Project Name: Effectiveness of Cochlear Implants in Adults with Sensorineural Hearing Loss
Project ID: AUDT0501

Table 1: Invited Peer Reviewer Comments

Reviewer[1]	Section[2]	Reviewer Comments	Author Response[3]
1	Executive Summary	Page ES-3, KQ1: Is it true that all CI indications specify the use of the HINT sentences specifically or do they simply refer to open-set sentence perception?	Advanced Bionics refers specifically to HINT scores, while Cochlear Americas only refers to open-set perception. The final document has been changed to reflect this.
	Introduction/ Background		
1	Page 1, Background	In the first paragraph there is reference to "two types of hearing loss" – conductive and sensorineural. However, it is important to acknowledge central hearing loss, particularly when considering an aging population who may acquire central auditory deficits secondary to strokes.	We have made changes to reflect this edit.
1	Page 1, Background 1st Line, 2nd paragraph	Sensorineural hearing loss is not best characterized by just an attenuation of the highest frequencies of sound. First, any frequency can be attenuated. Second, the attenuation is not necessarily the factor that causes the significant speech perception difficulties. For a pure attenuation loss acoustic amplification is an excellent options. 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.	We have made changes to reflect this edit.
1	Page 1, last line of background	Consider adding "or central" before "deafness."	We have made changes to reflect this edit.
1	Page 1, Cochlear	I find the word "arrange" to be quite unspecific. Aside from a	We have made changes to

	implantation, 2nd to last line on page	more complete description of sound processing, even replacement of the word with something like “analyzes and codes” would be more instructive.	reflect this edit.
1	Page 2, FDA labeled use, line 1	“users” should be possessive.	We have made changes to reflect this edit.
1	Page 2, FDA labeled use, line 5	The word insufficient seems to be incorrectly used here. If resideual hearing was insufficient then a hearing aid would be ineffectual. Consider replacing “insufficient” with “present.”	We have put the words "present but" immediately before "insufficient".
1	Page 2, Recent Health Technology Assessment, lines 10-11	There seems to be a grammatical problem here; it wasn’t the “guidelines” that conducted the additional analyses.	We have made changes to reflect this edit.
	Methods		
1	Page 6, Comparator of Interest	consider defining “non-auditory support.” Also, the last sentence of this paragraph is unclear.	We have clarified this statement.
1	Page 6, Outcomes of Interest	It is stated that “two-syllable or multi-syllable words are words that have equal emphasis on both of them…” Not all two-syllable words have equally stress. It appears that this section is referring to a specific type of two-syllable words – spondees.	Edited.
1	Page 6, Outcomes of Interest	Why wasn’t there consideration of perception of single-syllable words? I believe the assessment only found 2 studies that included two-syllable words. This is because those types of words are not often used in CI assessments. However, single syllable words are almost always included. They may be a more appropriate stimuli for uncovering binaural benefits as perception of single-syllable words occurs without the benefits of context that are provided by sentence-level stimuli. I find the lack of consideration of single-syllable word perception to be a limitation of this assessment.	"Outcome measures were chosen to respond to CMS' needs to assess day-to-day functional ability of subjects with cochlear implant."
1	Page 6, Outcomes of Interest, last sentence	Sensorineural hearing loss is not demonstrated by speech perception scores.	Corrected to “pre-implantation test scores”
1	Page 6, Study designs and sample size	There is no justification for eliminating studies with sample sizes less than 30 subjects. This would be helpful to the reader. I find this factor to be an unfortunate one. Given the size of the population of CI users, one can expect small-scale studies.	The clinical effectiveness of unilateral cochlear implantation has been well examined in prior systematic

		Further, many of the best CI research labs operate independently of CI programs that are most often located at medical centers. For this reason, is it not uncommon for papers that come out of research labs to have studied smaller groups of implant users. However, it is quite likely these studies are of significantly higher scientific merit and that they could add very important information and support to the central questions asked in the current assessment. I find the lack of inclusion of smaller-scale, yet potentially well-executed, studies a limitation of this assessment.	reviews. Sample size thresholds were chosen based primarily on practical consideration of available resources and time balanced with the likely amount of available literature. Including many more studies with smaller sample sizes would have increased the number of subjects evaluated, but would very rarely upgrade to good methodological quality.
1	Page 9, Candidates for Cochlear Implants	I find much of this paragraph could benefit from some word-smithing. For example “distinguish speech at higher thresholds” is non-specific and could be misinterpreted. Another example is “ability to detect an audiometric pure-tone average…” Finally the parenthetical information in the second-to-last line of this paragraph is unclear.	Edited
1	Page 12, Pre versus post unilateral cochlear implants	I find much of the second paragraph to be unclear.	Deleted
1	Page 19, 2nd line of last paragraph before Duration of Impaired hearing	consider replacing “of” with “at”	We have edited this sentence
1	Page 20, Older Age, 2nd paragraph	The 2nd and 3rd sentences seems to contradict each other. The 2nd says there were no differences between younger and older recipients while the 3rd sentences says that older patients had a significantly lower post-op score.	The sentence had been clarified.
1	Page 21, Preoperative Speech Perception Scores & Degree of Pre-Implant Residual Hearing	I don’t see how these two sections differ – they are both looking as preoperative speech perception/speech recognition or word understanding as a potential modifying factor postoperative speech perception or health-related quality of life outcomes. Why wouldn’t they all be considered together? :Degree of pre-implant hearing” perhaps needs better definition – is this just word perception or does it have to do with pure tone thresholds?	"degree of pre-implant hearing" has been changed to "degree of pre-implant hearing as defined by pure one thresholds. Therefore the two sections now are mutually exclusive.

1	Page 21, preoperative speech perception scores, last line	is r=0.0003 really correct?	The number was correct but we had clarified the number was beta coefficient from multivariate regression.
1	Page 30, study characteristics, 4th line	What does “immediate sequential second ear implant mean? Is this another way of saying simultaneous? If so, simultaneous would be much more clear to the reader.	The immediate sequential second ear implant occurred one month after first ear unilateral and we have clarified the same in the text.
	Page 30, study characteristics, 9th line from bottom	consider making “implant” plural.	Done.
1	Page 30, study results 4th line from bottom	What was 100% compared to?	Corrected.
1	Page 31, health-related quality-of-life:	Last two sentences are unclear.	Clarified.
1	Page 31, 5th line from bottom	The parenthetical (38%, P = 0.02) is hard to interpret. Is there some information missing here?	We have made changes to clarify this sentence.
	Discussion/Conclusion		
1	Page 35, 1st full paragraph, 4th sentence	There are some grammatical problems here	We have edited this sentence
1	Tables		
1	Table 1	Isn’t there in indication that refers to “≤ 60% in the unimplanted ear?”	Though preoperative, contralateral scores are discussed in the literature, our search did not reveal in the manufacturer's specifications of any indication with respect to the unimplanted ear.
1	Appendices	Due to time constraints, I did not take editorial notes on the content of the appendices. However, there were a couple of instances that popped-out as needing some editing	We have proof-read the tables.

2	General	The ability to evaluate the effectiveness of a treatment, in this case cochlear implants in the adult population, is based on numerous factors not least of which is a baseline knowledge and understanding of the area to be studied. And a lack of real understanding can be reflected in the lack of clarity in the writing. I found that to be so in this document. While there is much information included in the report, I had underlying sense that a 'feel' and true understanding of the subjective matter was missing. I found the choice of publications to include interesting. While I appreciate the group was attempting to hold to certain standards, the publications chosen were often not indicative of the leading publications in the field and therefore rather perplexing. While the conclusions were spot on, they did not seem to flow from the literature that was selected.	With peer review process, we think the clarity of the document would have improved. In general, leading publications with positive findings get cited more frequently than the studies with negative and/or null findings.
2	Executive Summary	The summary was understandable and succinct and reflected the document	Thank you.
2	Introduction/Background		
2	Page 1, paragraph 2	in sensorineural hearing all frequencies can be compromised to various degrees depending on the type, degree of the hearing loss.	We have made changes to reflect this edit.
2	General	The ability to evaluate the effectiveness of a treatment, in this case cochlear implants in the adult population, is based on numerous factors not least of which is a baseline knowledge and understanding of the area to be studied. And a lack of real understanding can be reflected in the lack of clarity in the writing. I found that to be so in this document. While there is much information included in the report, I had underlying sense that a 'feel' and true understanding of the subjective matter was missing. I found the choice of publications to include interesting. While I appreciate the group was attempting to hold to certain standards, the publications chosen were often not indicative of the leading publications in the field and therefore rather perplexing. While the conclusions were spot on, they did not seem to flow from the literature that was selected.	With peer review process, we think the clarity of the document would have improved. In general, leading publications with positive findings get cited more frequently than the studies with negative and/or null findings.
2	Page 1	why did the Background focus on the elderly? Adults of all ages	In the background, we have

		receive cochlear implants and have hearing loss. In fact, many of the articles cited in this review are not focused on the elderly. While one of the key questions relate to the elderly in terms of Medicare, my understanding is that all adults should be addressed as reflected in key question #1.	made changes to reflect this edit. When the data available is specific to the elderly, we have retained the focus to older adults. Often limited data is available for elderly, but the focus of the report is geared more towards the elderly.
2	Page 1, paragraph 4	the sentence reading '…unimpaired scores…? What does that mean? People with word recognition scores of 80% or less often do very well with hearing aids but this score is most likely not achieved in the presence of a severe-to-profound hearing loss	Deleted.
2	Introduction/ Background	The key questions are thorough although ambiguous in certain areas, for instance, the areas in 2a. Age at what? Time of implantation? And there are no studies that truly reflect the differences in outcome based on expertise of the center. Nor did I see any studies cited that discuss differences in outcome between devices. Since these questions cannot really be addressed, it would be appropriate to either eliminate them or explain the lack of data.	These are evaluation of pre-operative characteristics that may predict outcomes. We have clarified to age at implantation. When data were available, we have presented them and when there were no data, we have addressed them. Showing areas that lack of data is to identify areas that need future research. There is a section with small number of studies on differences between devices.
2	Methods	Why were the studies chosen limited to those with 30 or more subjects? There are numerous good studies with fewer subjects.	We have clarified this in the methods section.
2	Methods	the inclusion of the 'hybrid' device is inappropriate. This device is investigational and not yet approved by the FDA unless it is included in a special section to review investigational devices.	This has been moved to the end of the results section.
2	Methods	the standard/baseline evaluation tests are sentences and	"Outcome measures were

		monosyllabic word recognition, not multisyllabic words. This is evident in the published literature.	chosen to respond to CMS' needs to assess day-to-day functional ability of subjects with cochlear implant."
2	Methods	3 classification of grades were used and many of the articles were judged by the group to be poor (quality c) and of low validity. I think that either the articles need to be re-reviewed and re-classified or if they are indeed poor, why are they being used to develop Conclusions? The old phrase of garbage in, garbage out applies. Bad research should not be used to form Conclusions. My concern, however, is whether these articles have been appropriately classified and judged as well as the selection of references (see below).	The poor quality studies are neither utilized to evaluate overall body of evidence nor used for conclusions. This is clarified in the first sentence of overall body of evidence. We have reviewed the reference list and when studies met our eligibility criteria, they have been added to the review.
2	Methods	the inclusion of the 'hybrid' device is inappropriate. This device is investigational and not yet approved by the FDA unless it is included in a special section to review investigational devices.	This section with one study is moved to the end of the results section as a separate heading.
2	Results	The methods need to be addressed in order to have valid and reliable results (see above)	Clarified above.
2	Discussion/ Conclusion	While I agree wholeheartedly with the Conclusions, my concern is they are not supported by the facts as interpreted by the authors and presented in the document.	Thank you for your comment.
2	Tables	The tables are wordy and often unclear. Should be simplified.	Thank you for your comment.
2	Appendices	A bit wordy, perhaps reflective of a lack of familiarity of the topic	Thank you for your comment.
2	References	I am reasonably familiar with the cochlear implant literature and am frankly perplexed by some of the choices. Here are some additional suggestions: 1. Chang et al. Performance over time with simultaneous bilateral implants. J Am Acad Audiol. 2010 2. Berrettini et al. Benefit from bimodal hearing in a group of prelingually deafened adult cochlear implant users. Am J Otolaryngol 2010	We have included studies 3, 5, and 12. Others were ineligible because of sample size <10 for bilaterals, mixed populations, and duplicate publications. Ref 6 was already included in the draft.

		3. Noble et al. Younger and older age adults with unilateral and bilateral cochlear implants: speech and spatial hearing self-ratings and performance. Otol Neurotol 2009 4. Budenz et al. Effect of cochlear implant technology in sequentially bilaterally implanted adults. Otol Neurotol 2009. 5. Laske et al. Subjective and objective results after bilateral cochlear implantation in adults. Otol Neurotol 2009 6. Koch et al. Simultaneous bilateral cochlear implantation: prospective study in adults. Cochlear Implants Int. 2009 7. Eapen et al. Hearing in noise benefits after bilateral simultaneous cochlear implantation continue to improve 4 years after implantation. Otol Neurotol 2009 8. Loizou et al. Speech recognition by bilateral cochlear implant users in a cocktail party setting. J Acoust Soc Am 2009 9. Poissant et al. Impact of cochlear implantation on speech understanding , depression, and loneliness in the elderly. J Otolaryngol Head Neck Surg 2008 10. Mosnier et al. Speech performance and sound localization in a complex noisy environment in bilaterally implanted adult patients. Audiol Neurotol 2009 11. Noble et al: Unilateral and bilateral cochlear implants and implant-plus-hearing-aid profile. Int J Audiol 2008 12. Zeitler et al. Speech perception benefits of sequential bilateral cochlear implantation in children and adults: a retrospective analysis. Otol Neurotol 2008 13. Tyler et al. Speech perception and localization with adults with bilateral sequential cochlear implants. Ear Hear 2007 These are some suggestions. There are additional articles and I urge the authors to examine their exclusion criteria as they may not allow for inclusion of important and relevant clinical research while including literature that is not perhaps so relevant to the topic.	
3	Executive Summary, ES1	o Statement that “implant site” was not evaluated refers, I believe, to “implant center” (p. ES-4)	Edited
3	Methods	The screening system of report studies utilized seems to have excluded a large number of studies. I have provided a review of	Thank you, eligible studies have been added. Many

		bilateral implantation that includes a number of studies not assessed in the present report.	were ineligible because of sample size, mixed populations, and duplicate publications.
3	Results, KQ2	"there was a low level of evidence regarding the association between preoperative patient characteristics (…) and better postoperative speech outcomes. This statement that there are insufficient data to evaluate the predictors of outcome fails to acknowledge a large, extant literature on the effects of residual hearing on outcome. For example, two carefully done studies have looked at such variables carefully and modeled effects with predictive mathematical formulae (eg Rubinstein et al, 1999; Friedland et al, 2003).	Both studies were published before 2004, so were not included in our report.
3	Results, KQ2	"Studies provide insufficient evidence to draw a conclusion about the relationships between preopereative patient characteristics and postoperative health-related quality-of-life outcomes" fails to note studies such as Francis et al who showed positive correspondence between gains in speech recognition scores and those of HR-QoL.	This evidence is based on current literature published since 2004.
3	Discussion/Conclusion		
3	KQ3	NICE was careful to evaluate the 24-patient study of QoL in bilateral implantation. Ultimately, in response to concerns from Prof. Quentin Summerfield who conducted the study, they discounted the findings that included the single patient with greater tinnitus following the 2nd device. Their final, adjusted result indicated a positive utility resulting from the 2nd device. Of course, one should be mindful that utility ratings are very generic and thus their sensitivity to hearing acuity afforded by bilateral inputs is questionable. Further, sensitivity to real-world hearing connection is difficult to capture in surveys that are designed to evoke consideration of health status per se. Although it is clear from the literature (eg Palmer et al, that going from the severe-to-profound SNHL state (with unilateral implantation) to unilateral, electrical hearing produces robust effects, the "achievable" gains with the 2nd ear implant are naturally constrained. With reduced headroom for utility gains,	We have clarified that better hearing specific quality-of-life instruments are needed to assess the benefits reported by patients.

		one approach would be to evaluate the effect of both devices in producing the gain achieved over baseline hearing. In support of this approach, many patients note that they often need to rely on one device in the case of cord or battery failure. Thus 2 devices help to insure that the patient does not return to the deaf state.	
3	ES5, 2nd paragraph	it's stated that bilateral CI benefit under quiet conditions is unclear. This is to be expected and is generally not a test administered as it would provide little clinical value. The first-ear CI is likely to completely "ceiling out" the effects of the 2nd ear's implant under such lax listening conditions.	Edited.
3	KQ3	Sound-field expansion to provide direct access to the hemisphere of the 2nd ear implanted	
3	KQ3, ES5	The quote: "Small studies showed significant binaural head-shadow benefit, small benefits in binaural summation, and squelch effects in bilateral listening conditions over unilateral listening conditions, suggesting that subjects with bilateral cochlear implants may perform better in real world conditions." seems to downplay perceptual benefits with the adjective "small". Indeed, such perceptual skills are remarkably important in generating performance benefits related that stem from binaural hearing. The suggestion is, then, that the described benefits in head-shadow, binaural summation, and squelch are likely to contribute to binaural benefits that are critical to directional listening under challenging conditions.	We have discussed these effects in detail in discussion section.
3	KQ3, p33	The citation of the Gantz et al. study of Hybrid devices (ref #13) as a source of data on the complication of complete hearing loss seems non-compelling. This device is placed in ears that are uniquely different from	This section has been moved to the end of the results.
3	Tables. D3	Did this review make certain that pre- to post-operative change represented testing of the ear of implantation only? Testing of both ears to give the baseline performance, and testing of the implanted ear only post-operative is the norm, but does not provide rigor in testing the implanted ear only.	The studies described them as comparisons of pre-implant versus post-implant scores for the ear that had an implant.
	References	There are a number of typographical errors (eg, journal citations in #41 and 43).	We have made minor changes to reflect this edit.

3	General	It is now a virtual certainty that outside agencies' evaluation of the literature surrounding a clinical intervention such as the cochlear implant will conclude that extant assessments are of low quality. What's puzzling is why such evaluations fail to attempt to account for the underlying reasons for this. Without such considerations, results indicating patient safety and benefit—required for initial FDA approval—are not considered.	There were studies that were of fair quality and with sufficient numbers, it reached moderate overall body of evidence.
	General	After the initial manufacturer-based trials to gain FDA approval, randomization becomes ethically challenging. Large-scale, multisite, prospective studies are prohibitively expensive (eg, our current 6-center pediatric study is costing about $1.2M/y) and are unlikely to attract outside, independent funding. Even large single-center studies that would be of sufficient size to power through the expected variability in results would be unmanageably expensive. Further, given the established efficacy of the intervention based in FDA trials, NIH reviews for funding are often harsh when proposed studies attempt to assemble datasets already established as part of the regulatory process. In fact, the highest quality data are most likely to be found in the FDA trial databases—studies funded by manufacturers—that would not meet criteria for evaluation by the AHRQ.	Thank you for your comment.

[1] Peer reviewers are not listed in alphabetical order.

[2] If listed, page number, line number, or section refers to the draft report.

[3] If listed, page number, line number, or section refers to the final report.

Project Name: Effectiveness of Cochlear Implants in Adults with Sensorineural Hearing Loss
Project ID: AUDT0510

Table 2: Public Review Comments

Reviewer Name[1]	Reviewer Affiliation[2]	Section[3]	Reviewer Comments	Author Response[4]
Anonymous Reviewer 1	NA	General	As a sequential bilateral CI recipient I read this report with great interest. Sorry to say I was so disappointed with the lack of adequate credible research into the pre- & post-implant effects. I have been very successful as a recipient and will say without hesitation that bilateral is far better than unilateral (I was unilateral for 2 years). However, I will also say that none of the testing for word and sentence recognition even comes close to real world living conditions. The only one that even comes close is the one test with background "babble". The white noise tests are unrealistic & I have yet to encounter a sound-proof booth quiet environment in daily living. Overall I believe the report is well written and thorough based on the data available. The conclusions are good, especially about needing much more research.	Thank you.
Anonymous Reviewer 2	Cochlear Americas	General	Cochlear Americas, together with its parent and affiliate companies, is the global leader in implantable hearing solutions. Cochlear Americas offers the following comments to the draft Technology Assessment of the Effectiveness of Cochlear Implants in Adults with Sensorineural Hearing Loss (?TA?).	
Anonymous reviewer 2	Cochlear Americas		First, Cochlear Americas is pleased that AHRQ has addressed the issue of the effectiveness of cochlear implantation. It is well documented that unilateral cochlear implantation provides significant and substantial benefit to adults with severe to profound hearing loss as compared to a hearing aid. Available in the U.S. commercial market place	Thank you for your comment..

			for close to 30 years for adults, it is fair to say that cochlear implantation as a treatment modality has come to be considered the ?standard of care? for those individuals meeting its indications. The transition into bilateral implantation has naturally evolved as did the practice of unilateral hearing aid fitting to bilateral fittings over 20 years ago. The recognition of binaural hearing advantages is not disputed and individuals meeting indications for treatment of a mild to moderately severe bilateral hearing disability are routinely fit with bilateral hearing aids. A company review of over 100 articles specifically addressing the use of bilateral cochlear implants was completed last year (currently pending publication). In this review, the psychoacoustic benefits of binaural hearing (e.g. squelch effect, binaural summation and head-shadow effect) was well supported.	
Anonymous Reviewer 2	Cochlear Americas		Cochlear Americas would like to offer a few comments regarding the interpretation of some of the study outcomes, metrics and design that we feel affected the committee?s conclusions. They are as follows:	
Anonymous Reviewer 2	Cochlear Americas	General Comments	The lack of study outcomes indicating a bilateral advantage in speech perception ?in quiet? is not an indication of lack of effectiveness. Generally speech tests in quiet are not sensitive to differences between monaural and binaural hearing nor are they representative of ?real world hearing? ? another acknowledgement made by the committee. The study outcomes as summarized in the report Discussion and Conclusion sections support the benefit in speech perception ?in noise? with bilateral implantation as compared to unilateral.	We have clarified to reflect this section.
Anonymous Reviewer 2	Cochlear Americas	General Comments	A concern expressed in the same Discussion and Conclusion sections related to inadequate data supporting improvements in the psychoacoustic processes of squelch and binaural summation is misplaced. It is primarily an academic argument. The individual patient does not care nor benefit from the underlying physiological mechanism by which binaural listening provides benefit. It only matters that the patients are doing better with two ears rather than one. In	The tests are conducted in a laboratory setting and are not real world settings. We do not have sufficient data to evaluate real-world performance.

			fact, head-shadow effects are a very large issue in real world listening situations with background noise and the large benefits received via the second implant are thus a primary factor in the beneficial effects of bilateral implantation even if an individual patient receives less benefit attributable to binaural squelch.	
Anonymous Reviewer 2	Cochlear Americas	General Comments	Cochlear Americas is concerned that an omission from the study literature review was an examination of studies on the restoration of the ability to localize sound direction with bilateral implantation. The hearing science literature strongly supports the improvement in localization ability for individuals receiving bilateral hearing treatment (e.g. two hearing aids or two cochlear implants). This has significant safety implications in the ?real world? (ie. identifying the direction of emergency vehicular sirens) for all ages.	We have added these studies.
Anonymous Reviewer 2	Cochlear Americas	General Comments	The conclusion in the TA that long-term follow-up with bilaterals is necessary does not appear to be supported with data. There was nothing in the report to suggest that the incidence and types of adverse events would be any different with bilateral vs. unilateral over time. The one report on device non-use (reported at 4%) was inaccurate as it 'counted' Hybrid cochlear implant users (study of n=87) who experienced loss of hearing and discontinued use of an acoustic component (n=2) as 'non-users'. The subjects still successfully used their cochlear sound processor.	The latter part of this comment (regarding non-use) is referring to Gantz 2009, which states, "Total loss of hearing occurred in 2 cases within the first month after surgery". It is not clear that this is only acoustic loss (as discussed later in the article). Regardless, the 'Hybrid' parts of the report will be consolidated separately from the rest of the report.
Anonymous Reviewer 2	Cochlear Americas	Quality of life and cost effectiveness	Well known and recognized experts in the field have studied and addressed the quality of life improvements associated with cochlear implantation. Some key studies do not seem to have been included in the TA, even though they also represent the quality of papers that were included in the grading for the review. It is suggested that the TA be expanded to include some of these studies - - particularly, we would suggest the following studies be considered for	We have carefully reviewed your suggestions and included studies that met our eligibility criteria.

			inclusion.	
Anonymous Reviewer 2	Cochlear Americas	Quality of life and cost effectiveness	Bichey and Miyamoto (2008) illustrated the cost-utility and quality of life improvements for bilateral compared with unilateral implantation, using a group of subjects from the U.S. healthcare system that would be more representative than those from Britain used for the Summerfield et al. study often quoted in the TA. (Bichey BG, Miyamoto RT. Outcomes in Bilateral Cochlear Implantation. Otolaryngol Head Neck Surg 2008;138(5):655-661).	Excluded because of mixed population (children and adults).
Anonymous Reviewer 2	Cochlear Americas	Quality of life and cost effectiveness	Litovsky et al. (2006) also identified, in a large group of subjects representing typical U.S. patients, a significant improvement across questionnaire measures of hearing and perceived benefit with bilateral implantation versus unilateral. (Litovsky, RY, Parkinson, A, Arcaroli, J, Sammeth, C. Simultaneous bilateral cochlear implantation in adults: A multicenter study. Ear Hear 2006; 27(6): 714-731).	Yes, this study was already included in the draft report.
Anonymous Reviewer 2	Cochlear Americas	Quality of life and cost effectiveness	Finally, a recent study by Wyatt, Niparko and deLissovoy concluded that cochlear implants are second only to neonatal intensive care in terms of cost effectiveness, as shown in the figure below. This type of data would seem to be useful to the analysis in the TA.	The objective of the report is to assess clinical effectiveness of cochlear implants in adults.
Anonymous Reviewer 2	Cochlear Americas	Quality of life and cost effectiveness	Additionally, much of the Quality of Life (QOL) metrics reported in the TA are based upon QOL studies from outside the U.S., and especially from Europe. Europe and other countries use different QOL metrics than those used in the U.S. to measure changes in QOL. Because of this inconsistency, we question the applicability of many of the studies and tests cited in the TA as a measure of QOL. And again, we suggest the inclusion of more U.S. based studies, including those identified above.	Thank you for your comment..
Anonymous Reviewer 2	Cochlear Americas	Tinnitus	There are studies showing that cochlear implantation has a positive effect on tinnitus in that it is or can be reduced by cochlear implants, although there is also sometimes an increase in tinnitus immediately after implantation that subsides over time. Such studies did not seem to be addressed fully in the TA. By contrast, the Summerfield et al. study was referenced in the TA in relation to a possible	We have clarified this in our report.

			worsening of tinnitus after cochlear implantation for some of the subjects in that particular study. This does not represent the literature as a whole. For instance, that finding of reported worsening tinnitus after bilateral implantation is in opposition to a more recent report by Di Nardo et al., 2007. In the latter study, a majority of patients with intractible tinnitus reported a reduction or complete suppression of the tinnitus with bilateral cochlear implant use. (Di Nardo W, Cantore I, Cianfrone C, et al. Tinnitus modifications after cochlear implantation. Eur Arch Otorhinolaryngol 2007; 264(10): 1145-1149).	
Anonymous Reviewer 2	Cochlear Americas	Study sizes and population	The numbers of cochlear implant recipients are relatively less than the size of populations for other device or disease condition technology assessments. This smaller scope should be taken into account in evaluating the study data. In 2009, for example, there were 1,481 Medicare cochlear implant surgeries. In contrast to this, 58,500 hip replacements were done in 2009. Even though cochlear implant studies tend to use smaller subject numbers, the significance of the results is clearly seen across the more than 100 studies done on bilateral versus unilateral implantation, and, of note, the same significant findings and trends are seen consistently across all the studies despite differences in patient factors such as age, length of implant use, preoperative hearing aid use, and in experimental differences including language evaluated, loudspeaker setup, speech task employed and so on. It is a consistent and striking finding across the bilateral cochlear implantation literature as a whole that patients receive significant and substantial benefit from addition of the second implant. There have been no reports of a decrement in performance with addition of the second implant, with nearly all subjects receiving a number of reported benefits in terms of speech recognition, sound localization, and perceived improvement in quality of life.	Thank you for your comment.
Anonymous Reviewer 2	Cochlear Americas	Conclusion	The literature reviewed by the members of the Tufts committee may have been representative of the clinical and	Cochlear implantation is a safe procedure in adults. The

			scientific publications on cochlear implants but it failed to address key elements relevant to the safety and efficacy with unilateral and bilateral cochlear implantation. Those would include 1) there is no difference in the type and incidence of surgical and device specific adverse events in unilateral vs. bilateral implantation; 2) restoring the ability to localize is a key component to minimizing the disability of hearing loss; 3) not recognizing that the benefits of binaural hearing are an established fact and are not required to be re-assessed with electrical bilateral stimulation vs. acoustic; and 4) the lack of acknowledgement that the wide ?sweep? of quality of life tools may have not been appropriate for this population. Different QOL measures are more appropriate for different study designs and the perception of them as a ?whole? vs. individual was, perhaps, over-reaching.	main objective of this report is to assess the clinical effectiveness of cochlear implants in adults. We have added sound localization studies and have clarified that better tools are needed to assess patient performance in real-world setting.
Darla Franz	MED-EL Corporation	Executive Summary		
Darla Franz	MED-EL Corporation	KQ3, page ES4	The technology assessment evaluated a total of nine studies to answer this question, with respect to speech perception in noise, speech perception in quiet, and quality of life. We suggest some additional studies for consideration that show benefits for speech in noise (including head shadow, summation and squelch effects) as well as improvements in speech understanding in quiet. In addition, we suggest that the committee also consider evaluating studies of localization abilities. The ability to localize a sound in space relates to quality of life, although it is not a direct measure of quality of life per se. Rather, the ability to locate sounds provides not only a measure of safety in dealing with moving objects in daily life, but also it indirectly demonstrates the presence of binaural fusion. Localization requires the brain to demonstrate the ability to compare intra-aural timing and loudness differences (ITDs and ILDs respectively) between the ears. The ITD is particularly important in localizing low frequency sounds, such as the source of traffic noise, detecting an accelerating or oncoming vehicle, or in a reverberant environment. Localization of a sound source is	We have added localization studies in the current version of the draft.

			also necessary to determine its distance. Localization data show that bilaterally implanted cochlear implant listeners can often localize sound at minimal audible angles that are very similar to that of normal hearing listeners, while unilateral implant users guess, and most often their guess is biased toward sound coming from the direction of their only implanted ear. References to such studies are included in the Reference Section of the public comment interface. We include reference to a study of localization skills in unilateral implantees for comparison.	
Darla Franz	MED-EL Corporation	Discontinuation of Use, page ES4	In this section, the technology assessment reviews results from an ongoing clinical trial for a type of cochlear implant device that is intended for a completely different indication range than the current scope. Electric-acoustic stimulation (aka ?hybrid?) devices are studied in individuals with significant residual hearing ? so significant that they would not qualify for traditional cochlear implantation and do not match the criteria delineated by this Technology Assessment. Indeed one of the goals of such studies is to determine whether residual hearing can be reliably maintained using specialized electrode arrays and soft surgical techniques. Loss of residual hearing found as a preliminary result in these studies, therefore, does not and should not apply when considering traditional implant users with severe-to-profound sensorineural hearing loss preoperatively. In addition, loss of residual hearing is a known risk for cochlear implant surgery in general in the traditional CI candidate group, and is listed as such on the implant package insert.	The hybrid single study is moved to the end of the results section with a separate heading.
Darla Franz	MED-EL Corporation	Discussion Section, page ES5	The Executive Summary statement ?benefit under quiet conditions was unclear? could perhaps be clarified by the Mueller et al. and Mosnier et al. studies (complete cite listed in the comments on the Reference Section). In the Ramsden et al. study a bilateral benefit in quiet could not be shown because of ceiling effects in the unilateral listening conditions. Therefore, the absence of a significant effect is primarily due to a methodological flaw. Indeed, the Study Results section of the Technology Assessment (p 27)	Studies that met our eligibility criteria have been included in this current version.

			includes the statement ?All three studies tested HINT sentences in quiet, and bilateral cochlear implants scored statistically significantly better than the unilateral cochlear implants (Table 9).? These results are not reflected in the Executive Summary. The Summary should be modified to reflect this.	
Darla Franz	MED-EL Corporation	Executive Summary	Also in this section and several times throughout the work, the authors mention a result in one study that seems to indicate a possible worsening of tinnitus. Post-implant tinnitus is a known potential risk of cochlear implantation. The risk of potential tinnitus is mentioned on the cochlear implant package inserts accompanying all FDA approved devices, and is also listed as a known risk on the FDA website. In addition, it might be important to note that many cochlear implant patients report a post-implant reduction in pre-existing tinnitus and this is reported often in the literature. There is no clear evidence to date that supports a presumption that bilateral implantation might increase the risk of post-implant tinnitus over that reported in unilateral implant recipients. Indeed, on page 31 of the Technology Assessment the committee stated ?To evaluate the issue of worsening tinnitus, bilateral cochlear implants were compared with unilateral implants from the UKCISG that resulted in inconclusive results.? Therefore, these statements implying a relationship between bilateral implantation and tinnitus that is different from the relationship between unilateral implantation and tinnitus should be removed from the report.	Thank you for your comment.
Darla Franz	MED-EL Corporation	Conclusion, page ES5	We suggest that the statement ?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? either be revised with respect to localization data, or removed. As mentioned in the earlier comments to the Executive Summary, localization studies were not evaluated as a part of this technology assessment. Indirectly, fusion, i.e. binaural signal processing by the brain, can be argued by the significant presence of a squelch effect	We have included the sound localization studies.

			in a series of studies and more generally by the ability to discriminate ITDs in electrical stimulation. See the comments to the Reference List for a complete list of studies that could be evaluated here.	
Darla Franz	MED-EL Corporation	Future Research Needs, page 36	The Assessment calls for ?good quality studies? that ?include sufficient numbers of subjects? that provide ?long term follow-up data on patient outcomes? as well as ?identify the time period needed for [development of] sound localization, improved speech perception, and improved?quality of life.? In addition there is a call for improved test measures to study outcomes including 3D binaural fusion. Studies began on bilateral implantation in the 1990?s and continued to be published in greater numbers into the early part of the 2000?s. Since many significant studies occurred prior to 2004, it is perhaps helpful to widen the scope of review somewhat. This is perhaps an important point, in that we anticipate a decreasing level of interest across implant centers in beginning or pursuing large-scale studies looking at unilateral vs. bilateral performance. We believe this trend to be a result of the clinical research community?s growing agreement that bilateral implants are an accepted medical practice. Several research teams have even commented that it now presents an ethical dilemma for researchers to continue to enroll unilateral implant patients in studies when the benefits of bilateral implants are rather clear in their clinical practice; they are conflicted by the question of whether they should withhold a treatment that is considered accepted medical practice from a group of subjects simply for the benefit of data collection. Given the low-incidence of deafness as a whole, and the small numbers of cochlear implant subjects as compared to studies of other treatments, such as heart stents or new drug studies, it is unlikely that large scale studies looking at the benefit of bilateral implantation will continue to be undertaken. Regarding the time course of the development of various binaural processing skills, studies by Buss and Eapen (cites included in comments to the Reference Section) were not evaluated	We have included studies that meet our eligibility criteria. Buss et al is included, Eapen et al is not reviewed because of sample size issue but cited in the discussion section. Bichey et al used mixed population, no data is available for adults only.

			by the Technology Assessment but do provide some insight into the time course of the development of binaural benefits such as the squelch effect, which appears to be continuing to develop even one year post implant. Regarding quality-of-life, Bichey & Miyamoto found an improvement using HUI Mark III and a favorable cost-utility associated with bilateral cochlear implantation in patients with profound hearing loss.	
Darla Franz	MED-EL Corporation	Discussion/Conclusion	Finally, we would again suggest that the committee consider some of the studies looking at localization abilities to address issues indirectly related to quality of life and binaural fusion. For example, one paper by Mani et al. that directly addresses fusion tells us that there is some degree of fusion in quiet. Fusion can indirectly be found in a series of studies which showed the significant presence of a squelch effect. This effect requires the integration of binaural / bilateral inputs. More generally, the ability to fuse dichotic electric stimuli by the ability to discriminate ITDs in electrical stimulation is shown by Laback et al. and Majdak et al.	We have included studies that met our eligibility criteria.
Darla Franz	MED-EL Corporation	References	We would suggest the following studies for re-consideration in the literature search:	
Darla Franz	MED-EL Corporation	Speech in noise topic	Superiority of bilateral cochlear implantation over unilateral cochlear implantation in tone discrimination in Chinese patients. Au D; Hui Y.;Ignace W. Am J Otolaryngol , 24(1), 2003, p. 19-23 ?Shows significant benefit of bilateral CI in lexical tone discrimination at SNRs of 5 dB and lower Multicenter U.S. Bilateral MED-EL Cochlear Implantation Study: Speech Perception over the First Year of Use. Buss E.;Pillsbury H.;Buchman C.;Pillsbury C.;Clark M.;Haynes D.;Labadie R.;Amberg S;Roland P.;Kruger P.;Novak M.;Wirth J.;Black J;Peters R.;Lake J.;Wackym P.;Firszt J.;Wilson B.;Lawson D.;Schatzer R.;D'Haese P.;Barco A. Ear Hear, 29(1), 2008 Jan, p. 20-32 ?Shows head shadow and summation effects evident instantaneously; binaural squelch reliably observed after one year of bilateral CI use after simultaneous implantation	Ricketts et al has subjects overlap with Buss E et al study. The study with maximum number of patients is now included in the draft. Eapen et al has sample size <10 and is cited within the discussion section. Mosnier et al is included in the review. Au et al published before 2004.

			Hearing-in-Noise Benefits After Bilateral Simultaneous Cochlear Implantation Continue to Improve 4 Years After Implantation. Eapen RJ;Buss E;Adunka MC;Pillsbury HC;Buchman CA Otol Neurotol 30(2) 2009 p. 153-9 ?Shows head shadow and summation remain stable; squelch still develops after one year or more of bilateral implant use Speech recognition for unilateral and bilateral cochlear implant modes in the presence of uncorrelated noise sources. Ricketts T.;Wesley Grantham D.;Ashmead DH;Haynes D.;Labadie R. Ear Hear, 27, 2006, p. 763-773 ?Shows small but significant bilateral benefit in difficult conditions with multiple noise sources; combined effects of binaural squelch and diotic summation sum up to approximately 10% Speech Performance and Sound Localization in a Complex Noisy Environment in Bilaterally Implanted Adult Patients. Mosnier I;Sterkers O;Bebear JP;Godey B;Robier A;Deguine O;Fraysse B;Bordure P;Mondain M;Bouccara D;Bozorg-Grayeli A;Borel S;mbert-Dahan E;Ferrary E. Audiol Neurootol , 14(2), 2008 Oct 2, p. 106-114 ?Shows binaural benefit in in quiet of 10% ($p < 0.005$), and 8% in 15 dB SNR noise	
Darla Franz	MED-EL Corporation	Speech in quiet topic	Speech understanding in Quiet and Noise in Bilateral users of the MED-EL COMBI40/40+ cochlear implant system. M?ller J.;Sch?n F.;Helms J. Ear Hear, 23, 2002, p. 198-206 ??? average score for recognition of monosyllabic words was 18.7 percentage points higher with both cochlear implants than with one cochlear implant ? significant at the 5% level.?	Excluded because of publication before 2004.
Darla Franz	MED-EL Corporation	Localization / Bilateral Topic	Horizontal-plane localization of noise and speech signals by postlingually deafened adults fitted with bilateral cochlear implants. Grantham D.;Ashmead DH;Ricketts T.;Labadie R.;Haynes D. Ear Hear, 28(4), 2007, p. 524-541 Sound localization in bilateral users of the MED-EL COMBI 40/40+ cochlear implant. Nopp P.;Schleich P Ear Hear, 25, 2004, p. 205-214	Grantham et al, Nopp et al, and Schoen et al are included in the final draft. Senn et al. Excluded because of small sample size.

			Minimum audible angle, just noticeable interaural differences and speech intelligibility with bilateral cochlear implants using clinical speech processors. Senn P;Kompis M.;Vischer M.;H?usler R. Audiol Neurootol , 10, 2005, p. 342-352 Sound localization and sensitivity to interaural cues in bilateral users of the MED-EL COMBI 40/40+ cochlear implant system. Sch?n F.;M?ller J.;Helms J.;Nopp P. Otol Neurotol , 26, 2005, p. 429-437	
Darla Franz	MED-EL Corporation	Localization / Unilateral Topic	Localization by Postlingually Deafened Adults Fitted With a Single Cochlear Implant. Grantham D.;Ricketts T.;Ashmead DH;Labadie R.;Haynes D. Laryngoscope, 118(1), 2008 Jan, p. 145-151	Excluded because of small sample size.
Darla Franz	MED-EL Corporation	Fusion Topic	Dichotic speech recognition by bilateral cochlear implant users. Mania A, Loizoua PC, Shoupb A, Roland P, Kruger P. International Congress Series 1273, (2004) 466?469. ?Shows that in quiet, bilateral implant users were able to fuse the information presented dichotically Binaural jitter improves sensitivity to interaural time differences in electric and acoustic hearing. Laback B;Majdak P;Goupell MJ J Acoust Soc Am , 123(5), 2008 May, p. 3055 Lateralization discrimination of interaural time delays in four-pulse sequences in electric and acoustic hearing. Laback B;Majdak P;Baumgartner W J Acoust Soc Am , 121(4), 2007 Apr, p. 2182-2191 Effects of interaural time differences in fine structure and envelope on lateral discrimination in electric hearing. Majdak P;Laback B;Baumgartner WD J Acoust Soc Am, 120(4), 2006 Oct, p. 2190-2201	Excluded because of small sample sizes (<10 subjects)
Darla Franz	MED-EL Corporation	Quality of Life Topic	Outcomes in bilateral cochlear implantation. Bichey B;Miyamoto RT. Otolaryngol Head Neck Surg , 138(5), 2008 May, p. 655-661 ?Shows improvement in quality of life (HUI Mark III) and a favorable cost-utility associated with bilateral	Excluded because of mixed population (adults and children).

			cochlear implantation	
Alice E. Holmes	American Academy of Audiology	General	This report is an attempt to cover the relevant literature from 2004-2010 on the status of cochlear implant in adults. While the report is fairly comprehensive, there are some gaps and misunderstandings in the conclusions. In the report, electrical-acoustic systems (EAS)/Hybrids are often lumped with standard cochlear implant arrays. These EAS studies have different criteria for implantation, are still investigational and use different non-FDA approved internal cochlear implant arrays as compared to standard cochlear implants. Therefore the inclusion of these devices (EAS) and the study outcomes, could significantly skew the conclusions.	A single study on the hybrid implant is now moved to the last section of the results
Alice E. Holmes	American Academy of Audiology	General	Because this report limited its study to post 2004 investigations, it omitted a number of excellent reports on the quality of life benefits of unilateral implantation. An excellent review of these of studies can be found in John Niparko?s textbook: Cochlear Implants, Principles and Practices (2009 edition). Therefore, there is a question about the need for future studies investigating the quality of life in unilateral implant cases, as this has been studied fairly extensively. However, studies are needed on bilateral and bimodal implant cases using quality of life measures as these are more recently mainstream treatment options.	We have included studies that meet our eligibility criteria.
Alice E. Holmes	American Academy of Audiology	General	One area that was not well addressed in the report was the effectiveness of bimodal stimulation. Very few controlled studies on the benefits of bimodal stimulation have been conducted and there is currently no standard protocol for the hearing fitting component of the bimodal treatment option. The majority of bilateral implantation studies did not include the bimodal paradigm as a control condition. Some recent results in studies on bimodal hearing suggest that the hearing aid in the opposite ear may provide different and very important information on prosody that cannot be obtained from a cochlear implant (Chang, Bai & Zeng, 2006; Ching, et al, 2007; Cullington & Zeng, 2010, 2011).	We have added a section bilateral versus bimodal in adults.
Alice E. Holmes	American Academy	General	Because of the lack of controlled studies with bimodal stimulation, we agree with the conclusion that further studies,	When reported in studies, we have added the rates of

	of Audiology		especially longer-term prospective studies, are needed to assess the additional benefits (e.g., improved health-related quality-of-life) with bilateral CI. Additionally, these studies should explore potential risks of bilateral cochlear implantation as compared with unilateral implantation.	device discontinuation.
Alice E. Holmes	American Academy of Audiology	General	In general the report is accurate and the conclusions are appropriate with the aforementioned issues noted.	Thank you.
Alice E. Holmes	American Academy of Audiology	Executive Summary		
Alice E. Holmes	American Academy of Audiology	Page ES2	>40 & <50% ---- >50 <60 question	
Alice E. Holmes	American Academy of Audiology	Introduction/ Background		
Alice E. Holmes	American Academy of Audiology	Page 1, 2nd paragraph, 1st sentence	Need to insert qualifier. ?In most cases of sensorineural hearing loss, the higher frequencies of sound are attenuated.	We have made changes to reflect this edit.
Alice E. Holmes	American Academy of Audiology	Methods		
Alice E. Holmes	American Academy of Audiology	Page 6, Comparators of interest	Questionable inclusion of EAS/Hybrid studies in this analysis.	Moved to the end of results section; no conclusion drawn from this study.
Alice E. Holmes	American Academy of Audiology	Results		

Alice E. Holmes	American Academy of Audiology	Page 9, 1st paragraph, Question 1, last sentence	Left out Nuerelec Implant. The Digisonic cochlear implant by Nuerelec is used in the US but is being implanted in Europe.	The Nuerelec is not FDA approved and was therefore not included in this report.
Alice E. Holmes	American Academy of Audiology	Page 12, Hybrid Implantation	These studies in most cases were using a modified internal device with a shorter electrode array and should not be compared directly with standard cochlear implants. In addition the criteria for implantation in these investigational devices is quite different ? less stringent than the FDA approved devices.	Moved to the end of results section, no conclusion drawn from this one study.
Alice E. Holmes	American Academy of Audiology	Page 17, Last paragraph, last 2 lines and 1st study listed on Table 5 page 18	The Most 2009 study was done on prelingual adults and therefore should be considered separately.	Studies have often combined both prelingual and postlingual deafness.
Alice E. Holmes	American Academy of Audiology	Page 18	The authors are using the Hybrid studies for this -- all of the studies (minus the one Hybrid one) quoted in the previous section used the FDA criteria of <40 or <50% on sentence material.	We have made changes to reflect this edit. Only one of 22 studies reported on the implant indication criteria.
Alice E. Holmes	American Academy of Audiology		Gifford et al 2010 report results on 22 participants with pre-CI sentence scores from 21 to 92%. This study does not meet the 30 subject criteria but does provide evidence on the possible benefits of expanded CI criteria with standard implant arrays	Did not meet eligibility criteria based on sample size as well as the type of test evaluated.
Gerhard Roehrlein	Advanced Bionics	General	Thank you for the opportunity to provide comments on the Agency for Healthcare Research and Quality?s (AHRQ?s) draft technology assessment, Effectiveness of Cochlear Implants in Adults with Sensorineural Hearing Loss. Advanced Bionics is a global leader in cochlear implant technology, and is also a wholly-owned subsidiary of Sonova, a firm committed to the development of innovative hearing solutions to address a wide spectrum of patient needs.	Thank you for your comment.
Gerhard	Advanced	General	Overall, this technology assessment recognizes that the	

Roehrlein	Bionics		evidence supports the many improvements in clinical outcomes and health-related quality of life that advances in cochlear implant technology have provided for patients with severe to profound hearing loss. The assessment contains many references to ?small number of subjects? in studies and urges ?cautious interpretation of results? throughout the document. It is important to recognize that the population size and limited procedure volume of cochlear implantation constrain practical study design options. Data from the Medicare Hospital Outpatient Prospective Payment System indicates that in 2009 1,481 cochlear implant procedures were performed (APC 0259) compared to 20,657 coronary stent placements (APC 104). Consequently, the small number of subjects in cochlear implant studies reflects the small size of the implanted population and the low volume of procedures performed.	Thank you for your comment.
Gerhard Roehrlein	Advanced Bionics	General	Randomized study designs and the use of blinding in studies would be infeasible because subjects must give consent to undergo surgical placement of the device and will be able to detect if the device has been activated. Also, since unilateral and bilateral cochlear implantation are considered accepted medical practices for deafness by the medical community (Balkany, et al, 2008), patients would choose direct access to care rather than participation in a study in order to gain access to this treatment. These factors make it impractical to conduct large, randomized studies in this population.	We have not suggested conducting large randomized trial.
Gerhard Roehrlein	Advanced Bionics	General	We recognize that broad quality of life (QOL) evaluation of cochlear implantation is important for understanding the effectiveness of this intervention. However, we also agree with the authors on the need for improved instruments to assess the effects of changes in hearing on QOL. Some instruments available today, for example the Health Utilities Index Mark III (HUI-3), are reasonably sensitive to interventions such as unilateral cochlear implantation. Sudden loss of hearing may also be registered by instruments such as the EQ5D. However, progressive hearing loss, or more subtle interventions, including bilateral	We have emphasized on developing better measures for disease-specific health-related quality-of-life.

			cochlear implantation are likely to be more difficult to evaluate effectively using today?s measures. Part of the problem is that quality of life measures have tended to focus on disease and have applied terms such as ?depression.? While severe to profound hearing loss is widely and accurately viewed as highly disabling, many deaf people do not consider themselves ill as such. Thus, measures targeting illness do not capture cochlear implant benefits. Ongoing work related to EQ5D focuses on alternative terms, such as ?embarrassment? as opposed to ?depression.? Attempts are also being made to counter the natural changes which deaf people make to their lifestyles such as restrictions which tend to defeat common questions on how much impact deafness has on daily life.	
Gerhard Roehrlein	Advanced Bionics	General	The Nijmegen Cochlear Implant Questionnaire, which was referred to in the Technology Assessment, is an example of a sensitive measure that contains many ideas appropriate for the assessment of deafness. Factoring in communication and isolation issues specific to deafness appears wholly appropriate for a comprehensive QOL measure which seeks to capture a realistic picture of everyday life.	Agree, evaluations using disease-specific health-related quality-of-life data are very much needed in this population.
Gerhard Roehrlein	Advanced Bionics	General	Clearly, there is a need for measures which take a much more real world approach when assessing the impact of more severe to profound levels of deafness. For example, pediatric measures are required to look broadly from education right through to employment and factor in the potential impact which modern interventions have on independence and ability to compete effectively for higher level employment opportunities. An aging adult population with increased presbycusis will also require measures which capture lifestyle changes which are sometimes invisible to today?s QOL measures.	Thank you for your comment.
Gerhard Roehrlein	Advanced Bionics	General	We?ve included the above comments regarding population size and quality of life instruments in the General section because they apply to many findings throughout this assessment.	Thank you for your comment.
Gerhard	Advanced	Executive		

Roehrlein	Bionics	Summary		
Gerhard Roehrlein	Advanced Bionics	ES4, KQ3	In a randomized controlled trial evaluating sequential bilateral cochlear implants, the second ear implant resulted in negative results for quality of life after the first ear implant that may have been due to worsening tinnitus after the second ear implant.? Please see detailed comment on Key Question 3: Sequential Bilateral versus Unilateral Cochlear Implantation in the Results section.	Clarified.
Gerhard Roehrlein	Advanced Bionics	ES4, Discontinuation of Use	Please see detailed comment on Key Question 3a and 3b: Discontinued use of cochlear implant in the Results section.	
Gerhard Roehrlein	Advanced Bionics	ES5, Discussion	Of note, results from a randomized controlled trial that included 28 subjects indicated that the worsening of tinnitus after the second implant might have offset the positive binaural benefit.? Please see detailed comment on Key Question 3: Sequential Bilateral versus Unilateral Cochlear Implantation in the Results section.	Clarified
Gerhard Roehrlein	Advanced Bionics	Methods		
Gerhard Roehrlein	Advanced Bionics	Page 6, Interventions of Interest	Please see detailed comment on Key Question 2: Pre versus post unilateral cochlear implants: Hybrid implantation in the Results section.	Hybrid is moved to a separate section at the end of results section and has no bearing on the conclusions
Gerhard Roehrlein	Advanced Bionics	Page 6, Outcomes of Interest	We included data on device non-use and hearing loss after cochlear implantation.? Please see detailed comment on Key Question 2: Pre versus post unilateral cochlear implants: Hybrid implantation in the Results section.	Clarified
Gerhard Roehrlein	Advanced Bionics	Page 7, Predictors of Interest	Please see detailed comment on Key Question 2A: Implanted device in the Results section.	Edited
Gerhard Roehrlein	Advanced Bionics	Results		
Gerhard Roehrlein	Advanced Bionics	KQ1, Recalls	Two of the three manufacturers distributing cochlear implants in the U.S. import their products from another country. Different mechanisms apply for U.S. market withdrawals of medical products depending on whether the manufacturer is based in the United States or another country. Manufacturers	We have made changes to reflect these explanations.

			based in the U.S. are subject to product recalls while firms based outside of the U.S. may be subject to different mechanisms such as import bans which may not be found in the ?grey literature.? We would like to clarify a reference made to the November 2010 voluntary recall of Advanced Bionics? HiRes 90K cochlear implant. This voluntary recall was in response to a device malfunction which occurred within 8 to 10 days post device activation. This issue, which subsequently required explantation, has occurred in two of 28,000 devices. As written by the authors, the sentence inaccurately states that the issue required ?explantation within 8-10 days of device activation.	
Gerhard Roehrlein	Advanced Bionics	KQ2, Pre versus Post Unilateral	Hybrid implantation For the reasons explained below, literature and data concerning hybrid devices should be included in a separate assessment. The hybrid device is designed for a different population than a cochlear implant. Cochlear implants are prescribed for individuals with severe-to-profound hearing loss (? 70 dB HL average thresholds for 500, 1000, and 2000 Hz) who obtain limited benefit from hearing aids. In contrast, the hybrid device is targeted at individuals who have residual low-frequency hearing (profound loss only at frequencies greater than 1500 Hz) and who are still able to understand some speech with a hearing aid. More to the point, the hybrid device is designed for individuals who ?have too much residual hearing and speech perception to qualify for conventional cochlear implants? (Gantz et al. 2009, reference 12 on page 37). The hybrid device is not a conventional cochlear implant and is not approved by the FDA. As an experimental device, patient data associated with its use should not be combined with data from standard cochlear implants.	The single study is now moved to a separate section and no conclusions are made from this study.
Gerhard Roehrlein	Advanced Bionics	KQ2A	Key Question 2A is concerned with ?preoperative patient characteristics associated with successful attainment of	We had added AzBio score results reported in Spahr 2004

			?improved communication-related outcomes?.? Although this potential modifier of interest is not ?preoperative,? the assessment summarizes the outcomes associated with different types of devices by stating that ?none of the studies found significant differences?among patients who received different cochlear implant devices (page 21). The review failed to recognize that contemporary cochlear implant users demonstrate ceiling effects on the traditional tests of speech perception that are mentioned in that analysis (Gifford et al. 2008, reference 11). In fact, technology differences become apparent only when more difficult test materials are used. For example, one of the references cited (Spahr and Dorman 2004, reference 37) showed superiority of the Advanced Bionics CII implant over the Nucleus 3G implant when difficult speech test materials were used to evaluate subjects who had been matched by demographic variables and word recognition ability in quiet. Other studies which were not included in this assessment also show that technology can influence outcomes when test materials are designed to mimic real-world listening (Spahr et al. 2007, Haumann et al. 2010).	(ref 37). However, as this study was the only quality B study comparing Advanced Bionics CII implant with Nucleus 3G implant, our conclusion remains unchanged.
Gerhard Roehrlein	Advanced Bionics	KQ3	Sequential Bilateral versus Unilateral Cochlear Implantation On pages 26 and 30, the finding of ?worsening tinnitus? in patients who received bilateral implants needs clarification. A causal relationship does not appear to exist between tinnitus and bilateral implantation. Tinnitus is considered to be a potential complication of cochlear implantation in general. In fact, tinnitus is listed as a surgical risk of cochlear implantation on the FDA website and is included as a potential post-operative complication in the package inserts of the three cochlear implant manufacturers. Thus, increased tinnitus could occur with either unilateral or bilateral cochlear implantation.	We have edited to reflect exactly how the study reported.
Gerhard Roehrlein	Advanced Bionics	KQ3A&B	Discontinued use of cochlear implant It is important to note that complete hearing loss, the adverse result attributed to the hybrid by the authors, is actually an expected consequence of standard cochlear implantation. This	Hybrid implant has been moved to a separate section and no conclusions were derived from this study.

			information is included as a warning in the labeling of the three FDA-approved cochlear implant devices, and is an unremarkable finding.	
Gerhard Roehrlein	Advanced Bionics	Discussion/Conclusion		
Gerhard Roehrlein	Advanced Bionics	Page 34	Device non use rates secondary to hearing-related complications was 4.0 percent among subjects with cochlear implants.? Please see detailed comment on Key Question 2: Pre versus post unilateral cochlear implants: Hybrid implantation in the Results section.	Device non-use section has been expanded.
Gerhard Roehrlein	Advanced Bionics	Page 35	Potential limitations of our review?. Existing studies do not allow accurate conclusions to be drawn.? Please see detailed comment on impact of population size on studies in the General section.	Edited.
Gerhard Roehrlein	Advanced Bionics		We encourage AHRQ to develop methods of assessing technology that take into consideration the differences in the evidence available for recipients of cochlear implants and other interventions that provide significant clinical and HRQOL benefits to small segments of the population at large. We would be willing to work with AHRQ to develop technology assessment methods appropriate for smaller populations.	Thank you for your comment.
Gerhard Roehrlein	Advanced Bionics	Future Research Needs	Given the small size of the cochlear implant population, it would not be feasible to conduct ?good quality? studies as defined in this assessment (i.e., large study samples, randomized treatment designs) or to maintain a large database or registry sufficient for multivariate analyses.	We have not suggested designing new randomized studies or large study samples for future research. Observational studies, if well designed and appropriately analyzed can qualify to be good quality studies.
Gerhard Roehrlein	Advanced Bionics	Future Research Needs	A need exists 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. For example, new tests would incorporate listening to multiple talkers at various distances or listening in different types of noise or noisy environments. Future research also should focus on developing quality of life	Thank you, we have changed to reflect this edit.

			instruments specifically designed for people with severe-to-profound hearing impairment, so that subjective benefits associated with unilateral and bilateral cochlear implantation can be assessed quantitatively.	
Gerhard Roehrlein	Advanced Bionics	Future Research Needs	It is worthy to note that recent research indicates that an expanded population of individuals with hearing impairment may be able to benefit from cochlear implantation (Gifford et al., 2010). Individuals with some residual hearing who currently use hearing aids may, in fact, hear better with a cochlear implant than with conventional acoustic amplification. Future research should focus on expanding the candidacy profile of cochlear implants (e.g., degree of hearing loss, speech perception ability) and assessing consequent outcomes.	Thank you, we have changed to reflect this edit.
Gerhard Roehrlein	Advanced Bionics	References	Balkany T, et al. Editorial: William House Cochlear Implant Study Group Position Statement on Bilateral Cochlear Implantation. Otology & Neurotology, 2008; 29:107??108. Haumann S, Lenarz T, B?chner A. Speech perception with cochlear implants as measured using a roving-level adaptive test method. ORL 2010; 72:312?318. Spahr AJ, Dorman MF, Loiselle LH. (2007) Performance of patients using different cochlear implant systems: effects of input dynamic range. Ear and Hearing, 2007; 28:260?275. Gifford RH, Dorman MF, Shallop JK, Syndlowski SA. Evidence for the expansion of adult cochlear implant candidacy. Ear and Hearing, 2010; 31(2):186-194.	We have verified and included studies that met our eligibility criteria
Dan Sheridan	CI Recipient	General	I would like to see more discussion of what adverse effects as a result of the surgical procedure, if any, the CI recipients had. I'd also like to know how those adverse events differ between people with a single implant and those with two implants. The review does a good job exploring adverse effects that cause people to stop using the CI, but not adverse effects that people may experience while still using the CI.	Device non-use and reasons of device non-use were only outcome that was defined a priori as outcomes of interest.

Dan Sheridan	CI Recipient	General	When I was trying to decide whether to get a CI, I read a study which concluded that about 1/3 of CI recipients experience a delayed onset dizziness weeks or months after the surgery. It's been years since I read this article, so I don't remember the details, but I think the authors theorized that the dizziness was a delayed reaction by the cochlea as it healed from the "insult" of the surgery. When I discussed this study with several friends who have CIs, I learned that most of them have dizziness issues, but don't attribute it to the CI. One friend started having mysterious loss of balance episodes while riding a bicycle. Twice he crashed into trees along the road and was injured.	Thank you for your comment.
Dan Sheridan	CI Recipient	General	I did end up getting a CI. I'm very happy with it: the results are amazing and I have no dizziness issues. However, when I was exploring the idea of getting an implant, I would love to have seen objective information about the likelihood of disabling vertigo. That would have helped me to make a more informed decision. Should I ever consider getting a second implant, I'd like to know how that will change my risk of dizziness. Thank you.	We did not come across this outcome in studies that we reviewed.
Sarah Sydlowski Sarah Sydlowski	CCF, AAA	General	The study was overall well-organized and well-written. The general conclusions, that cochlear implantation is a safe and effective intervention option for adults with sensorineural hearing loss, is accurate and well stated. However, the authors also reported some degree of inconclusivity on several points, particularly related to outcome measures and bilateral cochlear implantations that raise some concerns about the study. The greatest concern is that the overall scope of this study is may be more narrow and limited than would be preferred. Specifically, inclusion criteria and summary comments were such that findings can only be generalized to a small sample of the adult CI recipient population.	We found many studies on patient reported outcomes on quality-of-life in unilateral implants although this sample was restricted by ≥30 and there was consistent benefit. However, we found only 3 studies that reported quality-of-life in bilateral implants although we used N≥10, and there were inconsistent results across various domains analyzed.
Sarah Sydlowski	CCF, AAA	General	The study needs to better define the population of interest. From the design and implementation of the review, it seems	Sensorineural deafness is the most prevalent form of

			that the focus is on cochlear implantation in adults and generalizing findings to the Medicare population. However, the background statements in both the Executive Summary and Introduction describe only presbycusis as the cause of sensorineural hearing loss in cochlear implant recipients. This is a narrow view of the adult population for which cochlear implantation is a viable and successful intervention.	hearing loss among adults, especially presbycusis is the most common type of hearing loss in the U.S.
Sarah Sydlowski	CCF, AAA	General	There are some concerns with the description of the methods of this study. In particular with the statement ?we thus excluded studies with only audiological outcomes and studies with music tests as the only outcomes? (page 6). The authors specifically state that outcomes of interest include speech perception outcomes including open-set sentences and two syllable or multi-syllable words, then proceed to exclude studies that provide this data in isolation. Additionally, there are a variety of outcome measures that may be utilized in clinical audiologic practice depending on patient performance; exclusion of these data would not necessarily provide a complete view of the benefits or performance differences between unilateral, bimodal, and bilateral CI recipients.	The current draft includes localization outcomes.
Sarah Sydlowski	CCF, AAA	General	There is concern the wording of the key questions to only include recipients who fall within a specific range of pre-implantation speech recognition scores. By confining outcome measures to such a narrow range, actual benefit by cochlear implant recipients may not be accurately represented. Recent research suggests that expansion of cochlear implant candidacy criteria may be warranted based on performance outcomes with cochlear implant(s) compared to hearing aids (Gifford et al, 2010; Trembly, Bergeron, & Fallon, 2008; Dowell, Hollow, & Winton, 2004). It would be a critical feature of this study to include patients with pre-implantation scores who may fall outside of traditional candidacy. Additionally, by excluding those patients with <40% open-set speech recognition, the current study completely excludes assessment of benefit for a large number of potential cochlear implant recipients. Rather, the	We did not exclude studies of patients <40% open-set speech recognition. In fact, our review states that there were two studies that enrolled patients with <40% open-set speech recognition. Only handful of studies mentioned this as an indication for cochlear implant and we state that this criterion is not clearly reported in studies.

			study focuses on benefit obtained for those individuals with open-set speech recognition between 40% and 60%, which is a newer potential recipient population.	
Sarah Sydlowski	CCF, AAA	General	There is concern that evaluation of audiological outcomes in this review did not appear to take into account the various levels of skill that different speech recognition measures assess. For example, BKB-SIN scores are presented along with HINT sentences. Reference was even made to HINT sentences not being presented in noise, presumably as a flaw of a study. In fact, HINT sentences were not designed to be presented in noise. They were designed as a pseudoadaptive hearing in noise test; these materials have been historically used for cochlear implant recipients although it is not necessarily the most appropriate test battery for evaluation. The differences in test measure and outcomes is an important distinction to make. The recommendation would be to re-evalute these results with this point in mind.	Studies report using HINT in quiet and noise and we have summarized accordingly. We recognize that some speech perception measures are different than others and it will not be very useful to create a table for each of these measures and evaluate evidence individually.
Sarah Sydlowski	CCF, AAA	General	Finally, the inclusion of hybrid cochlear implant in this review is somewhat of a concern. The clinical indications for hybrid cochlear implantation are very different from traditional, full insertion cochlear implantation. Specifically, greater levels of residual hearing are required and both acoustic and electric stimulation are utilized in the same ear. While hybrid implant is a viable intervention for appropriate candidates, it does not serve the same population as traditional implantation. For this reason, it may be preferable to consider its clinical viability in a separate report.	We have moved this single study to a separate section.
Sarah Sydlowski	CCF, AAA	Executive Summary		
Sarah Sydlowski	CCF, AAA	KQ2A	The authors suggest that there is a low level of evidence regarding the association between preoperative patient characteristics and better postoperative speech outcomes. In my clinical experience, it is generally recognized that certain characteristics such as residual hearing, shorter duration of deafness, greater spiral ganglia survival, and postlinguistic deafness (versus prelinguistic) result in overall better speech	We have clarified this section.

			recognition with cochlear implant.	
Sarah Sydlowski	CCF, AAA	KQ3	The authors state that the second ear implant may decrease quality of life due to worsening tinnitus in the second ear. This observation contradicts my clinical experience and I question whether this is an observable trend, or single situation. I would caution the authors to suggest generalizability of this statement.	We have clarified that the authors of the original study report that second ear implant may decrease quality of life due to worsening tinnitus in the second ear.
Sarah Sydlowski	CCF, AAA	Introduction/ Background	The background section is well-organized and well-written, however, it appears there is a narrowed focus beyond the population that this study purports to examine. While the information presented in this section is correct regarding hearing loss in the elderly, this report should be focusing on cochlear implant recipients ages 18 and older. As a result, etiologies beyond presbycusis should be discussed. Ototoxicity, progressive syndromic and non-syndromic hearing loss, otosclerosis, trauma, autoimmune disease, etc. are not mentioned and should be. Additionally, differentiation between sound detection and speech recognition and the differences between hearing aids and cochlear implants bear mentioning. This is an important omission. Clinical experience suggests despite variability in speech recognition, cochlear implant recipients, regardless of pre-CI characteristics, can detect sounds at or near normal hearing levels. Conversely, many hearing aid recipients with equivalent degrees of hearing loss may not possess this ability.	Hearing aids evaluation is not of interest to this report. Regarding various etiologies, we have made changes to reflect this edit.
Sarah Sydlowski	CCF, AAA	Methods	The technical expert panel, while including a physician with expertise in adult cochlear implantation, did not include an audiologist with the same expertise at the review and revisions stage. Because many of the outcomes of interest are related to audiologic measures, it would be important to have a cochlear implant audiologist as an expert technical contributor at all stages of development of this document.	Our current version includes localization outcomes.
Sarah Sydlowski	CCF, AAA	Results		
Sarah Sydlowski	CCF, AAA	KQ2&2A	Device characteristics do not reflect currently available technology for any manufacturer except for Advanced Bionics (and only internal devices are reported). As a result, these	We relied on published studies and we have reported results as available.

			findings are not generalizable to currently available cochlear implant technology.	
Sarah Sydlowski	CCF, AAA	KQ2	The reporting of unilateral CI vs. hearing aids was accurately and well-presented. It would have been beneficial to have seen data presented in this more specific manner throughout the paper.	Thank you for your comment.
Sarah Sydlowski	CCF, AAA	KQ2, page 18	The authors reported that there were no studies that used the results of open-set sentence tests for CI indication. We would submit that this finding is due to the limitations of the inclusion criteria that was employed for this study. Open-set sentence recognition is clinically the single most commonly used measure for CI evalution. This statement raises concerns regarding the generalizability of these findings. Additionally, the word recognition scores reported were for hybrid candidacy, not standard cochlear implant candidacy.	We recognize that the use of open-set sentence recognition is the most commonly used measure for CI evaluation, but published studies (except for a handful) have failed to mention this as their inclusion criteria. We have moved hybrid to a separate section.
Sarah Sydlowski	CCF, AAA	Discussion/Conclusion	Although bilateral cochlear implantation in adults is less common than unilateral cochlear implants, there is existing research that suggests improved performance with bilateral cochlear implants. Exclusion criteria in this study may have eliminated useful information in the evaluation of the efficacy of bilateral implantation (e.g., Chang et al, 2010; Litovsky, Parkinson, and Arcaroli, 2009; Budenz et al, 2009) due to only audiologic data being reported or small sample sizes (i.e., <30). The recommendation would be to revisit these exclusion criteria due to the small cochlear implant population (particulaly bilateral cochlear implant population) and the importance and usefulness of speech recognition measures as outcome data. Overall the discussion and conclusion are well-formulated and follow reported results. Positive outcomes generally observed clinically with cochlear implanation may be under-emphasized due to concerns previously described.	We included bilateral CI with sample size of at least 10 and speech perception tests using multi-syllable and open-set sentences. Litovsky et al 2009 is included. Other two studies did not meet eligiblility criteria (1. Chang et al – did not compare with unilateral CI or condition and has overlapping subjects with Dunn et al publications; 2. Budenz et al used CNC word lists).
Sarah Sydlowski	CCF, AAA	Tables	Well-organized, useful, easy to follow	Thank you.
Sarah Sydlowski	CCF, AAA	Appendices	Well-organized, useful, easy to follow. Would recommend considering more details in appendix describing inclusion strategy.	Thank you for your comment.

[1] Names are alphabetized by last name. Those who did not disclose name are labeled "Anonymous Reviewer 1," "Anonymous Reviewer 2," etc.

[2] Affiliation is labeled "NA" for those who did not disclose affiliation.

[3] If listed, page number, line number, or section refers to the draft report.

[4] If listed, page number, line number, or section refers to the final report.