Systematic review of the scientific literature on the economic evaluation of cochlear implants in adult patients

Revisione sistematica della letteratura scientifica sulla valutazione economica degli impianti cocleari in pazienti adulti

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SUMMARY

A systematic review of the economic literature of cochlear implants (CI) was conducted with the aim of summarizing the results of studies on the cost effectiveness of monolateral and bilateral (sequential/simultaneous) CI in adult patients affected by severe to profound prelingual and postlingual hearing impairment. The literature search was performed using "PubMed MEDLINE" and the Centre for Reviews and Dissemination search engines. Inclusion criteria related to economic evaluation included primary studies published in English language from January 2000 to May 2010 and aimed to quantify costs of CI and compare monolateral CI *vs.* acoustic prosthesis and bilateral (sequential/simultaneous) CI *vs.* monolateral CI in terms of cost per unit of effectiveness. Four articles were identified. The mean direct medical cost of the monolateral CI varied from € 30,026 to € 45,770 in postlingually deafened patients, and the cost of device represented the main cost component. Additional median costs of simultaneous and sequential bilateral CI were, respectively, € 21,831 and € 25,459. The mean direct medical cost of monolateral CI was € 31,942 in prelingually deafened patients. The monolateral CI in postlingually deafened patients represented a cost effective intervention as compared with no implant (€ /QALY varied from € 7,930, € 24,983 to € 33,094). Monolateral CI were not a cost effective intervention for traditional patients with more than 40 years of hearing impairment (€ 64,604/QALY) or for patients with marginal benefits from using acoustic prosthesis with more than 30 years of hearing impairment (€ 106,267/QALY). The cost effectiveness of monolateral CI worsened with increasing age (€ /QALY from € 23,439 for patients < 30 years old to € 55,369 for patients > 70 years). Bilateral CI in postlingually deafened patients were less cost effective than monolateral CI (from € 91,943/QALY to € 102,640/QALY). Monolateral CI were cost effective in prelingually deafened patients (€ /QALY: € 8,096). Given the few economic evaluation studies in literature, future researches are needed to support the cost effectiveness results of CI in adults and to evaluate the cost effectiveness of bilateral CI, as well as to estimate the non-medical direct and indirect cost components.

KEY WORDS: Hearing loss • Cochlear implant • Cost-analysis • Cost-effectiveness • Adults

RIASSUNTO

La revisione sistematica della letteratura economica sugli impianti cocleari (IC) è stata condotta con l'obiettivo di sintetizzare i risultati degli studi scientifici di costo efficacia degli IC monolaterali e bilaterali (sequenziali/simultanei) in pazienti adulti affetti da sordità prelinguale e postlinguale da grave a profonda. La ricerca della letteratura è stata effettuata attraverso le banche dati "PubMed MEDLINE" e "Centre for Reviews and Dissemination". Sono stati inclusi gli studi primari di valutazione economica pubblicati in lingua inglese dal 2000 al maggio 2010 e finalizzati a quantificare i costi degli IC e a confrontare gli IC monolaterali con le protesi acustiche e gli IC bilaterali (sequenziali/simultanei) con gli IC monolaterali in termini di costo per unità di efficacia. La revisione sistematica della letteratura ha consentito di identificare 4 articoli economici. I costi medi diretti sanitari variano da € 30,026 a € 45,770 nei pazienti con sordità postlinguale e il costo dell'impianto rappresenta la componente di costo principale. I costi addizionali mediani degli IC bilaterali simultanei e sequenziali sono rispettivamente € 21,831 e € 25,459. Il costo medio diretto sanitario degli IC monolaterali è pari a € 31,942 nei pazienti con sordità prelinguale. L'IC monolaterale nei pazienti con sordità postlinguale rappresenta un intervento costo efficace se confrontato con nessun impianto (€ /QALY varia da € 7,930, € 24,983 a € 33,094). L'IC monolaterale non è un intervento costo efficace per pazienti tradizionali con più di 40 anni di sordità (€ 64,604/QALY) e per pazienti con beneficio marginale dall'uso di protesi acustiche con più di 30 anni di sordità (€ 106,267/QALY). La costo efficacia degli IC monolaterali peggiora con l'aumentare dell'età (€ /QALY da € 23,439 per pazienti con età < 30 anni a € 55,369 per pazienti con età > 70 anni). Gli IC bilaterali in pazienti con sordità postlinguale sono meno costo efficaci che gli IC monolaterali (da € 91,943/QALY a € 102,640/QALY). Gli IC monolaterali sono costo efficaci in pazienti con sordità prelinguale (€ /QALY: € 8,096). Data l'esiguità degli studi di valutazione economica in letteratura, ulteriori future ricerche si rendono necessarie al fine di supportare i risultati di costo efficacia degli IC negli adulti, per valutare la costo efficacia degli IC bilaterali e per stimare i costi diretti non sanitari e i costi indiretti degli IC.

PAROLE CHIAVE: *Perdita di udito • Impianto cocleare • Analisi dei costi • Costo-efficacia • Adulti*

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Introduction and aims

A systematic review of the literature was carried out to summarize the results of studies published from January 2000 to May 2010 on the economic evaluation of cochlear implants (CI) in adult patients affected by severe to profound hearing impairment.
The CI considered are both monolateral and bilateral (sequential/simultaneous) and were analysed in: i) monolateral CI in adult patients; ii) monolateral CI in elderly patients; iii) monolateral CI in prelingual deaf adult patients; iv) bilateral (sequential or simultaneous) CI in adult patients.

Methods

This systematic review of the literature was conducted with the rationale of an explicit and reproducible methodology according to the criteria of The Cochrane Collaboration and others [1 2].

Research strategy
The systematic review of the economic literature was performed by a reviewer on September 2009 and updated on 31 May 2010, interrogating the databases "PubMed MEDLINE" and the Centre for Reviews and Dissemination (CRD). PubMed MEDLINE was interrogated using the keyword "Cochlear implants" AND (Costs OR "Cost Analysis" OR economics) and limiting the search to the adult population (age > 18 years), to publications in English from 2000 to May 2010. The database Centre for Reviews and Dissemination, which includes the Economic Evaluation Database (NHS EED) and HTA Database, was interrogated by the "MeSH descriptor Cochlear Implants explode all trees with qualifier: EC"; it was not possible to insert limits of time, population and language. The results obtained from database query were imported by RefWorks Version 6.0, a software for the management of bibliographic data which allows to remove any duplicate records. After identifying publications, two reviewers, working independently, reviewed the titles and the abstracts, applying the inclusion and exclusion criteria described below. Any differing opinions were resolved by discussion between the same reviewers.

Criteria of study selection
Inclusion criteria related to primary studies on CI with the following characteristics.

Types of study
- Partial economic evaluation studies estimating direct and indirect costs of CI;
- complete economic evaluation studies, including cost-effectiveness, cost-utility and cost-benefit analyses performed through observational and experimental studies. Studies published in English from 2000 up to the moment of the research (May 2010) were included.

Population
Adults affected by severe to profound hearing impairment.

Types of comparison
- Monolateral implants *vs.* acoustic prosthesis in prelingual deaf adult patients;
- monolateral implant *vs.* acoustic prosthesis in elderly postlingual deaf patients;
- simultaneous bilateral implant *vs.* monolateral implant in adult patients;
- sequential bilateral implant *vs.* monolateral implant in adult patients.

Outcomes
Direct and indirect costs and benefits have been considered. In particular:
- cost for unit of effectiveness measured in physical units through an incremental cost effectiveness ratio (ICER);
- cost for quality adjusted life years (QALY);
- cost for benefits measured in monetary units;
- direct and indirect costs of cochlear implantation.

Exclusion criteria
The studies that were not compliant to the inclusion criteria were excluded (in particular unpublished articles, unreviewed conference papers, case reports, letters and commentaries).
The selected studies were considered eligible, as well as those selected through the consultation of bibliographies of pertinent publications. Studies were carefully examined, assessing their methodology, using the available tools [3], to evaluate both internal and external validity.

Results

A total of 42 articles were obtained from the database search. Of these, 30 were extracted from Pubmed and 12 from the Centre for Reviews and Dissemination. Three duplicates were eliminated, while pre-defined inclusion and exclusion criteria applied to the remaining 39 titles and abstracts led to exclusion of 32 studies. The remaining 7 articles were considered eligible, and 1 study identified by bibliography research was added. The 8 articles were analyzed carefully; of these, 4 articles not compliant to the quality criteria defined by Evers et al. [3] were excluded from the review [4-7]. A total of 4 articles responding positively to the criteria of Evers et al. [3] were included (Francis et al. [8], Summerfield et al. [9], UK Cochlear Implant Study Group, UKCISG [10], Molinier et al.) [11].
The countries examined were the United States [8], Great Britain [9 10] and France [11]. The design was that of a cohort retrospective study [8 9] and of a prospective study [10 11]. One study was single centre [8] and three studies were multicen-

tre [9-11]. The two English studies [9 10] and the French study [11] considered adult patients with a mean age of around 50 years, while Francis et al. [8] considered older patients aged between 50 and 80 years and a mean age at recruitment of around 66 years. In three articles [8-10], patients were affected by postlingual deafness. The study by Francis et al. [8] also includes a group of 6 subjects affected by prelingual deafness, while Molinier et al. [11] do not specify the type of deafness, but postlingual hearing impairment can be hypothesized.

In the English studies [9 10], the implant received by the patients was monolateral; the study by Summerfield et al. [9], also evaluates the benefits from the use of bilateral cochlear implants. Two studies [8 11] do not state clearly whether the implants used are monolateral or bilateral, but it would seem that they are monolateral implants when unspecified. Furthermore, Summerfield et al [9] and UKCISG [10] divide the group of patients affected by postlingual deafness and using monolateral CI into traditional patients and patients with marginal benefits on the basis of the results of 2 speech intelligibility tests (Bamford-Kowal-Bench, BKB and City University of New York, CUNY) using acoustic device before surgery. Over the last 30 years, there has been an extension of the eligibility criteria for cochlear implantation, ranging from patients affected by profound and total deafness with no benefit from the use of acoustic devices to inclusion of patients with marginal benefit deriving from the use of acoustic devices. Both studies consider no intervention as an alternative to CI for traditional patients and the use of an acoustic device for patients with marginal benefit. In three cases, the observation period is prior to the year 2000 [8-10] and in one case after the year 2000 [11].

Economic assessment consisted in cost analysis [11] and cost-utility analysis [8-10]. In the cost-utility studies, the following were compared: monolateral implant *vs.* no CI [8-10], monolateral implant *vs.* acoustic device [9 10], simultaneous bilateral *vs.* monolateral implant, sequential bilateral implant *vs.* no additional implant, simultaneous bilateral implant *vs.* no intervention and simultaneous bilateral implant *vs.* acoustic device [9]. In all three articles, cost-utility estimates were obtained from measurements repeated on the same subjects before and after the CI.

Three studies adopted the healthcare prospective [9-11]; one study does not declare the prospective of analysis [8].

In this article, all costs are expressed in 2011 Euro. The cost data resulting from the articles were first inflated to 2011 and then converted in Euros in the case of different currencies. In order to inflate to 2011, the consumer price index, the hospital and community health services (HCHS) pay and price index [12], and the gross domestic product deflator index for the euro zone were used for the following currencies: USA dollars, English pounds and Euros, respectively. Conversion from USA dollars to euro ($ 1 = € 0.70) and from English pounds to Euros (£ 1 = € 1.13) was performed on 14 June 2011.

Analysis of cochlear implant costs

Table I summarizes the results of cost analysis performed on the studies included in the review. The costs of cochlear implantation are estimated in all the four articles considering the preoperative, operative and postoperative phases. The costs evaluated are those related to healthcare, and the article by Molinier et al. [11] also takes into consideration the non-medical components. Indirect costs were not considered. One study [9] presents the median costs, while the other three studies [8 10 11] deal with the mean costs. Francis et al. [8] do not specify the method of evaluation of the costs; the English studies [9 10] use the top-down approach, while the French study [11] adopts a bottom-up approach using the micro-costing method.

Francis et al. [8] evaluated the direct healthcare costs of cochlear implantation taking into account the following components: preoperative assessment, CI costs, surgeon's and anaesthetist's fees, hospitalization charges and postoperative expenses including insurance, planning, CI warranty and hardware costs. The costs were € 30,026 for all patients. Total discounted costs for the group of prelingual patients was € 31,942.

The mean costs estimated by Summerfield et al. [9] for monolateral cochlear implantation were € 4,276 for preoperative assessment, 79% of which is represented by personnel expenses, and € 26,221 for surgical implantation, 79% of which related to the costs for the implanted system. Personnel costs represented the largest part (81%) of the average costs for rehabilitation in the first year after surgery and were € 5,115; maintenance costs in the following years were € 1,055.

For surgical implantation, additional median costs evaluated for simultaneous bilateral cochlear implantation were € 21,831 (95% of which was for the implanted system and the remaining 5% by personnel costs). Median additional costs evaluated for sequential bilateral cochlear implantation were € 25,459 for surgical implantation, 81% of which was represented by the costs for the implanted system, 7% by personnel expenses and 6% by the surgical session. In case of lack of implantation, management costs of the hearing aid were estimated by clinicians to be equal to a trial visit (€ 149) and a hearing aid (€ 372) every three years for about 50% of patients, and to therapeutic rehabilitation (€ 447) each year for about 10% of patients.

In the same way as for [9], for UKCISG [10] costs were evaluated on the basis of phase and year of treatment using the same cost calculation method. Unlike [9], UKCISG [10] examined only monolateral CI and analyzed the cost components in greater detail. The phases examined per year of treatment refer to preoperative assessment and surgical graft (1st year), activation and mapping of the CI and ther-

Table I. Cost analysis results of the studies included in the review of cochlear implants in adults.

Author, year of publication, country	Cost components, prospective of analysis, follow-up	Results (Euro, 2011)
Francis et al., 2002, USA [8]	Direct healthcare costs. Undefined prospective. Undefined follow-up.	Total costs for cochlear implant: - € 30,026 for all patients; - € 30,026 for postlingual deaf patients; - € 31,942 for prelingual deaf patients.
Summerfield et al., 2002, UK [9]	Direct healthcare costs. Health prospective. 4 years follow-up.	Median cost for different types of cochlear implant: - preoperative evaluation: € 4,276 ICU*, € 0 SBCI**, € 508 ABCI***; - implantation: € 26,221 ICU, € 21,831 SBCI, € 25,459 ABCI; - rehabilitation in 1st year: € 5,115 ICU, € 512 SBCI, € 548 ABCI; - maintenance in 2nd and 3rd year: € 1,055 ICU, € 512 SBCI, € 548 ABCI; - maintenance in 4th year: € 1,055 ICU, € 512 SBCI, € 548 ABCI.
UKCISG, 2004, UK [10]	Direct healthcare costs. Health prospective. 4 years follow-up.	Mean cost (range) of unilateral cochlear implant: - evaluation and implantation in 1st year: € 45,770 (€ 43,161 - € 48,528); - mapping in 2nd year: € 8,426 (€ 7,489 - € 8,932); - maintenance in 3rd year: € 1,698 (€ 1,271 – € 2,283); - maintenance in 4th year: € 1,629 (€ 931 - € 2,283); - maintenance in nth year: € 1,379 (€ 931-€ 1,818).
Molinier et al., 2009, France [10]	Direct costs for health and non-health. Healthcare prospective. 1 year follow-up.	Mean cost (± standard deviation) total of cochlear implant € 37,030 (± 3,166) in 1st year, of which: - preoperative evaluation: € 756 (± € 589), - implantation: € 28,991 (± € 2,011), - rehabilitation: € 4,677 (± € 2,087) and - travel: € 2,605 (± € 2,008).

** UCI, unilateral CI, ** SBCI: simultaneous bilateral CI; *** ABCI: additional sequential bilateral CI*

apeutic rehabilitation (2nd year) and maintenance of the patients and their CI (3rd and successive years). The costs of the hearing aid supplied to the patients before cochlear implantation were estimated to be € 656 for the trial visit and a new hearing aid for each patient in the first year of treatment. In the 1st year, the average costs for monolateral cochlear implantation were estimated to be € 45,770 for the phases of evaluation and implantation; 76% of these were absorbed by implantation of the system, 13% by hospitalization charges and 6% by the surgical session. The mapping phase of the implanted system in the 2nd year of treatment had an average cost of € 8,426, of which 95% for hospitalization fees and the remaining 5% for replacements and repairs. The phases of maintenance for the CI in the third and fourth years after implantation and mapping were estimated to be € 1,698, 75% for hospitalization costs and the remaining 25% for replacement and repair expenses, and € 1,629, of which 74% was absorbed by hospitalization charges and the remaining 26% by replacements and repairs. It was estimated that costs in the successive years will decrease to € 1,379, 70% of which will be assigned to hospitalization charges and the remaining 30% to replacements and repairs. The authors estimated an additional cost of € 9,851 every 10 years for upgrading the CI processor.

The French prospective and multicentre study [11] evaluated direct healthcare and non-healthcare costs of monolateral cochlear implantation in the preoperative, operative and rehabilitative phases. The total mean cost (± standard deviation) of cochlear implantation was estimated € 37,030 ± 3,166 per patient, of which 2% was due to the costs of preoperative evaluation, 78% to implantation costs (hospitalization € 3,517 ± 2,075 for an average period of 5 ± 3 days, implantation of the device € 25,557 ± 735), 13% to rehabilitation and 7% (€ 2,605 ± 2,008) to travel costs. Implantation costs for the device made up the largest part of expenses.

There are three cost-utility studies included in the present systematic review [8-10].

Analysis of utility gains with cochlear implants

Three articles [8-10] used the HUI to evaluate the quality of life of patients using monolateral CIs. HUI is a general, multi-attribute and preference-based questionnaire that quantitatively measures the general state of health using a health utility index score varying from 0.00 (death) to 1.00 (perfect health). The versions Mark II (HUI2) and Mark III (HUI3), which distinguish deficits in auditory and visual functions, were used.

Francis et al. [8] concluded that cochlear implantation was as-

sociated with a significant increase in quality of life: HUI-3 scores increased from an average preoperative value of 0.37 to an average postoperative value of 0.61 with significant mean difference of 0.24 ($p < 0.0001$). A significant increase in the scores of HUI-3 after surgery (0.25, $p < 0.0001$) was observed for 41 postlingual deaf patients, while the appreciated increase for the 6 patients affected by prelingual deafness did not reach statistical significance (0.21, $p \pm 0.1$). Twenty-seven patients with postlingual deafness (66%) and 3 (50%) patients with prelingual deafness reported that their quality of life had significantly improved since they started to use CIs.

The study by Summerfield et al. [9] concluded that monolateral implantation, compared to no-intervention (traditional candidates), allows an average utility gain of 0.188. Monolateral implantation, compared to a hearing aid, allowed reacing an average utility gain in patients (candidates with marginal benefit) of 0.077. Similar results were obtained in a group of volunteers. The utility gain in the group of volunteers was 0.031 both for the simultaneous bilateral implant and monolateral implants, and for the sequential bilateral implant compared to no additional intervention.

UKCISG [10] claimed that the estimated average utility gain with CI was 0.197 for all patients. Traditional patients have an average utility gain which is higher than that of patients with marginal benefit (0.214 *vs.* 0.151); in fact, the CI had stronger subjective impact on the former patients who passed from a lack of word intelligibility to the comprehension of some words compared to the latter patients whose understanding of a word increased thanks to the intervention.

Analysis of cost-utility ratio in cochlear implants

Table II summarizes the results of cost utility analyses in the studies included in the review [8-10]. Cost-utility is expressed in terms of ratio of cost effectiveness and QALY gained.

Francis et al. [8] considered an expected average number of years of usage of the implant based on 21-year life expectancy (average age of patients of 63 years). The QALY gained are 3.78 for all patients, 3.80 for the postlingual group and 3.96 for the prelingual group. Estimated cost-utility was € 7971 for QALY for all patients, € 7,930 for QALY for patients affected by postlingual deafness and € 8,096 for QALY for prelingual deaf patients. The Authors concluded that CI in adult patients is a highly cost-effective intervention for both post-lingual and prelingual deaf patients.

Summerfield et al. [9] evaluated costs and gains of the implant on the basis of an expected average usage of 30 years. From the evaluation of the authors it may be concluded that:

- compared to no intervention, monolateral implantation allows an incremental gain of 2.45 (2.08-2.83) QALY with respect to an incremental cost of € 61,265 which, in terms of QALY/cost (plausible range), was € 24,983 (€ 21,524-29,508);
- compared with hearing aids, monolateral implantation allows an increase of 1.42 (1.15-1.70) QALY with respect to an increased cost of € 58,127 which, expressed in cost/QALY (plausible range), was € 40,810 (€ 34,275-50,050);
- compared to monolateral implantation, simultaneous bilateral implantation allows an incremental gain of 0.44 (0.26-0.62) QALY with respect to an incremental utility cost of € 40,213 which, in terms of cost/QALY (plausible range) was € 91,943 (€ 65,394-154,775); sequential bilateral implantation compared to no additional implant allowed an incremental gain of 0.44 (0.26-0.62) QALY with respect to an incremental cost of € 44,892 which, expressed in cost/QALY (plausible range), was € 102,640 (€ 73,004-172,781);
- compared to no implant, simultaneous bilateral implant allows an incremental gain of 2.89 (2.45-3.33) QALY with respect to an incremental cost of € 101,479 which, in terms of cost/QALY (plausible range), was € 35,116 (€ 30,466-41,441); simultaneous bilateral implant compared to a hearing aid allowed an increment of 1.86 (1.52-2.21) QALY for an incremental cost of € 97,053 which, expressed in cost/QALY (plausible range), was € 52,130 (€ 43,979-63,990).

Cost-utility ratios for simultaneous and sequential bilateral implants (compared to monolateral implants and no additional implant, respectively) ranged from 3 to 4 times more than cost-utility ratios for monolateral implants, although the costs for monolateral implants were incrementally higher than those for bilateral implants. Therefore, the authors concluded that the second implant was less cost-effective than the first. In order for the bilateral implant to be competitive with the monolateral implant, the gain in utility of the second implant was 3 to 4 times higher than estimated.

UKCISG [10] estimated that mean life expectancy of recruited patients is around 30 years. The results of the analysis show that the increased average number of QALYs gained (95% interval of confidence) thanks to the use of the cochlear implant was 2.46 (2.19-2.73) with an average incremental cost of € 81,712 (€ 80,774-82,703), the cost-utility ratio (€/QALY) was € 33,094 (€ 29,911-36,972) for all patients. Cost-effectiveness of CI differed according to the type of patients: the cost-utility ratio for patients with marginal benefit was significantly higher than that of traditional patients, € 40,860 (€ 32,551-54,196) and € 30,892 (€ 27,665-34,928), respectively, and therefore cost-effectiveness of the CI was less competitive for patients with marginal benefit than for traditional patients. The patients with marginal benefit could use the CI for a greater number of years, incurring higher total costs for a longer period than traditional patients;

Table II. Results of the cost-utility analysis of the studies included in the review on cochlear implants in adults.

Author, year of publication, country	Type of comparison	Cost components, outcomes, discount rate	Results (Euro, 2011)
Francis et al., 2002, USA [8]	Cochlear implant *vs.* no cochlear implant.	Direct healthcare costs. Estimated utilities with HUI-III*. Yearly discount rate of 3%.	Cost/QALY**: € 7,971 for all patients; € 7,930 for patients with postlingual deafness; € 8,096 for patients with prelingual deafness.
Summerfield et al., 2002, UK [9]	i) Monolateral implant *vs.* no intervention; ii) Monolateral implant *vs.* hearing aid; iii) Simultaneous bilateral implant *vs.* monolateral implant; iv) Additional implant *vs.* no additional implant; v) Simultaneous bilateral implant *vs.* no intervention; vi) Simultaneous bilateral implant *vs.* hearing aid.	Direct healthcare costs. Estimated utilities by the time trade-off method to evaluate changes from the monolateral and bilateral implants. Yearly discount rate of 6%.	Cost/QALY** (plausible range): i) Monolateral implant *vs.* no intervention € 24,983 (€ 21,524 - € 29,508); ii) Monolateral implant *vs.* hearing aid € 40,810 (€ 34,275 - € 50,050); iii) Simultaneous bilateral implant *vs.* monolateral implant € 91,943 (€ 65,394 - € 154,775); iv) Sequential bilateral implant *vs.* no additional implant € 102,640 (€ 73,004 - € 172,781); v) Simultaneous bilateral implant *vs.* no intervention € 35,116 (€ 30,466 - € 41,441); vi) Simultaneous bilateral implant *vs.* hearing aid € 52,130 (€ 43,979 - € 63,990).
UKCISG, 2004, UK [10]	Monolateral cochlear implant *vs.* no cochlear implant.	Direct healthcare costs of CI. Estimated utilities with HUI-III*. Yearly discount rate of 6%.	Cost/QALY** (95% confidence interval): € 33,094 (€ 29,911 - € 36,972) for all patients; € 30,892 (€ 27,665 - € 34,928) for traditional patients; € 40,860 (€ 32,551 - € 54,196) for patients with marginal benefit.

* HUI-III: Health Utility Index Mark III; ** QALY: Quality Adjusted Life Years.

indeed, the patients in the former group were younger than those of the traditional group (mean age at implantation of 46 years *vs.* 53 years) and had a longer life expectancy, and therefore greater use of the CI (mean age expectancy of 34 *vs.* 28 years, respectively). However, the results of the analysis showed a minor gain in terms of average incremental number of QALY for the group with marginal benefit compared to the traditional group (1.99 QALY *vs.* 2.64 QALY) and few differences in average incremental costs (€ 81,513 *vs.* € 81,784). The unilateral CI was a cost-effective intervention for the cohort of patients under study, and was less competitive but in any case acceptable for patients with marginal benefit compared to traditional patients.

By analyzing cost/QALY in relation to age at implantation, the authors demonstrated that cost-effectiveness decreases with the age of the subjects at implantation but within an acceptable range; indeed, the average cost to gain a QALY increased from € 23,439 for subjects younger than 30 years to € 55,369 for subjects older than 70 years, as the latter have fewer remaining years on which to accumulate QALYs. Instead, considering the duration of profound deafness in the implanted year, the utility gain deriving from the use of cochlear implantation diminished with the increase of the duration of deafness and under the best preoperative condition, passing from a gain of 0.24 utilities for traditional patients with deafness duration inferior to 10 years to 0.10 QALY for those with deafness duration longer than 40 years and from a utility gain of 0.18 for patients with marginal benefit, with deafness duration inferior to 10 years at 0.06 utility for those with deafness duration higher than 30 years. CI were not cost-effective for traditional patients with more than 40 years of profound deafness (€ 64,604/QALY) or for patients with more than 30 years of profound deafness, with marginal benefit from the use of the hearing aid (€ 106,267/QALY). Therefore, the authors concluded that CI is a cost-effective intervention for the majority of subjects, including patients older than 70 years at age of implant, while the extension of the criteria of eligibility to intervention for patients with marginal benefit reduces cost-effectiveness.

Discussion

The cost-utility of cochlear implants in adult patients has been examined in only a few studies on economic evalu-

ation. A meta-analysis of the literature prior to the year 2000 demonstrated that cochlear implantation provides a total average improvement of 0.26 utilities in adult patients affected by profound deafness with cochlear implantation costs of € 12,127 for QALY [12]. Therefore, to provide an updated synthesis of the results of studies published since 2000, a systematic review of literature was conducted through a rigorous screening process, which made it possible to identify 4 studies on economic evaluation responding to the selection criteria established in the present review protocol.

The limited number of studies included in the review and the differences between countries, samples, study design, follow-up, utility measures, cost components make it difficult to compare the results obtained or to perform a quantitative synthesis of the results through meta-analysis. The results of the studies cannot be pooled due to the different features utilized. Furthermore, meta-analysis is possible when the same treatment is evaluated in a considerable number of studies, but in this case meta-analysis applied to few heterogeneous studies would produce results that would be unreliable and difficult to reproduce.

With regard to economic evaluations in general and cochlear implants in particular, the specific features of the different contexts (e.g. in terms of organization of the healthcare systems) render healthcare resources and associated costs highly variable within the same country and between countries, so that generalizability and transferability of cost and cost-effectiveness estimates may be limited to areas other than the specific case.

From the results of the articles included in this review, we conclude that cochlear implantation is a highly expensive intervention. Total direct healthcare costs for monolateral cochlear implantation in patients affected by postlingual deafness varies, on average, from about € 30,026 [8] to € 45,770 [10], including preoperative evaluation and intervention, in which the expenses for the hearing aid represent the main component.

Mapping costs for monolateral CIs in the second year after the intervention and of maintenance in the successive years decrease over time (from € 8,426 in the second year to € 1,379 in the years successive to the fourth year [10]). Additional average costs for simultaneous and sequential bilateral implants were € 21,831 and € 25,459 respectively [9], including preoperative evaluation and intervention. The total costs for monolateral CI was € 31,942 according to the estimates of Francis et al. [8].

In patients affected by postlingual deafness, the mean utility gain from the preoperative condition with monolateral CI varies from 0.20 [10] to 0.25 [8]. The mean utility gain was higher in traditional patients who did not benefit from acoustic devices to patients who benefited only marginally from the use of acoustic devices (0.21 *vs.* 0.15 [10], 0.17 *vs.* 0.08 [9]). Mean gain in terms of simultaneous or sequential bilateral implantation was inferior to the gain with monolateral implantation (0.03 [9]). Patients with prelingual deafness had a mean utility gain of 0.21 [8].

Monolateral CIs in patients affected by postlingual deafness represent a cost-effective intervention when compared to no-implant for the studies included in the review (€ /QALY: € 7,930 according to Francis et al. [8]; € 24,983 according to Summerfield et al. [9]; € 33,094 according to UKCISG [10]). Cost-effectiveness of monolateral CI were less competitive but in any case acceptable in patients with marginal benefit from the acoustic device compared to traditional patients without benefit (€ /QALY: € 40,860 *vs.* € 30,892 [10]). According to UKCISG [10], monolateral CIs were not cost effective for traditional patients with a duration of deafness over 40 years affected by profound hearing impairment (€ 64,604/QALY) and for patients with more than 30 years of profound deafness receiving marginal benefit from the use of an acoustic device (€ 106,267/QALY). With regard to the age at implantation, UKCISG [10] concluded that cost-effectiveness of monolateral cochlear implants decreased with increasing age, remaining however within an acceptable range (€ / QALY from € 23,439 for younger subjects 30 years of age to € 55,369 for those older than 70 years). Bilateral implants in patients affected by postlingual deafness are less cost-effective than monolateral implants (simultaneous bilateral implant *vs.* monolateral implant € 91,943/ QALY; bilateral sequential implant *vs.* no additional implant € 102,640/QALY) [9]. Monolateral CIs are also cost-effective in patients affected by prelingual deafness (€/ QALY: € 8,096 according to Francis et al. [8]). The estimates provided by the studies analyzed – although variable and context-dependent – should however be considered as references in the literature after the year 2000.

With regard to the design of the study, the retrospective cohort studies [8 9] could be affected by the recall bias, namely the reduced capacity of patients to remember past events that may have influenced outcomes relative to the estimates of preoperative utility. The studies analyzed [8-10] measured the utilities through repeated measurements (before and after CI), and therefore did not compare cases (patients with CI) with controls (patients without CI); they did not indicate what would happen to patients without CI, thus limiting the analysis. However, as profound bilateral deafness allows neither spontaneous recovery nor regression, it displays none of the typical features which normally limit the design with repeated measurements.

Concerning the cost components analyzed, the study by Francis et al. [8] does not report explicitly the prospective of analysis adopted in the study and it is therefore difficult to establish whether all the significant cost categories have been considered. The prospective of society can however be excluded, since the indirect costs are not taken into account. The study does not specify the method employed to calculate costs and does not describe in detail the consumed resources and associated cost units. Furthermore,

sensitivity analyses were not performed, and for this reason the results can hardly be extended to other contexts.
These limits, as well as the exiguity of the sample and the retrospective and single centre study design are partly responsible for the lower estimates of cost and cost utility presented by the authors with respect to the studies considered. These estimates can only be referred to the centre and to the categories of patients analyzed.
Compared to the other studies [8-10], the estimate of costs performed by Molinier et al. [11] over a single year covers a shorter follow-up period which affects expenses: the longer the period of observation, the higher the costs, in particular when the expenses for post-operative rehabilitation were considered.
Not only does the brief follow-up affect the rehabilitation costs, but it also influences a number of important cost components that are not taken into account. These include adverse events and repair or replacement of CI. Unlike other investigations [8-10], the French study [11] is the only one that considered direct non-medical travel expenses, but not the costs for informal care, i.e. the time dedicated by relatives and friends to assist the deaf patient. Another important cost component neglected by all the four studies is indirect costs, including the losses of productivity that were totally or partially supported by the patients and relatives, e.g. work days lost by the patient for treatment and healthcare assistance, the work time lost in terms of the patient's lower work productivity, and work days lost by relatives assisting the patients (Vantrappen et al. [14] estimated that the indirect costs represent 8.9% of total costs).
The analysis of costs and cost-utility of simultaneous and sequential bilateral CIs is limited to the study by Summerfield et al. [9] who only assess the utilities deriving from bilateral implantation not in hearing impaired patients, but in normal hearing volunteers (using the time trade off method) not affected by deafness and eventual comorbidity. Furthermore, they estimated the resources absorbed by the implants as the minimal resources considered plausible by clinicians. Recent contrasting outcomes on cost-utility of bilateral implants were published by Bichey and Miyamoto [15]. This study was not included herein, as the authors analyzed a sample of postlingual deaf patients aged 6 to 79 years with very different characteristics, without stratifying the results on the basis of paediatric or adult patients. Unlike Summerfield et al. [9], the outcomes of the study showed an overall improvement of 0.48 utilities after bilateral implant with favourable cost/QALY of € 17,132. In order to clarify the relation between age at implantation and duration of deafness and quality of life of patients using cochlear implants, it would be necessary to assess larger samples with respect to those of Francis et al. [8] who analyzed 47 elderly patients. Moreover, in the future it will be necessary to perform studies on braoder samples of patients to estimate the cost-utility of cochlear implantation in patients affected by prelingual deafness, as only one study [8] deals with a group of 6 patients.

Conclusions

The examination of four articles on economic evaluation published after 2000 and included in our systematic literature review allowed identification of the high costs supported by the healthcare sector for cochlear implantation in adult patients affected by post-lingual deafness. Of the four articles concerning economic assessment, three studies performed complete cost-quality analyses indicating that monolateral cochlear implantation is generally a cost-effective intervention. When compared to non-intervention, monolateral cochlear implantation has QALY/costs varying from about € 25,000/QALY [9] to € 33,000/QALY [10] for patients affected by postlingual deafness. Cost/QALY estimates indicate that monolateral cochlear implantation is also a cost-effective intervention for elderly patients, while the extension of eligibility criteria to patients marginally benefiting from the use of hearing aids showed a reduction in cost-effectiveness. Cochlear implantation is not cost-effective for patients who obtained a benefit from the use of hearing aids with a duration of profound deafness in the ear receiving the implant that was over 30 years [10].
Therefore, the duration of deafness should be taken into account to establish the eligibility criteria for cochlear implantation. Bilateral implants are less cost-effective than monolateral implants as shown by the study by Summerfield et al. [9]
This systematic review of the literature included only one study [8] on adult patients affected by prelingual deafness showing that monolateral cochlear implantation was also cost-effective for this group. The insufficient number of patients examined by the study and the lack of references in the literature make it necessary to perform future research on a wider sample of patients to study the utility costs of cochlear implantation in adult patients with prelingual deafness. Since the studies analyzed consider only direct healthcare costs, except for one article which also assessed the non-medical direct costs for travelling, future economic assessment studies should consider the other categories of non-medical direct costs and indirect costs. There is a limited number of articles published, so that the results cannot easily be generalized to contexts different from those specific to individual studies. Future searches through economic assessment studies will thus be necessary to:

a. support the cost-effectiveness results of CIs in adults;
b. evaluate cost-effectiveness of simultaneous and sequential bilateral implants;
c. evaluate the components of direct and indirect non-medical costs as well as direct medical costs in cost-effectiveness analysis.

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