6	nd	bilateral severe (81.5 and 77.3 dB)	20.0 yr	nd	nd	Advanced Bionics: 55%, Nucleus 22: 5%; Nucleus 24: 40%	
		43 bilateral profound HL patients	56.1	nd	bilateral profound (110.9 and 108.5 dB)	19.3 yr	nd	nd	Advanced Bionics: 67.4%, Nucleus 22: 16.3%; Nucleus 24: 16.3%	
Bodmer 2007	Retrospective 1	252	49.3	60	nd	nd	nd	nd	Advanced Bionics (a variety of models) and	C; univariate analysis only,

[22] The original study was a multicenter study but only patients in UK center were included for the BKB-SIN test

Study	Study design, followup (y)	Cochlear implant (N)	Mean age	Male (%)	Degree of deafness	Duration of deafness	Mean time (range) between deafness and implant	Implant indication	Device coding strategy	Study quality (comments)
Canada									Nucleus (a variety of models)	only 56% patients were included in the analyses.
Green 2007 UK	Retrospective 9 months	117	51	50.4	Frequencies btw 250Hz-kHz with residual hearing; 0 (30%); 1 (1%); 2 (2%); 3 (14%); 4 (14%); 5 (4%)	15.5	nd	nd	Multi-peak (20%), spectral peak (55%), continuous interleaved sampling (24%); and advanced combination encoders (1%)	B; patients are not representative of the population.
Spahr 2004 U.S. Canada	Prospective nd	30	56	nd	101 dB	15.8	1.7 yr	nd	Hi-resolution sound processing strategy/ Nucleus 24 electrode array	B; followup duration was not reported; small sample size.
Nascimento 2005 Brazil	Cross-sectional	40	43.5	47.5	nd	5.8	2 yr (6 mo-5.9 yr)	nd	Nucleus 22 (SPEAK), Nucleus 24 (ACE), Combi 40, Combi 40+, Clarion bipolar enhanced 1.2 (CIS)	C; small sample size, no adjustment for confounding factors.
Matterson 2007 Australia	Retrospective 1 yr	59	66 (41-84) yr	56%	nd	8 (1 – 59) yr	23 (1-59) yr	Severe - profound postlinguistic deafness due to otosclerosis.	Cochlea corporation CI	B; retrospective study; undertook multiple regression analysis.
Haensel 2005 Germany	Cross-sectional	26 elderly patients (*47 younger patients)	elderly: 69y (*young: 37yr)	38.5	nd	13yr	1yr	Best-aided condition: monosyllabic word recognition of < 30% (open-set; 70 dB	Cochlear Nucleus 22-M, MED-EL Combi-40, Advanced Bionics CLARION, Advanced Bionics CLARION (HiFocus/CII, (MPEAK/SPEAK/ACE/CIS	C; no information of characteristics of younger patients, only postimplant assessment for

Study	Study design, followup (y)	Cochlear implant (N)	Mean age	Male (%)	Degree of deafness	Duration of deafness	Mean time (range) between deafness and implant	Implant indication	Device coding strategy	Study quality (comments)
								SPL)	/HiRes)	quality-of-life.
Friedland 2010 U.S.	Retrospective cohort (for elderly cohort) 1	78	74yr	nd	nd	16y (1-74yr)	nd	nd	nd	C; only <50% patients had postimplantation outcome data.
	Retrospective , case-control (for case-control part of study) 1	56	Elderly: 73yr Younger: 47yr	nd	nd	nd	nd	nd	nd	B; matched based on preimplantation performance on the HINT-Q and duration of deafness.
Carlson 2010 US	Retrospective 12 mo	232	80.6%: 55.4y 19.4%: 84.8yr	nd	nd	nd	nd	nd	Nucleus Freedom (CI24RE), Advanced Bionics HR90k, or Med-El Sonata	C; no adjustment for confounders

BKB-SIN test = Bamford-Kowal-Bench Speech-in-Noise Test, dB = decibel, HL = hearing loss, HINT-Q = Hearing in Noise Test (quiet conditions), nd = no data, SPL = sound pressure level.

Table D.7 Preoperative patient characteristics associated with postimplant improvement in communication and health outcomes: summary of study results

Potential modifying factor	Number of Studies Total patients (range) Quality	HINT[23]	CUNY[24]	BKB[25]	HRqol		Other Outcomes
					General	Hearing specific	
Longer duration of impaired hearing	7 627 (28 to 311) 5 B;[13, 14, 24, 35, 39] 2 C[12, 37]	Hay-McCutcheon, 2005 [16222216]: r= 0.86; P= 0.003 (age<65 yr); NS (age≥65 yr)	Matterson, 2007 [17468676]: r=-0.32; P<0.05 but NS in noise UK CI, 2004 [15292774]: Effectiveness declined with increasing duration of profound deafness[26]	Green, 2007 [17479968]: r=-0.56; P<0.0001[27] Rotteveel, 2010 [19690406]: NS[28]	Hawthorne, 2004 [15250122]: NS Klop, 2008 [18451751]: r= 0.0003; P=0.03[29]	Hawthorne, 2004 [15250122]: NS Klop, 2008 [18451751]: r= 0.3; P=0.03[30]	

[23] HINT in quiet unless otherwise noted
[24] CUNY in quiet unless otherwise noted
[25] BKB in quiet unless otherwise noted
[26] The effectiveness was measured by both BKB and CUNY scores
[27] Multivariate analysis with independent variables: duration of hearing loss; Multi-peak (MPEAK) as the speech-processor strategy. Findings: additional year of deafness prior to implantation (OR=1.09, CI=1.06-1.13, p<0.001)
[28] High performer (BKB score >47%) versus low performer (BKB score ≤47%). This definition of high speech performance, that is BKB score >47 percent, was based on the 25th percentile of the BKB data among study participants was 47 percent correct.
[29] Multivariate model with 8 preoperative variables: sex, cause, cochlear implant model, and educational background, preoperative hearing thresholds, preoperative CVC scores, duration of deafness, and age at implant
[30] Multivariate model with 8 preoperative variables: sex, cause, cochlear implant model, and educational background, preoperative hearing thresholds, preoperative CVC scores, duration of deafness, and age at implant

Potential modifying factor	Number of Studies Total patients (range) Quality	HINT[23]	CUNY[24]	BKB[25]	HRqol		Other Outcomes
					General	Hearing specific	
Younger age at implantation	7 593 (29 to 252) 3 B;[14, 35, 39] 4 C[12, 28, 30, 32]	Hay-McCutcheon, 2005 [16222216]: NS Fiedland, 2010 cohort study [20479370]: NS but r= 0.40; P= 0.05 for HINT-N Bradley, 2010 [20927155]: NS for HINT A and HINT AV in noise[31]	Matterson, 2007 [17468676]: NS in both quiet and noise	Green, 2007 [17479968]: NS		Klop, 2008 [18451751]: -0.48; P<0.0001	Bomer, 2007 [17585277]: NS, poor performers vs. excellent performers[32]
Older age (≥65 yr) vs. younger age (<65 yr)	7 807 (34 to 232) 7 C[12, 20, 25, 30, 31, 33, 40]	Hay-McCutcheon, 2005 [16222216]: NS Fiedland, 2010 case-control study [20479370]: 70% vs. 83%; P=0.02 but NS for HINT-N Vermeire, 2005 [15793403]: NS[33] Chatelin, 2004 [15129109]: NS[34]	Orabi 2006 [16620330]: NS	Orabi 2006 [16620330]: NS in both quiet and noise Carlson 2010 [20729782]: NS in noise[35]	Vermeire, 2005 [15793403]: NS[36]	Vermeire, 2005 [15793403]: NS[37]	Haensel, 2005 [16303673]: Speech perception, NS Chatelin, 2004 [15129109]: CID, NS[38] Carlson 2010 [20729782]: AzBio sentences, 85% (≥80 yr) vs. 78.5% (18-79 yr), P=0.03

[31] Age at implant 20-44y, 45-59y, vs. ≥60y groups
[32] Poor performers were patients who realized a worsening, no improvement, or an improvement of <10% in their audiologic scores. Excellent performers were patients who scored between 91 and 100% postimplantation.
[33] Young (≤ 55 yr), middle (56-69 yr) vs. geriatric (≥ 70y) groups
[34] Elderly adults (≥ 70y) vs. younger adults (<70y) groups
[35] Younger (18-79 yr) vs.geriatric (≥ 80y) groups
[36] Young (≤ 55 yr), middle (56-69 yr) vs. geriatric (≥ 70y) groups
[37] Young (≤ 55 yr), middle (56-69 yr) vs. geriatric (≥ 70y) groups

Potential modifying factor	Number of Studies Total patients (range) Quality	HINT[23]	CUNY[24]	BKB[25]	HRqol		Other Outcomes
					General	Hearing specific	
Type of implanted device	7 625 (28 to 252) 2 B;[35, 38] 5 C[28, 29, 32, 36, 37]	Spahr, 2004 [15148187]: NS Bradley, 2010 [20927155]: HINT A score – 89% (Nucleus Freedom) vs. 73% (Nucleus 22&24), P=0.01; HINT AV score – NS	Spahr, 2004 [15148187]: NS in both quiet and noise[39]	Green, 2007 [17479968]: NS[40] Rotteveel, 2010 [19690406]: NS[41]			Bomer, 2007 [17585277]: 53% vs. 47% Advanced Bionics, poor performers vs. excellent performers[42] Nascimento, 2005 [16446956]: CPA recognition test,[43] NS Spahr, 2004 [15148187]: AzBio scores, 75% (Advance Bionics CII) vs. 61% (Nucleus 3G), p=0.01 Lazard, 2010 [20446821]: "speech perception open-set sentences", 75% (Digisonic® SP) vs. 49% (Digisonic® Convex), P<0.05

[38] Elderly adults (≥ 70y) vs. younger adults (<70y) groups
[39] Patients with Advanced Bionics CII versus those with nucleus 3G implants. Two groups of patients were matached by preimplant CNC score and age.
[40] Univariate analysis by implanted device was not significant. Multivariate analysis with independent variables: duration of hearing loss; Multi-peak (MPEAK) as the speech-processor strategy. Findings: speech processor, no difference to the regression.
[41] High performer (BKB score >47%) versus low performer (BKB score ≤47%)
[42] Poor performers were patients who realized a worsening, no improvement, or an improvement of <10% in their audiologic scores. Excellent performers were patients who scored between 91 and 100% postimplantation.
[43] Centro de Pesquisas Audiológicas recognition test at different noise ratios

Potential modifying factor	Number of Studies Total patients (range) Quality	HINT[23]	CUNY[24]	BKB[25]	HRqol		Other Outcomes
					General	Hearing specific	
Preoperative speech recognition or word understanding	5[44] 468 (44 to 232) 2 B;[14, 30] 3 C[28, 30, 40]	Fiedland, 2010 cohort study [20479370]: preoperative HINT score r= 0.44; P=0.02 Fiedland, 2010 case-control study [20479370]: preoperative HINT score r=0.31; P=0.02 Bradley, 2010 [20927155]: NS[45]	nd	Carlson 2010 [20729782]: NS in noise	Klop, 2008 [18451751]: preoperative CVC score r= 0.0003; P=0.02[46]		Carlson 2010 [20729782]: AzBio sentences, NS
Degree of preimplant residual hearing	4 423 (34 to 232) 2 B;[13, 35] 2 C[34, 40]	Francis, 2004 [15454765]: NS[47]	nd	Green, 2007 [17479968]: NS[48] Carlson 2010 [20729782]: NS in noise	Hawthorne, 2004 [15250122]: profound deafness improved more than severe-moderate deafness (P=0.08)	Hawthorne, 2004 [15250122]: NS	Carlson 2010 [20729782]: AzBio sentences, NS
Associated ear or bone disease	2 280 (28 to 252) 2 C[32, 37]	nd	nd	Rotteveel, 2010 [19690406]: extent of otosclerosis, NS[49]			Bomer, 2007 [17585277]: 97% vs. 91% normal temporal bone, poor performers vs. excellent performers[50]

[44] There are two studies (case-control and cohort study) included in Fiedland, 2010[30] publication
[45] Preimplant A (0, 1-15, or ≥ 16) or AV scores (0-60, 67-78, or ≥ 78) were not significantly related to long-term HINT A or HINT AV scores
[46] Multivariate model with 8 preoperative variables: sex, cause, cochlear implant model, and educational background, preoperative hearing thresholds, preoperative CVC scores, duration of deafness, and age at implant
[47] Severe-profound vs. bilateral severe patients (i.e., presence of residual hearing vs. no residual hearing in the implanted ear)
[48] Residual hearing as assessed by number of frequencies with an audiometric response
[49] High performer (BKB score >47%) versus low performer (BKB score ≤47%)

Potential modifying factor	Number of Studies Total patients (range) Quality	HINT[23]	CUNY[24]	BKB[25]	HRqol		Other Outcomes
					General	Hearing specific	
Pre vs. postlingual deafness	2 339 (87 to 252) 2 C[9, 32]	Bassim, 2005 [16148696]: worse	Bassim, 2005 [16148696]: worse	nd			Bomer, 2007 [17585277]: 43% vs. 88% postlingual deafness; P<0.0001, poor performers vs. excellent performers[51]
Later age of onset of hearing loss	2 62 (28 to 34) 2 C[12, 37]	Hay-McCutcheon, 2005 [16222216]: r= 0.92; P= 0.0004 (age<65 yr); NS (age≥65 yr)	nd	Rotteveel, 2010 [19690406]: NS[52]			
Choice of implanted ear	1 101 1 B[18]	Morris, 2007 [17195742]: NS[53]	Morris, 2007 [17195742]: NS[54] in both quiet and noise	nd			

CVC, consonant-vocal-consonant word list; HINT-N, Hearing in Noise Test

[50] Poor performers were patients who realized a worsening, no improvement, or an improvement of <10% in their audiologic scores. Excellent performers were patients who scored between 91 and 100% postimplantation.

[51] Poor performers were patients who realized a worsening, no improvement, or an improvement of <10% in their audiologic scores. Excellent performers were patients who scored between 91 and 100% postimplantation.

[52] High performer (BKB score >47%) versus low performer (BKB score ≤47%)

[53] Left ear vs. right ear. In the event of significant differences in preoperative charateristics between groups, grouped linear regression with analysis of covariance (ANCOVA) was used to control for these possible covariates.

[54] Left ear vs. right ear. In the event of significant differences in preoperative charateristics between groups, grouped linear regression with analysis of covariance (ANCOVA) was used to control for these possible covariates.

Table D.8 Effectiveness of bilateral cochlear implants, sequential and simultaneous: summary of general study characteristics

Study Yr Country PMID	Followup (yr)	Population(N) [Cochlear implant]	Indication for cochlear implant	Mean age (yr)	Male (%)	Degree of deafness	Duration of deafness	Mean time (range) between deafness and implantation	Device coding strategy	Study quality (comments)
Simultaneous bilateral implant										
Koch 2009 U.S. 19247979	Prospective 0.5 yr	15	Open-set sentence scores ≤50% in the best-aided condition	51	NR	≥ 70 dB HL Severe-to-profound hearing loss	Right ear: 9yr Left ear: 10yr	Right/Left ear (1-17yr)	Harmony HiResolution® CIS+HiRes	B; selection process unclear.
Buss 2008 18091099 Grantham 2007 17609614 Ricketts 2006 17086085 U.S. (Multicenter)	Prospective 1 yr	26	HINT sentence scores ≤40% in quiet under auditory-only testing conditions	48.3 (25.3 – 76.6)	31	Average 70 dB HL or poorer at 0.5, 1, 2 KHz Severe-to-profound hearing loss	<15 y in either ear	nd	MED-EL COMBI 40+ TEMPO+	B; selection process unclear, 10% excluded from analysis.
Litovsky 2006 U.S. 17086081 (multicenter)	Prospective 0.5 yr	37	HINT sentence scores ≤50% in the best-aided condition	53.6 (15.3)	38	Hearing thresholds from 70dB to no response (postlinguistic)	5.6 yr (1 mo – 15yr)	nd	Nucleus 24 Contour SPEAK, ACE, CIS	B; some patients not accounted for.
Litovsky 2009 U.S. (multicenter) 19455039	Prospective cohort 0.5 yr	17	nd	52.7 yr	47	Severe to profound hearing loss with no benefit from hearing aids	6.5 yr in the right ear 9.7 yr in the left ear	nd	Nucleus 24 Contour SPEAK, ACE, CIS	B; selection process unclear; population represent data collected for a multicenter trial.
Litovsky 2004 U.S. (single center) 15148192	Prospective cohort 0.25 yr	17 (14 postlingual deaf; 3 prelingually deaf)	nd	52.7 yr	47	nd	8 yr in the right ear and 13 yr in the left ear	nd	C124R(CS)	B; selection bias

Study Yr Country PMID	Followup (yr)	Population(N) [Cochlear implant]	Indication for cochlear implant	Mean age (yr)	Male (%)	Degree of deafness	Duration of deafness	Mean time (range) between deafness and implantation	Device coding strategy	Study quality (comments)
Mosnier 2009 France (multicenter) 18832816	Prospective cohort 1 yr	27	nd	45 (24-69) yr	nd	Postlingual bilateral profound or total hearing loss	3 (1-9) yr [profound hearing loss]	nd	Med-El Combi 40+ CIS	B; unclear if they were consecutive subjects with bilateral implant; unclear recruitment process.
Dunn 2010 U.S. 19858720	Cross-sectional	30 simultaneous bilateral implant, 30 unilateral implant	nd	55 (14.4) 56 (14.7)	nd	96-102 dB HL; Preoperative hearing level within 5 and 6 dB for right and left ear	6.5 (8.4) yr 7.2 (9.3) yr	nd	Nucleus; Clarion CL Hi Focus CII, CL Hi Res 90K, CL 1.0, NU 22, 24M, 24R, RPS, ACE, SPEAK, RIS	B; matched for age at implantation, duration of profound deafness, and preoperative pure-tone hearing loss (0.5, 1, and 2 kHz) in the right and left ears, respectively.
Noble 2008 U.S. 18091100	Cross-sectional	(183)	nd	61.8	43.2	nd	nd	nd	nd	C; cross-sectional.
		Unilateral implant 71		60.6 (15.1)	50.7					
		Unilateral implant+HA 40		61.9 (15.9)	30					
		Bilateral implant 35		64.3 (15.5)	42.9					
Dunn 2008 U.S. 18453885	Cross-sectional	66	nd	54 (at implantation)	nd	nd	11 yr	3.5yr	nd	C; cross-sectional; performance values not explicitly given. No recruitment information.

Study Yr Country PMID	Followup (yr)	Population(N) [Cochlear implant]	Indication for cochlear implant	Mean age (yr)	Male (%)	Degree of deafness	Duration of deafness	Mean time (range) between deafness and implantation	Device coding strategy	Study quality (comments)
Sequential Bilateral implant										
Summerfield 2006 UK 16938781	Group1 (Bi immediate): 9 mo Group2 (Bi delayed): 9 mo RCT	28	nd	Median 56	nd	nd	nd	Median 2.7 years (1-6 years, a unilateral implant)	Nucleus CI24; SPEAK processing strategy	B; allocation concealment not clearly reported.
Ramsden 2005 UK 16151348 (part of Summerfield)	Prospective cohort 0.75 yr	31 (27)	30% open set recognition with BKB in quiet	57 (29 – 82)	nd	102.79 – 108.06 dB HL	6.14 – 8.48 yr	ND for 1st implant 1-7 y for 2nd implant	CI24M or CI24R(ST) MAP ACE SPEAK	B; confounders not discussed; nor how they were analyzed addressed.
Verschuur 2005 U.K. (part of subjects included in Ramsden 2005) 18792387	Prospective cohort 0.75 yr	29 (20)	30% open set recognition with BKB in quiet	61 (33 -82)	nd	Severe or profound deafness <15 year in either ear	First ear 9 yr	Between first and Second ear implant ~3 yr	Nucleus 24M or 24K	C; Selection criteria not explicit; confounders not discussed; nor how they were analyzed addressed.
Gifford, 2008 U.S. 18212519	Cross-sectional	156 (13 bilateral implant)[55]	nd	59.5	~45.6%	nd	nd	0 – 15.8 yr	CII, C124RCS, C124RE, C124RCA, HR90K, C122M, C124M, HiFocus C1.2 (SPEAK/ACE/CIS/HiRes/HiRes120)	C; cross-sectional, no multivariate analysis.
Laske, 2009 Switzerland 19318885	Clinical trial (cross-sectional)	34 (29)[56]	nd	Age at first implant 31.0 (16)	nd	Severe to profound hearing loss	5.4 (6.4) yr	5.6 (5.7) yr time to second implant	Nucleus device Esprit 3G, Esprit 22, Esprit 23, SP-12 or the Nucleus Freedom Auditory Processor	C, (although matching was reported, it was not relevant for the outcomes of interest)
Schleich, 2004	Cross-	18	nd	44 (17.5 –	nd	Prelingual or	12.9 (0.6	nd	MED-EL COMBI 40 or COMBI 40+	C (cross-

[55] Of the 13 subjects, 12 had sequential bilateral implant and one had simultaneous bilateral implant
[56] Of the 29 subjects, 27 had sequential bilateral implant and two had simultaneous bilateral implant

Study Yr Country PMID	Followup (yr)	Population(N) [Cochlear implant]	Indication for cochlear implant	Mean age (yr)	Male (%)	Degree of deafness	Duration of deafness	Mean time (range) between deafness and implantation	Device coding strategy	Study quality (comments)
Nopp, 2004 Austria 15179111 15179112	sectional			66.5) yr		postlingual deafness	– 47.8) yr		CIS+	sectional)
Zeitler 2008 U.S. 18494140	nd	26 (22)	nd	46 (1st implant) 52 (2nd implant)	46	Profound deafness	32.1 yr	nd time between sequential implants 5.6 yr	Nucleus; Advanced Bionics; Med-EL CIS, HiRes, SPEAK, ACE	B (retrospective data; unclear selection and 15% attrition.
Both										
Laszig 2004 Switzerland 15547426	Prospective cohort 0.5 yr	37	nd	46	nd	Bilateral, severe to profound hearing loss	10.4yr	nd	ACE	C ; prospective; does not account for missing subject data.
Cullington 2010 U.S.; U.K. 21178567	Cross-sectional	26 (13 bilateral implant)	nd	56 yr bilateral implant 63 yr bimodal	46% bilateral implant 38% bimodal	Progressive hearing loss	7.5 yr bilateral implant 16.5 bimodal	nd	Nucleus 24, 22; HiRes 90k; Med-EL C40+; Freedom; Clarion	C; cross-sectional, no matching or multivariate analysis.

BKB = HINT = Hearing in Noise Test, nd = no data, RCT = randomized controlled trial.

Table D.9 Effectiveness of bilateral cochlear implants, sequential and simultaneous: summary of study results

Study Yr Country PMID	Specific outcome	Intervention group (n analyzed/N total) mean (95% CI)	Control group (n analyzed /N total) mean (95% CI)	p-value	Descriptive analysis
Speech Tests					
Koch 2009 U.S. 19247979	HINT (speech in quiet)	Bilateral implant	Right ear alone	<0.05	Bilateral scores greater than right ears
	HINT (speech in quiet)	Bilateral implant	Left ear alone	<0.05	Bilateral scores greater than left ears
	HINT (speech in quiet)	Right ear alone	Left ear alone	NS	No significant differences btw two groups
Buss 2008 18091099 Grantham 2007 17609614 U.S. (Multicenter)	CUNY sentences in Noise	Bilateral implant 26/29	Right ear alone and Left ear alone 26/29		Stable head shadow estimates at the 6 and 12 month test intervals. (37.5%) Binaural summation estimates had no statistically significant difference at the 6 and 12 month test intervals (2.0% to 5.7%). A highly significant increase from 3.3% to 10.6% in binaural squelch effect.
Litovsky 2006 U.S. 17086081	BKB-SIN overall: noise from left, from right, and from front	29/37	Right ear alone and Left ear alone 29/37	P<0.0001	Bilateral implant was significantly better than either unilateral implant at all times. Holding listening condition constant, significant effects of noise location for left implant alone, right implant alone, and bilateral (all at $p < 0.0001$). For the bilateral listening condition performance was significantly poorer for noise from the front than from either side, but there was no difference between noise from the left and from the right.
	HINT at 6 mo followup	33/37 31/33 subjects (94%) had a higher bilateral score compared with at least one of the unilateral scores 19/33 subjects (58%) had a better bilateral score than both unilateral scores.	Right ear alone and Left ear alone 33/37	<0.008	Bilateral Ci was significantly better than either unilateral implant at all times except for 3 mo postimplant. No significant differences were found between the left-alone and right-alone conditions at any time interval.
Litovsky 2009 U.S. (multicenter) 19455039	BKB-SIN speech in babble task	Bilateral implant 17/17	Right ear alone and Left ear alone	nd	Bilateral benefit was 60% at 3 mo and 53% at 6 mo. About 40% showed no benefit at 3 mo and 47% at 6 mo. The head shadow effect and squelch were significantly higher at 6 mo than 3 mo for both ears and left ear only, respectively. Summation was reduced at 6 mo for the right ear comparison only.
Litovsky 2004 U.S. (single center) 15148192	BKB-SIN speech in babble task	Bilateral implant 14/17	Right ear alone and Left ear alone	nd	Bilateral benefit against better ear was minimal when babble was near better ear. Bilateral benefit against poorer ear had advantage when babble was near poorer ear.

Mosnier 2009 France (multicenter) 18832816	Disyllabic words in noise	Bilateral implant 27/27	Better ear 27/27	NS (3 mo) <0.05 at 6 mo, 12 mo	Statistical significance for bilateral vs. unilateral was achieved at 6 mo for an SNR +dB, and at 12 mo for SNRs +5 and +15 dB.
	Disyllabic words in quiet			<0.05 at 12 mo	Speech performance in quiet at 12 month postactivation with an improvement of 10±0.3% for disyllabic words. The magnitude was slightly lower in noise.
Dunn 2008 U.S. 18453885	HINT sentences in quiet (rationalized arcsine scores transformed from % correct)	Bilateral implant (33/33) ~104	Uni-implant (33/40) ~82	< 0.01	two-tailed *t* (d.f. 64) = -3.06
	HINT sentences in quiet (rationalized arcsine scores transformed from % correct)	Bilateral implant (33/33) ~104	Right implant only (same subjects) ~88	< 0.001	Bonferroni adjusted two-tailed *t* (d.f. 32) = -4.92
	HINT sentences in quiet (rationalized arcsine scores transformed from % correct)	Bilateral implant (33/33) ~104	Left implant only (same subjects) ~96	< 0.05	Bonferroni adjusted two-tailed *t* (d.f. 32) = -2.90
Multi-syllable Test					
Dunn 2010 U.S. 19858720	Speech test - Multiple-jammers test Signal to noise ratio (SNR) scores	Bilateral implant nd (total 48/55) -3dB	Unilateral implant +2 dB	<0.05	Bilateral implant subjects were able to listen against significantly higher noise levels to identify the words 50% of the time compared with the implant-only subjects (t[50] = -2.66)
Sound localization					
Koch 2009 U.S. 19247979	Horizontal-plane sound localization	Bilateral implant 15/15	Right implant only and Left implant only 15/15	nd	The mean accuracy improves with bilateral implants than just one, although the accuracy is still below that of normal. Bilateral accuracy did not improve appreciably over time.
Buss 2008 18091099 Grantham 2007 17609614 U.S. (Multicenter)	Horizontal-plane sound localization	Bilateral implant 22/22	Right implant only and Left implant only18/22	<0.001	Subjects performed better with bilateral condition for both the noise stimulus and for the speech stimulus. Speech signal was more accurately localized than the noise signal.
Dunn 2008 U.S. 18453885	Everyday Sounds Localization test	Bilateral implant 12/33	Right implant only and Left implant only 12 (matched for age and duration of deafness)	<0.001	Sounds were presented one of eight loudspeakers at 70dB, an arc of ~108^{O} in the frontal horizontal plane. Significantly greater benefit of localization for listeners using bilateral implant over those using unilaterally.
Litovsky 2009 U.S. (multicenter) 19455039	Horizontal-plane sound localization	Bilateral implant 17/17	Right ear alone and Left ear alone 17/17	nd	At 3 mo 82% demonstrated bilateral benefit when right or left discrimination was evaluated. In contrast, 47% subjects showed a bilateral benefit when sound localization was evaluated.
Litovsky 2004 U.S. (single center) 15148192	Sound localization	Bilateral implant 17/17	Right ear alone and Left ear alone 17/17	nd	Bilateral subjects identified sound source better than either ear unilaterally. Either ear alone had significant error compared to bilateral condition and post-hoc

					analysis suggested no significant differences between the right and left ears.
Mosnier 2009 France (multicenter) 18832816	Sound localization in noise with cocktail party background	Bilateral implant 27/27	Better ear 27/27		
HRqol					
Noble 2008 U.S. 18091100	HHIE --emotional distress	Bilateral 40/183 1.67 (1.0)	Unilateral 71/183 1.31 (1.1)	NS	
	HHIE --emotional distress	Bilateral 40/183 1.67 (1.0)	Unilateral +HA 35/183[57] 0.85 (0.9)	0.002	Unilateral implant+HA group had higher rating (worse) than Bil implant
	HHIE – social restriction	Bilateral 40/183 0.37 (0.9)	Unilateral 71/183 1.21 (1.5)	0.009	Bil implant had lower score (better)
	HHIE – social restriction	Bilateral 40/183 0.37 (0.9)	Unilateral +HA 35/183[58] 1.35 (1.4)	0.006	Bil implant had lower score (better)
	HHQ - emotional distress	Bilateral 39/183 2.82 (0.8)	Unilateral +HA 35/183 2.12 (0.8)	0.002	Greater handicap in implant+HA group
	HHQ – social restriction	Bilateral 39/183 3.15 (0.8)	Unilateral +HA 35/183 2.38 (0.8)	<0.001	Greater handicap in implant+HA group
Sequential Bilateral implant					
Speech test					
Ramsden 2005 UK 16151348	CUNY in quiet	27/31 91% (SD 9)[59]	28/31 89% (SD 11)	NS	No significant advantage over the first ear at 3, 9 mo
	CUNY in noise	27/31 Difference 5.4 (SD 5)[60] Difference 12.6 (SD 5.4)[61]	28/31	<0.001[62]	With CUNY tests in noise, bilateral implant scores were better than the first ear scores both at 3 and 9 month
Laske, 2009 Switzerland 19318885	OLSA in quiet	Bilateral implant 23/29	Better ear unilateral implant	NS	There was no difference between the bilateral implant and the better ear for percentage of correctly understood words for a fixed presentation level of 65dB SPL with signal presented at 0-degree azimuth. The summation, squelch, and speech discrimination in quiet were better than in the unilateral condition but the difference was not statistically significant.
			Poorer ear unilateral implant	<0.05	Speech understanding was better by 18% in the bilateral condition compared with results from the poorer ear.

[57] Unilateral implant + HA group
[58] Unilateral implant + HA group
[59] From figure 4
[60] At 3 month
[61] At 9 month
[62] At 3 and 9 month

Gifford, 2008 U.S.	AzBio sentences	6 Bilaterals – 81.2% correct (Total N=137)	49 Unilaterals – 72.1% correct 29 Bimodals – 83.5% correct 53 Hearing aid users – 47.3% correct	NS vs unilateral or bimodal	Unilateral, bilateral, and bimodal were not found to be significantly different from one another.
	BKB-SIN	Bilaterals – 9.8 dB SNR (Total N=231)	145 Unilaterals – 11.4 dB SNR 20 Bimodals – 8.7 dB SNR	NS vs unilateral or bimodal	Unilateral, bilateral, and bimodal were not found to be significantly different from one another.
	HINT-Q	13 Bilaterals – 89.6% correct (Total N=189)	115 Unilaterals – 84.8% correct 15 Bimodals - 94.1% correct	NS vs unilateral or bimodal	Unilateral, bilateral, and bimodal were not found to be significantly different from one another.
Schleich 2004 Austria 15179111	OLSA	Bilateral 18/21	Right implant only and Left implant only	<0.001: head shadow <0.001 Bilateral summation <0.001 left ear squelch NS right ear squelch	Speech tests were performed for three different noise conditions. The noise signal was presented from either the front, from the left, or from the right. For all values positive values indicate a beneficial effect. When averaged across listening conditions and noise conditions, respectively, the head shadow effect = 6.8 dB, the squelch effect = 0.9 dB, and the summation effect = 2.1 dB. The only effect that was not significant was squelch effect in noise.
Zeitler 2008 U.S. 18494140	HINT-Q	Bilateral implant 22/29	First ear implant	0.010	Bilateral implant had significant benefit over unilateral implant.
	BKB-SIN	Bilateral implant 11 matched pair data	First ear implant	0.05	
Sound localization					
Verschuur 2005 U.K. (part of subjects included in Ramsden 2005) 18792387	Sound localization in the horizontal plane	Bilateral implant 20/29	Right implant only and Left implant only	<0.001	Bilateral implant had marked improvement in horizontal plane localization abilities compared with unilateral implant. Mean error with bilateral implant was 24^{O} compared with means of 67^{O} for right implant and left implant.
Nopp 2004 Austria (same as Schleich 2004) 15179112	Frontal horizontal plane localization task	Bilateral implant 18/20	Either ear unilateral implant 18/20	<0.05	Substantial significant benefit for bilateral implant group over unilateral implant except for two subjects who were early deafened and had late implantation.
Laske 2009 Switzerland 19318885	Sound localization in the horizontal plane	Bilateral implant 29	Either ear unilateral implant 29	<0.05	Bilateral implants had a mean deviation from the actual sound source of 57 degrees.
HRqol					
Summerfield 2006 UK 16938781	GHSI	Bilateral Immediate implant (N=12)	Bilateral Delayed implant (N=12)	<0.05[63]	Non-significant difference between two groups Significant improvement 9 months postimplant second ear
	HUI3	Bilateral Immediate implant (N=12)	Bilateral Delayed implant (N=12)	NS	Non-significant difference between two groups

[63] Within group significant improvement of the score

	VAS	Bilateral Immediate implant (N=12)	Bilateral Delayed implant (N=12)	NS	Non-significant difference between two groups, with worsening after bilateral implant
	EQ-5D	Bilateral Immediate implant (N=12)	Bilateral Delayed implant (N=12)	<0.05	Non-significant difference between two groups. Significant decrease increase after Bil implant vs. first implant (p <0.05) –within group.
	GHSI	Bilateral implant (Immediate+Delayed) (N=24) Non-significant decrease after intervention vs. preintervention (ES = -0.3)	Unilateral implant (N=188) Significant increase after intervention vs. preintervention (p <0.001) (ES = + 1.1)		
	HUI3	Bilateral implant (Immediate+Delayed) (N=24) Non-significant decrease after intervention vs. preintervention. (ES = -0.1)	Unilateral implant (N=188) Significant increase after intervention vs. preintervention (p <0.001) (ES = + 0.9)		
	VAS	Bilateral implant (Immediate+Delayed) (N=24) Non-significant decrease after intervention vs. preintervention (ES = -0.3)	Unilateral implant (N=188) Significant increase after intervention vs. preintervention (p <0.001) (ES = +0.5)		
	EQ-5D	Bilateral implant (Immediate+Delayed) (N=24) Significant decrease increase after intervention vs. preintervention (p <0.05) (ES = -0.5)	Unilateral implant (N=188) Significant increase after intervention vs. preintervention (p <0.05) (ES = +0.1)		Non-significant difference between two groups. Significant decrease increase after Bil implant vs. first implant (p <0.05) –within group.
Both simultaneous and sequential bilateral					
Speech test					
Laszig 2004 Switzerland 15547426	OLSA in quiet	Bilateral implant (19) 79%	Better ear (19) 75%	0.03	
			Poorer ear (19) 73%	0.0004	
	HSM in quiet	Bilateral implant (14) 82%	Better ear (14) 80.4%	> 0.3	
			Poorer ear (14) 69%	0.01	
	HSM in noise	Bilateral implant (23) 53%	Better ear (23) 49%	0.1	
Cullington 2010 U.S.; U.K. 21178567	HINT	Bilateral implant (13)	Bimodal (13)	NS	No difference between bilateral and bimodal group.
Sound localization					
Laszig 2004 Switzerland	Horizontal plane sound localization	Bilateral implant 16/37	Either ear unilaterally	<0.00005	Horizontal plane sound localization with 12 speaker locations. Bilateral implant had significantly improved

15547426	localization abilities than either ear unilateral implant.

BKB-SIN = Bamford-Kowal-Bench Speech-in-Noise Test, CUNY = City University of New York tests, EQ-5D = EuroQoL 5 dimensions, GHSI = Glasgow Health Status Inventory, HHIE = Hearing Handicap Inventory for the Elderly, HHQ = Hearing Handicap Questionnaire, HRQoL = health-related quality-of-life, HSM = Hochmair, Schultz and Moser sentence test, HUI3 = Health Utilities Index Mark III, OLSA = Oldenburg sentence test, SNR = signal to noise ratio, VAS = Visual Analogue Scale.

Table D.10 Effectiveness of hybrid implant: summary of study results

Study	Study design, followup (yr)	Cochlear implant (N)	Mean age	Male (%)	Degree of deafness	Duration of deafness	Mean time (range) between deafness and implant	Implant indication	Device (coding strategy)	Study quality (comments)
Gantz 2009 U.S. 19390173	Prospective cohort 1 yr	87	nd	nd	Severe-to-profound hearing loss >2000 Hz	nd	nd	CNC word scores: 10-60% (preimplant ear) & up to 80% (contralateral ear)	Iowa/Nucleus 10-mm Hybrid implant (Standard CIS)	C (poor reporting)

Study	Outcome category	Specific outcome	Preimplant group (n/N) mean (95% CI)	Postimplant group (n/N) mean (95% CI)	p-value	Descriptive analysis
Gantz 2009 US 19390173	Speech perception	Respondee recognition in multitalker babble threshold values	nd	nd	nd	The result indicated that speech recognition in noise exists unless the low-frequency postoperative hearing levels approach profound levels.
Gantz 2009 US 19390173	Speech perception	% of people with improved BKB-SIN speech reception threshold	nd	41/61 total evaluated. 74% (SD nd)	nd	14 subjects did not show any significant enhancement with a decline on one of 2 speech measures. 7 subjects were not assessed on the BKB-SIN test.

BKB-SIN = Bamford-Kowal-Bench Speech-in-Noise Test,

Table D.11 Adverse events from hybrid implant

Study	Outcome category	Specific outcome	Descriptive analysis
Gantz 2009 U.S.	Adverse events	Total hearing loss	2 cases within 1st month of implant; 6 between 3 and 24 mo

Appendix E. References of Included Studies

(1) Sprinzl GM, Riechelmann H. Current trends in treating hearing loss in elderly people: a review of the technology and treatment options - a mini-review. *Gerontology* 2010;56(3):351-8. PMID: 20090297

(2) Gates GA, Rees TS. Hear ye? Hear ye! Successful auditory aging. *West J Med* 1997 October;167(4):247-52. PMID: 9348755

(3) Bond M, Mealing S, Anderson R et al. The effectiveness and cost-effectiveness of cochlear implants for severe to profound deafness in children and adults: a systematic review and economic model. *Health Technol Assess* 2009 September;13(44):1-330. PMID: 19799825

(4) Isaacson B, Lee KH, Kutz JW, Roland PS, Sargent EW. Cochlear Implants, Indications. *emedicine medscape com* 2010 June 25;Available at: URL: http://emedicine.medscape.com/article/857164-print.

(5) Huart SA. Unidentified and Underserved: Cochlear Implant Candidates in the Hearing Aid Dispensing Practice. *www audiology online* 2009 August 17;Available at: URL: www.audiologyonline.com/articles/pf_article_detail.asp?article_id=2272. AccessedSeptember 20, 2010.

(6) Disability Programs. *www socialsecurity gov* 2010 August;Available at: URL: http://www.ssa.gov/disability/professionals/bluebook/2.00-SpecialSensesandSpeech-Adult.htm#2_10.

(7) NICE. Cochlear implants for children and adults with severe to profound deafness. *National Institute for Health and Clinical Excellence* 2009 January 28;Available at: URL: http://www.nice.org.uk/TA166.

(8) Bai Z, Stephens D. Subjective outcome measures after cochlear implantation: Overall measures. *Audiological Medicine* 2005;3(4):212-9. PMID: None

(9) Bassim MK, Buss E, Clark MS et al. MED-EL Combi40+ cochlear implantation in adults. *Laryngoscope* 2005;115(9):1568-73. PMID: 16148696

(10) Damen GWJA, Beynon AJ, Krabbe PFM, Mulder JJS, Mylanus EAM. Cochlear implantation and quality of life in postlingually deaf adults: Long-term follow-up. *Otolaryngology - Head and Neck Surgery* 2007;136(4):597-604. PMID: 17418258

(11) Gifford RH, Shallop JK, Peterson AM. Speech recognition materials and ceiling effects: considerations for cochlear implant programs. *Audiol Neurootol* 2008;13(3):193-205. PMID: 18212519

(12) Hay-McCutcheon MJ, Pisoni DB, Kirk KI. Audiovisual speech perception in elderly cochlear implant recipients. *The Laryngoscope* 2005;115(10):1887-94. PMID: 16222216

(13) Gantz BJ, Hansen MR, Turner CW, Oleson JJ, Reiss LA, Parkinson AJ. Hybrid 10 clinical trial: preliminary results. *Audiol Neurootol* 2009;14 Suppl 1:8-13. PMID: 19390173

(14) Hawthorne G, Hogan A, Giles E et al. Evaluating the health-related quality of life effects of cochlear implants: a prospective study of an adult cochlear implant program. *Int J Audiol* 2004;43(4):183-92. PMID: 15250122

(15) Klop WMC, Boermans PPBM, Ferrier MB, Van Den Hout WB, Stiggelbout AM, Frijns JHM. Clinical relevance of quality of life outcome in cochlear implantation in postlingually deafened adults. *Otology and Neurotology* 2008;29(5):615-21. PMID: 18451751

(16) Krueger B, Joseph G, Rost U, StrauÃŸ-Schier A, Lenarz T, Buechner A. Performance groups in adult cochlear implant users: Speech perception results from 1984 until today. *Otology and Neurotology* 2008;29(4):509-12. PMID: 18520586

(17) Liu B, Chen XQ, Kong Y et al. Quality of life after cochlear implantation in postlingually deaf adults. *National Medical Journal of China* 2008;88(22):1550-2. PMID: 18956638

(18) Mawman DJ, Bhatt YM, Green KMJ, O'Driscoll MP, Saeed SR, Ramsden RT. Trends and outcomes in the Manchester adult cochlear implant series. *Clinical Otolaryngology and Allied Sciences* 2004;29(4):331-9. PMID: 15270818

(19) Morris LG, Mallur PS, Roland J, Waltzman SB, Lalwani AK. Implication of central asymmetry in speech processing on selecting the ear for cochlear implantation. *Otology and Neurotology* 2007;28(1):25-30. PMID: 17195742

(20) Most T, Shrem H, Duvdevani I. Cochlear implantation in late-implanted adults with prelingual deafness. *Am J Otolaryngol* 2010 November;31(6):418-23. PMID: 20015795

(21) Orabi AA, Mawman D, Al-Zoubi F, Saeed SR, Ramsden RT. Cochlear implant outcomes and quality of life in the elderly: Manchester experience over 13 years. *Clinical Otolaryngology* 2006;31(2):116-22. PMID: 16620330

(22) Rama-Lopez J, Cervera-Paz FJ, Manrique M. Cochlear implantation of patients with far-advanced otosclerosis. *Otology and Neurotology* 2006;27(2):153-8. PMID: 16436983

(23) Roditi RE, Poissant SF, Bero EM, Lee DJ. A predictive model of cochlear implant performance in postlingually deafened adults. *Otology and Neurotology* 2009;30(4):449-54. PMID: 19415041

(24) Firszt JB, Holden LK, Skinner MW et al. Recognition of speech presented at soft to loud levels by adult cochlear implant recipients of three cochlear implant systems. *Ear Hear* 2004;25(4):375-87. PMID: 15292777

(25) UK Cochlear Implant Study Group. Criteria of candidacy for unilateral cochlear implantation in postlingually deafened adults III: prospective evaluation of an actuarial approach to defining a criterion. *Ear Hear* 2004;25(4):361-74. PMID: 15292776

(26) Vermeire K, Brokx JPL, Wuyts FL, Cochet E, Hofkens A, Van De Heyning PH. Quality-of-life benefit from cochlear implantation in the elderly. *Otology and Neurotology* 2005;26(2):188-95. PMID: 15793403

(27) Vermeire K, Brokx JPL, Wuyts FL et al. Good speech recognition and quality-of-life scores after cochlear implantation in patients with DFNA9. *Otology and Neurotology* 2006;27(1):44-9. PMID: 16371846

(28) Wanscher JH, Faber CE, Grontved AM. Effect on quality of life of cochlear implantation in deaf adults. *Ugeskr Laeger* 2006;168(33):2656-9. PMID: 16942684

(29) Bradley J, Bird P, Monteath P, Wells JE. Improved speech discrimination after cochlear implantation in the Southern Cochlear Implant Adult Programme. *New Zealand Medical Journal* 2010;123(1321):34-44. PMID: 20927155

(30) Lazard DS, Bordure P, Lina-Granade G et al. Speech perception performance for 100 post-lingually deaf adults fitted with Neurelec cochlear implants: Comparison between Digisonic(R) Convex and Digisonic(R) SP devices after a 1-year follow-up. *Acta Otolaryngol* 2010 November;130(11):1267-73. PMID: 20446821

(31) Friedland DR, Runge-Samuelson C, Baig H, Jensen J. Case-control analysis of cochlear implant performance in elderly patients. *Archives of Otolaryngology - Head and Neck Surgery* 2010;136(5):432-8. PMID: 20479370

(32) Haensel J, Ilgner J, Chen YS, Thuermer C, Westhofen M. Speech perception in elderly patients following cochlear implantation. *Acta Otolaryngol (Stockh)* 2005;125(12):1272-6. PMID: 16303673

(33) Bodmer D, Shipp DB, Ostroff JM et al. A comparison of postcochlear implantation speech scores in an adult population. *Laryngoscope* 2007;117(8):1408-11. PMID: 17585277

(34) Chatelin V, Kim EJ, Driscoll C et al. Cochlear implant outcomes in the elderly. *Otology and Neurotology* 2004;25(3):298-301. PMID: 15129109

(35) Francis HW, Yeagle JD, Brightwell T, Venick H. Central effects of residual hearing: Implications for choice of ear for cochlear implantation. *Laryngoscope* 2004;114(10 I):1747-52. PMID: 15454765

(36) Green KMJ, Bhatt YM, Mawman DJ et al. Predictors of audiological outcome following cochlear implantation in adults. *Cochlear Implants Int* 2007;8(1):1-11. PMID: 17479968

(37) Nascimento LTd, Bevilacqua MC. Evaluation of speech perception in noise in cochlear implanted adults. *Rev Bras Otorrinolaringol (Engl Ed)* 2005;71(4):432-8. PMID: 16446956

(38) Rotteveel LJC, Snik AFM, Cooper H, Mawman DJ, Van Olphen AF, Mylanus EAM. Speech perception after cochlear implantation in 53 patients with otosclerosis: Multicentre results. *Audiology and Neurotology* 2010;15(2):128-36. PMID: 19690406

(39) Spahr AJ, Dorman MF. Performance of Subjects Fit with the Advanced Bionics CII and Nucleus 3G Cochlear Implant Devices. *Archives of Otolaryngology - Head and Neck Surgery* 2004;130(5):624-8. PMID: 15148187

(40) Matterson AG, O'Leary S, Pinder D, Freidman L, Dowell R, Briggs R. Otosclerosis: Selection of ear for cochlear implantation. *Otology and Neurotology* 2007;28(4):438-46. PMID: 17468676

(41) Carlson ML, Breen JT, Gifford RH et al. Cochlear implantation in the octogenarian and nonagenarian. *Otology and Neurotology* 2010 October;31(8):1343-9. PMID: 20729782

(42) Dunn CC, Tyler RS, Oakley S, Gantz BJ, Noble W. Comparison of speech recognition and localization performance in bilateral and unilateral cochlear implant users matched on duration of deafness and age at implantation. *Ear Hear* 2008;29(3):352-9. PMID: 18453885

(43) Dunn CC, Noble W, Tyler RS, Kordus M, Gantz BJ, Ji H. Bilateral and unilateral cochlear implant users compared on speech perception in noise. *Ear Hear* 2010;31(2):296-8. PMID: 19858720

(44) Koch DB, Soli SD, Downing M, Osberger MJ. Simultaneous bilateral cochlear implantation: Prospective study in adults. *Cochlear Implants Int* 2009;11(2):84-99. PMID: 19247979

(45) Litovsky R, Parkinson A, Arcaroli J, Sammeth C. Simultaneous bilateral cochlear implantation in adults: a multicenter clinical study. *Ear Hear* 2006;27(6):714-31. PMID: 17086081

(46) Noble W, Tyler R, Dunn C, Bhullar N. Hearing handicap ratings among different profiles of adult cochlear implant users. *Ear Hear* 2008;29(1):112-20. PMID: 18091100

(47) Buss E, Pillsbury HC, Buchman CA et al. Multicenter U.S. bilateral MED-EL cochlear implantation study: Speech perception over the first year of use. *Ear Hear* 2008;29(1):20-32. PMID: 18091099

(48) Grantham DW, Ashmead DH, Ricketts TA, Labadie RF, Haynes DS. Horizontal-plane localization of noise and speech signals by postlingually deafened adults fitted with bilateral cochlear implants. *Ear Hear* 2007;28(4):524-541. PMID: 17609614

(49) Litovsky RY, Parkinson A, Arcaroli J et al. Bilateral Cochlear Implants in Adults and Children. *Archives of Otolaryngology - Head and Neck Surgery* 2004;130(5):648-55. PMID: 2873678

(50) Litovsky RY, Parkinson A, Arcaroli J. Spatial hearing and speech intelligibility in bilateral cochlear implant users. *Ear Hear* 2009;30(4):419-431. PMID: 19455039

(51) Mosnier I, Sterkers O, Bebear JP et al. Speech performance and sound localization in a complex noisy environment in bilaterally implanted adult patients. *Audiol Neurootol* 2009;14(2):106-14. PMID: 18832816

(52) Quentin Summerfield A, Barton GR, Toner J et al. Self-reported benefits from successive bilateral cochlear implantation in post-lingually deafened adults: randomised controlled trial. *Int J Audiol* 2006;45 Suppl 1:S99-107. PMID: 16938781

(53) Ramsden R, Greenham P, O'Driscoll M et al. Evaluation of bilaterally implanted adult subjects with the nucleus 24 cochlear implant system. *Otology and Neurotology* 2005;26(5):988-98. PMID: 16151348

(54) Schleich P, Nopp P, D'Haese P. Head shadow, squelch, and summation effects in bilateral users of the MED-EL COMBI 40/40+ cochlear implant. *Ear Hear* 2004;25(3):197-204. PMID: 15179111

(55) Laske RD, Veraguth D, Dillier N, Binkert A, Holzmann D, Huber AM. Subjective and objective results after bilateral cochlear implantation in adults. *Otology and Neurotology* 2009;30(3):313-8. PMID: 19318885

(56) Nopp P, Schleich P, D'Haese P. Sound localization in bilateral users of MED-EL COMBI 40/40+ cochlear implants. *Ear Hear* 2004;25(3):205-14. PMID: 15179112

(57) Verschuur CA, Lutman ME, Ramsden R, Greenham P, O'Driscoll M. Auditory localization abilities in bilateral cochlear implant recipients. *Otology and Neurotology* 2005;26(5):965-71. PMID: 16151344

(58) Zeitler DM, Kessler MA, Terushkin V et al. Speech perception benefits of sequential bilateral cochlear implantation in children and adults: A retrospective analysis. *Otology and Neurotology* 2008;29(3):314-25. PMID: 18494140

(59) Laszig R, Aschendorff A, Stecker M et al. Benefits of bilateral electrical stimulation with the nucleus cochlear implant in adults: 6-Month postoperative results. *Otology and Neurotology* 2004;25(6):958-68. PMID: 15547426

(60) Cullington HE, Zeng Fg. Bimodal hearing benefit for speech recognition with competing voice in cochlear implant subject with normal hearing in contralateral ear. *Ear Hear* 2010;31(1):70-73. PMID: 19858722

(61) Noble W, Tyler RS, Dunn CC, Bhullar N. Younger- and older-age adults with unilateral and bilateral cochlear implants: speech and spatial hearing self-ratings and performance. *Otology and Neurotology* 2009;30(7):921-929. PMID: 19692936

(62) Ray J, Wright T, Fielden C, Cooper H, Donaldson I, Proops DW. Non-users and limited users of cochlear implants. *Cochlear Implants Int* 2006;7(1):49-58. PMID: 18792374

(63) Eapen RJ, Buss E, Adunka MC, Pillsbury HC, Buchman CA. Hearing-in-noise benefits after bilateral simultaneous cochlear implantation continue to improve 4 years after implantation. *Otology and Neurotology* 2009;30(2):153-159. PMID: 19180675

(64) Harrell FE, Jr., Lee KL, Califf RM, Pryor DB, Rosati RA. Regression modelling strategies for improved prognostic prediction. *Stat Med* 1984 April;3(2):143-52. PMID: 6463451