Cost-effectiveness of Pediatric Bilateral Cochlear Implantation in Spain

Jorge Pérez-Martín, M.Eng.; Miguel A. Artaso, M.Eng.; Francisco J. Díez, Ph.D.
Department of Artificial Intelligence, Universidad Nacional de Educación a Distancia (UNED),
Madrid, Spain.

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Conflicts of Interest

F. J. Díez is the father of a bilaterally implanted child.

ABSTRACT

Objective: To determine the incremental cost-effectiveness of bilateral versus unilateral cochlear implantation for one-year-old children suffering from bilateral sensorineural severe to profound hearing loss from the perspective of the Spanish public health system.

Study Design: Cost-utility analysis.

Methods: We conducted a general-population survey to estimate the quality of life increase contributed by the second implant. We built a Markov influence diagram and evaluated it for a life-long time horizon with a 3% discount rate in the base case.

Results: The incremental cost-effectiveness ratio (ICER) of simultaneous bilateral implantation with respect to unilateral implantation for one-year-old children with severe to profound deafness is €10,323 per quality-adjusted life year (QALY). For sequential bilateral implantation, it rises to €11,733/QALY. Both options are cost-effective for the Spanish health system, whose willingness to pay is estimated at around €30,000/QALY. The probabilistic sensitivity analysis shows that the probability of bilateral implantation being cost-effective reaches 100% for that cost-effectiveness threshold.

Conclusions: Bilateral implantation is clearly cost-effective for the population considered. If possible, it should be done simultaneously, i.e., in one surgical operation, because it is as safe and effective as sequential implantation, and saves costs for the system and for users and their families. Sequential implantation is also cost-effective for children who have received the first implant recently, but it is difficult to determine when it ceases to be so because of the lack of detailed data. These results are specific for Spain but the model can easily be adapted to other countries.

Key Words: Bilateral cochlear implantation; cost-effectiveness analysis; state-transition model; Markov influence diagrams.

Level of Evidence: 2C

Address correspondence to J. Pérez-Martín, Dept. Artificial Intelligence, UNED.
Juan del Rosal 16, 28040 Madrid, Spain. E-mail: jperezmartin@dia.uned.es

INTRODUCTION

Cochlear implantation (CI) is the most effective treatment for severe to profound hearing loss, which affects around one in 1,000 newborn children and an increasing number of elderly people. In this situation, a cochlear implant has a great impact on quality of life, as it entails a transition from not hearing to hearing. This impact is especially significant for prelingually deafened children because a cochlear implant allows them to learn to speak and integrate in society. A second cochlear implant provides additional advantages, as it allows the user to locate the source of sound, to understand language better, especially in noisy environments, and to continue hearing when the first implant fails.¹⁻⁴ The issue is whether these advantages outweigh the economic costs of implantation.

Cost-effectiveness analysis, the most common method for economic evaluation, consists in comparing the health benefit provided by an intervention with its economic cost. In this paper, we identify effectiveness with quality-adjusted life time, measured in quality-adjusted life years (QALYs). Economic evaluations assume that each decision maker—in this case, each health care system—has a specific willingness to pay, also called cost-effectiveness threshold, which determines the economic value of a QALY for that decision maker. This way it is possible to determine whether an intervention is cost-effective with respect to the alternatives for a certain health condition.⁵

In the 1990s it was demonstrated that unilateral cochlear implantation (UCI) is cost-effective (with respect to no intervention) both in children and adults.⁶⁻⁸ In contrast, the first economic evaluation of bilateral cochlear implantation (BCI) asserted that it is not cost-effective (with respect to UCI) for adults.⁹ Two studies, carried out in Spain by the regional health technology assessment agencies of Catalonia¹⁰ and Madrid,¹¹ also asserted, after brief analyses, that BCI is not cost-effective, even for children. At the same time, the National Institute for Health and Clinical Excellence (NICE) commissioned a study in the UK, which by means of a systematic review and a Markov model concluded that BCI might be cost-effective for children, with great uncertainty, but not for adults;^{12,13} that study led to the policy of providing simultaneous BCI (i.e., putting two implants in one surgery session) for all children in the UK. Another study, carried out in the United States, found that BCI is cost-effective for both adults and children.¹⁴ Summerfield et al. concluded that pediatric BCI is cost-effective, but with a probability of only 48%.¹⁵ Recent studies suggest that BCI is cost-effective in children¹⁶ and adults.¹⁷⁻²⁰ For a systematic review, see ²¹⁻²³.

Because of the lack of conclusive evidence, at least until the last few years, there is a high variability in BCI coverage in Spain: in some regions, all the children who qualify for BCI receive two implants, in others they receive only one, and in yet others the probability of getting the second one depends on the hospital and on the availability of devices at the moment when the child arrives, thus resulting in the so-called zip code lottery. For this reason, we decided to conduct a cost-effectiveness analysis of BCI vs. UCI in Spain that might contribute to reducing that variability. Our study focuses on one-year-old children suffering from bilateral sensorineural severe to profound hearing loss, because this is the condition for which there was controversy and that is the age at which children are usually implanted. We adopted the perspective of the Spanish public health system, which means that we only included the costs that it currently covers. However, given that the Spanish authorities are considering the possibility of assuming some of the maintenance costs that in other countries are reimbursed by the public health system, we have also analyzed the cost-effectiveness for that scenario.

This paper describes the Markov model and the analyses in accordance with the Consolidated Health Economic Evaluation Reporting Standards, CHEERS.²⁴

MATERIALS AND METHODS

When an intervention, B , is more effective than another one, A , but more expensive, they are compared by computing the incremental cost-effectiveness ratio (ICER):

$$ICER(B, A) = \frac{c_B - c_A}{e_B - e_A}, \quad (1)$$

where c stands for cost and e for effectiveness. In this paper, we identify effectiveness with quality-adjusted life time, measured in quality-adjusted life years (QALYs). Quality of life is measured on a scale where 0 corresponds to being dead and 1 to perfect health.

One of the parameters that most affect the ICER of BCI with respect to UCI is the increase in quality of life contributed by the second implant. Because of the great variability of the estimates in previous studies, as explained in the discussion, we conducted a survey with students of our university, as representatives of the general population, which recruited 583 respondents. We used the time trade-off method, which consists in asking the subjects whether they prefer to live for a certain amount of time in a certain health state or living for a shorter time in a healthier state. We framed the questions in three different ways to analyze the effect of psychological biases on the quality of life estimates. The study is described in detail in a technical report.²⁵ We also conducted a survey with 273 CI users who were asked not only about quality of life but also about maintenance costs (paper in preparation).

We then built a state-transition model (Figure 1) implemented as a Markov influence diagram,²⁶ which is described in more detail in the appendix and available at www.probmodelxml.org/networks. It assumes that the child is severely to profoundly deaf, has not been implanted previously, and will receive one or two implants when he/she is one-year old. The model contains one decision, with three options: *simultaneous BCI* (i.e., putting two implants in one surgical operation), *sequential BCI* (two implants in different surgical operations) and *UCI* (only one implant). It has four states, indicating how many implants the patient is using at each moment: both, only the first one, only the second one, and none. The model includes several possible hazards, such as surgical complications, failures of the external and internal components, natural death, etc., as well as their impact on quality of life and their associated costs. In Figure 1, “CS” denotes the costs covered by the health system (cochlear implant device, surgery, replacement of the external components after a certain period of time, etc.), while “CF” denotes the costs that in Spain are currently covered by users and their families; these are the maintenance costs, which include cables, batteries, repairs, etc.

Tables 1 and 2 contain the parameters of the model. The most relevant parameter in Table 1 is the increase in quality of life contributed by the second implant, $\Delta QoL_{1 \rightarrow 2}$; in a conservative approach in favor of UCI, we took the smallest value obtained from our general-population survey.²⁵ The uncertainty about the parameters was represented by associating second-order distributions to them, as explained in the appendix.

The Markov model was evaluated for a horizon of 100 cycles, i.e., until the age of 101 years. Following the recommendations of the *Panel on Cost-Effectiveness in Health and Medicine* convened by the U.S. Public Health Service,²⁷ in the reference case we applied an annual discount rate of 3% on both costs and effectiveness—the same value as in other economic evaluations of BCI.^{11,17,28} We performed a probabilistic sensitivity analysis with 10,000 simulations as well as deterministic sensitivity analyses for the discount rate and for several parameters.

RESULTS

Reference Case Analysis

When considering only the costs currently covered by the Spanish health system, the incremental effectiveness of simultaneous BCI with respect to UCI was 3.163 QALYs and the incremental cost was €32,649, which leads to an ICER of €10,323/QALY. For sequential BCI the effectiveness is the same as for simultaneous BCI, the incremental cost is \$37,109, and the ICER €11,733/QALY. If the health system covered all the maintenance costs (at the current prices) the ICER with respect to UCI would be €15,035/QALY for simultaneous BCI and €16,446/QALY for sequential BCI.

Given that the willingness to pay—also known as cost-effectiveness threshold—of the Spanish health system accepted as a consensus among experts is €30,000/QALY,²⁸ BCI turns out to be clearly cost-effective in all cases.

Sensitivity Analyses

In all the 10,000 simulations of the probabilistic sensitivity analysis the ICER of both simultaneous and sequential BCI with respect to UCI was below €30,000, which implies that for this willingness to pay BCI is always cost-effective with virtually 100% certainty—see the acceptability curves in Figures 2A and 2B, which represent the probability of BCI being cost-effective.

If the health system covered all the maintenance costs, the acceptability curves for BCI would increase more slowly (Figures 3A and 3B), but it is still virtually certain that both interventions are cost-effective with respect to UCI—the probability is 99.98% for simultaneous BCI and 99.92% for sequential BCI.

Given that the most influential parameter (together with the price of the device) and the most uncertain parameter is the increase in quality of life from UCI to BCI, $\Delta QoL_{1 \rightarrow 2}$, we performed a deterministic sensitivity analysis for it. If we assume that the other parameters take the same values as in the reference case and the willingness to pay is €30,000/QALY, a value as low as $\Delta QoL_{1 \rightarrow 2} = 0.037$ suffices to make simultaneous BCI cost-effective (see Figure 4); if the health system covered all the maintenance costs, it would be cost-effective when this parameter is above 0.054. We will show in the discussion that the average value obtained for $\Delta QoL_{1 \rightarrow 2}$ in the literature is 0.073.

We have also analyzed the impact of the discount rate. It is more relevant for CI than for other health technologies because a significant part of the cost (40%) is paid at the moment of implantation, while the benefit (the effectiveness) is gathered along the user's lifetime. If we raise the discount from 3% to 5% and 7%, as recommended by a panel of experts,²⁷ the ICER for simultaneous BCI increases from 10,323 to 13,703 and 17,353 euros per QALY respectively. In the absence of discounts, the ICER would reduce to €6,422/QALY. The changes in the ICER for sequential BCI are analogous. In all cases the ICER remains clearly below €30,000/QALY.

DISCUSSION

Our study has focused on one-year-old children with bilateral severe to profound hearing loss who qualify for bilateral CI. Unlike other studies,^{12,15,16} the only comparator in our analysis was UCI. We did not consider the option “no implant” because in developed countries all children with severe to profound deafness receive at least one implant when it is clinically feasible. We did not compare BCI with “UCI plus a contralateral hearing aid” because the benefit of a hearing aid depends on the degree of hearing loss in that ear: in mild to moderate losses a hearing aid provides better audition than a cochlear implant, while in severe to profound deafness it is almost useless.

Simultaneous BCI clearly dominates sequential BCI because it is as safe and effective, but less expensive. Therefore, children that need two implants should receive them in one surgical operation. However, because of current policies, many children in Spain have received one implant. If they get the second within a short time interval—say less than a year—it will be cost-effective according to our model, but its effectiveness decreases with age and with the lag between implantations. Unfortunately, the lack of detailed effectiveness data in the literature makes it impossible to specify with precision in which cases sequential BCI is cost-effective.

Our results agree with those of previous studies^{12,15,16} and with the guidelines of the British National Institute for Health and Care Excellence (NICE), which recommend simultaneous BCI for newborn children and admit the possibility of a second implant for children who already have one.¹³ The main difference is that in our study the probability of BCI being cost-effective is much higher than in previous probabilistic sensitivity analyses.^{12,15,16} In contrast, our conclusions disagree with the recommendations of the two studies conducted by Spanish regional agencies ten years ago.

The principal limitation of our analysis—and of all other cost-effectiveness analyses of BCI—is the uncertainty about the increase in quality of life from one to two implants, $\Delta QoL_{1 \rightarrow 2}$. The studies aimed at measuring it have returned very disparate estimates, mainly due to the use of different elicitation methods. Quality of life indexes, such as the HUI-3,²⁹ have yielded estimates from -0.003 ³⁰ to 0.11 .¹⁴ An additional drawback of these indexes is their low sensitivity to improvements in audition.^{18,20,31,32} In our opinion, the most reliable technique for this purpose is the time trade-off method (TTO), mentioned above, because it is preference-based and does not suffer from that lack of sensitivity. Previous estimates of $\Delta QoL_{1 \rightarrow 2}$ with the TTO have returned the values 0.031 ,³³ 0.05 ,¹⁵ 0.12 ,¹⁸ and 0.09 ,²⁰ with an average of 0.073 and a median of 0.070 . In the survey we conducted for this project, the values obtained with the TTO ranged from 0.106 to 0.293 , depending on the different ways of framing the questions.²⁵ In our model we have taken the value 0.106 , the lowest in this range, because it is closer to the average of previous studies and because we decided to take a conservative approach in favor of UCI to make the conclusions more compelling. Given that all the studies except the oldest one³³ have returned values above the threshold of 0.042 derived in our sensitivity analysis (Figure 4), we can conclude that sequential BCI is cost-effective for the Spanish public health system beyond any reasonable doubt.

There are minor sources of uncertainty—such as the probability of voluntary non-use, the risk of meningitis, and the possibility of discounts on the price of the devices—which we have not considered in our sensitivity analyses for the reasons explained in the appendix.

We should finally mention that some aspects of our model are specific for current policies in Spain: in most implantation centers the cost of programming is covered by manufacturers; users and their families assume most of the maintenance costs, including batteries and cables, lost coils, the repairs of the processor (and its replacement, if necessary) between the third and the sixth year of use; the cost of surgery when the internal device fails is always covered by the health system, even during the guarantee period; etc. However, our study has proved that even if the health system covered all the maintenance costs, as in other countries, BCI would still be cost-effective. Additionally, researchers interested in the ICER of BCI for other health systems can easily modify the prices and reimbursement policies in this model using the graphical user interface of OpenMarkov,^a an open-source program developed by our group. This is one of the reasons for making our model publicly available.

^a www.openmarkov.org.

Another reason is to allow everyone to reproduce our results, modify the parameters of the model, and perform other sensitivity analyses, since transparency is essential for the credibility of a study that has been partially supported by a manufacturer of the technology evaluated.

CONCLUSION

Our study has proved that BCI is clearly cost-effective for the Spanish public health system. Even if the system took over all the maintenance costs, which in Spain are partially covered by users and their families, it would still be cost-effective, but with a small amount of uncertainty, mainly due to the imprecise estimation of the quality of life increase from one to two implants. From the societal perspective, BCI would be even more cost-effective because of savings in education and better employment opportunities.

Given that putting both implants in one surgical operation saves costs for the health system (additional surgery and (re)habilitation) and for users and their families (traveling, work hours lost...), bilateral implantation should be performed simultaneously. For young children who already have one implant, it is cost-effective to give them a second one. In this case, the benefit decreases with age and with the gap between implantations, but the uncertainty about the increase in quality of life makes it impossible to specify with precision when sequential BCI ceases to be cost-effective.

Our analysis agrees with recent studies that concluded that BCI is cost-effective for children,^{12,15,16} at least when performed simultaneously, and possibly also for adults,¹⁷⁻²⁰ and contradicts the two studies that asserted, after brief analyses, that it was not cost-effective (in Spain) even for children.^{10,11}

Taking into account that reproducibility and the ability to build on the work of others are fundamental principles of scientific research, we have made our model publicly available at www.probmodelxml.org/networks so that other researchers can verify the results presented in this paper and adapt this study to other countries.

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^b See www.cisiad.uned.es/implante-coclear/encuestas.php.

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APPENDIX: DETAILED DESCRIPTION OF THE MODEL

We describe here in further detail the state-transition model built for analyzing the cost-effectiveness of bilateral cochlear implantation.

Markov Influence Diagrams

Probabilistic graphical models (PGMs)³⁴ consists of nodes, links, and variables. Every node represents a variable and for this reason we speak indifferently of nodes and variables. A PGM may contain three types of nodes: chance, decision, and value. *Decision nodes* represent choices available to the decision maker. A *chance node* represents a variable that is not under the direct control of the decision maker; for example, the gender or the age of the patient, the outcome of a test, or an adverse event. *Value nodes*, also known as *utility nodes* in the PGM literature, represent the decision maker's values, such as costs and effectiveness. Links usually represent causal relations. The qualitative information of a PGM consists of a set of probability distributions and value functions.

Markov influence diagrams are a particular type of PGM proposed recently for encoding state-transition models and performing cost-effectiveness analysis.²⁶ They can contain variables that evolve over time (for example, the patient's age) and others that do not change (for example, the gender). As in other Markov models, time is discretized into cycles of fixed duration, such that the state of the system (in this case, the patient) is assumed to be constant along each cycle. OpenMarkov^c is an open-source package for building and evaluating PGMs, including Markov influence diagrams.

Markov Influence Diagram for Cochlear Implantation

Structure of the Model

The model used in our study represents the state of the CI user and the events that may occur throughout his/her life. The cycle length is one year. We assume that the child is severely to profoundly deaf, has not been implanted previously, and receives one or two implants when he/she is one-year old.

Figure 1 shows the graph of the model. It contains one decision, *Intervention decided*, drawn as a blue rectangle, with three possible options: *simultaneous BCI* (i.e., putting two implants in one surgical operation), *sequential BCI* (two implants in different surgical operations) and *UCI* (only one implant). Given that in developed countries the standard practice is to give at least one implant to all children with severe to profound deafness, we did not include the option *no implant*.

Chance nodes are drawn as rounded rectangles. The node *Intervention applied* represents whether the patient receives one implant, two implants simultaneously, or two implants sequentially. In general, this variable takes the same value as *Implantation decided*, unless it turns out to be impossible to put the two implants in one operation, as discussed below. The six nodes in the upper right zone of the graph represent the gender and age of the patient, and whether he/she is alive. *Gender* does not have a temporal index because it is an atemporal variable, i.e., its value does not change. Variables whose value can change over time have indexes, written in square brackets, which denote the period of time. Thus, *Implants used [i]* indicates how many implants the patient is using in the *i*-th cycle; it has four states: *both implants*, *only first implant*, *only second implant*, or *none*. The numbers 1 and 2 written in the name of a variable outside the brackets denote the first or the second implant respectively. For example, *Elective non use 2* indicates whether the person decides to use the second implant or not. When the value of a chance variable is known with certainty, the node is

^c OpenMarkov is available at www.openmarkov.org.

colored in gray; in this model we know with certainty that the child is initially one year old and alive (nodes *Age [0]* and *Alive [0]*), and all the external and internal components of the implant are brand new (nodes *Processor 2 age [0]*, *Internal device 1 age [0]*, and *Internal device 2 age [1]*).

Value nodes are drawn as green hexagons. $\Delta QoL_{0 \rightarrow 1}[i]$ and $\Delta QoL_{1 \rightarrow 2}[i]$ denote the increase in quality of life from no implant to one implant and from one implant to two implants respectively; the effectiveness accrued in the i -th cycle is proportional to the quality of life and to the cycle length, and depends on the number of implants used in that cycle. The other value nodes represent monetary expenditures. The prefix “CS” means “cost for the (health) system” and “CF” means “cost currently covered by the family”. The three child nodes of *Intervention applied* represent the cost of implantation; they are temporal because they are paid only once. The other costs depend on the number of implants used in each cycle and on the occurrence of adverse events.

Probabilities

When there is a link $A \rightarrow B$ in the graph, we say that A is a parent of B and B is a child of A . Every chance variable in the model has a conditional probability distribution for each configuration of its parents in the graph. The node *Gender* has no parent; therefore, its probability is just the prior probability of being male or female; we obtained it from the database of the National Institute of Statistics (INE) for January 1st, 2015. The probability of dying in the i -th cycle, represented by *Death [i]*, depends on *Gender* and *Age [i]*; it is therefore the annual mortality rate, also taken from the INE.

If *Intervention decided* takes the value *UCI* or *sequential BCI*, then *Intervention applied* takes the same value, with probability 1, but when *Intervention decided* = *simultaneous BCI* the probability of *Intervention applied* is 89% for *simultaneous BCI*, 10% for *sequential BCI*, and 1% for *UCI*. We assigned these probabilities because in the 50 cases reported by Ramsden et al.³⁵ it was always possible to put both implants in one surgery, as planned, but in another 50 cases planned for simultaneous BCI³⁶ it was possible only in 39 patients—in 10 cases the second ear had to be implanted later and one patient received only one implant, for unknown reasons.

In some cases the child variable depends deterministically on the values of its parents. For example, *Alive [i]* = *true* if and only if the user was alive in the previous cycle and has not died, i.e., if *Alive [i - 1]* = *true* and *Death [i - 1]* = *false*. Similarly, the value of *Implants used [0]* is determined by the intervention applied: if *Intervention applied* = *UCI*, then the patient is initially in the state *only first implant*, whereas if the intervention is either *simultaneous BCI* or *sequential BCI*, the initial state is *both implants*. In subsequent cycles, *Implants used [i]* takes the same value as in the previous cycle except when the user dies, when he/she decides not to use the second implant, or when the internal device has been explanted and could not be reimplanted.

The probability of a failure of the external device (the sound processor) was set to 0.115 for the first two years, 0.095 between the third and the fifth, 0.104 for the sixth and seventh, and 0.16 afterwards.¹²

Revision surgery may be due to a failure of an internal device or to a major medical/surgical complication. In accordance with previous studies^{12,15} we set the probability of internal device failure to 0.001 for the first 9 years and 0.003 afterwards, and the probability of major complication (other than a failure) to 0.041 in the first year and 0.004 afterwards. Some manufacturers have reported lower failures rates,^{37,38} but due to discrepancies in their reports and in published studies,^{39,40} we decided to use the same probabilities as in the studies of Bond et al.¹² and Summerfield et al.¹⁵, thus taking a conservative position in favor of UCI. We also followed those authors in assuming that a failing internal device can be replaced, but a major

complication may make it impossible to reimplant the device; we set the probability of permanent explantation in case of major complication to 0.043.⁴¹

The possibility of dying during revision surgery, mainly because of the complication of anesthesia, slightly reduces the effectiveness of bilateral implantation. The peri-operative mortality rate is less than 1/10,000 for children⁴² and less than 20/10,000 for adults.⁴³ Taking again a conservative approach in favor of UCI, we set those probabilities to 0.0001 until the age of 18 and 0.002 afterwards.

Table 1 summarizes the probabilities used in the model.

Effectiveness

In cost-utility analysis, the effectiveness is identified with life duration, adjusted by the quality of life at each moment, $QoL(t)$:

$$e = \int QoL(t) \cdot dt \quad (2)$$

In our model, the quality of life only depends on the number of implants used, as shown in Figure 1. Therefore, the incremental effectiveness of BCI with respect to UCI mainly depends on the difference in quality of life between having one and two implants, $\Delta QoL_{1 \rightarrow 2}[i]$. In our general-population survey the estimates for this parameter ranged from 0.106 to 0.293, depending on the elicitation technique.²⁵ In our model we used the lowest value, 0.106, for two reasons: because that was the value obtained with the version of the time trade-off method most commonly used in quality of life studies, and because we wished to take a conservative approach in favor of UCI.

Costs

According to Equation 1, the ICER does not depend on the absolute costs of interventions—simultaneous BCI, sequential BCI, or UCI—but on the differences between them. For this reason, we have not explicitly included in our model the costs common to the three interventions, such as the cost of the first implant system.

The price of the second implant was set to €21,000, the average of the prices we obtained from a manufacturer and a distributor of another manufacturer for our country. We also asked the third main manufacturer, but received no answer. We assumed no discount on the devices, for the reasons discussed below.

In the case of simultaneous BCI, we assumed that surgery requires 100 more minutes than UCI²⁰ at a cost of €229/hour, including personnel and materials; this value is the average of €169/h⁴⁴ and €289/h.⁴⁵ Sequential BCI has an extra cost of €1,000 for the pre-surgical selection and exploration assessment (50% of the corresponding cost for UCI), plus €3,500 for the surgical operation and €600 for rehabilitation,⁴⁶ the same as for UCI. These are conservative estimates in favor of UCI, because in general the pre-surgical assessment made for UCI is also valid for the second implantation, and because if the gap between implantations is short, both ears can be rehabilitated at the same time.

If the internal device fails during the first ten years, the manufacturer provides a new one; after the guarantee period, the health system pays €13,000 for it (communication from a manufacturer). In all cases the health system takes over the cost of surgery.

If the external processor fails during the first two years, it is replaced by the manufacturer. After the seventh year, it is replaced by the health system.

Between the third and the sixth year, the user must cover the repairs; we have included this expense in maintenance costs, together with coils, microphones, cables, and batteries, which

in Spain are covered by users and their families. According to our study with CI users, these costs amount to €675/year for users under the age of 18 and €373/year for adults.

In our model we did not include the incremental cost of programming the second implant because in most cases it is covered by manufacturers, whose experts travel to hospitals in different cities; in the few cases in which the processors are programmed by the personnel of the implantation center, the marginal cost is low.

Please note that all the costs have been obtained from Spanish sources. Given that all the costs relative to the cochlear implant have been obtained in the last year, we did not convert them to current euros. We did not update the costs of surgery, obtained from the literature, because there is no evidence that they have increased at the same rate as inflation, and they might have even decreased due to austerity measures. In any case, the effect of these adjustments in the context of low inflation would be much smaller than the uncertainty about these parameters.

Table 2 summarizes the quality of life increases and the economic costs used in the model.

Second-Order Uncertainty

The uncertainty of the model was represented by adding second-order distributions to the main parameters.⁴⁷ Each parameter denoting a probability p in the reference case was assigned a beta distribution $B(\alpha;\beta)$ with a mean of p , i.e., $\alpha / (\alpha + \beta) = p$; when p was taken from a study that did not indicate the number of subjects involved, we assumed a sample size of 100, which is implemented by making $\alpha + \beta = 100$.⁴⁸ Therefore $\alpha = 0.01p$ and $\beta = 100 - \alpha$.

We modeled the increment in QoL from one to two implants, $\Delta QoL_{1 \rightarrow 2}$, with a Gamma with $k=22.832$ and $\theta = 0.004$, as this is the distribution that better fitted the data from our general-population survey.²⁵

Following the recommendation of Briggs et al.,⁴⁷ costs were modeled with Gamma distributions. We used a Gamma with $k = 155.96$ and $\theta = 4.314$ for the maintenance costs of users under 18, and $k = 37.49$ and $\theta = 9.866$ for adults. In the remaining cases, each parameter denoting a cost c was assigned a Gamma distribution with a mean $\mu = c$ and a standard deviation $\sigma = \mu / 5 = 0.2 c$.^{15,49}

These choices of equivalent sample size and standard deviations are debatable, but our sensitivity analyses confirmed that their effect is virtually null for a willingness to pay of €30,000/QALY.

Further details

In this last section of the appendix we discuss some parameters and hypotheses of our model that are not mentioned in the body of the paper because they have no relevant impact on the cost-effectiveness results.

First, the probability of a major complication is 4.1% in the first year and 0.4 in subsequent years; in 4.3% of these cases it is not possible to reimplant the same ear. In UCI it might also be impossible to reimplant the contralateral ear. In BCI it might occur that both implants must be explanted and none can be reimplanted. Even though this scenario is extremely unlikely, our model needs to assign a value for the quality of life with no hearing at all; more precisely, it needs a value for the parameter $\Delta QoL_{0 \rightarrow 1}$, which represents the difference between having no implant and having one. As in our surveys we did not measure it, we took the value 0.106 from Summerfield et al.,¹⁵ which is, by coincidence, the same as the lowest value for $\Delta QoL_{1 \rightarrow 2}$ obtained in our survey. It might be argued that $\Delta QoL_{0 \rightarrow 1}$ should be greater than $\Delta QoL_{1 \rightarrow 2}$, but

the sensitivity analysis confirms that the value of $\Delta QoL_{0 \rightarrow 1}$ is irrelevant: if we vary it from 0.05 to 0.20, the ICER of simultaneous BCI only varies from 10,354 to 10,269 euros per QALY gained.

Second, previous models^{12,15} have taken into account that some users decide not to use the second implant. However, the cases reported in the literature always refer to adolescents and adults who received it a long time after the first one. The experts we consulted could not recall any case of a child who refused one or both implants after receiving them at a very early age; therefore in our reference case we set the probability of *Elective non use 2* to zero. If we had set that probability to a value as high as 1%, the ICER of simultaneous BCI would have been €10,392/QALY instead of 10,323, an irrelevant change.

Third, unlike those studies^{12,15} we did not take into account the risk of meningitis due to CI. Some years ago that was a serious concern, but nowadays its incidence has decreased,^{50,51} mainly because in many cases meningitis was caused by electrode positioners that are no longer used. In other cases it was due to “congenital abnormalities of the cochlea which predispose [deaf people] to meningitis even prior to implantation”.⁵² Additionally, in Spain all children are vaccinated against several types of meningitis, and some receive prophylactic perioperative antibiotic treatment before CI surgery, with no extra cost in the case of simultaneous BCI and a negligible cost for sequential BCI. For these reasons we assumed that BCI neither increases significantly the risk of meningitis nor requires additional expenditures to prevent it.

Finally, we have not taken into account the discounts that manufacturers may offer when a device is purchased for BCI. According to the technical report of Bond et al.,⁴⁹ in the UK the discount were sometimes “equivalent to 40% or more for the second implant” and were decisive for the approval of BCI in that country.¹³ However, the journal version of that paper did not consider the effect of discounts because “the continued presence and size of these discounts in the future is impossible to guarantee”.¹² More importantly, in the Spanish health system the devices are acquired in batches at hospital-specific tenders, without stipulating how each one will be used, which prevents the possibility of obtaining discounts for BCI.

Figures

Figure 1: Markov influence diagram for cochlear implantation.

Figure 2: Acceptability curves for bilateral cochlear implantation: (A) simultaneous and (B) sequential, including only the costs currently covered by the Spanish health system. They represent the probability of BCI being cost-effective with respect to unilateral CI.

Figure 3: Acceptability curves for (A) simultaneous and (B) sequential BCI with respect to UCI if the health system covered all the maintenance costs.

Figure 4: Sensitivity analysis: incremental cost-effectiveness ratio (ICER) of simultaneous BCI with respect to UCI as a function of the increase in quality of life from having one implant to having two. Under the current coverage policy (orange curve), BCI is cost-effective when the increment is above €0.037/QALY. If the system covered all the maintenance costs (blue line), BCI would be cost-effective for values higher than €0.054/QALY.

Figure legends abbreviations:

- BCI: Bilateral Cochlear Implantation
- CI: Cochlear Implantation

Tables

Parameter	Value	Source
Being male	0.4914	National Institute of Statistics
Major complication device age < 1 year	0.041	Bond et al. ⁴⁹ Summerfield et al. ¹⁵
Major complication device age ≥ 1 year	0.004	Bond et al. ⁴⁹ Summerfield et al. ¹⁵
Permanent explantation major complication.	0.043	Wang et al. ⁴¹
Surgical mortality age < 18 years	0.0001	Gonzalez et al. ⁴²
Surgical mortality age ≥ 18 years	0.002	Braz et al. ⁴³
External device failure 1st year	0.16	Bond et al. ⁴⁹
External device failure 2nd year	0.115	Bond et al. ⁴⁹
External device failure 3rd - 4th years	0.095	Bond et al. ⁴⁹
External device failure 5th - 6th years	0.104	Bond et al. ⁴⁹
External device failure ≥ 7th years	0.16	Bond et al. ⁴⁹
Internal device failure < 8th years	0.001	Bond et al. ⁴⁹
Internal device failure ≥ 8th years	0.0035	Bond et al. ⁴⁹

Table 1. Probabilities in the model. The annual mortality rate, which is not shown in this table because it depends on age and gender, was also taken from the Spanish National Institute of Statistics.

Parameter	Value	Source
$\Delta QoL_{1 \rightarrow 2}$	0.106	Artaso et al. ²⁵
CS: Device	€21,000	manufacturers
CS: Surgery (increase for simultaneous BCI)	€382	Palà et al. ⁴⁵ Herranz Amo et al. ⁴⁴ Smulders et al. ²⁰
CS: Surgery (increase for sequential BCI)	€4,500	de la Torre et al. ⁴⁶
CS: Habilitation (increase for sequential BCI)	€600	de la Torre et al. ⁴⁶
CS: Processor 2 replace	€6,300	manufacturers
CS: Internal device 2 replace	€13,000	manufacturers
CF: Maintenance (per implant per year)	€675 (< 18 y.o.) €373 ($\geq$ 18 y.o.)	CI users survey

Table 2. Quality of life increase (which determines the effectiveness) and economic costs. “CS” stands for “cost covered by the health system” and “CF” for “cost currently covered by users and their families”.