Supplementary Digital Content 1

Estimates of the gain in health-related quality of life (health utility) associated with bilateral cochlear implantation compared with unilateral cochlear implantation in bilaterally severely-profoundly post-lingually deafened adults

(This document is supplementary to the paper by Summerfield, Kitterick, and Goman entitled 'Development and critical evaluation of a condition-specific preference-based measure sensitive to binaural hearing in adults: the York Binaural Hearing-related Quality of Life System'.)

1. Introduction

1.1. Estimates of the gain in health utility associated with bilateral implantation compared with unilateral implantation in bilaterally severely-profoundly post-lingually deafened adults have been obtained in three ways: a retrospective study (Bichey and Miyamoto 2008), scenario analyses (Summerfield, Marshall, Barton, et al. 2002; Kuthubutheen, Mittmann, Amoodi, et al. 2015), and prospective randomized controlled trials (Summerfield, Barton, Toner, et al. 2006; Smulders 2016; Smulders, van Zon, Stegeman, et al. 2016).

1.2. This supplementary digital content evaluates these studies. We start by considering estimates of health utility associated with unilateral implantation measured prospectively in patients. These estimates can be used to calibrate the results of some of the methods used to estimate the gain associated with bilateral implantation.

2. Unilateral implantation

2.1. Table 1 lists mean values of health utility obtained with the HUI3 in the United States from a group of 46 adults before and 12-months after they received unilateral implants in comparison with a group of 16 non-implanted controls (Palmer, Niparko, and Wyatt 1999). Before implantation, there was no difference in mean health utility between the groups. Twelve months after implantation, there was a difference of +.20. The control group showed no change in mean health utility. The implanted group showed an improvement of +.20.

2.2. Table 2 lists mean values of health utility obtained with the HUI3 in the United Kingdom from a group of 311 patients before and 9-months after unilateral implantation (UK Cochlear Implant Study Group 2004). Despite the UK patients reporting poorer health than their US counterparts both before and after implantation, the improvement in health utility attributable to implantation was the same as the US estimate at +.20 (after rounding).

3. Bilateral implantation

3.1. <u>Retrospective study (Bichey and Miyamoto 2008)</u>

3.1.1. Twenty three users of bilateral implants completed the HUI3 three times. They considered their state of health 'for the time period just before receiving the first cochlear implant, just before receiving the second implant, and at the most recent time of sampling' (Bichey and Miyamoto 2008, p. 656). Table 3 lists the resulting mean values of health utility and the changes in utility between no implant and one implant, and between one implant and two. The last of these – the difference in health utility between unilateral and bilateral implantation – was +.12 (95% CI .09 to .14).

3.1.2. Two limitations of retrospective studies should be borne in mind in assessing this estimate. First, retrospective studies may recruit only those participants who have achieved successful outcomes. Restricted selection may arise either by design or because only those patients displaying successful outcomes are willing to participate.

As a result, benefits may be exaggerated compared to those which would be measured in a prospective cohort that included the patients experiencing less successful outcomes. In the case of the study reported by Bichey and Miyamoto, the authors state that they reviewed the database of their research laboratory ‘to identify all cochlear implant users currently using bilateral implants. Twenty-three patients were identified. All patients were currently using both cochlear implants …’. It is not clear whether the 23 participants included all of the patients who had undergone bilateral implantation in their facility or whether other patients had received bilateral implants but were not current users of both implants.

3.1.3. A second limitation of retrospective studies is that participants’ recollection of health states experienced some years previously may be inaccurate. Having achieved an improved health state, they may recall previous health states as being less advantageous than they actually were. It not possible to be confident whether this effect influenced the results in Table 3. We note, however, that the mean utility before receiving a first implant (.33, .27 to.39) is significantly lower than the corresponding values measured in the prospective studies reviewed in Section 2 of this supplementary digital content. Those values were .58 (.53 to .63) reported by Palmer, Niparko, & Wyatt (1999) in the US (Table 1), and .43 (.41 to .46), reported by the UK Cochlear Implant Study Group (2004) (Table 2). The mean utility before receiving the second implant measured by Bichey and Miyamoto, .69 (.64 to.75), is also significantly lower than the corresponding value of .78 (.73 to .83) measured by Palmer, Niparko, and Wyatt (1999), though it is not lower than the value of .63 (.61 to .65) measured by the UK Cochlear Implant Study Group (2004). The values measured by Bichey & Miyamoto for no implant and one implant are also lower than values measured from patients in the study by Kuthubutheen, Mittmann, Amoodi, et al. (2015) which is described in the next section.

3.1.4. In summary, the retrospective design of the study reported by Bichey and Miyamoto (2008) may have meant that their data were affected by selection bias and recall bias in ways that exaggerated the improvements in health utility measured with the HUI3 for the comparison of unilateral implantation with no intervention, and for the comparison of bilateral implantation with unilateral implantation.

3.2. <u>Scenario analyses (Summerfield, Marshall, Barton, et al. 2002; Kuthubutheen, Mittmann, Amoodi, et al. 2015)</u>

3.2.1. In scenario analyses, researchers describe two or more states of health, typically in the form of written vignettes. Informants are asked to consider that the states apply to them and to value the states. Valuations may be conducted in several ways: using a Generic PBM, the time trade-off, the standard gamble, or a visual analogue scale. The aim is to determine whether valuations of the states differ. The difference may then be used to inform an exploratory cost-effectiveness analysis.

3.2.2. Summerfield, Marshall, Barton, et al. (2002) wrote vignettes describing four states: (1) profound post-lingual deafness with no benefit from acoustic hearing aids (‘Traditional candidates’ for cochlear implantation); (2) profound post-lingual deafness with marginal benefit from acoustic hearing aids (‘Marginal hearing-aid users’); (3) experiencing typical outcomes from unilateral implantation; and (4) experiencing typical outcomes from bilateral implantation. A group of 70 clinicians and researchers with knowledge of hearing loss and cochlear implantation used the time trade-off to value the four states. They were asked to imagine that they would live until they were

75 years old and to declare the number of years in their remaining life expectancy that they would give up to be free of the limitations described in the vignette. If their current age was *y* years and they were prepared to give up *x* years, then their valuation was calculated as *(75-y-x)/(75-y).*

3.2.3. The entries in the fourth column of the 1st to 4th lines of Table 4 are the mean values of the resulting valuations of the four states. The authors, in order to validate their results, compared the estimates for states involving no implant and one implant with corresponding values measured in patients. Those measures were obtained with the Mark II Health Utilities Index and are listed in the fourth column of the 5th to 8th lines of Table 4. The values measured with patients are significantly lower than the values estimated by volunteers. The authors hypothesized that the values from patients reflected comorbidities which were absent from the considerations of the volunteers. Accordingly, the authors re-scored the measures from patients after setting each patient to the highest levels of the *Hearing* and *Speech* dimensions. The resulting values are in the 5th column of Table 4. The authors then calculated the difference between the values in the 4th and 5th columns in order to estimate the loss of utility among the patients that might be attributed to problems with hearing and speaking. These differences did not differ significantly from the corresponding differences calculated from the estimates of volunteers. The authors suggested that this statistical similarity gave credibility to the volunteers' valuations, including their estimate of the utility associated with the state of benefitting from bilateral implantation, which are listed in Table 5. The mean value of utility of the state of benefitting from bilateral implants estimated by volunteers was .965. The mean value of the utility of the state of benefitting from a unilateral implant was .934. The difference was +.031 (+.018 to +.042) and was taken as an estimate of the incremental gain in utility associated with bilateral compared with unilateral implantation.

3.2.4. Kuthubutheen, Mittmann, Amoodi, et al. (2015) wrote vignettes describing typical states of being severely-profoundly hearing impaired with (1) no intervention, (2) a unilateral cochlear implant, and (3) bilateral cochlear implants. The vignettes were valued by four groups of informants: patients with severe-profound deafness who were eligible for cochlear implantation (N=30); patients with severe-profound deafness who were users of a unilateral implant (N=30); patients with severe-profound deafness who were users of bilateral implants (N=30); and clinical professionals with knowledge of deafness and cochlear implantation (N=52). Each member of each group valued each scenario using each of four methods: HUI3, EQ5D-3L, EQ-VAS, and TTO with a time frame of 30 years.

3.2.5. Table 6 reproduces Table II in Kuthubutheen et al. (2015). Considering all of the groups of informants together, the estimates of the incremental change in utility between unilateral and bilateral implantation are +.035 (HUI3), +.04 (EQ5D-3L), +.07 (EQ-VAS), and +.12 (TTO).

3.2.6. The results reported by Summerfield et al. (2002) may be susceptible to two limitations of scenario analyses which were largely avoided by the inclusion of groups of patients in the study reported by Kuthubutheen et al. (2015). First, vignettes may not describe health states in ways that are understood by informants. Second, the imagination of a health state by an informant may differ from the reality of experiencing it as a patient. Both studies are susceptible to a third limitation which is that vignettes usually describe typical good outcomes from treatments. They do not capture negative side-effects or poor outcomes. Thus, while scenario analyses reflect individual differences in the valuation of an outcome, they do not reflect the heterogeneity of outcomes themselves. For these reasons, scenario analyses may provide estimates of the values of health states which are towards the upper end of the range of values that would be reported by patients.

3.3. Randomized controlled trials (Summerfield, Barton, Toner, et al. 2006; Smulders, van Zon, Stegeman, et al. 2016)

3.3.1. Randomized controlled trials (RCTs) compare outcomes between two or more alternative treatments for a condition. Patients who meet criteria of candidacy for both treatments are randomized to receive one. Random assignment controls for covariates, both known and unknown, which might otherwise bias outcomes. Two RCTs have been reported which have provided measures of the gain in utility between unilateral and bilateral implantation in post-lingually deafened adults.

3.3.2. Summerfield, Barton, Toner, et al. (2006) randomized 24 users of unilateral implants to two groups of 12. Group 1 received a second implant immediately. Group 2 waited 12 months before receiving a second implant during which time they acted as controls for late-emerging benefits of the first implant. Measures were obtained from both groups at baseline and then 3 and 9 months after Group 1 received a second implant. Additional measures were obtained from Group 2 3 and 9 months after they received their second implant. The measures included HUI3, EQ5D-3L, EQ-VAS, SSQ (separate measures for Speech Hearing, Spatial Hearing, and Other Qualities of Hearing), the Glasgow Health Status Index (GHSI), and Annoyance due to Tinnitus.

3.3.3. The authors reported two analyses. The first compared measures between the groups 3 and 9 months after Group 1 received their second implants. In the second analysis, the two groups were combined and 'before-and-after' comparisons were made between baseline measures and measures obtained 3 and 9 months after patients received their second implant.

3.3.4. Table 7 reports results of the first analysis. The values in the table are the amounts by which the change in a measure in Group 1 exceeded the change in Group 2 calculated while controlling for differences among patients at baseline (Vickers and Altman 2001). The only outcome measure which shows a consistently significant advantage for bilateral over unilateral implantation is the measure of spatial hearing from the SSQ. None of the generic measures of HRQL shows a significant difference.

3.3.5. Table 8 reports the results of the second analysis. The values in the table are the mean differences between the baseline value of a measure and the value obtained 3 months and, separately, 9 months after patients received their second implant. The condition-specific measures from the SSQ that show consistently significant advantages for bilateral over unilateral implantation. The generic measures of HRQL do not show significant differences.

3.3.6. Smulders (2016; Smulders et al. 2016) randomized 38 patients either to receive a unilateral implant (N=19) or to receive simultaneous bilateral implants (N=19). Quality-of-life-related outcomes were measured before implantation and then one and two years after implantation. Table 9 lists values of each outcome measure, and the difference between them, at each time point. All but one of the differences between the groups were small and not significant. The HUI3, for example, yielded a difference of .03 one year after implantation and of .04 two years after implantation.

3.3.7. In principle, RCTs provide the best evidence of the effects of alternative treatments. However, both RCTs described here were under-powered statistically. The following analyses put that statement into context. First, consider that the standard deviation of values of health utility measured with HUI3 is of the order of 0.2 (Tables 1 and 2). Suppose that there is an increase in health utility between unilateral and bilateral implantation and that its size is .03. If so, then two groups of 698 participants would be required to achieve a probability of .8 of rejecting the null hypothesis (that there is no difference in health utility) when the alternative hypothesis (that there is a difference of .03) is true at a significance level of $p<.05$ (e.g. https://clincalc.com/stats/samplesize.aspx). Thus, neither trial came close to recruiting the required number of participants to achieve adequate statistical power.

3.3.8. The theoretical probability of rejecting the null hypothesis with two groups of 12 is .056 and with two groups of 19 is .067 (e.g. https://clincalc.com/stats/Power.aspx). We ran simulations of each trial in order to elaborate on these predictions. We defined two normal distributions of values of health utility each with a standard deviation of 0.2 and a difference between their means of .03. We then sampled randomly from each distribution and compared the two samples with a 2-tailed t-test. The sample sizes were 12 in simulating the trial reported by Summerfield et al. (2006) and 19 in simulating the trial reported by Smulders et al. (2016). We ran 1000 simulations of each trial. In 11 out of 1000 simulations of the trial reported by Summerfield et al. (2006), the mean utility for the bilateral group was significantly smaller than the mean utility for the unilateral group; in 935, there was no significant difference; and in 53 the mean utility for the bilateral group was significantly larger than the mean utility for the unilateral group. The corresponding numbers from simulations of the trial reported by Smulders et al. (2016) were 9, 932, and 59. Thus, the proportions of simulations giving significant results were .064 and .068, which are similar to the theoretical predictions from the power calculations. Thus, the most likely outcome from each trial was the finding of no significant difference in health utility measured with the HUI3 between unilateral and bilateral implantation. This was what each trial reported.

4. Conclusions

4.1. There are limitations in each of the studies which have sought to estimate the gain in health utility associated with bilateral implantation compared with unilateral implantation in bilaterally severely-profoundly post-lingually deafened adults. In the case of the retrospective study and the two scenario analyses, weaknesses in the experimental design make it difficult to draw confident conclusions. In the case of the two RCTs, the design is intrinsically powerful, but its implementation was underpowered.

4.2. Where some or all of the evidence has been assessed in systematic reviews (Bond et al. 2009; Lammers et al. 2011; Health Quality Ontario 2018), authors have concluded that there probably is an increase in HRQL associated with bilateral implantation, but its size is small – in the range from .03 (Bond et al. 2009) to .035 (Health Quality Ontario, 2018) – and that studies with better designs and greater statistical power are needed to reduce the uncertainty.

5. References

Bichey, B.G., Miyamoto, R.T. (2008). Outcomes in bilateral cochlear implantation. *Otolaryngology—Head and Neck Surgery*, 138, 655-661.

Smulders, Y.E. (2016) *Unilateral versus simultaneous bilateral cochlear implantation in adults; a randomized controlled trial.* Doctoral Thesis, University of Utrecht, the Netherlands.

Smulders, Y.E., van Zon, A., Stegeman, I., et al. (2016). Cost-utility of bilateral versus unilateral cochlear implantation in adults: a randomized controlled trial. *Otol Neurotol* 37, 38-45.
Summerfield, A.Q., Marshall, D.H., Barton, G.R., et al. (2002). A cost-utility scenario analysis of bilateral cochlear implantation. *Archives of Otolaryngology Head Neck Surgery*, 128, 1255-1262.
Summerfield, A.Q., Barton, G.R., Toner, J., et al. (2006). Self-reported benefits from successive bilateral cochlear implantation in post-lingually deafened adults: randomised controlled trial. *International Journal of Audiology,* 45 (Supplement 1), S99-S107.
Kuthubutheen, J., Mittmann, N., Amoodi, H., et al. (2015). The effect of different utility measures on the cost-effectiveness of bilateral cochlear implantation. *The Laryngoscope,* 125, 442-447.
Palmer, C.S., Niparko, J.K., Wyatt, J.R., et al. (1999). A prospective study of the cost-utility of the multichannel cochlear implant. *Arch Otolaryngol Head Neck Surg,* 125, 1221-1229.
United Kingdom Cochlear Implant Study Group (2004). Criteria of candidacy for unilateral cochlear implantation in postlingually deafened adults II: cost-effectiveness analysis. *Ear Hear* 25, 336-360.
Bond, M., Mealing, S., Anderson, R., et al. (2009). 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* 13: 1-330.
Lammers, M.J.W., Grolman, W., Smulders, Y.E., Rovers, M.M. (2011). The cost-utility of bilateral cochlear implantation: a systematic review. *The Laryngoscope* 121, 2604-2609.
Health Quality Ontario (2018). Bilateral cochlear implantation: a health technology assessment. *Ont Health Technol Assess Ser [internet],* 18, 1-139.
Vickers, A.J., Altman, D.G. (2001). Analysing controlled trials with baseline and follow up measurements. *BMJ* 323, 1123-1124.

Table 1 Values of health utility obtained with the HUI3 from a group of 46 patients before and 12-months after unilateral implantation in comparison with a control group of 16 non-implantees at equivalent time points (Palmer, Niparko, and Wyatt 1999). (SD, standard deviation)

	Before unilateral implantation		12 months after unilateral implantation	
	Mean	SD	Mean	SD
Implantees (N=46)	.58	.17	.78	.17
Non-implantees (N=16)	.58	.20	.58	.23
Difference between groups	.00		.20	
Significance of difference	n.s.		p<.01	

Table 2 Values of health utility obtained with the HUI3 from a group of 311 patients before and 9-months after unilateral implantation (United Kingdom Cochlear Implant Study Group 2004). (SD, standard deviation; CI, confidence interval of mean; Change, difference between pre- and post-operative values of health utility)

	Before unilateral implantation		9 months after unilateral implantation		Change	
	Mean (SD)	95% CI	Mean (SD)	95% CI	Mean (SD)	95% CI
Implantees (N=311)	.433 (.198)	.411 to .455	.630 (.198)	.608 to .652	.197 (.189)	.176 to .218

Table 3 Values of health utility obtained with the HUI3 from 23 users of bilateral implants reporting their state now with two implants and recalling their states before receiving their first implant and before receiving their second implant (Bichey and Miyamoto 2008).

	Mean	95% CI
Before 1st implant	.33	.27 to .39
Before 2nd implant	.69	.64 to .75
Change (no implant to one implant)	.36	.28 to .44
With two implants	.81	.77 to .85
Change (one implant to two implants)	.12	.09 to .14

Table 4[a] Estimates of the utility of health states relevant to unilateral and bilateral implantation from a scenario analysis reported by Summerfield, Marshall, Barton, and Bloor (2002).

Health state	Informants	Sample size	Mean utility[b] (95% CI)[c]	Mean utility[d] (95% CI)	Loss of utility[e] (95% CI)
Profoundly hearing impaired, no benefit from acoustic hearing aids ('Traditional Candidate')	Volunteers	70	.765 (.730 to .800)	1[f]	.235 (.200 to .270)
Severely-profoundly hearing impaired, marginal benefit from acoustic hearing aids ('Marginal Hearing-aid User')	Volunteers	70	.836 (.807 to .865)	1[f]	.164 (.135 to .193)
Benefitting from a unilateral cochlear implant	Volunteers	70	.934 (.915 to .954)	1[f]	.066 (.046 to .085)
Benefitting from bilateral cochlear implants	Volunteers	70	.965 (.952 to .978)	1[f]	.035 (.022 to .048)
Profoundly hearing impaired, no benefit from acoustic hearing aids ('Traditional Candidate')	Patients	87	.562 (.527 to .596)	.843 (.805 to .880)	.281 (.255 to .308)
Severely-profoundly hearing impaired, marginal benefit from acoustic hearing aids ('Marginal Hearing-aid User')	Patients	115	.725 (.693 to.794)	.870 (.839 to .900)	.145 (.123 to .167)
Traditional candidate benefitting from a unilateral cochlear implant	Patients	87	.750 (.705 to .794)	.813 (.769 to .857)	.063 (.048 to .078)
Marginal hearing-aid user benefitting from a unilateral cochlear implant	Patients	115	.802 (.767 to .838)	.851 (.815 to .887)	.049 (.039 to .059)

[a]This table largely reproduces Table 2 in Summerfield, Marshall, Barton, and Bloor (2002).
[b]Mean utility measured with Mark II Health Utilities Index (patients) and with time trade-off (volunteers).
[c]CI = confidence interval.
[d]Mean utility after placing patients at the highest levels of the *Hearing* and *Speech* dimensions.
[e]Mean loss of utility due to impaired hearing and speech.
[f]Assuming a utility of unity in the absence of impairments to hearing and speech.

Table 5[a] Estimates of the difference in utility between health states relevant to unilateral and bilateral implantation from a scenario analysis reported by Summerfield, Marshall, Barton, et al. (2002).

Patient group	Intervention and alternative	Informants	Difference in utility (95% CI)[b]
Traditional candidates	Unilateral implantation compared with no intervention	Patients	+.188 (+.150 to +.226)
Marginal hearing-aid users	Unilateral implantation compared with management with acoustic hearing aids	Patients	+.077 (+.045 to +.110)
Traditional candidates	Unilateral implantation compared with no intervention	Volunteers	+.169 (+.143 to +.195)
Marginal hearing-aid users	Unilateral implantation compared with management with acoustic hearing aids	Volunteers	+.098 (+.080 to +.117)
All candidates	Bilateral implantation compared with unilateral implantation	Volunteers	+.031 (+.018 to +.042)

[a]This table largely reproduces Table 3 in Summerfield, Marshall, Barton, and Bloor (2002).
[b]CI = confidence interval.

Table 6[a] Estimates of the utility of health states relevant to unilateral and bilateral implantation from a scenario analysis reported by Kuthubutheen, Mittmann, Amoodi, et al. (2015).

		Utility measures across different groups Groups						
		A	B	C	D	Patients	All Groups	
Utility measure	Scenario	Deaf	Unilateral CI[b]	Bilateral CI[b]	Professionals	A+B+C	A+B+C+D	Incremental utility gain by second cochlear implant
HUI3	1	.51	.57	.55	.35	.54	.495	
	2	.74	.78	.79[c]	.75	.77	.765	
	3	.77	.81	.79[c]	.83	.79	.800	.035
EQ5D-3L	1	.78	.78	.82	.62	.79	.75	
	2	.85[c]	.90	.94[c]	.87	.89[c]	.89	
	3	.90[c]	.93	.93[c]	.95	.92[c]	.93	.04
EQ-VAS	1	.73	.72	.77	.51	.74	.68	
	2	.79	.83	.84	.78	.82	.81	
	3	.86	.88	.89	.89	.88	.88	.07
TTO	1	.64	.63	.62	.72	.63	.65	
	2	.78	.79	.84	.87	.80	.82	
	3	.89	.95	.96	.95	.93	.94	.12

[a] This table reproduces Table II in Kuthubutheen et al. (2014).

[b] CI = Cochlear Implant.

[c] The increase in utility compared to Scenario 1 is not statistically significant (p>.05) on Wilcoxon Signed Rank Test.

Table 7[a] Results of analyses of covariance from Summerfield, Barton, Toner, et al. (2006) comparing outcomes between the implanted group and the control group. Values in columns headed 'Difference' are the amounts by which the change in a measure in the implanted group exceeded the change in the control group while adjusting for participants' baseline scores. Columns A-C report analyses of differences between baseline and 3 months after the implanted group had received second implants. Columns D-F report analyses of differences between baseline and 9 months after the implanted group had received second implants.

	Time after implanted groups received second implants					
	3 months			9 months		
	A	B	C	D	E	F
Measure	Difference	95% CI[b]	Sig.[c]	Difference	95% CI[b]	Sig.[c]
SSQ(Speech)	1.148	-.043 to 2.340	n.s.	1.055	-.278 to 2.388	n.s.
SSQ(Spatial)	1.414	.456 to 2.372	p<.01	1.683	.616 to 2.750	p<.01
SSQ(Qualities)	.532	-.274 to 1.339	n.s.	1.687	.697 to 2.677	p<.01
HUI3	.092	-.109 to .293	n.s.	.105	-.073 to .282	n.s.
EQ5D-3L	-.036	-.124 to .053	n.s.	-.006	-.091 to .078	n.s.
EQ-VAS	-1.41	-9.35 to 6.52	n.s.	-2.66	-9.21 to 3.90	n.s.
GHSI	.128	-7.97 to 8.22	n.s.	3.80	-4.97 to 12.57	n.s.
Annoyance due to tinnitus	9.62	-5.48 to 24.71	n.s.	13.69	-1.78 to 29.16	n.s.

[a] This table reproduces the data plotted as 'Between groups' in Figure 3 of Summerfield, Barton, Toner, et al. (2006).

[b] CI = confidence interval.

[c] Sig. = Significance of the difference; n.s. = Not significant.

Table 8[a] Differences between scores obtained prior to receiving a second implant and 3- and 9-months after receiving a second implant for 24 participants from Summerfield, Barton, Toner, et al. (2006). Columns A-C report comparisons of baseline measures and measures obtained 3 months after participants received a second implant. Columns D-F report comparisons of baseline measures and measures obtained 9 months after participants received a second implant.

	Time after receiving a second implant					
	3 months			9 months		
	A	B	C	D	E	F
Measure	Difference	95% CI	Sig.	Difference	95% CI	Sig.
SSQ(Speech)	.631	.0371 to 1.224	p<.05	0.813	.168 to 1.458	p<.05
SSQ(Spatial)	1.560	.953 to 2.167	p<.001	2.001	1.471 to 2.531	p<.001
SSQ(Qualities)	.879	.455 to 1.303	p<.001	1.188	.686 to 1.691	p<.001
HUI3	-.026	-.122 to .070	n.s.	-.015	-.110 to .079	n.s.
EQ5D-3L	-.063	-.155 to .029	n.s.	-.063	-.120 to .005	n.s.
EQ-VAS	-3.26	-10.15 to 3.63	n.s.	-4.41	-11.59 to 2.77	n.s.
GHSI	2.29	-.86 to 5.43	n.s.	4.46	.78 to 8.13	p<.05
Annoyance due to Tinnitus	11.96	.578 to 23.34	p<.05	8.24	-3.07 to 19.56	n.s.

[a] This table reproduces the data plotted as 'Within group' in Figure 3 of Summerfield, Barton, Toner, et al. (2006).

[b] CI = confidence interval.

[c] Sig. = Significance of the difference; n.s. = Not significant.

Table 9[a] Quality-of-life-related outcomes from a randomized controlled trial comparing unilateral (N=19) and simultaneous bilateral (N=19) implantation in bilaterally severely-profoundly post-lingually deafened adults (Smulders 2016). Mean and median values of outcome measures are listed for the group that received unilateral implants (Unilateral CI) and the group that received bilateral implants (Bilateral CI) at three time points: before implantation (Preoperative), one year after implantation (1 year postoperative), and two years after implantation (2 years postoperative). The p-value comes from a Mann-Whitney test of the hypothesis that the scores for the bilateral group are higher than the scores for the unilateral group. (NS = Not Significant).

Measure	Time of measurement		Unilateral CI (A)	Bilateral CI (B)	Difference (B - A)	p-value unilateral vs bilateral CI
HUI3, Utility [b]	Preoperative	Mean	.58	.56	-.02	
		Median	.57	.59	.02	NS
	1 Year postoperative	Mean	.68	.71	.03	
		Median	.78	.78	.00	NS
	2 Years postoperative	Mean	.68	.72	.04	
		Median	.74	.78	.04	NS
EQ-5D, utility[c]	Preoperative	Mean	.95	.93	-.02	
		Median	1.00	1.00	.00	NS
	1 Year postoperative	Mean	.93	.90	-.03	
		Median	1.00	1.00	.00	NS
	2 Years postoperative	Mean	.94	.92	-.02	
		Median	1.00	1.00	.00	NS
EQ-5D, thermometer[d]	Preoperative	Mean	84.16	81.42	-2.74	
		Median	80.00	80.00	.00	NS
	1 Year postoperative	Mean	80.05	79.47	-0.58	
		Median	80.00	75.00	-5.00	NS
	2 Years postoperative	Mean	82.61	77.32	-5.29	
		Median	85.00	77.00	-8.00	NS
TTO[e]	Preoperative	Mean	NA	NA		
	1 Year postoperative	Mean	.91	.99	.08	
		Median	1.00	1.00	.00	NS
	2 Years postoperative	Mean	.90	.99	.09	
		Median	1.00	1.00	.00	NS
VAS, hearing[f]	Preoperative	Mean	.16	.13	-.03	
		Median	.10	.10	.00	NS
	1 Year postoperative	Mean	.63	.74	.11	
		Median	.65	.80	.15	p<.02
	2 Years postoperative	Mean	.57	.72	.15	
		Median	.66	.75	.09	NS
VAS, health[g]	Preoperative	Mean	.66	.72	.06	
		Median	.70	.80	.10	NS
	1 Year postoperative	Mean	.79	.75	-.04	
		Median	.80	.80	.00	NS
	2 Years postoperative	Mean	.80	.78	-.02	
		Median	.80	.80	.00	NS

[a] This table reproduces Table 3 in Chapter 4 of Smulders (2016) with the addition of the column entitled 'Difference (B-A)'.

[b] Health utility from the HUI3.

[c] Health utility from the EQ5D-3L.

[d] Value recorded the visual-analogue scale incorporated in the EQ5D-3L questionnaire. Respondents are asked to indicate how good or bad their own health is today by making a cross on a scale ranging from 0, labelled 'Worst imaginable health state', to 100, labelled 'Best imaginable health state'.

[e] Informants were asked to state how many of their expected remaining years of life they would give up in order to live the rest of their expected years with perfect hearing. A value of HRQL was calculated as *(l-x)/l,* where *l* was the informant's life expectancy and *x* was the number of years they would be willing to give up.

[f] Value recorded on a visual-analogue scale with end-points of 0, (inferred to correspond to no hearing), and 1, (inferred to correspond to perfect hearing).

[g] Value recorded on a visual-analogue scale with end-points of 0, (inferred to correspond to worst imaginable quality of life), and 1, (inferred to correspond to best imaginable quality of life).