Systematic review of the literature on the clinical effectiveness of the cochlear implant procedure in paediatric patients

Revisione sistematica della letteratura sull'efficacia clinica della procedura di impianto cocleare in età pediatrica

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SUMMARY

The aim of this systematic review of the literature was to summarize the results of scientific publications on the clinical effectiveness of the cochlear implant (CI) procedure in children. The members of the Working Group first examined existing national and international literature and the principal international guidelines on the procedure. They considered as universally-accepted the usefulness/effectiveness of unilateral cochlear implantation in severely-profoundly deaf children. Accordingly, they focused attention on systematic reviews addressing clinical effectiveness and cost/efficacy of the CI procedure, with particular regard to the most controversial issues for which international consensus is lacking. The following aspects were evaluated: post-CI outcomes linked to precocity of CI; bilateral (simultaneous/sequential) CI *vs.* unilateral CI and *vs.* bimodal stimulation; benefits derived from CI in deaf children with associated disabilities. With regard to the outcomes after implantation linked to precocity of intervention, there are few studies comparing post-CI outcomes in children implanted within the first year of life with those of children implanted in the second year. The selected studies suggest that children implanted within the first year of life present hearing and communicative outcomes that are better than those of children implanted after 12 months of age. Concerning children implanted after the first year of life, all studies confirm an advantage with respect to implant precocity, and many document an advantage in children who received cochlear implants under 18 months of age compared to those implanted at a later stage. With regard to bilateral CI, the studies demonstrate that compared to unilateral CI, bilateral CI offers advantages in terms of hearing in noise, sound localization and during hearing in a silent environment. There is, however, a wide range of variability. The studies also document the advantages after sequential bilateral CI. In these cases, a short interval between interventions, precocity of the first CI and precocity of the second CI are considered positive prognostic factors. In deaf children with associated disabilities, the studies analyzed evidence that the CI procedure is also suitable for children with disabilities associated with deafness, and that even these children may benefit from the procedure, even if these may be slower and inferior to those in children with isolated deafness, especially in terms of high communicative and perceptive skills.

KEY WORDS: Cochlear implant • Bilateral cochlear implant • Severe to profound hearing loss • Disabilities

RIASSUNTO

L'obiettivo della revisione sistematica della letteratura è stato quello di sintetizzare i risultati degli studi scientifici pubblicati sull'efficacia clinica della procedura di impianto cocleare (IC) nel bambino. I componenti del Gruppo di Lavoro, viste le evidenze della letteratura nazionale ed internazionale e analizzate le principali linee guida internazionali riguardanti la procedura in oggetto, decidono di considerare come universalmente accettata l'utilità/efficacia della procedura di IC unilaterale nelle sordità gravi/profonde del bambino e di focalizzare la review sulle tematiche più attuali e più discusse, per per le quali non esiste ancora un consenso internazionale. In particolare, si è proceduto alla valutazione dei seguenti aspetti: risultati post-IC in rapporto alla precocità dell'IC; IC bilaterale (simultaneo/sequenziale) vs. IC unilaterale e vs. stimolazione bimodale; beneficio derivato dalla procedura di IC in bambini con disabilità associate alla sordità. Riguardo ai risultati post-IC in relazione alla precocità del'intervento, sono pochi gli studi della letteratura che confrontano i risultati post-IC di bambini impiantati entro il primo anno di vita con quelli di bambini impiantati nel secondo anno di vita. Gli studi selezionati evidenziano comunque che bambini impiantati entro il primo anno di vita presentano risultati uditivi e soprattutto comunicativi migliori rispetto a quelli impiantati dopo i 12 mesi di età. Per quanto riguarda i bambini impiantati dopo il primo anno di vita, tutti gli studi documentano un vantaggio in relazione alla precocità di impianto, e tra questi molti documentano un vantaggio in bambini sottoposti alla procedura entro i 18 mesi di vita rispetto a quelli impiantati in epoche successive. Riguardo all'IC bilaterale, gli studi selezionati dimostrano che l'IC bilaterale rispetto all'IC unilaterale offre vantaggi nell'ascolto nel rumore, *nella localizzazione sorgente sonora, durante l'ascolto nel silenzio. E'comunque presente una ampia variabilità nei risultati. Gli studi documentano vantaggi anche dopo IC bilaterale sequenziale. In questo caso vengono considerati fattori prognostici positivi un breve intervallo tra i due interventi, la precocità del primo IC, la precocità del secondo IC. Per quanto riguarda la procedura di IC in bambini con disabilità associate, gli studi selezionati documentano che la procedura di IC è indicata anche in bambini con disabilità associate alla sordità e che questi bambini presentano benefici dalla procedura, anche se più lenti e inferiori rispetto ai bambini con sordità isolata, soprattutto in termini di abilità comunicative e percettive elevate.*

PAROLE CHIAVE: *Impianto cocleare • Impianto cocleare bilaterale • Sordità grave-profonda • Disabilità*

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Introduction and aim

The aim of this systematic literature review was to summarize the results of scientific publications on the clinical effectiveness of the cochlear implant (CI) procedure in children. The members of the Working Group first examined existing evidence from national and international literature and the main international guidelines concerning the procedure [1]. They considered as universally accepted the usefulness/effectiveness of unilateral cochlear implantation in severely-profoundly deaf children. Accordingly, they focused their attention on systematic reviews addressing clinical effectiveness and cost/efficacy of CI procedure, with particular regard to the most controversial issues for which international consensus does not yet exist.
For preparation of the review article on the clinical effectiveness of CI in children, the following aspects were evaluated:
1. post-CI outcomes linked to precocity of CI;
2. bilateral (simultaneous/sequential) CI *vs.* unilateral CI and *vs.* bimodal stimulation;
3. benefits derived from the CI procedure in deaf children with associated disabilities.

Methods

A systematic review of the literature was undertaken using explicit and reproducible methodology aimed at minimizing any possible distortions, biases or erroneous conclusions caused by the exclusion of important studies, according to the recommendations made by the *Systematic Reviews CRD's guidance for undertaking reviews in health care* [2].

Search strategy
A systematic review of the literature was performed using the following databases: PubMed Medline and Cochrane Systematic Review Database. Furthermore, the major Internet sites and guidelines from national and international scientific societies were consulted. Bibliographical research was completed by assessing the bibliographical entries of pertinent, previously selected publications.

Research Issues
Bibliographical research performed on databanks using the *MeSH descriptor* or a combination of keywords was limited to articles published in English. The search in PubMed Medline was conducted on works published after the year 2000. Owing to the rapid progress of technology and the rapidly-expanding indications to CI procedure, papers published before the year 2000 were excluded.
The first bibliographical search was undertaken in 2009. At a later stage, bibliographic research was updated for the period of publication from 2009 to 31 May 2010.

Bibliographical research characteristics
- PubMed Medline: "Cochlear Implants"[Mesh] AND (("2000"[PDat]:"2009"[PDat]) AND (English[lang]) AND ((infant[MeSH] OR child[MeSH] OR adolescent[MeSH]))) ⇒ 929 results.
- Cochrane Systematic Review Database: MeSH descriptor cochlear implants explode all trees. A total of 107 results up to 31 May 2010. All studies retrieved by the Cochrane Systematic Review Database were also selected by PubMed Medline.

Outcomes assessed
Studies reporting one or more of the following outcomes were evaluated: audiological results and language and communication results.

Exclusion criteria
Articles which did not present the above-listed characteristics were not considered. Articles presented at congresses but not submitted to peer-reviewing, as well as case reports, letters, commentaries and non-English studies published before the year 2000 were also excluded. The inclusion criteria were applied by one reviewer and then checked by a second. Any dissenting opinions were resolved through discussion.

Strategy to assess the quality of studies
The publications identified according to the search criteria described above were examined by two independent reviewers. Any dissenting opinions were resolved through discussion. A preliminary selection was made

on the basis of titles and abstracts. The works were then examined in full-text format, and assessed in terms of methodological quality and usefulness of the reported results for the type of analysis to be conducted. Methodological quality was assessed using the available tools, according to the criteria specified in the report *Systematic Reviews CRD's guidance for undertaking reviews in health care* [2].

Strategy of data extraction

The data were extracted by a reviewer and checked by a second. Any dissenting opinions were resolved through discussion. Tables summarizing the main information on each study included were produced, including Authors' name, year of publication, title of the journal, sample population and other data concerning methods, devices and results (Tables I-III).

Results

A total of 929 studies on the clinical effectiveness of the CI procedure in paediatric patients were identified using the research criteria listed in the *Aims*. A preliminary evaluation was performed on the basis of the titles and abstracts, and 138 works were selected and examined in full text format. A total of 49 studies on CI in children were chosen and used for the review. The principal documents containing the guidelines for the procedure of national and international CI were examined. A summary of the review and assessment of the literature studies is shown in Figure 1.

Bearing in mind the purpose of this review, the following articles were selected which concerned clinical effectiveness of the CI procedure in paediatric age: 22 articles on "post-CI results related to CI precocity"; 20 articles on "bilateral (simultaneous/sequential) CI *vs.* unilateral CI and *vs.* bimodal stimulation"; 7 articles on the "benefit derived from the CI procedure in children with disabilities associated with deafness".

Tables I, II and III include the articles selected, subdivided according to subject with detailed information on the authors, title, journal and year of publication, as well as sample features, most relevant data on the methods adopted, results and conclusions.

With regard to the analysis of the results, it was not possible to perform a meta-analysis. Study design, type of comparison and results of the articles selected for inclusion in the review were different, and therefore it was difficult to define the features on which to base variations in outcome. The studies included in the review presented variability related to type of interventions and outcomes (clinical differences), and study design and error risk (methodological differences). Therefore, the studies presented variabilities in the effects of intervention, and consequently statistical differences resulting from both methodological and clinical diversity. Therefore, a meta-analysis was not feasible, as the studies included in the review were not sufficiently consistent in terms of types of participants, interventions and outcomes, and therefore could not provide statistically significant results.

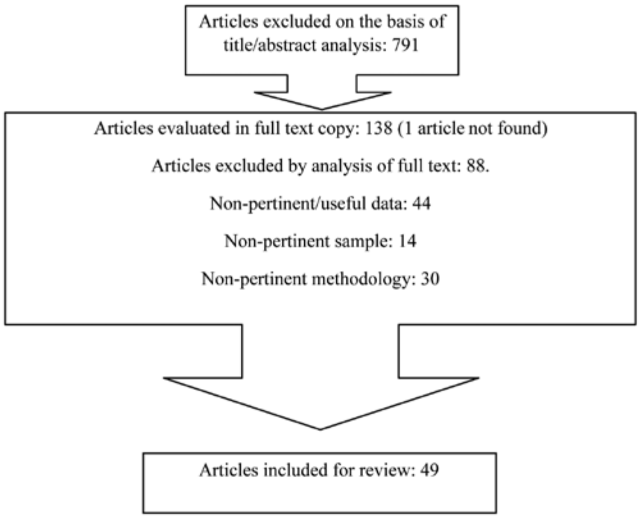

Fig. 1. Summary of selection of literature articles.

The two most recent systematic reviews on the procedure [3 4] reported the same difficulty in performing a meta-analysis, and were therefore limited to a narrative description of previous studies.

Results

Post-CI results in relation to early cochlear implantation

A total of 22 studies were selected from the literature (Table I). Considering the introduction of CI in children younger than twelve months, few studies in the literature have compared post-CI results in children implanted within the first year of age, compared to those implanted between 12 and 24 months.

The results in children implanted in their first year of life are reported in 7 studies. However, statistical significance of the data is not confirmed in all studies submitted to statistical analysis (Table I). Furthermore, the data in the selected publications is insufficient to assess whether the advantages identified in children implanted in their first year of life is retained over time and to what extent they are influenced by a longer period of usage of the implant.

Dettman et al. [5] observed improved language outcomes in children implanted within the first year compared to those implanted between 12 and 24 months. Moreover, language development in children implanted within the first 12 months of life seems to be similar to that of their hearing peers. However, it is not clear whether this advantage identified in children implanted in their first year of life is retained over time and whether the results are influenced by a longer period of usage of the implant.

Table I. Summary of selected literature studies on "Post-CI results in relation to early CI" (paediatric age).

Authors	Title	Journal, year	Sample size and other methodology	Type of CI/ processing strategy	Results evaluated	Conclusions/opinions
Niparko et al. [15]	Spoken language development in children following cochlear implantation	JAMA 2010	188 children implanted before five yrs of age. Group 1 children implanted < 18 mths. Group 2 children implanted 18-36 mths. Group 3 children. implanted aged > 36 mths. Follow-up: 3 yrs.	Not specified	Language development in relation to age. Raynell Developmental Language Scales (RDLS). Speech Recognition Index (SRI).	Children implanted earlier (Group 1) achieve better language results and present a steeper learning curve.
Hayes et al. [16]	Receptive vocabulary development in deaf children with cochlear implants: achievement in an intensive auditory-oral educational setting	Ear & Hear 2009	65 children implanted at < 5 yrs. All children were submitted to oral education. Case studies relative to the period 1991-2004.	Technology was not specified	Assessment of receptive vocabulary through annually-submitted PPVT.	Implanted children present levels of receptive vocabulary inferior to those of their hearing peers, but growth velocity in vocabulary achievement is more rapid. Implanted children < 2 yrs have velocity of receptive vocabulary development > children implanted at a later stage (2-5 yrs).
Ching et al. [10]	Early language outcomes of children with cochlear implants: interim findings of the NAL study of longitudinal outcomes of children with hearing impairment	Cochlear Implants Int 2009	16 implanted children < 12 mths. 23 implanted children > 12 mths. They specify mean age at CI, but not age range.	Not specified	Results of language development: Preschool Language scale (PLS-4, Zimmermann et al. 2002). Follow-up: test at 6-12-24 mths post-CI.	They compare the post-CI results in children implanted before and after 12 mths. Implanted children < 12 months present language outcomes (in understanding and production) similar to their hearing peers and have abilities of language development similar to those of normal-hearing peers. Implanted children > 12 mths lag behind with respect to normal-hearing peers, in terms of abilities as well as rates of language development.
Colletti [8]	Long-term follow-up of infants (4-11 months) fitted with cochlear implants	Acta Otolaryngol 2009	Group I: 13 children CI 4-11 mths. Group II: 18 children CI 12-23 mths. Group III: 22 children CI 24-36 mths. Follow-up 4-9 yrs.	Nucleus 24M	Perceptive abilities: Category of Auditory Performance (CAP). Receptive Language: Peabody Picture Vocabulary Test (Revised) (PPVT-R). Receptive grammar-language development: Reception of Grammar (TROG). Language comprehension: SIR.	Perceptive abilities: Category of Auditory Performance (CAP). All children reach maximum level, but those of II and III groups with delay. Statistically significant. Receptive language: Peabody Picture Vocabulary Test (Revised) (PPVT-R). Only children of first group follow a trend similar to that of normal-hearing children. The other children never reach the levels of normal-hearing peers even after 9 yrs of age. Statistically significant. Receptive grammar-language development: Reception of Grammar (TROG). Better and more rapid results in former group. Statistically significant. Language comprehension: SIR. Outcomes in II and III groups were slightly worse, but at 5 yrs the differences were not significant.

(continues)

Table I. *(follows)*

Holt & Svirsky [11]	An exploratory look at pediatric cochlear implantation: is earliest always best?	Ear Hear 2008	96 children implanted before 4 yrs of age. Subdivided into 4 groups: CI at 1, 2, 3, 4 yrs of age. Follow-up > 2 yrs.	Not specified	Assessment of language development (receptive and expressive language) and of the rate of language development. Evaluation of perceptive abilities (recognition).	Limited advantage in children implanted within 12 months of age and those implanted in second yr of life.
Miyamoto RT et al. [6]	Language skills of profoundly deaf children who received cochlear implants under 12 months of age: a preliminary study	Acta Oto-Laryngologica 2008	8 children CI < 12 mths. 38 children CI 12-23 mths. 45 childen 24-36 mths. Follow-up 2-3 yrs.	SAS, CIS, SPEAK, ACE	Comprehension and production language tests: Reynell Developmental Language Scales (RDLS) or the Preschool Language Scale (PLS).	Children implanted < 24 mths show better results than those of children implanted at 24-36 mths, but data are not statistically significant. Better results in earlier implanted children, but the number of children implanted before 12 mths is too small to draw conclusions.
Nicholas & Geers [18]	Will they catch up? The role of age at cochlear implantation in the spoken language development of children with severe to profound hearing loss	J Speech, Lang Hear Res 2007	76 children CI 1-3 yrs ± 2. tests performed at 3.5 and 4.5 yrs.	Medel, Clarion, Cochlear	Expressive language sample transcribed from video recording. Preschool Language Scale - Third Edition (Zimmerman et al., 1992).	Children implanted < 24 mths present language similar to that of normal-hearing peers at 4.5 yrs. Children implanted earlier generally show improved language outcomes.
Dettman et al. [5]	Communication development in children who receive the cochlear implant younger than 12 months: risks vs. benefits	Ear Hear 2007	11children CI < 1 yrs, 36 children CI 12-24 mths.	ACE, SPEAK SPrint, ESPrit 3G, Freedom	Evaluation of language in terms of comprehension and expression RI-TLS (Rossetti, 1990).	The first group shows language outcomes in terms of comprehension and production which are similar to those of normal-hearing children.
Wu et al. [22]	Effect of age at cochlear implantation on open-set word recognition in Mandarin speaking deaf children	Int J Pediatr Otorhinolaryngol 2006	15 children CI < 3yrs. 13 children CI > 3 yrs. Follow-up > 3 yrs.	Nucleus 24 M, ACE	Verbal perception test in Mandarin (open-set): Mandarin Lexical Neighborhood Test (M-LNT).	Implanted children < 3 yrs better results than those of implanted children > 3 years (open set). Statistically significant. Mandarin speaking deaf children.
Nicholas & Geers [17]	Effects of early auditory experience on the spoken language of deaf children at 3 years of age	Ear Hear 2006	76 children implanted 12-38 mths.		Evaluation of language at 3.5 yrs: analysis of language in 30 min video recording, Mc Arthur (parents), Scales of Early Communication Skills for Hearing-Impaired Children (teachers).	The children with better pre-op threshold and longer usage of CI present better language outcomes. Statistically significant.
Lee et al. [23]	Spoken word recognition in children with cochlear implants: a five-year study on speakers of a tonal language	Ear Hear 2005	15 children CI 1-3 yrs. 18 children CI 3-6 yrs. 31 children CI > 6 yrs.	Nucleus 22, Nucleus 24	Verbal perception test in Cantonese (recognition).	Children implanted < 3 yrs have better results than those of children implanted > 6 yrs of age. Statistically significant. These outcomes also remain at long-term (5 yrs follow-up). Cantonese.

(continues)

Table I. *(follows)*

Colletti et al. [7]	Cochlear implantation at under 12 months: report on 10 patients	Laryngoscope 2005	10 children CI < 12 mths. Control groups: children CI 12-23 mths (24 children), 24-35 mths (21 children), 36-59 mths (12 children) and 60-72 mths (5 children). Follow-up: 1-3-6-12-24 mths post-CI.		Perceptive categories. Onset of babbling.	Perceptive categories, more rapid improvement in children implanted < 12 mths. Results progressively slower in children implanted later. Onset of babbling in children implanted < 12 mths: no statistically significant differences with respect to normally hearing peers (Control group: 10 children).
Lesinsky-Schiedat et al. [9]	Pediatric cochlear implantation in the first and second year of life: a comparative study	Cochlear Implants Int 2004	27 children CI < 12 mths. 89 children CI 12-24 mths. Follow-up: 3-6-12 mths and then annually post-CI.	Nucleus 24M/Contour, Advanced Bionics	Test of verbal perception: - FDA test battery (Lesinsky-Sheidat 1999): closed- and open-set. - MAIS and MUSS.	After 2 yrs from CI the group of children receiving CI < 12 mths resulted better than the other children in open set. Not statistically significant.
Manrique et al. [20]	Advantages of cochlear implantation in prelingual deaf children before 2 years of age when compared with later implantation	Laryngoscope 2004	36 children CI < 2 yrs, 94 children CI 2-6 yrs. Follow-up: 5 yrs.	Processing strategies: SPEAK, CIS, ACE, MPEAK (modified in SPEAK during the study)	Verbal perception in *closed* and *open* set. Language development: Peabody Picture Vocabulary + Reynell general oral expression scale.	Implanted children < 2 yrs achieve better results in verbal perception. Statistically significant. Implanted children < 2 yrs obtain better language outcomes (in line/slight delay with respect to the normally hearing population). Those implanted 2-6 yrs have benefits, but are inferior to those of the other group.
Manrique et al. [21]	Prospective long-term auditory results of cochlear implantation in prelinguistically deafened children: the importance of early implantation	Acta Otolaryngol 2004	94 children CI 0-3 yrs. 36 yrs CI 4-6 yrs. 30 yrs CI 7-10 yrs. 22 yrs CI 11-14 yrs.	Nucleus 22 and 24, SPEAK	Tone audiometry, CL. Verbal perception test in Spanish. Language test: Peabody Picture Vocabulary test and Reynell's general oral scale.	Children implanted < 3 yrs show better outcomes both in verbal perception and in language development. Children who receive CI < 6 years achieve the better results. After 6 yrs no differences at the time of CI are observed between children implanted before and after.
Svirsky et al. [12]	Development of language and speech in congenitally profound deaf children as a function of age at cochlear implantation	Audiol Neurotol 2004	20 children CI 12-24 mths. 34 children 24-36 mths. 29 children 36-48 mths.		Receptive and expressive language evaluation. Raynell Development Language Scale (RDLSIII). Mc Arthur early language development.	CI performed in second year of life leads to improved results in terms of verbal perception and language development. Interindividual variability.
McConkey Robbins et al. [13]	Effect of age at a cochlear implantation on auditory skill development in infants and toddlers	Arch Otolaryngol Head Neck Surg 2004	100 implanted children. Group 1: 45 children CI < 18 mths. Group 2: 32 children CI 19-24 mths. Group 3: 30 children CI 25-36 mths.	Device: Clarion Multi Strategy	Perceptive abilities evaluated by IT-MAIS.	All children improved. Groups 1 and 2 result to be more rapid than group 3. Group 1 achieves before group 2 at IT-MAIS results similar to those of normally hearing children and group 2 before group 3. They document the advantage of receiving CI before 18 mths with respect to 18-24 mths.
Nikolopoulos et al. [26]	Development of spoken language grammar following cochlear implantation in prelingually deaf children	Arch Otolaryngol Head Neck surg 2004	82 implanted children	Devices: CI Nucleus	Grammar competence and receptive language (TROG: Test for Reception of Grammar).	Statistically significant improvement after follow-up of 3-5 yrs. Children receiving CI within 4 yrs reach better (statistically significant) results than those of children implanted after 4 yrs.

(continues)

Table I. *(follows)*

Anderson et al. [19]	Cochlear implantation in children under the age of two - what do the outcomes show us?	Int J Pediatr Otorhinolaryngol 2004	37 children CI < 2 yrs (10-23.9 mths). 26 children CI 2-4 yrs. 27 children CI 4-6 yrs. Follow-up 3 yrs.	MED-EL COMBI 40/ COMBI 40+TIME+ speech processor/CIS PRO+ body-worn processor.	Test of verbal and language perception of the EARS protocol.	The 37 children implanted < 2 yrs show better results than those implanted 2-4 yrs and 4-6 yrs. More rapid and better results, with particular regard to language development.
Sainz [24]	Assessment of auditory skills in 140 cochlear implant children using the EARS protocol	ORL J Otorhinolaryngol Relat Spec 2003	140 implanted children. Follow-up: 2 yrs.	Device: Medel Combi 40/40+	Perceptive abilities evaluated by EARS protocol.	Improved perceptive abilities more evident in terms of CI precocity. Children implanted within 3 yrs obtain better results than those implanted at later stages.
Hassanzadeh et al. [25]	The effects of age on auditory speech perception development in cochlear-implanted prelingually deaf children	Otolaryngol Head Neck Surg 2002	119 subdivided into 2 groups (CI < 3 yrs and CI > 3 yrs). Follow-up 24 mths.	CI 22 (Spectra 22 speech processor), Nucleus CI 24 (Sprint speech processor), processing strategy SPEAK, ACE	Tests of verbal perception closed-set and open-set in Persian.	Children receiving CI < 3 yrs have better results in verbal perception tests. Statistically significant results.
Novak et al. [14]	Cochlear implants in infants and toddlers	Ann Otol Rhinol laryngol Suppl 2000	15 children implanted between 9 and 25 mths.	Devices Nucleus 22 and 24, Advanced Bionics1.2 and S-Series	Evaluation of verbal perception, language production.	Children implanted before 18 mths present better and more rapid linguistic results than those implanted between 18 and 25 mths.

Miyamoto et al. [6] documented the best results in language development (comprehension and production) in children implanted before the first year of age, but owing to the limited sample they were unable to draw any definite conclusions.

Colletti V. et al. [7], and later Colletti L. [8], reported better results in terms of development of verbal perception, receptive language and verbal understanding in children implanted within the first year of age compared to those implanted in the second and third years of age. This data was statistically significant.

Lesinsky et al. [9] recorded better results of verbal perception in *open* set in children implanted before the first 12 months of age than in those implanted during the second year of age, at 2-year follow-up. However, the results were not statistically significant.

Ching et al. [10] confirmed better and more rapid outcomes in terms of perception and production related to linguistic development in children implanted within the first year of life compared to those implanted at a later stage; however, the Authors did not specify the age of implantation in this latter group of children.

Holt and Svirsky [11] found no evident advantages in children implanted before 12 years of age compared to those implanted in the second year of life. There were only a small number of case studies of children implanted within the first year of life (n ± 6).

According to the studies selected [12], the advantages of CI *after the first year of life* were more favourable in relation to implant precocity. The studies evaluated were heterogeneous for the age ranges analyzed and outcomes evaluated. In particular, the different age ranges examined in these studies is likely to be related to the different periods in which the investigations were performed. Moreover, the statistical analysis did not always provide statistically significant outcomes (Table I).

As far as perceptive abilities are concerned, Robbins et al. [13] documented results which were better in children implanted before 18 months of age vs those implanted between 18 and 25 months. Similarly, Novak et al. [14] reported better and more rapid language outcomes in children implanted before 18 months vs children implanted between 18 and 25 months.

Niparko et al. [15] also referred better and more rapid language outcomes in children implanted before 18 months of age vs those implanted at later stages.

Hayes et al. [16] documented higher development velocity in terms of perceptive vocabulary in children implanted within the first two years of age compared to children implanted between 2 and 5 years of age.

Miyamoto et al. [6] and Svirsky et al. [12] found better results in terms of language development (comprehension and production) in children implanted within the first two years of age vs those implanted after two years (in Svirsky et al.; the comparison was with children implanted between 2 and 4 years of age).

Holt and Svirsky [11] recorded an advantage in expressive and receptive language in terms of implant precocity and more rapid development in earlier implanted children than in a group of children who received CI within the first 4 years of age. However, as far as development of word recognition ability is concerned, no differences were found in relation to early implantation.
Nicholas and Geers [17] demonstrated better outcomes in children implanted earlier, with regard to children implanted between 12 and 38 months of age.
Nicholas and Geers [18] observed improved results in children implanted before two years of age compared to those implanted at later stages. Anderson et al. [19] documented better and more rapid results in terms of verbal perception and of language development in children implanted in the first 2 years of age compared to those implanted between 2-4 and 4-6 years.
Manrique et al. [20] recorded better results in terms both of verbal perception and language development in children implanted before three years of age than in children implanted at later stages. In a study carried out in the same year by Manrique et al. [21], the same group confirmed better results of verbal perception and language development in a group of children implanted before the age of two compared to children implanted between 2 and 6 years of age.
Wu et al. [22], Lee et al. [23] and Sainz [24] documented better verbal perception in children implanted within the third year of age vs those implanted at a later stage. Hassanzadeh et al. [25] document better results in the verbal perception of children implanted within the third year of age vs those implanted at later stages. Nikolopoulos et al. [26] demonstrated better grammar competence in children implanted within the first 4 years of age vs those implanted at later stages.
In summary, there are few studies in literature comparing post-CI outcomes in children implanted within the first year of life with those of children implanted in the second year. The selected studies suggest that children implanted within the first year of life present hearing and especially communicative outcomes that are better than those of children implanted after 12 months of age. Unfortunately, only a limited number of studies have been published, and even fewer report statistical significance; the long-term results are unknown. Moreover, it is impossible to establish what influence duration of CI usage rather than precocity of implant may have on outcomes, with particular regard to language.
Concerning children implanted after the first year of life, all studies confirm an advantage with respect to implant precocity, and many document an advantage in children who received cochlear implants before 18 months of age compared to those implanted at a later stage. However, the cut-off in the different studies is variable, and not all studies report statistical significance. However, a "sensitive" period has been identified before 24-36 months, after which hearing and communicative outcomes are significantly inferior.

Bilateral (simultaneous/sequential) CI vs. unilateral and vs. bimodal stimulation in children

A total of 20 studies were selected on this issue (Table II).
All the studies examined except for one – Schaefer et al. [27] – documented advantages derived from bilateral CI stimulation with respect to unilateral CI stimulation. In the studies in which the outcomes of children with bilateral CI were compared with those of children with unilateral CI, no effective control group exists with the exception of the study by Beijen et al. [28], in which the results of children with bilateral CI were compared with those of a control group formed by unilateral CI users. Nineteen studies have reported on the advantages of bilateral stimulation both in verbal perception of noise and the capacity of identifying the sonorous source, despite the variability of results seen in some investigations [29-47].
Gordon and Papsin [40], Scherf F et al. [41] and Peters et al. [44] reported on the advantages of bilateral compared to monolateral CI, even when hearing occurs in a silent environment.
Bilateral CI can be performed *simultaneously or sequentially* (namely by two independent surgical interventions, with the time interval between the two operations ranging from months to years). In the case of sequential CI, no definitive data exists concerning the influence of duration of the time interval between the two interventions and the benefits following the second implant. An advantage derived from the second implant is reported in all the literature studies on the issue, even in the cases of a long interval between the two interventions, despite wide interindividual variability. However, long interval and long duration of hearing deprivation in the second ear seem to negatively influence outcomes after the second implant [32 33 40-45]. Scherf F et al. [41] reported that there were advantages from the second CI even in children who received the second implant at a considerable distance from the first (> 6 years of age): however, these results appear to be slower than those achieved by children receiving the second implant after a short delay (< 6 years). Galvin KL et al. [35] reported a benefit from the second implant even in adolescents or young adults affected by pre-lingual deafness and already using unilateral CI.
Peters et al. [44] and Wolfe et al. [33] documented that in some of the cases in which the second ear was implanted at an early age (within 4 years of age in Wolfe et al. and 5 years in Peters et al.), the outcomes with the second CI reached those obtained for the first implanted ear.
Furthermore, a number of studies have demonstrated an advantage in the use of bilateral CI in patients who received the first implant at an early stage. In this respect, Van Deun [43] report better outcomes with bilateral CI in

children who received the first implant very early (< 2 years of age) and in those with a small time interval between the two interventions. An advantage in relation to precocity of the first implant was also reported by Gordon and Papsin [40] and Zeitler et al. [46].
None of the selected studies compared the results obtained in children who received bilateral CI by simultaneous and sequential procedures. The study by Scherf et al. [42] suggests that there are subjective benefits derived from the use of a second implant in bilaterally implanted children with sequential procedure, evaluated by parental questionnaires and interviews.
In 4 studies, the benefits derived from bilateral hearing were compared in two groups of patients: bilateral CI users and bimodal stimulation users. In 2 studies, Litovsky et al. [36 37] reported on the advantages (in verbal perception, noise, and localization of the sonorous source) deriving from bilateral stimulation in both situations, although the advantages were more evident in bilateral CI patients.
No hearing advantages derived from bilateral stimulation (via bilateral CI or bimodal stimulation) in noisy environments were documented by Shaefer et al. [27]. Instead, the authors reported that there were benefits obtained using the frequency modulation (FM) system. Mok et al. [47] recorded the advantages produced by bilateral stimulation in both groups of patients when listening in a noisy environment, but noticed a greater advantage in the second device in children using bimodal stimulation.
In conclusion, the selected studies demonstrate that compared to unilateral CI, bilateral CI offers advantages in terms of hearing in noise (+++), localization of the sonorous source (+++) and during hearing in a silent environment. There is however a wide range of variability.
None of the studies have analyzed the benefits of bilateral vs monolateral CI in terms of language and learning development. Concerning simultaneous *vs.* sequential bilateral CI, no study has compared outcomes in patients who received simultaneous and sequential CI.
The studies also documented some advantages after sequential bilateral CI. In these cases, a short interval between interventions, precocity of the first CI and precocity of the second CI were considered positive prognostic factors. The precise interval limit between the two operations after which the sequential procedure is contraindicated is not reported, but long intervals generally seem to be associated with slower and fewer benefits from the second implant.

Benefit derived from CI procedure in deaf children with associated disabilities

A total of 7 articles were selected on this issue (Table III). The groups of children analyzed were heterogeneous with regard to type of disability associated with deafness and number of associated disabilities, as well as other variables conditioning post-CI results (age at time of CI, use of hearing aids before CI, type of rehabilitation performed, etc.).
All the selected studies reported post-CI benefits in this category of children, although they were inferior and slower compared to those generally reached by implanted children with isolated deafness [48-54].
None of the studies examined auditory/communicative/quality of life results in implanted children with disabilities associated with deafness compared to those obtained in children in the same category (children with disabilities associated with deafness), treated by traditional hearing aids. The post-CI results obtained in children with disabilities associated with deafness have been compared to those obtained by children affected by isolated deafness in only one study [48].
In summary, the studies analyzed suggest that the CI procedure is also suitable for children with disabilities associated with deafness. However, there are some rare cases linked to modest outcomes, and some authors considered that there are contraindications for the procedure (severe form of autism, serious psychotic disturbances and severe to profound mental retardation).
From the studies included in the review, it emerges that even children with disabilities associated with deafness may draw benefits from the procedure, even if they are slower and inferior to those of children with isolated deafness, especially in terms of high communicative and perceptive skills (e.g. development of oral language, open set recognition abilities).
In these cases, it can be difficult to assess post-implant benefits with regards to perceptive abilities and language development using standardized tests; furthermore, the results of these tests may not reflect the actual benefits obtained and reported by parents in terms of quality of life. Therefore, literature studies underline the need for assessment tools that are different from those commonly employed, which can allow assessment of benefits in various aspects of everyday quality of life (e.g. questionnaires).

Discussion and conclusions

The purpose of this report was to assess the clinical effectiveness of cochlear implants for children. The members of the WG, after examining existing research evidence of the national and international literature and the main international guidelines, considered as universally accepted the usefulness/effectiveness of unilateral cochlear implantation in severely-profoundly deaf children. Within the context of the current review, two systematic reviews on CI procedure have been published [3 4], and both concluded that there was consistent evidence that cochlear implantation is a safe, reliable and effective strategy for children with severe to profound sensorineural deafness.
As a consequence, the members of the WG focused their attention on clinical effectiveness of CI procedure, with

Table II. Publications included for review on "Bilateral (simultaneous/sequentiale) *vs.* unilateral CI and *vs.* bimodal stimulation" (paediatric age).

Authors	Title	Journal year	Size of sample and other data on methods adopted	Type of implant/ processing strategy	Evaluated results	Conclusions/opinions
Mok et al. [47]	Speech perception benefit for children with a cochlear implant and a hearing aid in opposite ears and children with bilateral cochlear implants	Audiol Neurotol 2010	Bimodal 9 children, bilateral 4 children.	ESPRIT 3G Processing strategies: ACE/SPEAK	Outcomes: verbal perception in noise (0 degrees front and 90 degrees on the side of CI/first CI): CNC test. The Authors evaluate perception of phonemes, words, consonants and vowels.	Bimodal: advantages from bimodal to CI alone, statistically significant. Bilateral: advantages from bilateral only if the noise comes from the side of the first CI, statistically significant. Comparison between bilateral and bimodal advantages: bimodal children achieve better results from the use of the latter device, both in the case of the noise released at 0° front, at 90° on the side of CI/first CI). Importance of providing implanted children with a second device. If the child can use a hearing aid in the second ear it is better to place the prosthesis. On the other hand, the second CI yields better results when the II ear is used alone.
Van Deun [43]	Earlier intervention leads to better sound localization in children with bilateral cochlear implants	Audiol Neurotol 2010	30 children: bilateral sequential CI (delay 10 mths-9 yrs)	Nucleus SPRINT/3G/ Freedom. Processing strategy ACE/SPEAK	Analysis of sound localization (by test and questionnaire submitted to parents).	Better localization in children who received the first CI < 2 yrs and in those who received CI at a later stage and used the hearing aid. With regard to age at the second CI, younger age is associated with better results. Good results also in those with long interval who used a contralateral hearing aid.
Galvin et al. [35]	Can adolescents and young adults with prelingual hearing loss benefit from a second, sequential cochlear implant?	Int J Audiol 2010	9 adolescents or young adults (> 10 yrs) with CI and prelingual hearing loss receiving sequential CI. Follow-up: around 1 yr.	IC1: Cochlear (Spectra, ESPRIT 3G, Freedom) IC2: Cochlear (ESPRIT 3G, Freedom) Processing strategy SPEAK, ACE	Test of verbal perception with each implant and with both. Questionnaire derived from SSQ and from monthly interviews.	In all cases patients reported improvement with the second CI. In 7/9 cases the first CI gave better results. In 2/9 cases the results with the two CI are similar.
Lovett et al. [34]	Bilateral or unilateral cochlear implantation for deaf children: an observational study	Arch Dis Chlid 2010	30 children with bilateral CI (sequential and simultaneous). 20 children with unilateral CI. Age: 18 mths - 16 yrs.	Advanced Bionics Corporation, Cochlear, MedEl	Outcomes are compared in the two groups. Localization: left right discrimination test, localization test, movement tracking test. Listening to the sound: Spatial Release from Masking (SRM). Spatial Speech and Quality of hearing (SSQ).	Outcomes in the group of children with bilateral CI are statistically better than those in the group of unilateral CI children. The results of the questionnaire are also better in children with bilateral CI. No advantages were recorded in terms of quality of life in groups of children with unilateral compared to bilateral CI.

(continues)

Table II. *(follows)*

Scherf et al.	Three-year post implantation auditory outcomes in children with sequential bilateral cochlear implantation	Ann Otol Rhinol Laryngol 2009	35 children with bilateral sequential CI. Follow-up at 36 mths.	Processore: Nucleus Freedom, Nucleus 3G, Nucleus Sprint Laura Max	Evaluation of recognition in environments both silent and with background noise.	All children show better results with binaural listening, even those with greater interval between 2 children (comparison between delay < and > 6 yrs. The benefits derived from the second CI are slower to appear than in children who receive the second CI at a later stage. Interindividual variability.
Gordon & Papsin	Benefits of short interimplant delays in children receiving bilateral cochlear implants	Otol Neurotol 2009	51children first CI < 3 yrs second CI after 6-12 mths or after a period > 2 yrs. 7 children first CI > 3 yrs second CI after a period > 2 yrs. Follow-up: 6-12-18-24-36 months after bilateral use.		Verbal perception tests appropriate to age, in silence and with noise.	Benefit from second CI superior in children with shorter duration of bilateral deafness and inferior interval between the two implantations. Not statistically significant. Follow-up: 6-12-18-24-36 mths after bilateral use.
Sherf et al. [41]	Functional outcome of sequential bilateral cochlear implantation in young children: 36 months postoperative results	Int J Pediatr Otorhinolaryngol 2009	18 children who received second CI < 6 yrs. 17 children who received second CI > 6 yrs. Follow-up: 3 yrs from second CI.		Categories of Auditory Performance (CAP), Speech Intelligibility. Rating (SIR), communication mode, school attendance, parents' witness and Wurzburg's questionnaire.	Benefits from the second implant obtained in all children. Improved benefits in the group of children who received the second CI within 6 yrs (both verbal perception and quality of life).
Scherf et al. [42]	Subjective benefits of sequential bilateral cochlear implantation in young children after 18 months of implant use	ORL J Otorhinolaryngol Relat Spec 2009	Comparison of benefit from second CI in 2 groups: 17 children who received second CI < 6 yrs, 16 children who received second CI > 6 yrs. Follow-up: tests performed, before activation of second CI, at 1-3-6-12-18 mths post-second CI.	Processor used: Nucleus Spectra, Nucleus SPRINT, 3G, Freedom, LauraMax	Subjective results: - Questionnaires submitted to parents. - Evaluation of perceptive abilities and categorization in the CAP, according to the information given to parents.	Subjective results: all parents documented improvements derived from the use of second CI in everyday life. Category of auditory performance also improved, but no statistically significant results were found.
Galvin et al. [32]	Speech detection and localization results and clinical outcomes for children receiving sequential bilateral cochlear implants before four years of age	Int J Audiol 2008	10 children who received second CI within 4 yrs of age.	Nucleus Contour/Contour Advance/Freedom with softip ACE	Detection of language in noisy environment. Localization (right/left). Parents' opinion.	9 children reported benefit in the detection test in noisy environment and the majority of children in the localization test. Improved results linked to precocity of second CI. 1 child refused second CI at activation.

(continues)

Table II. *(follows)*

Zeitler et al. [46]	Speech perception benefits of sequential bilateral cochlear implantation in children and adults: a retrospective analysis	Otol Neurotol 2008	43 children: bilateral sequential CI. 22 adults: bilateral sequential CI. Follow-up 3 mths.	Nucleus, Clarion, Medel CIS, SPEAK, ACE	Test of verbal perception: - Adults: Consonant-Vowel-Consonant (CNC) and Hearing in Noise sentence test in quiet environment(HINT-Q), BKBSIN in noisy environment. - Children: Glendonald Auditory Screening Procedure (GASP), Phonetically Balanced Kindergarten (PBK), Multisyllabic Lexical Neighborhood Test (MLNT), Lexical Neighborhood Test (LNT), CNC and HINT paediatric version. Test performer before second CI and 3 months after second CI.	Significant improvements with bilateral hearing. Better outcomes are related to precocity of first implant.
Peters et al. [44]	Importance of age and postimplantation experience on speech perception measures in children with sequential bilateral cochlear implants	Otolo Neurotol 2007	30 children (first CI within 5 yrs) Three groups: I: second CI 3-5 yrs. II: second CI 5-8 yrs. III: second CI 8-13 yrs Follow-up 3-6-12 mths post second CI	First AU: Nucleus 22/24/24 Contour Second AU: Nucleus 24 Contour/Contour Advance	Outcomes with bilateral CI, right CI, left CI. Verbal perception test in silence: MLNT words (group I); LNT words (groups II and III); HINT-C sentences in silence (group III). Test of verbal perception with background noise: CRISP test.	Results in relation to age (second CI). Benefit in all children. More benefit in children who receive second CI earlier. In children who receive CI within 5 yrs, second implant reaches same performance as first (after 1 yr). No control group. Children act as control (cf before and after CI)
Wolfe et al. [33]	1-year postactivation results for sequentially implanted bilateral cochlear implant users	Otol Neurotol 2007	12 children (first CI < 3 yrs) second CI: 22 mths-9.5 yrs	First AU: Advanced Bionics/90K Nucleus 24 Second AU: Advanced Bionics/90K Nucleus 24 Freedom	Verbal perception in silence and in noise settings. Multisyllabic Lexical Neighborhood Test (MLNT), Central Institute for the Deaf (CID) Early Speech Perception (ESP) test.	All children obtain benefits from use of bilateral CI when listening to noise, independent of age at second CI. Children receiving second CI earlier (< 4 yrs from onset of deafness) obtain better results from second ear (listening in silent setting is similar to the first implanted ear).
Galvin et al. [30]	Perceptual benefit and functional outcomes for children using sequential bilateral cochlear implants	Ear Hear 2007	11 children (age > 4 yrs)	First AU: Nucleus 22/24/24 Contour Second AU: Nucleus 24/24 Contour/Contour Advance Strategies of processing SPEAK, ACE	Verbal perception in noise: AdSpon (Adaptive Spondee Discrimination Test). Localization. Questionnaire distributed to parents.	Benefit from sequential bilateral CI. However, results are variable. Patients are unable to perceive real binaural hearing and to identify variables conditioning the results.
Galvin et al. [31]	12-month post-operative results for older children using sequential bilateral implants	Ear Hear 2007	6 children (5-15 yrs) first CI < 2.5 yrs second CI 4.5-10 yrs 12 mths follow-up with second CI		Parents' report on use of II CI. Verbal perception test in noise: AdSpon (discrimination). Localization Test. Cf I CI and bil. CI outcomes.	No better localization was reported with bilateral CI compared to first CI. Significant benefit only in some children for verbal discrimination in noise.

(continues)

Table II. *(follows)*

Beijen et al.[28]	Sound localization ability of young children with bilateral cochlear implants	Otolo Neurotol 2007	5 children. Simultaneous bil. CI (1 seq 6 mths interval): study group. 5 children. Unilateral CI control group. Follow-up > 11 mths.	Nucleus Contour Advance and processor SPRINT	Localization Test (90/-90 30/-30). Questionnaires SSQ (The functional Speech, Spatial and Qualities of Hearing. Scale) and PedsQL 4.0 (health related quality of life).	Children with bilateral CI have better results in localization of sonorous source (statistically significant). Questionnaire SSQ: children with bilateral CI achieve better results only in localization domain (statistically significant). Questionnaire PedsQL 4.0: the two groups had similar results.
Scherf et al.	Hearing benefits of second-side cochlear implantation in two groups of children	Int J Pediatr Otorhinolaryngol 2007	Cf benefit from second CI in 2 groups: 17 children received second CI < 6 yrs, 16 children who received second CI > 6 yrs. Tests performed, first activation of first CI, at 1-3-6-12-18 mths post-second CI.	Processor: Nucleus Spectra, Nucleus SPRINT, 3G, Freedom, LauraMax	Results (first CI, second CI, first and second CI): - hearing threshold with CI - verbal perception in silent and noisy setting.	Hearing threshold with CI: threshold with second CI better than with only one CI in both groups. Verbal perception in silence and noise: benefits in both groups, in silence. Benefits stat sign. Benefits only in children who received second CI < 6 yrs when hearing in noise.
Schafer et al.[45]	Speech recognition in noise in children with cochlear implants while listening in bilateral, bimodal and FM-systems arrangments	Int J Audiol 2006	12 children bilateral CI. 10 children bimodal. 3-12 yrs. Use first CI > 6 yrs, use of second CI > 4 mths.		Verbal perception in noise (sentences): they determine speech in noise threshold.	Verbal perception in noise (sentences): no improvement of verbal perception with use of contralateral stimulation via CI or HA. Use of FM.
Litovsky[36]	Benefits of bilateral cochlear implants and/or hearing aids in children	Inte J Audiol 2006	10 children with bilateral CI (sequential interval between first and second CII > 12 mths). 10 bimodal children.	Bilateral CI group: Nucleus 24, Nucleus 22, Clarion. Bimodal group: Nucleus 22, 24 or Freedom) MedEl C40+	Verbal perception in quiet and noise: CRISP test. Localization (MMA Minimum Audible Angle: smallest variation of sonorous source position that can be identified).	Bilateral CI *versus* bimodal hearing. Advantages of bilateral stimulation in both groups, but better for bilateral CI (for both verbal perception and sonorous source localization).
Litovsky et al.[37]	Bilateral cochlear implants in children: localization acuity measured with minimum audible angle	Ear Hear 2006	13 children: bilateral CI (sequential). 6 children bimodal stimulation.	Bilateral CI group: Nucleus 24, Nucleus 22, Clarion (Platinum Auria). Bimodal group: Nucleus 24 or 24. Contour, Clarion II HiFocus MedEl C40+ Some children are post-verbal.	Localization: (MMA Minimum Audible Angle): smallest variation of sonorous source position that can be discriminated).	Bilateral CI *versus* bimodal hearing. Bilateral CI offers advantage in both groups, but the results are variable; greater variability in bimodal group, where some children are disadvantaged. Bilateral CI group: results with I CI are better than those with II CI. Bilateral CI shows better advantage than bimodal hearing. Experience in use of bil CI helps improve performances. Children with non congenital deafness are better-off in this test. Similar to what is reported for post-lingual adults.

Table III. Summary table of selected articles for review on "Benefit derived from the CI procedure in children with deafness-associated disabilities".

Authors	Title	Journal Year	Size of sample and other data on the methods adopted	Type of implant/ processing strategy	Evalauted results	Conclusions/opinions
Wiley et al. [48]	Auditory skills development among children with developmental delays and cochlear implants	Ann Otol Rhinol Laryngol 2008	14 children with deaf-associated disabilities. 21 children with no other disabilities. Follow-up: 1 yr.	Device: non specified	Evaluation of auditory benefits using the Auditory Skills Checklist (ASC) which is a tool they have validated. Comparison between ASC and cognitive DQ (developmental quotient).	The ASC improvement rate is equal in children with and without multiple disabilities, the ASC improvement rate is associated with DQ, rather than in presence or absence of multiple disabilities. Children with DQ < 80 (mean) have progress rate which is ½ those with DQ > 80. Children with DQ < 80 do not reach high abilities of verbal perception, e.g. identification and perception, but only detection and discrimination.
Nikolopoulos et al. [49]	Speech production in deaf implanted children with additional disabilities and comparison with age-equivalent implanted children without such disorders	Int J Pediatr Otorhinolaryngol 2008	67 implanted children with additional disabilities. Control group: 100 children without such disorders. All children were implanted before 5 yrs. Follow-up: 5 yrs post-CI. Case studies relative to the period following 1997.	Nucleus	Speech intelligibility: SIR (Speech Intelligibility Rating).	SIR (Speech Intelligibility Rating): 70% of patients with disabilities reaches intelligible speech, although only 16% reaches the highest categories (mostly children with visual impairment). In children without disorders the results were better. Statistically significant results.
Wiley et al. [50]	Perceived qualitative benefits of cochlear implants in children with multi-handicaps	Int J Pediatr Otorhinolaryngol 2005	20 implanted children with associated disabilities. Some children use sign language. Follow-up 0.5-8 yrs.	Not specified	Subjective post-CI results, collected through a questionnaire they prepared.	All parents report perceptive and communicative benefits, also in daily life.

(continues)

Table III. *(follows)*

Frush Holt & Kirk [51]	Speech and language development in cognitively delayed children with cochlear implants	Ear Hear 2005	19 implanted children with associated disorders (slight cognitive delay), 50 implanted children with no associated disorders. Some children use Total communication.	CI: Nucleus 22/24 Processor: MSP, SPECTRA, SPRINT Processing Strategy: SPEAK/ACE	Perceptive and linguistic results between implanted children without disabilities and implanted children with slight cognitive delay. Tests: IT-MAIS, Grammatical Analysis of Elicited Language: Pre-Sentence Level Test (GAEL-P), Mr. Potato Head Task, Pediatric Speech Intelligibility Test, Peabody Picture Vocabulary Test-Third Edition, Reynell Developmental Language Scales.	Children with mild developmental delays have benefits, but slower and minor, in particular in the more difficult tests (production, sentence recognition).
Donaldson et al. [52]	Measuring progress in children with Autism spectrum disorder who have cochlear implants	Arch Otolaryngol Head Neck Surg 2004	7 children affected by autism spectrum disorders who received CI.	Devices: Nucleus 24 and Clarion.	Circulation of a questionnaire concerning the benefits perceived by the parents, tests on verbal perception and language development (administered partially).	They demonstrate benefits in verbal perception. One child developed oral language. They also led to benefits in quality of life.
Waltzman et al. [53]	Performance of multiply handicapped children using cochlear implants	Am J Otol 2000	29 children with associated disabilities.	Nucleus 22/24 Clarion	Evaluation of perceptive abilities, in closed and open-settings. Test: Central Institute for the Deaf Early Speech Perception (ESP) Test, Northwestern University Children's Perception of Speech Test (NU-CHIPS), Glendonald Auditory Screening Procedure (GASP), Phonetically Balanced Kindergarten Word (PBK) test, Multisyllabic Lexical Neighborhood Test (MLNT), Lexical Neighborhood test (LNT), Common Phrases sentence test.	Slower and inferior improvement in verbal perception with respect to improvement observed in implanted children with no other disabilities.
Filipo et al. [54]	Cochlear implants in special cases: deafness in the presence of disabilities and/ or associated problems	Acta Otolaryngol 2004	18 implanted children with associated disabilities.	Clarion 1.2, Clarion CII, Clarion Hi Focus, Medel Processing strategies: CIS, SAS, HiRes	Assessment of perceptive abilities, independence and family/social relations.	Heterogeneous case studies, adults and children. Pre- and post-language adults. Associated disabilities are variable. (neuropsychiatry, visual impairment, bilingualism, family problems). In general, they report post-CI benefits.

particular regard to the most controversial issues for which international consensus is still lacking.

The first topic the WG analyzed was the age at implantation in a paediatric age. According to most international guidelines, the lower limit is 12 months and the appropriateness of the procedure in the first year of life is widely discussed. In cases of cochlear ossification, CI is also permitted under 12 months of age.

With regards to hearing levels in relation to age at implantation, international guidelines indicate different levels of hearing over which CI is indicated. Some guidelines refer to the PTA (pure tone audiometry between 0.5-1-2 kHz), while others refer to the mean threshold between 2 and 4 kHz (UK) [55].

For example, in children over 2 years of age, according to the Food and Drug Administration (FDA), CI is indicated with a PTA > 70 dB, while according to Belgian guidelines with a PTA > 85 dB associated with auditory brainstem responses (ABR) threshold ≥ 90 dB HL [55]. The British Cochlear Implant Group (BCIG) considers CI appropriate for children over 2 years of age with thresholds between 2 and 4 kHz > 90 dB [55]. Italian guidelines allow CI in children over 36 months of age with PTA > 75 dB [1].

With regards to the lower limit of age in relation to hearing threshold, generally CI between 12 and 24 months is accepted only in the case of profound deafness, but Italian guidelines consider 36 months the lower limit of age to implant a child with severe deafness [1 55].

Concerning hearing aid training and rehabilitative results with traditional hearing aids, most of the international guidelines indicate that training with traditional hearing aids for a period longer than 3 months is necessary before implantation, and generally CI is admitted in the case of unsatisfactory perceptive and communicative results with hearing aids [1 55]. Other guidelines indicate different limits, as Belgian ones refer to 30% as the limit under which CI is indicated in children [55].

With regard to the age of implantation in children, none of the existing systematic reviews [3 4] analyzed the topic of the lower limit of age for CI in children; they both report that greater benefits are found with earlier implantation and a shorter duration of deafness prior to implantation.

The WG of the present project drew the following recommendations.

In *children under 2 years of age* CI is indicated when all three of the following criteria are satisfied:

- Age: ≥ 12 months. The actual level of evidence does not justify systematic implantation in the first year of life. This indication should be limited to cochlear ossification or to selected cases reliably evaluated by experienced teams, with a definite diagnosis with regard to hearing threshold, aetiology and site of lesion.
- Hearing threshold level: CI is indicated in children with bilateral profound deafness (mean threshold between 0.5-1-2 kHz ≥ 90 dB HL), detected with both subjective and objective methods.
- Results with hearing aids: no significant communicative and hearing results after a period of 3-6 months with hearing aids and speech therapy training (except in the case of documented incipient cochlear ossification).

In *children between 2 and 18 years of age*, CI is indicated when all three of the following criteria are satisfied:

- Hearing threshold level: CI is indicated in children with bilateral severe to profound hearing loss (mean threshold between 0.5-1-2 kHz > 75 dB HL) detected with both subjective and objective methods.
- Results with hearing aids: no significant [a] communicative and hearing results after a period of 3-6 months with hearing aids and speech therapy training (except in the case of documented incipient cochlear ossification).
- Speech perception abilities: evaluation of speech perception abilities is recommended using materials appropriate to age and speech development. CI is indicated if the open-set speech recognition score is ≤ 50% in the best aided condition without lip reading. In selected cases, CI is indicated if open-set speech recognition score is ≤ 50% in the best aided condition without lip reading with background noise (signal to noise ratio SNR + 10).

The other topic the WG analyzed was the clinical effectiveness of *bilateral CI in children*. To our knowledge, no international guidelines exist on this issue. According to NICE guidance [4], simultaneous bilateral CI is cost-effective in children with severe to profound sensorineural deafness; the guidance accept sequential procedures only for children previously unilaterally implanted. According to Bond et al. [3], the clinical evidence for bilateral implantation suggests that there is additional gain from having two devices.

Regarding bilateral CI in children, the WG drew the following recommendations. Bilateral CI in children is indicated in the following conditions:

- Children with bilateral profound sensorineural hearing loss, who cannot achieve significant benefits with bimodal hearing.
- Children with deafness and initial bilateral cochlear ossification (ex. post-meningitic).
- Deaf-blind children.
- Unsatisfactory results with unilateral CI, if better results are achievable with a contralateral CI.
- Children with CI failure if reimplantation in the same ear is contraindicated.
- Children with multiple disabilities (case by case evaluation).

[a] *Speech, language and listening skills appropriate to age, developmental stage and cognitive ability.*

Both simultaneous and sequential procedures are admitted, although the simultaneous procedure is recommended. In the case of sequential bilateral implantation, a short delay between surgeries is recommended.

The third topic the WG analysed was *CI in deaf children with additional disabilities*. It is an emerging issue which CI teams have to face. To our knowledge, none of the international guidelines or existing systematic reviews have specifically analysed this issue [3 4]. The WG recommended the following.

CI in children with multiple disabilities is indicated. Indications and prognosis should be considered on a case-by-case basis. Comprehensive counselling with family members and caregivers is mandatory. Benefits after implantation can be expected both in terms of speech and language improvements and in quality of life.

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