Age-Dependent Cost-Utility of Pediatric Cochlear Implantation

Yevgeniy R. Semenov,[1] Susan T. Yeh,[2] Meena Seshamani,[1] Nae-Yuh Wang,[3,4] Emily A. Tobey,[5] Laurie S. Eisenberg,[6] Alexandra L. Quittner,[7] Kevin D. Frick,[2] John K. Niparko,[1,8] and the CDaCI Investigative Team[9]

Objectives: Cochlear implantation (CI) has become the mainstay of treatment for children with severe-to-profound sensorineural hearing loss (SNHL). Yet, despite mounting evidence of the clinical benefits of early implantation, little data are available on the long-term societal benefits and comparative effectiveness of this procedure across various ages of implantation—a choice parameter for parents and clinicians with high prognostic value for clinical outcome. As such, the aim of the present study is to evaluate a model of the consequences of the timing of this intervention from a societal economic perspective. Average cost utility of pediatric CI by age at intervention will be analyzed.

Design: Prospective, longitudinal assessment of health utility and educational placement outcomes in 175 children recruited from six U.S. centers between November 2002 and December 2004, who had severe-to-profound SNHL onset within 1 year of age, underwent CI before 5 years of age, and had up to 6 years of postimplant follow-up that ended in November 2008 to December 2011. Costs of care were collected retrospectively and stratified by preoperative, operative, and postoperative expenditures. Incremental costs and benefits of implantation were compared among the three age groups and relative to a nonimplantation baseline.

Results: Children implanted at <18 months of age gained an average of 10.7 quality-adjusted life years (QALYs) over their projected lifetime as compared with 9.0 and 8.4 QALYs for those implanted between 18 and 36 months and at >36 months of age, respectively. Medical and surgical complication rates were not significantly different among the three age groups. In addition, mean lifetime costs of implantation were similar among the three groups, at approximately $2000/child/year (77.5-year life expectancy), yielding costs of $14,996, $17,849, and $19,173 per QALY for the youngest, middle, and oldest implant age groups, respectively. Full mainstream classroom integration rate was significantly higher in the youngest group at 81% as compared with 57 and 63% for the middle and oldest groups, respectively ($p < 0.05$) after 6 years of follow-up. After incorporating lifetime educational cost savings, CI led to net societal savings of $31,252, $10,217, and $6,680 for the youngest, middle, and oldest groups at CI, respectively, over the child's projected lifetime.

Conclusions: Even without considering improvements in lifetime earnings, the overall cost-utility results indicate highly favorable ratios. Early (<18 months) intervention with CI was associated with greater and longer quality-of-life improvements, similar direct costs of implantation, and economically valuable improved classroom placement, without a greater incidence of medical and surgical complications when compared to CI at older ages.

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INTRODUCTION

Hearing loss is the most common sensory deprivation in developed countries, with severe-to-profound sensorineural hearing loss (SNHL) affecting 1 in 1000 children born in the United States (Smith et al. 2005). The lifetime cost of onset of deafness before a child acquires speech and language capabilities (approximately 3 years of age) exceeds $1 million per child and currently affects as many as 60,000 children (Mohr et al. 2000; Blanchfield et al. 2001). Cochlear implantation (CI) has been shown to be highly effective in treating deafness, with significantly improved spoken language and auditory outcomes observed at earlier ages of implantation (McConkey Robbins et al. 2004; Svirsky et al. 2004; Nicholas & Geers 2007; Holt & Svirsky 2008; Niparko et al. 2010). An economic evaluation of CI provides an opportunity to model the societal cost-utility of an early intervention for a significant childhood disability. The purpose of a cost-utility analysis is to determine the ratio between the cost of a health-related intervention and the benefits, expressed in quality-adjusted life years (QALYs), which allows for health states that are considered less preferable to full health to be given quantitative values and for those values to vary over time.

Despite increasing evidence in support of early implantation and successful implementation of universal newborn hearing screening programs, implantation at younger ages continues to face considerable resistance. Barriers to early implantation include delayed identification of hearing loss, slow assessment and referrals from interventionists, parental delays, concerns regarding complications with early surgical intervention, lack of health insurance reimbursement for the substantial travel costs, and lost earnings due to CI-related medical visits, which may present a considerable burden for low-income families (Moeller 2000; Lester et al. 2011).

As a result, families and healthcare professionals may devote a substantial amount of time in a developmentally critical period to trials of hearing aids and less expensive and intensive alternatives to CI. Concerns surrounding early CI would be reduced if the perceptual, developmental, and lifetime benefits of early implantation were shown to be substantial.

Previous investigations have shown CI to be highly cost effective in the overall pediatric population in the United States

[1]Department of Otolaryngology, The Johns Hopkins University School of Medicine, Baltimore, Maryland, USA; [2]Department of Health Policy and Management, The Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland, USA; [3]Department of Medicine, The Johns Hopkins University School of Medicine, Baltimore, Maryland, USA; [4]Department of Biostatistics, The Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland, USA; [5]University of Texas at Dallas, Callier Center for Communication Disorders, Dallas, Texas, USA; [6]House Research Institute, Los Angeles, California, USA; [7]University of Miami, Department of Psychology, Miami, Florida, USA; [8]Department of Epidemiology, The Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland, USA; [9]Childhood Development after Cochlear Implantation Study.

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but were limited in population size, duration of follow-up, and generalizability of the model (Cheng et al. 2000; Bichey & Miyamoto 2008). In one of the most comprehensive analyses of pediatric CI, a study by the Peninsula Technology Assessment Group (PenTAG) in the United Kingdom identified lack of longer-term health-utility data and analyses of potentially confounding factors such as age at intervention as major limitations to cost-utility analyses of pediatric CI (Bond et al. 2009). Building on these findings, the present study aims to evaluate the comparative societal benefits of pediatric CI by age at implantation through the first cost-utility analysis of pediatric CI using data from a multicenter, longitudinal study in the United States. The effects of long-term postoperative complications, differences in costs of care, and differential educational savings at the three different cohort ages of implantation are analyzed.

MATERIALS AND METHODS

Study Design and Study Population

A detailed discussion of the inclusion and exclusion criteria and the overall study design can be found in a previous publication (Fink et al. 2007). The Childhood Development after Cochlear Implantation (CDaCI) study is a multicenter, prospective cohort study aimed at measuring the outcomes of early childhood CI in the United States. Children with severe-to-profound SNHL were recruited at six academic medical centers, including The Johns Hopkins University, University of Miami, University of Michigan, University of Texas Southwestern, House Research Institute, and University of North Carolina. CI participants in the study had to be under 5 years of age at baseline, be pre- or postlingually deaf (onset of deafness before or after onset of speech and language acquisition), and have developmental scores on the Bayley Scales of Infant Development Mental Scale or Motor Scale (BSID II) of at least 70. A total of 188 children with severe-to-profound SNHL were enrolled in the study. The study was approved by each center's institutional review board, and written informed consent was obtained from the parents of each enrolled child.

For this cost-utility study, 175 cochlear implanted children with up to 6 years of postimplant follow-up, which concluded in November 2008 to December 2011, were grouped in three cohorts corresponding to their age at implantation: younger than 18 months, 18 to 36 months, and older than 36 months of age at implantation. Given that a 3- to 6-month hearing aid trial is required as part of the cochlear implant candidacy evaluation process (Zwolan et al. 1998), 13 cochlear implanted children who had an onset of hearing loss at an age more than 12 months were excluded to minimize selection bias into the three implantation age categories.

This study includes both unilaterally and bilaterally implanted children. As the decision for bilateral implantation was made by the family on an individual basis, the effect of bilateral implantation was factored out in both the costs and the benefits calculations. The health-utility effect of the second implantation was controlled by creating a flag variable within the data set, which was "switched on" whenever a child received a second implantation. This allowed for the isolation of all health-utility gains that were strictly associated with the second implantation. Removing the costs associated with the second implantation was more straightforward because the costs were developed in an itemized "ingredients based" approach.

Perspective and Time Horizon

A societal perspective was adopted for this analysis, in that both direct and indirect costs were examined. All costs, as well as QALYs related to CI were considered over an expected 77.5-year average lifetime (74.9 years for men and 79.9 years for women) of children born in the United States (Expectation of Life at Birth, and Projections 2012). All costs and outcomes were discounted annually at 3%(Gold et al. 1996).

Measurement of Costs

Costs and reimbursements, in U.S. dollars, were collected retrospectively at the individual patient level from the study center with largest number of participants, Johns Hopkins University (JHU). These were further stratified into direct medical costs, including preoperative, operative, and postoperative medical costs; and indirect costs, including lost wages, educational savings, and transportation costs incurred by the families. Full access to cost data from other study centers was prohibited by U.S. antitrust regulations that prevent sharing of medical pricing information among individual hospitals. Instead, costs from other centers were based on clinical care models provided by these institutions, which were priced out according to JHU costs and were incorporated as ranges in sensitivity analyses. In addition, a cost-adjustment factor (see the Appendix, Supplemental Digital Content 1, http://links.lww.com/EANDH/A92), determined by differences between JHU and the national average in payer mix and geographically adjusted healthcare utilization rates, was calculated using data provided by University HealthSystem Consortium (UHC), an alliance of 116 academic centers and 272 of their affiliated hospitals representing approximately 90% of the U.S. nonprofit academic medical centers, to adjust costs collected at JHU into more generalizable ones that reflect the payer mix and healthcare utilization rate of the greater part of the United States (University HealthSystem Consortium 2012). All six of the CDaCI study centers are nonprofit academic medical centers.

The costs used in this study represent direct hospital and physician charges for procedures and medical visits associated with CI and do not represent true economic (opportunity) costs. The latter would be obtained by determining the value of the next best use of each resource that is used to treat the children who receive CI and each resource that is saved as a result of CI rather than not having an implantation. Given the proven clinical superiority of CI over hearing aids in severe-to-profoundly deaf children, enrolling a hearing aided control group for the purposes of the present study would not be ethically justified. As such, direct cost data were not available for hearing aided nonimplanted children. The exclusion of such data yields considerably less favorable cost-utility ratios (as charges are greater than costs) than would be present when considering true economic costs, which are not truly zero for the nonimplantation group.

Educational costs were calculated based on classroom placement, which was tracked through annual parental questionnaires with classroom placement options including: (1) school for the deaf, (2) self-contained program within a mainstream school, (3) partially mainstream classroom placement with at least 50% of children having hearing impairment, and (4) a fully mainstream placement with mostly normal hearing children.

For the youngest cohort, with 6 years of follow-up data, classroom placement distribution was available through second grade. For the middle and oldest cohorts, classroom placement data were tracked through third and fourth grades, respectively. It was noted that beyond 4 years postimplantation, there tended to be little further transition in classroom placement, and therefore, for the remaining school years, an assumption was made that educational placement would hold steady at the last observed distributions. Composite educational costs were calculated based on the weighted proportion of children in each type of classroom setting and the associated costs for these placements as provided by the U.S. Department of Education. Costs were calculated through second, third, and fourth grades for the young, middle, and oldest age cohorts, respectively. Similarly, the educational costs for severe-to-profoundly deaf, nonimplanted children were obtained using data on classroom placement from the Gallaudet Research Institute's (GRI) Annual Survey of Deaf and Hard of Hearing Children and Youth (Gallaudet Research Institute 2009) and applying similar composite educational cost calculations. The GRI survey is conducted annually and offers a representative sample of hearing-impaired children and adolescents in the United States across all levels of hearing impairment. GRI classroom placement data were analyzed for 1517 severe-to-profoundly deaf, nonimplanted, school-aged children, who comprise a subset of the overall population tracked by the GRI annual survey. Educational savings for implanted children were then calculated as the difference between the educational costs for cochlear implanted children in the present study and those calculated for the nonimplanted children derived from the GRI annual survey. All educational costs or savings were discounted annually at 3%.

Average expected cost of complications was stratified by costs of minor (nonsurgical) complications, costs of revisions, and costs of reimplantations, as calculated using prevalence of these events (complication rate) in the CDaCI cohort over 6 years of follow-up. When more than 1 revision/reimplantation event took place, costs for the first and second corrective surgeries were added in determining the average cost of corrective surgery for the overall cohort.

Measurement of Health Utility

Parent-proxy questionnaires were used at baseline and also at yearly postimplantation intervals to assess the health utility of cochlear implanted children in the CDaCI study. The measurement instrument in this study uses questions from both the Health Utility Index (Horsman et al. 2003) Mark II (HUI2) and the Health Utility Index Mark III (HUI3) surveys. These surveys provide measurements of general health status and health-related quality of life stratified by hearing, speech, vision, emotion, pain, ambulation, dexterity, cognition, and self-care domains of health. Respondents' overall health states were calculated using the prescribed methodology provided for the HUI3 instrument. Although not specifically designed for use in children under 5 years of age, parent-proxy questionnaires for HUI2 and HUI3 instruments have been used widely in younger children both in CI and non-CI literature (Barr et al. 1999; Insinga et al. 2002; Oostenbrink et al. 2002; Brisson & Edmunds 2003; Barton et al. 2006b).

Analysis of the repeated measures of health-utility scores at baseline and at 12, 24, 36, 48, 60, and 72 months postimplantation was conducted. Generalized estimating equations (GEE) was used to estimate the parameters of a generalized linear model while allowing for correlation between observations. GEE can be used despite the unknown structure of correlation between measures of health utility at different times since implantation. Children implanted between 18 and 36 months of age were used as the reference group in estimating HUI scores at baseline and at each subsequent follow-up period. This allowed for adjustment for baseline differences in health utilities and projected health utility gains stratified by age at implantation over a 77.5-year average life expectancy in the United States ("Expectation of Life at Birth, and Projections," 2012), taking baseline individual ages and gender into account. Change in QALYs for the three cochlear implanted groups was then calculated by annually compounding the difference in health utility between each of the three cochlear implanted groups and the nonimplanted baseline across the projected life expectancy of each of the three implanted groups.

Cost-Utility Ratios and Sensitivity Analysis

All costs were reported in 2011 U.S. dollars. Base case results were calculated for each age group at implantation, using an average of 4 hours of lost wages based on an average 2-hr hospital stay and a 2-hr round trip travelling time as observed at the JHU study center, a once-a-year lifetime frequency of audiology appointments past study follow-up period, with and without consideration of educational savings, and the partial absorption of the device cost by the manufacturer warranty in instances of reimplantation due to device failures. One-way sensitivity analyses were performed varying these underlying assumptions, with sensitivity analysis parameters centered around those used in the base case.

Statistical Analysis

Baseline demographic, socioeconomic, and medical history factors, as defined in Table 1, were characterized as means and standard deviations for continuous variables and as frequency distributions and percent of total for categorical variables. Baseline comparisons stratified by age at implantation were tested using analysis of variance for continuous variables and χ^2 for categorical variables. Classroom placement and complication rates were compared across age groups at implantation, using analysis of variance.

Health-utility gains from baseline to 72 months, at yearly intervals, after CI were modeled using the results of GEE analysis, allowing for consideration of within-subject correlation over time in the repeated measures. Independent variables included dichotomous indicators for age group at implantation, dichotomous indicators for time of follow-up (a value of 0 or 1 was assigned to indicate whether a given observation occurred at a particular time of follow-up), interaction terms between age group and time of follow-up, and an indicator for bilateral implantation.

A decision tree (Supplementary Fig. 1, Supplementary Digital Content 2, http://links.lww.com/EANDH/A93) was used to compare the costs and outcomes of CI for the three age cohorts. Subsequent to the decision on the age of implantation, each child is faced with a chance node of a CI procedure that results in: no complications, minor complications, revision surgery, or reimplantation surgery. Revision surgeries include surgical procedures that are required to ensure correct functioning of the cochlear device without replacing the initial implanted device. Reimplantations most often result from device failures,

TABLE 1. Characteristics of cohorts

	Cochlear Implantation		
	<18 mos (n = 60)	18–36 mos (n = 71)	>36 mos (n = 44)
Characteristics, No.			
Age at implantation, mos, mean (SD)	13.2 (2.4)	26.4 (5.7)	47.0 (7.9)
Duration of deafness, mos, mean (SD)†	13.0 (2.8)	25.4 (6.8)	45.2 (8.3)
Female (%)†	25 (42)	36 (51)	31 (70)
Hispanic (%)	7 (12)	18 (25)	11 (25)
Congenital SNHL (%)†	51 (85)	34 (48)	20 (45)
Four-tone hearing threshold average, dB, better ear†	107.5 (16.3)	106.7 (15.3)	99.6 (16.0)
Race, No. (%)			
White	49 (82)	48 (68)	34 (77)
Black	4 (7)	9 (13)	2 (5)
Asian	2 (3)	4 (6)	3 (7)
Other	5 (8)	10 (14)	5 (11)
Maternal education, No. (%)			
<8th grade	0 (0)	0 (0)	1 (2)
Some high school	1 (2)	5 (7)	5 (11)
Graduated high school	11 (18)	11 (15)	3 (7)
Some college	13 (22)	23 (32)	14 (32)
Completed college	35 (58)	32 (45)	21 (48)
Household income, No. (%)‡			
<$15,000	1 (2)	8 (11)	4 (9)
$15,000–$29,000	7 (12)	9 (13)	5 (11)
$30,000–$49,999	8 (13)	20 (28)	10 (23)
$50,000–$74,999	14 (23)	8 (11)	7 (16)
$75,000–$99,999	12 (20)	10 (14)	3 (7)
>$100,000	11 (18)	10 (14)	9 (20)
Income <$50,000†	16 (27)	37 (52)	19 (43)
HUI scores,* mean (SD)			
Before implantation†	0.26 (0.14)	0.31(0.17)	0.37 (0.21)
Six years after implantation	0.76 (0.14)	0.72 (0.20)	0.71 (0.17)
Change†	0.51 (0.21)	0.41 (0.24)	0.34 (0.24)
Cognitive status score, mean (SD)			
Bayley PDI (<2y)†	96.2 (17.4)	95.0 (18.9)	76.2 (19.0)
Leiter-R Brief IQ (>2y)	113.5 (15.8)	94.8 (16.0)	106.2 (21.0)
Combined**	100.4 (18.1)	95.6 (20.1)	91.4 (25.5)

Bayley PDI, Bayley Psychomotor Development Index; HUI, Health Utilities Index; Leiter-R Brief, Leiter International Performance Scale-Revised; SNHL, sensorineural hearing loss.
**Health Utilities Index was measured using Mark III transforms—unadjusted scores (see Fig. 1A).*
†Statistically significant differences among children undergoing cochlear implantation at <18 months, 18 to 36 months, and >36 months of age (P< 0.05).
‡Although household income was not significantly different among implant age groups using the six aforementioned family income categories, grouping by family income of less than $50,000 results in significantly lower frequencies among families of children implanted at younger ages (p = 0.012).
***Cognitive status measured by the Bayley Physical Developmental Index for children under 24 months of age and by Leiter Brief Intelligent Quotient Composite Score for children 24 months of age or older.*

requiring the surgical team to replace the device in the same or opposite ear. The probabilities and costs of these events were based on clinical outcomes from the CDaCI study.

Microsoft Excel 2010 (Microsoft Corp., Redmond, WA) was used for decision tree modeling, and STATA version 12 (StataCorp, College Station, TX) was used for all other analyses.

RESULTS

Study Population

A total of 175 children were followed for 72 months after CI. Of these, 60 children were implanted before 18 months, 71 between 18 and 36 months, and 44 after 36 months of age, with a mean age at implantation of 13.2, 26.4, and 47.0 months, respectively. Table 1 shows the baseline characteristics of the study population stratified by age of implantation. The three groups differed by gender, age at onset of deafness, duration of deafness, four-tone hearing threshold average (PTA)—a measure of preimplantation residual hearing, socioeconomic status, baseline HUI scores, and baseline Bayley psychomotor development index, but were not significantly different by race, maternal education level, and other measures of baseline IQ.

Measurement of Health Utility

Children implanted at <18 months of age gained an average unadjusted health-utility improvement of 0.51 points in the first 6 years after implantation, compared with 0.41 points for the 18- to 36-month group, and 0.34 points for the >36-month age group at implantation ($p < 0.0001$). Adjusting for differences in baseline HUI3 scores and controlling for rate of bilateral implantation using the GEE model led to a 0.49 point health-utility gain for the youngest group, a 0.44 point gain for the middle group, and a 0.43 point gain for the oldest group, which resulted in lifetime projected QALY gains of 10.7, 9.0, and 8.4 QALYs, respectively (Fig. 1, Supplemental Digital Content 2,

http://links.lww.com/EANDH/A93; and Table 1, Supplemental Digital Content 3, http://links.lww.com/EANDH/A94).

Due to the absence of a specific hearing aided control group in the CDaCI study, these utility gains were calculated relative to a nonimplanted control constructed from the baseline HUI scores of the three cochlear implanted groups as estimated by the GEE model (0.25, 0.30, and 0.38 for the youngest, middle, and oldest groups, respectively). This approach was used for two reasons: (1) this crossover construct helps reduce potential biases that may be present if the nonimplanted data were instead derived from outside literature, and (2) allows for short-run consideration of effect of maturation on health utilities of nonimplanted children. A weakness of this approach arises from the confounding effect of differences in baseline levels of hearing impairment across the three cochlear implanted groups, a variable associated with HUI scores(Barton et al. 2006a). Barton et al. (2006) demonstrated that higher HUI scores were associated with a more favorable level of hearing loss in nonimplanted children. As a result, one would expect the oldest group at CI (group with lowest 4-tone hearing threshold average at baseline) to attain highest preimplantation HUI scores, as was indeed the case in the present study. The incorporation of this group would, therefore, conservatively bias the health-utility gains identified in the present analysis, particularly for the youngest and middle groups, making the results of the study less favorable.

Measurement of Costs

Classroom placement by 7 years of age (last year of follow-up for youngest cohort) differed significantly among the three cohorts, with the youngest having a higher rate of mainstream integration (81%) and a lower rate of school for the deaf attendance (5%) than the two older implantation groups (55% and 50% mainstream integration, respectively) (Table 2 and Fig. 2). Follow-up of the older two cohorts for 6 years allowed for an assessment of their educational placement at ages older than 7 years, with full mainstream integration increasing to 57% and 56% for the middle and oldest groups, respectively by 8 years of age, and to 63% for the oldest group by 9 years of age. As a result, at 6 years of implant use, the youngest group had a significantly higher rate of mainstream integration at 81% as compared with 57% and 63% for the middle and oldest age groups, respectively ($p < 0.05$). Moreover, GRI-derived classroom placement for severe-to-profoundly deaf hearing aided nonimplanted children had lower rates of mainstream integration than all implant cohort groups (12% for full and 14% for partial mainstream), a higher proportion of self-contained placement (28%), and a 46% attendance at schools for the deaf (Gallaudet Research Institute 2009). With these weights, the mean projected educational costs for severe-to-profoundly deaf hearing aided children were $293,070 from first through 12th grade. This represented mean educational cost savings of $191,705, $170,805, and $167,736 per child for the youngest, middle, and oldest implanted groups, respectively, over the same time period.

Direct medical costs were calculated on an individual patient basis for the entire duration of the CDaCI study, with mean costs presented in Table 3. Total medical cost differences between the three age groups were driven by differences in mean reimplantation rates, which were 5.9%, 7.5%, and 11.5% for the youngest, middle, and oldest groups, respectively ($p = 0.40$) across the 6 years of follow-up (see Table 4). However, none of these differences were significant. Revision surgery rates were 2.4%, 3.2%, and 3.9% for the youngest, middle, and oldest groups, respectively; again, none of these differences reached significance ($p = 0.95$). As a result, total medical and surgical complication rates (see Table 4), which also included minor complications, were not statistically different among the three cohorts ($p = 0.59$). The resulting total lifetime medical costs were $160,453 for the youngest group, $160,638 for the middle group, and $161,056 for the oldest group (Table 5). Incorporating the significantly different educational cost savings from first through 12th grade across the three groups resulted in net lifetime societal savings of $31,252, $10,217, and $6,680 for the youngest, middle, and oldest cohorts, respectively. That is, early CI is estimated to yield more than $20,000 per child lifetime societal savings over implantation at older ages.

Cost-Utility Ratios and Sensitivity Analyses

Driven by these findings, CI for the youngest subgroup dominated the other two alternatives in the base case and sensitivity analyses (Table 5). The base case analysis yielded $14,996/QALY gained when compared with nonimplantation alternatives for the youngest group, $17,849/QALY for the middle group, and $19,173/QALY for the oldest age group at implantation. When incorporating lifetime educational cost savings, these net costs become negative (reflecting net societal savings from pediatric CI), preventing the use of cost-utility ratios as outcome measures.

Sensitivity analyses were conducted by varying underlying assumptions of the model. By increasing the lifetime audiology appointments to twice a year, cost per QALY increases slightly to a range of $15,610 to $20,531. In addition, assuming four audiology visits per year increases the $/QALY ratio to $18,312 to $24,071. Relaxing the assumption that a reimplantation is partially covered by manufacturer's warranty increased the cost of reimplantation to be equal to that of the initial surgery and yielded a cost-utility ratio of $14,426 to $19,194 per QALY gained. Last, sensitivity analyses were performed on health-utility attainment of the constructed nonimplanted control group. These included comparing each implanted group only with their own preimplantation baseline on one extreme and allowing for more significant effects of maturation on health utility in the nonimplanted group on the other extreme. In the latter scenario, a new nonimplanted baseline was modeled after the HUI3 attainment of a group of hearing aided adults reported by Barton et al. (2005).

The study reported an average HUI3 health-utility score of 0.56 for a group of patients with a mean age of 69.5 years and four-tone hearing threshold average of 39 dB (better ear). Despite the considerably lower average level of hearing loss in the study by Barton et al. (2005) than in the present study, a conservative assumption was made to linearly model a health-utility increase from the last known HUI3 score of the nonimplanted group (0.38 at 46 months of age) to an HUI3 score of 0.56 by 21 years of age, after which the health utility of the nonimplanted control does not continue to grow. This scenario yielded cost-utility ratios of $23,254, $30,892, and $35,012 for the youngest, middle, and oldest groups, respectively. Of note, cost-utility ratios for the youngest age group consistently outperformed those for the older cohorts across all the sensitivity analyses. Moreover, even in the most conservative scenarios, these ratios did not approach the $50,000/QALY threshold for cost-effective procedures used in the United States (Owens 1998).

TABLE 2. Educational placement and cost savings

	Classroom Placement*				Difference From Nonimplanted Cohort				Costs and Savings†	
Age Group	Full Mainstream (%)	Partial Mainstream (%)	Self-Contained (%)	School for Deaf (%)	Full Mainstream (%)	Partial Mainstream (%)	Self-Contained (%)	School for Deaf (%)	Grade 1–12 Educational Costs ($)	Educational Cost Savings ($)
<18 mos (n = 42)	81	14	0	5	69	0	–28	–41	101,365	**191,705**
18–36 mos (n = 53)	55	28	2	15	43	14	–26	–21	122,215	**170,805**
36+ mos (n = 32)	50	34	0	16	38	20	–28	–30	125,334	**167,736**
Not implanted‡	12	14	28	46	0	0	0	0	293,070	**0**

**Second-grade classroom placement (average age 7 yrs for each of the groups) is reported in this table. Mean classroom placement was statistically different between the three age groups; p = 0.04. A portion of the children did not report classroom placement in each age group (18 children for youngest group, 18 for middle group, and 12 for oldest group at implantation).*
†On the basis of costs provided by the U.S. Department of Education, inflation adjusted to 2011 U.S. dollars: $7, 042 for full mainstream, $8, 540 for partial mainstream, $20,300 for self-contained in a regular school, and $39,480 for school for deaf placement. Educational costs and savings were calculated using differences between annually reported classroom placement for each of the three age groups at implantation during the Childhood Development after Cochlear Implantation study follow-up period. Costs were discounted annually at a 3% rate for entire duration of secondary schooling.
‡Classroom placement of severe-to-profoundly deaf, nonimplanted children obtained from data provided by Gallaudet Research Institute.

DISCUSSION

These data show that even without considering improvements in lifetime earnings, pediatric CI remains cost effective in any age group (<$50,000/QALY; Owens 1998). The $50,000/QALY threshold also translates to approximately one times the per capita U.S. gross domestic product, which is noted by the World Health Organization to be highly cost effective (World Health Organization 2012). Early implantation (<18 months) consistently dominated all quality of life and societal cost outcomes, with equal or lower rates of postoperative complications when compared with 18 to 36 months and >36 months of age at implantation. Although the middle cohort consistently outperformed the oldest age group at implantation, the differences in outcome metrics between these two groups were marginal and significantly lower than the difference between the middle to youngest age group at implantation. This suggests the presence of a critical age threshold below 18 months of age, after which benefits from CI are significantly reduced and are not regained with longer-term experience with the implant.

Barriers to early implantation are, in part, due to concerns of heightened risk in implanting young children. The present analysis demonstrates that, when performed at academic medical institutions with large, established CI programs, early implantation is as safe as implantation at later ages, with statistically equivalent, though lower rates of revision and reimplantation surgeries. Across all age groups at intervention, implanted children had no mortalities or life-threatening postoperative complications; encountered complications were minor, but there were several that required reoperation. These findings are in agreement with recent literature demonstrating the safety of CI in children under 12 months of age (James & Papsin 2004; Colletti et al. 2005; Miyamoto et al. 2005; Dettman et al. 2007; Valencia et al. 2008). In contrast to the present analysis, these studies reported lower or no complications after implantation but were limited to a smaller and less representative sample (less than 25 children, all from 1 study center; James & Papsin 2004; Colletti et al. 2005; Miyamoto et al. 2005; Valencia et al. 2008) and shorter follow-up duration (Dettman et al. 2007). Previous studies using larger patient populations (all pediatric cochlear implant recipients) and longer duration of follow-up reported similar rates of complications to those observed in the present analysis (Kempf et al. 1999; Bhatia et al. 2004; Kandogan et al. 2005).

Another barrier to early implantation relates to potential uncertainty surrounding the initial diagnosis and treatment

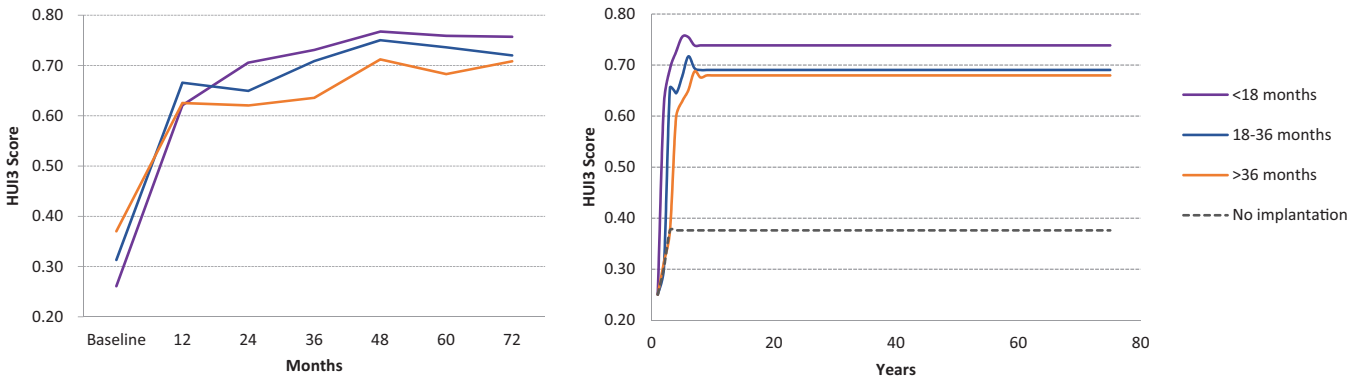

Fig. 1. Health-utility gains after cochlear implantation by age at baseline. Left panel shows unadjusted HUI Mark III gains in the first 6 years after implantation as observed in the Childhood Development after Cochlear Implantation study. Right panel includes lifetime health-utility projections after adjusting for differences in baseline HUI scores and rates of bilateral implantation between the three age groups. Health-utility differences and gains from baseline were significantly different among all three age groups at implantation through 6 years of follow-up on generalized estimating equations analysis ($p < 0.05$). Average projected lifetime quality-adjusted life years gained: 10.7 for <18 month group, 8.9 for 18–36 month group, and 8.2 for >36 month group. HUI, Health Utilities Index.

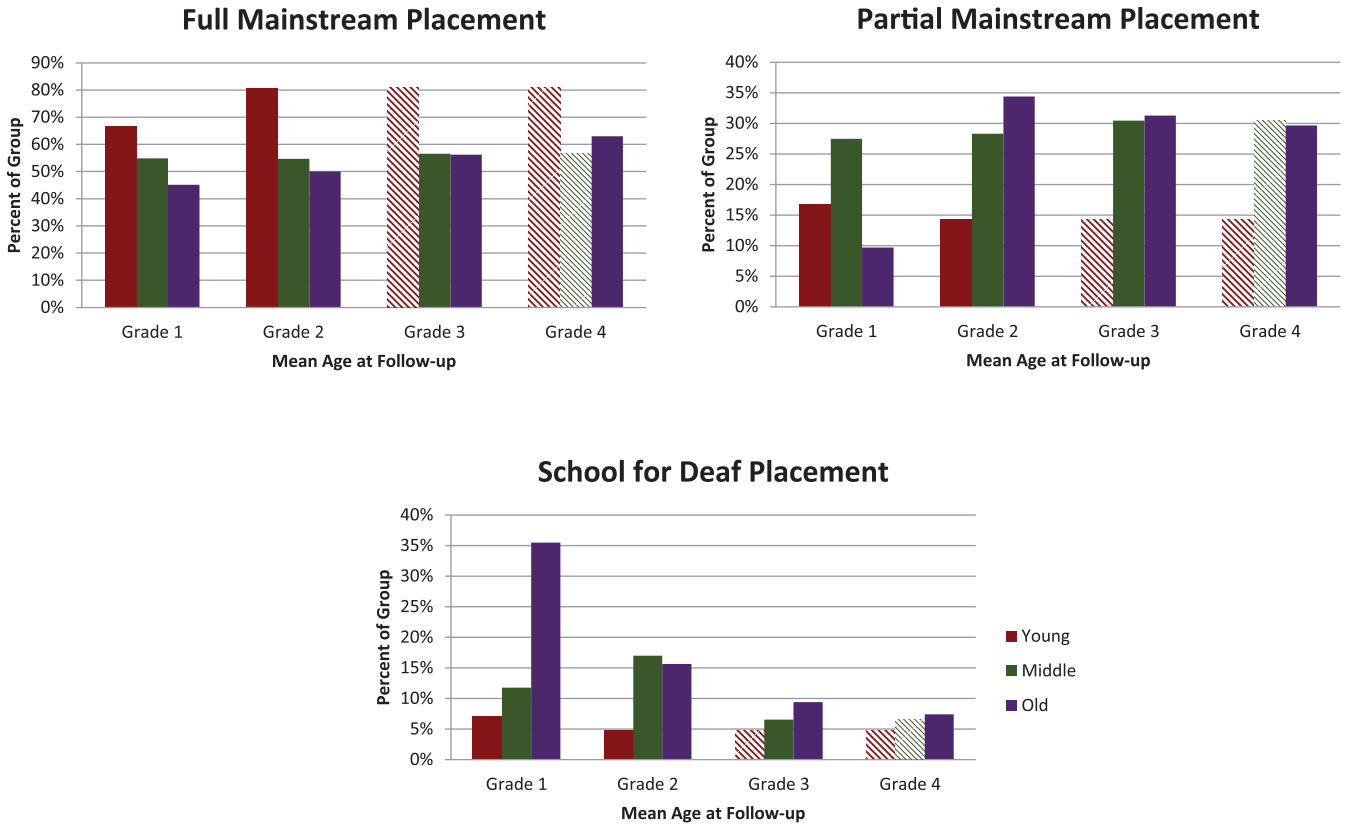

Fig. 2. Classroom placement after cochlear implantation by primary school grade level and age at implantation. Top left panel shows full mainstream placement, top right panel shows partial mainstream placement, and bottom panel shows school for deaf placement. Young, middle, and old correspond to <18 months, 18–36 months, and >36 months of age at implantation, respectively. Mean classroom placement was significantly different among the three groups ($p < 0.05$) in grades 1 and 2. All groups were followed for 72 months after implantation—striped bars are projections based on last known observation for that age group. Self-contained placement omitted because of small subgroup size.

follow-up (White et al. 2010). Though newborn hearing screening (NBHS) programs have been widely adopted in the United States since the early 1990s, increasing the detection of congenital hearing loss in infants from 3% to 94% over the last two decades, a nearly 2% false-positive rate (Clemens et al. 2000) requires further audiologic testing to rule out transient hearing loss and artifact-associated test errors, and to determine the etiology of hearing loss in those with confirmed hearing impairment. Despite the importance of early intervention, significant delays continue to exist in patient follow-up for confirmatory testing and in subsequent treatment for prelingual deafness (Morton & Nance 2006; White et al. 2010). The main factors associated with these delays include shortage of qualified pediatric audiologists, lack of knowledge among health providers about the importance and urgency of follow-up testing (particularly primary care physicians who rarely encounter pediatric hearing loss), and family delays in seeking treatment (Shulman et al. 2010; Lester et al. 2011). Recognizing these delays, the seven national goals for Early Hearing Detection and Intervention (EHDI) programs developed by the CDC include implementation of a confirmatory audiologic evaluation before 3 months of age and appropriate early intervention services by 6 months of age for all infants who screen positive on NBHS (Kemp 1978). The success of these initiatives will largely depend on additional training of health professionals (Sorkin 2011) and implementation of more effective patient tracking and record-management systems to enable timely follow-up and treatment compliance on the part of the patient's family.

These data also show that families with lower annual income were less likely to seek early implantation (in our study setting where onset of all SNHL was before 1 year of age), which may present a critical target for national hearing care initiatives. Prior literature has identified a similar association between delays in implantation and lower socioeconomic class (Fortnum et al. 2002), with some studies specifically linking delayed CI to the presence of Medicaid insurance, likely serving as an indicator for socioeconomic status (Lester et al. 2011). Although patients with Medicaid may receive the same access to medical care as those using private insurance (Morton & Nance 2006), the considerable expenses imposed on families of implanted children by the indirect and downstream costs of implantation, as shown in our analyses, are not reimbursed by health insurance and may present a challenge for low-income families (Chang et al. 2010). Specifically, the preimplantation evaluation process and extensive follow-up require considerable parental involvement and missed time from work, involving several hours of travel to the nearest CI center. Several of the centers participating in this study, for example, recommend at least 2 years of weekly rehabilitation appointments after surgery to achieve maximal benefit from implantation. In turn, these responsibilities are communicated to parents during the initial screening process and may serve as a deterrent to early

TABLE 3. Average lifetime costs of unilateral pediatric cochlear implantation (2011 U.S. dollars)*

Direct Costs	Number of Years	Probability (%)	Reimbursement (US$)
Preoperative			
Audiology	1	100	1284
Physician	1	100	100
Other	1	100	287
Operative			
Cochlear implant device	1	100	34,440
Hospital and surgery charges	1	100	5,724
Medical complications cost			
Minor complications	1–6	4.76	459
Revision	1–6	3.03	5,534
Reimplantation cost	1–6	7.79	9,370
Processor upgrade	1–75	100	11,743
Extended warranty	3–75	100	11,859
Insurance	1–75	100	8,671
Rechargeable batteries	1–75	100	1,485
Postoperative			
Physician	1–75	100	125
Audiology	1–75	100	23,291
Rehab	1–75	100	12,151
Total Direct Costs			126,523
Indirect Costs			
Lost wages†	1–75		30,799
Transportation cost‡	1–75		17,789
Educational savings	1–75		–176,944
Total Indirect Costs			–128,356
Total Costs			–1,833

*Using average age at implantation of 2.3 yrs, 75.2 remaining years of life, a 3% discount rate, once-a-year lifetime frequency of audiology follow-up, 4 hrs of lost wages per medical visit, seven processor upgrades at $2,834 average reimbursement for each upgrade, a $50 annual battery replacement cost, $400 annual extended warranty fee, and $289 annual device insurance fee.
†Lost wages were calculated based on a $23.50 hourly rate and 4 hrs away from work. Wage rate was obtained from the Bureau of Labor Statistics (http://www.bls.gov/eag/eag.us.htm).
‡Transportation cost was calculated based on 100 miles in travel and a travel reimbursement rate of $0.555/mile.

implantation and lead to the alternative of placing a longer emphasis on treatments requiring less intensive follow-up. Unfortunately, prolonging the decision to seek implantation incurs greater downstream costs to the implanted children, their families, and the society at large.

These data also show that the major cost drivers related to CI included the cost of the device and warranty, the surgery, and postoperative rehabilitation and audiology follow-up. Varying all of these factors to 150% of the base case level continued to yield favorable cost-utility ratios—under $25,790/QALY for all age groups at implantation—among the most cost-effective procedures undertaken in the United States (Tengs et al. 1995). Improvements in postimplantation classroom placement were among the largest value drivers of the present analysis. Though limited in duration of follow-up, these data show that early CI had a significantly higher and sustained rate of mainstream integration than the two older groups. This result agrees with the findings of a previous analysis by Schulze-Gattermann et al. (2002), which tracked classroom placement of 158 children in Germany by age at implantation (Schulze-Gattermann et al. 2002). When considering these differential educational cost savings, early pediatric CI actually leads to net societal savings up to $31,000 per child relative to nonimplantation (negative cost-utility ratios). This finding can be put in perspective with the following results: beta blocker therapy to reduce mortality from cardiovascular disease has a positive cost-utility ratio of $5,000/QALY (Weinstein & Stason 1985); combination antiretroviral therapy for human immunodeficiency virus—$23,000/QALY (Freedberg et al. 2001); and dialysis for end-stage renal disease—$50,000–$60,000/QALY (Garner & Dardis 1987).

TABLE 4. Postoperative complications

Age Group	Number of People Implanted	Number of Ears Implanted	Minor Complications* n (%)	Revision Surgeries* n (%)	Reimplantation Surgeries* n (%)	Total Complications* n (%)
<18 mos	60	85	5 (5.88)	2 (2.35)	5 (5.88)	12 (14.12)
18–36 mos	71	94	4 (4.26)	3 (3.19)	7 (7.45)	14 (14.89)
36+ mos	44	52	2 (3.85)	2 (3.85)	6 (11.5)	10 (19.23)
All groups	175	231	11 (4.76)	7 (3.03)	18 (7.79)	36 (15.58)

*All complication rates are shown as a percentage of number of ears implanted; none of the complication rates was statistically different at the 5% level between age groups—analysis of variance p values of 0.80, 0.95, 0.40, and 0.59 for minor complications, revision surgeries, reimplantation surgeries, and total complications across all age groups at implantation, respectively.

TABLE 5. Cost utility and sensitivity analysis

Cost-Utility Ratios	Total Lifetime Cost Without Educational Savings	Total Lifetime Savings With Educational Savings	QALYs Gained	Cost/QALY Without Educational Savings	Interpretation
<18 mos	$160,453	$31,252	10.7	$14,996	Dominated
18–36 mos	$160,638	$10,217	9.0	$17,849	—
36+ mos	$161,056	$6,680	8.4	$19,173	—
Sensitivity Analysis			<18 mos	18–36 mos	36+ mos
Variables	Base Estimate	Range of Estimate (Best to Worst)	Cost-Utility Cost per QALY (Base $14,996)	Cost-Utility Cost per QALY (Base $17,849)	Cost-Utility Cost per QALY (Base $19,173)
Discount rate	3%	0–6	$10,716–$29,005	$12,761–$34,504	$13,723–$37,018
Direct medical cost					
Frequency of lifetime audiology	1/yr	1–4	$14,996–$19,060	$17,849–$22,681	$19,173–$24,351
Reimplantation cost	$9,370	$0–$40,164	$15,165–$14,944	$18,103–$17,771	$19,045–$19,596
Extended warranty	$400/yr	$300–$500	$14,718–$15,273	$17,519–$18,178	$18,820–$19,526
Frequency of device upgrade	7/lifetime	5–10/lifetime	$14,660–$15,452	$17,448–$18,387	$18,740–$19,615
Total lifetime medical cost	$111,968	$55,984–$167,953	$9,801–$20,190	$11,673–$24,024	$12,557–$25,790
Time off work, hours per visit	4	3–5	$14,304–$15,686	$17,026–$18,669	$18,292–$20,053
Parent salary, hourly wage	$23.50	18–30	$14,322–$15,792	$17,048–$18,795	$18,315–$20,187
Nonimplanted health utility	0.38	0.26–0.56	$11,143–$23,254	$14,472–$30,892	$19,173–$35,012

QALY, quality-adjusted life year.

The use of the national CDaCI study, with access to baseline and long-term multicenter data, detailed tracking of educational placement, direct medical costs and reimbursements, and long-term quality-of-life outcomes, allows for greater generalizability of results than previously feasible. In particular, the inclusion of longer-term health-utility follow-up and subgroup analysis by age at implantation addresses two of the limitations of the PenTAG report (Bond et al. 2009). By tracking actual hospital and physician reimbursement data at the individual patient level across the entire duration of the study, this model expands prior analyses of pediatric CI, which relied on Centers for Medicare and Medicaid Services reimbursement data or shorter-term patient follow-up—factors that appear to understate the costs associated with this procedure. As a result, at approximately $112,000 across all age groups, the total direct lifetime cost of CI was considerably higher after inflation adjustment than that reported by Cheng et al. (2000). Despite these higher costs, the substantial gains in health utility over the lifetime of an implanted child still resulted in highly favorable cost-utility ratios, particularly at younger ages.

The approximate average increment of $20,000 of realized lifetime savings from early CI, relative to that observed with implantation in the two older groups, results in nearly $1.26 billion of societal savings over the lifetime of the current 60,000 pediatric cochlear implant candidates in the United States. An average 1.5-yr delay in CI, the age difference between the youngest and middle groups, would diminish these savings to $212 million and would abolish all saving with a 3-yr delay in implantation. This steep transition from the youngest to middle groups at implantation further supports the presence of a critical threshold period, which has also been suggested from a spoken language and auditory perspective (McConkey Robbins et al. 2004; Svirsky et al. 2004; Nicholas & Geers 2007). The significant association between baseline PTA threshold and age at implantation in the present study, with children implanted at younger ages having more severe hearing impairment at baseline, is in agreement with the results of the aforementioned investigations. These investigations concluded that age at implantation was strongly influenced by progression and degree of hearing loss, and, therefore, related to the extent of auditory experience with hearing aids preimplant. Although potentially confounding the effect of age at implantation on post-CI outcomes, these findings suggest that despite allowing for higher preimplantation PTA thresholds from longer hearing aid use, delaying CI in the hope of longitudinally assessing hearing aid benefit can lead to significant and sustained declines in patient quality of life, poorer educational outcomes, and, in turn, lost educational and societal savings.

There are several limitations to the use of CDaCI data, which may influence our findings. The inability to conduct a randomized controlled trial because of ethical considerations forces the use of preimplantation health-utility scores as proxies for quality-of-life attainment of children who would be cochlear implant candidates. The inability to measure costs directly from all study centers due to antitrust regulation led to the need to estimate these by using adjustment factors from a third-party source to generalize the detailed cost data collected at the JHU study center to other geographically dispersed academic medical centers. In addition, classroom placement was used as a proxy for educational costs, but truly assessing costs associated with each type of classroom placement for cochlear implanted children requires more detailed data than currently available. As noted, the use of parent-proxy questionnaires in measuring HUI score is recommended in children over 5 years of age (Horsman et al. 2003), which could decrease the reliability of the utility measures used in our study. However, because the present study longitudinally compares health-utility gains between three implanted groups and a nonimplanted control constructed from their preimplantation baselines, these potential biases would be systematically present across all age groups and time periods, and should be partially mitigated in the ensuing comparisons (Franks et al. 2006).

CONCLUSIONS

The results of this study add an important dimension to existing evidence on the benefits of early CI on auditory and language outcomes, informing policy makers and clinicians of the societal savings and improved economic outcomes that arise from earlier critical assessment and implantation of cochlear implant candidates. As a result, emphasizing intensive early intervention and bolstering early support of families of implanted children could help mitigate the factors associated with auditory deprivation and permanent delays in spoken language learning associated with delayed intervention, thus improving the lives of implanted children and leading to considerable societal savings.

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Dr. Niparko reported serving on advisory boards without remuneration for two cochlear implant manufacturers, Advanced Bionics Corporations and the Cochlear Corporation, and serving on the board of directors for a school for children with hearing loss, which has received gifts from cochlear implant manufacturers. The terms of these arrangements are being managed by The Johns Hopkins University in accordance with its conflict-of-interest policies. External advisors received honoraria for their review of the study protocol and progress reports.

The sponsors had no role in the design and conduct of the study; in the collection, analysis, and interpretation of the data; or in the preparation, review, or approval of this article.

The members of the CDaCI Investigative Team are listed in the Appendix (Supplemental Digital Content 4, http://links.lww.com/EANDH/A113).

Address for correspondence: John K. Niparko, The Johns Hopkins Outpatient Center, Department of Otolaryngology, Head & Neck Surgery, 601 N. Caroline Street, 6th Floor, Room 6161, Baltimore, MD 21287, USA. E-mail: jnipark@jhmi.edu

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