Bilateral vestibular deficiency: quality of life and economic implications

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Abstract

Importance—Bilateral vestibular deficiency (BVD) causes chronic imbalance, unsteady vision, and greatly increases the risk of falls; however, its effects on quality of life (QOL) and economic impact are not well defined.

Objective—Quantify disease-specific and health-related quality of life, health care utilization and economic impact suffered by individuals with BVD in comparison to those with unilateral vestibular deficiency (UVD)

Design—Cross-sectional survey study of BVD, UVD, and healthy individuals

Setting—Academic medical center

Participants—Fifteen BVD, 22 UVD and 23 healthy individuals. Vestibular dysfunction was diagnosed by caloric nystagmography

Intervention—Survey questionnaire

Main Outcomes and Measures—Health status was measured using the Dizziness Handicap Index (DHI) and Health Utility Index Mark 3 (HUI3). Economic burden was estimated using participant responses to questions on disease-specific health care utilization and lost productivity.

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Author Contributions

Dr. Sun, Dr. Ward, and Mr. Semenov had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Ward, Carey, Della Santina

Acquisition of data: Ward, Sun

Analysis and interpretation of data: Sun, Ward, Semenov, Carey, Della Santina

Drafting of the manuscript: Sun, Semenov

Critical revision of the manuscript for important intellectual content: Sun, Ward, Semenov, Carey, Della Santina

Statistical analysis: Semenov

Administrative, technical, and material support: Carey, Della Santina

Study supervision: Carey, Della Santina

Results—In comparison to UVD and normal controls, BVD patients had significantly worse DHI and HUI3 scores. Multivariate regression analysis showed UVD, BVD, increasing number of dizziness-related emergency department (ED) visits, and increasing dizziness-related work-place absenteeism were associated with worse HUI3 scores. BVD and UVD patients incurred annual economic burdens of $13,019 and $3,531 per patient, respectively.

Conclusions and Relevance—BVD significantly decreases quality of life and imposes substantial economic burdens on individuals and society. These results underscore the limits of adaptation and compensation in BVD. Furthermore, they quantify the potential benefits of prosthetic restoration of vestibular function both to these individuals and to society.

INTRODUCTION

Vestibulo-ocular and vestibulo-spinal reflexes normally maintain stable gaze and posture during head movement. Individuals with bilateral vestibular deficiency (BVD) often suffer from oscillopsia (blurring of vision due to image slip across the retinae during head movement), disequilibrium and postural instability that together confer a 31-fold increase in risk of falling.[1] Most individuals with unilateral vestibular deficiency (UVD) ultimately compensate for their loss by using information from the remaining labyrinth, and those with mild or moderate BVD often compensate by integrating residual labyrinthine input with other sensory cues. However, severe BVD can be devastating if adaptation and compensation strategies fail to overcome the sensory deficit.[2, 3] Individuals with BVD often suffer from chronic imbalance and instability of vision and posture that render routine daily activities such as walking and driving difficult.

Ototoxicity due to aminoglycosides such as gentamicin is the most common cause of acquired BVD among adults. Other causes include genetic abnormalities, Ménière's disease[4], labyrinthitis, meningitis, ischemia autoimmune disease, and idiopathic or iatrogenic injury.[5–7]

In contrast to the extensive literature on deafness[8] and blindness[9], the epidemiology of severe BVD has been studied infrequently, perhaps because lack of diagnostic standardization, screening programs, and effective treatments hinder accrual of information on prevalence, incidence, and health care utilization[10]. However, recent data from the United States National Health Interview Survey suggest a severe/profound BVD prevalence of 28/100,000 U.S. adults, or 64,046 Americans[1]. Although rare enough to merit designation as an orphan disease[11] in the US, BVD is a chronic disabling condition that can impose life-long socioeconomic costs while negatively impacting quality of life. Few studies[12, 13] have quantitatively investigated the socioeconomic and personal burden of BVD; however, these are important considerations for development of potential treatments for BVD, such as a multichannel vestibular prosthesis[38]. The objective of this study was to characterize the health-related quality of life in individuals with BVD and to quantify their disease-specific socioeconomic burden in comparison to individuals with UVD and to healthy controls. Utilizing the quality of life data obtained here, we provide a projected cost-utility estimate of a vestibular prosthesis.

METHODS

Study design and study population

Approval for this study was obtained from the Johns Hopkins Medicine Institutional Review Board. We identified patients with chronic unilateral or bilateral vestibular deficiency and recruited normal controls without a history of dizziness or inner ear disease. Participants with UVD after unilateral intratympanic gentamicin injection for treatment of unilateral Ménière's disease or BVD confirmed by history and examination were recruited from the neurotologic practice of the Johns Hopkins Department of Otolaryngology – Head and Neck Surgery. Normal control participants were recruited using community-based advertisements. An electronic survey was distributed to all subjects. Some subjects also received an identical paper-based survey, depending on participant preference, and results were then entered electronically by study investigators. For UVD and BVD participants, each respondent's medical chart was reviewed, and only subjects with vestibular deficiency confirmed by both history and caloric nystagmography (sum of peak slow phase eye speeds for warm and cool ear canal irrigations ≤10°/s in the affected ear(s)) were included in the study.

Study questionnaire

The survey questionnaire elicited participant demographics, clinical history of dizziness and balance symptoms, health care utilization, history of falls and effects on productivity attributed to dizziness and balance deficits. Clinical history of dizziness and balance symptoms was elicited using a set of questions that has been validated in a previous study[1] to be discriminatory for severe-to-profound BVD. Also embedded in the survey were the Dizziness Handicap Index (DHI) and Health Utility Index Mark 3 (HUI3). The DHI is a commonly used instrument to evaluate the specific impacts of dizziness and balance symptoms on quality of life[14]. It consists of a 25-item questionnaire that evaluates a respondent's performance along 3 dimensions: physical, emotional, and functional. Subjects respond with 'yes' (4 points), 'sometimes' (2 points), or 'no' (0 points) to each question. The total score ranges from 0 ('no difficulty') to 100 ('maximum difficulty'), so higher DHI scores imply greater self-reported handicap. HUI3 is a 15-item, population-based, validated health utility instrument that measures the respondent's general health status and health-related quality of life along 8 specific "attributes": vision, hearing, speech, ambulation, dexterity, emotion, cognition, and pain each with a 5 or 6 level of ability/disability. For example, for the ambulation domain, scores of 1 and 6 indicate no dysfunction and complete inability to walk, respectively, with intermediate scores determined by degree of reliance on others/equipment for ambulation. The responses for these individual attributes of health are then aggregated using a population-validated utility transformation function, yielding a total HUI3 score ranging from 1 (perfect health) to 0 (death), with lower HUI3 scores indicating poorer self-reported quality of life.[15] It has been used extensively in health economic analyses, including studies of cochlear implantation[16]. In the present study, each respondent's overall health utility was calculated using methods prescribed for analysis of HUI3 data[15], yielding a total HUI3 score ranging from 1 ('perfect health') to 0 ('death'), with lower HUI3 scores indicating poorer self-reported quality of life.

Economic burden

The annual, per patient economic burden for each study group was estimated based on responses to survey questions on health care utilization and lost productivity specifically attributed by the participant to dizziness and balance deficits. Economic analysis was conducted from a societal perspective and included both direct costs (e.g., health care utilization) and indirect costs (e.g., lost productivity). Cost of health care utilization was calculated by multiplying self-reported disease-specific annual frequency of clinic and emergency department (ED) visits by the estimated cost for each visit. The cost of each physician office visit was estimated using Medicare reimbursement figures for level III follow-up clinic visits ($145.00, CPT 99213). The per-visit cost of emergency room care for dizziness or balance complaints attributable to otologic/vestibular causes was estimated to be $768.33[17], which represents the national mean aggregate cost of each evaluation of dizziness, after adjusting for inflation. Other potential health care utilization costs such as costs related to falls, medication usage, vestibular physical therapy, diagnostic testing outside of the ED, treatment of depression or other sequelae of BVD, and alternative health practices such as acupuncture were neither addressed in the survey nor included in the analysis. The cost of lost productivity was calculated by multiplying the number of reported annual work hours missed by $22.60, the average wage for United States workers in 2012 as estimated by the US Bureau of Labor Statistics[18]. All economic analyses are expressed in 2012 dollars using a discount rate of 3%[19].

Prospective cost-utility analysis a multi-channel vestibular prosthesis (MVP)

Cost-utility is defined as cost per quality-adjusted life-year ($/QALY). The projected costs of a multi-channel vestibular prosthesis (MVP) can be modeled using estimates derived from the cochlear implant experience (eTable 1)[16, 20] due to the similarities in technology, surgical procedure, and post-operative care. Life-years following implantation are calculated by subtracting the average age of BVD respondents in this study from the age- and gender-matched life expectancy found in the U.S. Centers for Disease Control and Prevention (CDC) actuarial life tables [21]. Change in QALY's between the two vestibular deficiency groups are then calculated by annually compounding the difference in health-utility between the UVD and BVD groups across the projected average life-expectancy of the study population.

Statistical analysis

Baseline demographic, socioeconomic and medical history factors (Table 1) were characterized by mean and standard deviation for continuous variables and by frequency distributions and percentage of total for categorical variables. Baseline comparisons stratified by type of vestibular deficiency were tested using analysis of variance (ANOVA) for continuous variables and χ^2 for categorical variables.

Respondents' overall health states were calculated using the prescribed methodology provided for the HUI3 instrument. Baseline differences in health utilities were explored using a multivariate generalized linear model, allowing response variables that have both Gaussian and non-Gaussian distributions. Covariates included demographic and clinical characteristics, annual clinic and emergency room visits, economic variables related to lost productivity measured by days of work missed; and morbidity characteristics related to annual falls. Associations were adjusted for demographic characteristics including gender, race, age, and education status. STATA 12 (Stata Corp, College Station, TX) was used for all statistical analyses.

RESULTS

Survey response rates for BVD, UVD, and normal control groups were 64%, 52%, and 92%, respectively, with an overall response rate of 65%. In the BVD and UVD groups, 15 and 22 respondents, respectively, met inclusion criteria for having caloric-proven vestibular deficiency. Twenty-three normal controls were recruited. The etiologies of BVD in the study group were: ototoxicity from intravenous aminoglycoside use (27%), bilateral chemical labyrinthectomy for Ménière's disease (20%) (performed elsewhere), Lyme disease (1%), trauma (1%), and idiopathic (6%). For respondents who met inclusion criteria, there was 100% completion rate for the survey questions analyzed in this study, including DHI, HUI3, health care utilization and lost productivity. All BVD patients reported a clinical history consistent with severe-to-profound BVD.

Review of medical records indicate that for UVD subjects, vestibular physical therapy sessions at our institution occurred between 2003 and 2007 (6–9 years prior to survey), with the duration ranging from one session to several years. For BVD patients, vestibular physical therapy occurred between 2001 and 2010 (3–12 years prior to survey), spanning several months to years. Regimens consisted of balance and gait training, as well as visual adaptation, with little, if any benefit perceived by subjects. In 13 BVD subjects with available audiometric data, 9 showed pure tone averages (PTA) within normal range bilaterally while 4 showed high frequency loss consistent with presbycusis. Although audiometric data is not available in the remaining 2 BVD subjects, they both denied significant hearing loss on the hearing assessment portion of the HUI questionnaire. UVD subjects demonstrated greater unilateral hearing impairment with an average PTA of 59 dB (standard deviation, 26 dB) in the ear treated for Ménière's disease. Review of medical records indicated mild medical comorbidities including hypertension, hyperlipidemia, and gastroesophageal reflux in most subjects while only 1 BVD subject had a serious medical cormorbidity of cardiac arrhythmia with pacemaker dependence.

The demographic and clinical characteristics of study subjects are shown in Table 1. Statistically significant between-group differences were observed for age ($p=0.005$), DHI ($p<0.001$), number of falls during the previous year ($p<0.001$), annual days of work missed due to dizziness complaints ($p=0.03$), and annual physician office visits for dizziness ($p<0.001$).

Mean HUI3 overall health utility and attribute-specific scores of study group are shown in Table 2. Statistically significant between-group differences were observed for overall score ($p<0.001$), and for specific attributes including vision ($p<0.001$), hearing ($p<0.001$), ambulation ($p<0.001$), emotion ($p<0.001$), and pain ($p<0.001$). Generalized linear model analysis of clinical variables associated with HUI3 scores after adjustment for other variables (including gender, race, education, age, and frequency of dizziness-related visits to an outpatient clinic) showed decreased health utility was significantly associated with presence of UVD ($p<0.001$) or BVD ($p<0.001$), increased dizziness-related emergency room visits ($p=0.002$), and increased dizziness-related missed work days ($p<0.001$) to be independently associated with worse HUI3 scores.

The estimated annual per-patient societal economic burden of each study group is shown in Table 3. Normal controls incurred no costs due to dizziness-related complaints, whereas patients with UVD and BVD had estimated annual, per-patient economic burdens of $3,531 (range, 0 – 48,442) and $13,019 (range 0 – 48,830), respectively.

DISCUSSION

This study investigated the quality of life of individuals lacking vestibular sensation unilaterally or bilaterally using two validated instruments. In this study, DHI scores of BVD respondents indicated a “severe” handicap, compared to a “mild” handicap for UVD respondents[14]. BVD respondents were more likely to report worse handicap along the “functional” and “emotional” dimensions, reflecting the impact of chronic imbalance on perceived social and self well-being. These figures are consistent with DHI scores previously reported for BVD and UVD patients[12, 22].

The HUI3 is a well-validated health-related quality of life instrument that has not been previously applied to individuals with vestibular deficiency. The results are remarkable for the severity with which BVD respondents rated their general health status. The mean score of 0.39 reported by BVD respondents is similar to the score of 0.37 reported by a group of similarly-aged individuals with profound deafness[23] and those suffering from other debilitating chronic conditions such as untreated rheumatoid arthritis (HUI3=0.39)[24], while the HUI3 score of 0.63 reported by UVD respondents is similar to that reported for patients with congestive heart failure (CHF) severe enough to have required an implantable cardiac defibrillator (HUI3=0.64)[25] (Table 5). In contrast, individuals with chronic kidney disease (CKD) requiring hemodialysis reported a mean HUI3 score of 0.73, higher (i.e., better) than both BVD and UVD cohorts.[26]

The quality of life data for BVD patients reported herein are consistent with previously published results. Guinand *et al.*[12] used another health-related QOL instrument on a group of BVD patients and found impairment in overall health state to a degree similar to those with chronic low back pain[27], a condition that also carries considerable functional limitations. These figures reveal that although clinicians and third-party payors often consider BVD and UVD to be benign chronic conditions with negligible health impact, individuals suffering with these conditions report pervasive negative impact on health-related quality of life.

Attribute-specific HUI3 scores reveal that the impact of chronic oscillopsia and imbalance on the quality of life of BVD patients occurred not only in the expected attributes of ‘vision’ and ‘ambulation’, but also in others such as ‘emotion’, ‘cognition’, and ‘pain’. This may be due in part to the psychological toll of chronic disequilibrium and difficulty performing routine daily activities. For instance, on average, BVD patients rated their emotional state between ‘occasionally’ and ‘often’ ‘fretful, angry, irritable, anxious, or depressed’ on the HUI3 questionnaire. Moreover, compared to UVD subjects, the overall HUI3 scores of BVD subjects were significantly decreased despite actually scoring better in the hearing “attribute”, reflecting both the prevalence of Ménière’s-associated hearing loss in UVD individuals and the overwhelming impact of BVD. Consistent with their poor health status on HUI3, BVD patients also reported significant functional limitations in daily activities such as difficulty “walking in a straight line”, “walking through a doorway without bumping into the sides” or “walking on uneven surfaces”. BVD respondents also reported on average almost 19 falls a year. Although the health and economic impact of fall-related injuries could not be directly determined from data accrued in the present study, prior studies have shown that falling is often the proximate cause of large health care expenditures and reductions in functional status[28]. Finally, it is also possible that conditions such as depression, which may be more prevalent in individuals with BVD (either coincidentally or because BVD and chronic dizziness engender secondary depression[29]), may play a confounding role in the self-reported health status of respondents.

Although the normal controls in our study were younger on average than those in the BVD and UVD groups and had HUI3 scores higher than existing age-adjusted, population-based normative data[30], our multivariate statistical model found that respondent age was not associated with worse HUI3 scores in this study. Perhaps not surprisingly, decreasing vestibular function, number of ED visits due to dizziness, and dizziness-related work-place absenteeism were all independently associated with worse HUI3 scores. Number of falls was also considered in the statistical model but was found to be co-linear with other clinical variables such as the number of emergency room visits.

In estimating the socioeconomic impact of BVD, we found that the annual, per-patient economic burden of BVD is considerably higher than UVD and comparable to that of other chronic health conditions such as diabetes mellitus, non-congenital deafness, congestive heart failure, and osteoarthritis (Table 4)[31, 32]. Most of the increased burden in the BVD cohort can be attributed to higher rates of dizziness-specific work-place absenteeism. Our economic analysis is limited by its reliance on self-reported data that cannot be independently verified. Additional assumptions include that all clinic visits occurred with a physician rather than ancillary care provider, and that annual disease-specific health care utilization and productivity losses for the year prior to survey completion accurately reflect values for prior and future years. Furthermore, although survey questions were addressed with respect to each participant’s “main problem” of “dizziness and imbalance”, participants were not asked to distinguish between dizziness and balance complaints. We also assumed that all ED visits resulted in a work-up typical[17] for inner-ear-related vertigo, which may overestimate costs for BVD patients who have a known diagnosis and therefore may undergo neuroimaging less frequently. Despite these assumptions, the economic burden reported is likely a conservative estimate, as it does not include costs related to medications or other interventions, injuries due to falls, diagnostic testing outside of the ED, treatment of secondary conditions BVD/UVD patients fail to attribute to their vestibular loss (e.g., depression) and inpatient admission, a costly outcome that occurs in approximately 10% of dizziness presentations to the ED[33].

The large difference in self-reported quality of life between BVD and UVD patients likely reflects relative inadequacy of vestibular reflexes and vestibular rehabilitation outcomes for those with severe bilateral vestibular loss compared to individuals with a single working labyrinth.[34, 35] Restoring the function of one labyrinth through gene therapy[36], stem cell interventions[37] or prosthetic interventions[38–46] yield significant benefits. For example, a multi-channel vestibular prosthesis (MVP) currently in development may partly restore unilateral semicircular canal function to BVD patients, thereby improving vestibulo-ocular reflex performance, visual acuity during head movement and postural stability[38, 39, 43–46]. An important consideration in its development is the device's cost-utility. Based on data presented here, we can estimate the projected cost-utility of MVP implantation.

Since pre-implantation health utilities are known, we projected post-implantation health states as a percentage of unilateral vestibular restoration, with achievement of the reported health state of UVD individuals equating to 100% restoration (best-case scenario). By conducting this sensitivity analysis, we estimate the cost-utility of an MVP to be $28,490 per quality-adjusted life-year (QALY), $37,986/QALY, and $56,979/QALY for 100%, 75%, and 50% restoration, respectively. Additional cost-sensitivities with respect to other variables are shown in Table 5. These figures compare favorably with the cost-utility of existing interventions[47, 48] for other chronic conditions (Table 4) and with the existing standard of economic feasibility in the United States, which considers medical interventions costing ≤$50,000/QALY to be highly cost-effective.[49, 50]

Several limitations exist in this study, including sample sizes that are small (although evidently large enough to reveal significant findings) and biases inherent to cross-sectional survey studies relying on patient self-reporting. Reported health states are vulnerable to selection bias as individuals with poorer functional status are more likely to respond to the survey. Although estimates of BVD prevalence and incidence have been computed from National Health Interview Survey data for a large population,[1] the absence of large-scale, high quality epidemiological data that also include objective, specific assessments of labyrinthine function makes it difficult to determine how well our study population represents the spectrum of health-related quality of life among BVD and UVD individuals. Furthermore, the study is limited by the scope of the survey questionnaire, which, for instance, does not specifically address variability in respondents' medical comorbidities that may impact HUI3 scores.

CONCLUSION

In comparison to normal controls and to subjects with UVD, BVD patients had significantly decreased health-related quality of life as measured by the DHI and HUI3. They reported an increased frequency of falls, increased health care utilization, and decreased productivity due to dizziness-related workplace absenteeism. Taken together, these findings suggest that BVD significantly degrades quality of life for affected individuals, imposes a significant socioeconomic burden on society, and merits development of interventions that can restore function with cost-utility comparable to that of treatments that are already the standard of care for similarly disabling conditions.

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REFERENCES

1. Ward BK, Agrawal Y, Hoffman HJ, Carey JP, Della Santina CC. Prevalence and impact of bilateral vestibular hypofunction: results from the 2008 United States National Health Interview Survey. JAMA Otolaryngol Head Neck Surg. 2013; 139(8):804–810.
2. Minor LB. Gentamicin-induced bilateral vestibular hypofunction. JAMA. 1998; 279(7):541–544. [PubMed: 9480366]
3. Brandt T. Bilateral vestibulopathy revisited. Eur J Med Res. 1996; 1(8):361–368. [PubMed: 9360934]
4. Verstreken M, Declau F, Wuyts FL, et al. Hereditary otovestibular dysfunction and Meniere's disease in a large Belgian family is caused by a missense mutation in the COCH gene. Otol Neurotol. 2001; 22(6):874–881. [PubMed: 11698812]
5. Gillespie MB, Minor LB. Prognosis in bilateral vestibular hypofunction. Laryngoscope. 1999; 109(1):35–41. [PubMed: 9917037]
6. Rinne T, Bronstein AM, Rudge P, Gresty MA, Luxon LM. Bilateral loss of vestibular function: clinical findings in 53 patients. J Neurol. 1998; 245(6-7):314–321. [PubMed: 9669481]
7. Zingler VC, Cnyrim C, Jahn K, et al. Causative factors and epidemiology of bilateral vestibulopathy in 255 patients. Ann Neurol. 2007; 61(6):524–532. [PubMed: 17393465]
8. Mohr PE, Feldman JJ, Dunbar JL, et al. The societal costs of severe to profound hearing loss in the United States. Int J Technol Assess Health Care. 2000; 16(4):1120–1135. [PubMed: 11155832]
9. Bourne R, Price H, Taylor H, et al. New systematic review methodology for visual impairment and blindness for the 2010 Global Burden of Disease study. Ophthalmic Epidemiol. 2013; 20(1):33–39. [PubMed: 23350553]
10. Vibert D, Liard P, Häsler R. Bilateral idiopathic loss of peripheral vestibular function with normal hearing. Acta Otolaryngol. 1995; 115(5):611–615. [PubMed: 8928631]
11. [Accessed July 28, 2013] Office of Orphan Products Development, U.S. Food and Drug Administration. http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/OfficeofScienceandHealthCoordination/ucm2018190.htm
12. Guinand N, Boselie F, Guyot J-P, Kingma H. Quality of life of patients with bilateral vestibulopathy. Ann Otol Rhinol Laryngol. 2012; 121(7):471–477. [PubMed: 22844867]
13. Loughran S, Gatehouse S, Kishore A, Swan IR. Does patient-perceived handicap correspond to the modified clinical test for the sensory interaction on balance? Otol Neurotol. 2006; 27(1):86–91. [PubMed: 16371852]
14. Jacobson GP, Newman CW. The development of the dizziness handicap inventory. Arch Otolaryngol Head Neck Surg. 1990; 116(4):424–427. [PubMed: 2317323]
15. Horsman J, Furlong W, Feeny D, Torrance G. The Health Utilities Index (HUI(R)): concepts, measurement properties and applications. Health Qual Life Outcomes. 2003; 1(1):54. [PubMed: 14613568]
16. Cheng AK, Rubin HR, Powe NR, Mellon NK, Francis HW, Niparko JK. Cost-utility analysis of the cochlear implant in children. JAMA. 2000; 284(7):850–856. [PubMed: 10938174]
17. Saber Tehrani AS, Coughlan D, Hsieh YH, et al. Rising annual costs of dizziness presentations to U.S. emergency departments. Acad Emerg Med. 2013; 20(7):689–696. [PubMed: 23859582]
18. [Accessed February 20, 2013] Bureau of Labor Statistics. www.bls.gov
19. Gold, MR.; Siegel, JE.; Russell, LB.; Weinstein, MC. Cost-effectiveness in health and medicine. New York, NY: Oxford University Press; 1996.
20. Semenov YR, Yeh ST, Seshamani M, et al. Age-dependent cost-utility of pediatric cochlear implantation. Ear Hear. 2013; 34(4):402–412. [PubMed: 23558665]

21. [Accessed March 1, 2013] United States Centers for Disease Control and Prevention actuarial life tables. http://www.cdc.gov/nchs/data/nvsr/nvsr61/nvsr61_03.pdf
22. Jacobson GP, Calder JH. Self-perceived balance disability/handicap in the presence of bilateral peripheral vestibular system impairment. J Am Acad Audiol. 2000; 11(2):76–83. [PubMed: 10685673]
23. Francis HW, Chee N, Yeagle J, Cheng A, Niparko JK. Impact of cochlear implants on the functional health status of older adults. Laryngoscope. 2002; 112(8):1482–1488. [PubMed: 12172266]
24. Strand V, Rentz AM, Cifaldi MA, Chen N, Roy S, Revicki D. Health-related quality of life outcomes of adalimumab for patients with early rheumatoid arthritis: results from a randomized multicenter study. J Rheumatol. 2012; 39(1):63–72. [PubMed: 22045836]
25. Noyes K, Corona E, Veazie P, Dick A, Zhao H, Moss A. Examination of the effect of implantable cardioverter-defibrillators on health-related quality of life. Am J Cardiovasc Drugs. 2009; 9(6): 393–400. [PubMed: 19929037]
26. Heidenheim AP, Muirhead N, Moist L, Lindsay RM. Patient quality of life on quotidian hemodialysis. American Journal of Kidney Diseases. 2003; 42(Supplement 10):36–41. [PubMed: 12830442]
27. Garratt AM, Ruta DA, Abdalla MI, Buckingham JK, Russell IT. The SF36 health survey questionnaire: an outcome measure suitable for routine use within the NHS? BMJ. 1993; 306(6890):1440–1444. [PubMed: 8518640]
28. Sterling DA, O'Connor JA, Bonadies J. Geriatric falls: injury severity is high and disproportionate to mechanism. J Trauma. 2001; 50(1):116–119. [PubMed: 11231681]
29. Hoffman, HJ.; Li, C-M.; Losonczy, KG.; Sklare, DA.; Cohen, H.; Della Santina, CC. Paper presented at: 141st American Public Health Association Annual Meeting. Boston, MA: 2013. Impact of dizziness and balance problems and other chronic health conditions on falling risk in United States adults.
30. Trakas K, Oh PI, Singh S, Risebrough N, Shear NH. The health status of obese individuals in Canada. Int J Obes Relat Metab Disord. 2001; 25(5):662–668. [PubMed: 11360148]
31. Foley RN, Collins AJ. The growing economic burden of diabetic kidney disease. Curr Diab Rep. 2009; 9(6):460–465. [PubMed: 19954692]
32. Le TK, Montejano LB, Cao Z, Zhao Y, Ang D. Healthcare costs associated with osteoarthritis in US patients. Pain Prac. 2012; 12(8):633–640.
33. Newman-Toker DE, Camargo JCA, Hsieh Y-H, Pelletier AJ, Edlow JA. Disconnect between charted vestibular diagnoses and emergency department management decisions: a cross-sectional analysis from a nationally representative sample. Acad Emerg Med. 2009; 16(10):970–977. [PubMed: 19799573]
34. Leigh, R.; Zee, D. The neurology of eye movement. New York, NY: Oxford University Press; 1999.
35. Herdman SJ. Vestibular rehabilitation. Curr Opin Neurol. 2013; 26(1):96–101. [PubMed: 23241567]
36. Baker K, Brough DE, Staecker H. Repair of the vestibular system via adenovector delivery of Atoh1: a potential treatment for balance disorders. Adv Otorhinolaryngol. 2009; 66:52–63. [PubMed: 19494572]
37. Ronaghi M, Nasr M, Heller S. Concise review: inner ear stem cells—an oxymoron, but why? Stem Cells. 2012; 30(1):69–74. [PubMed: 22102534]
38. Della Santina CC, Migliaccio AA, Patel AH. A Multi-channel Semicircular Canal Neural Prosthesis Using Electrical Stimulation to Restore 3D Vestibular Sensation. IEEE Trans Biomed Eng. 2007; 54(6 Pt 1):1016–1030. [PubMed: 17554821]
39. Davidovics N, Rahman M, Dai C, Ahn J, Fridman G, Della Santina C. Multichannel vestibular prosthesis employing modulation of pulse rate and current with alignment precompensation elicits improved VOR performance in monkeys. J Assoc Res Otolaryngol. 2013; 14(2):233–248. [PubMed: 23355001]

40. Valentin NS, Hageman KN, Dai C, Della Santina CC, Fridman GY. Development of a multichannel vestibular prosthesis prototype by modification of a commercially available cochlear implant. IEEE Trans Neural Syst Rehabil Eng. 2013; (5):830–839. [PubMed: 23649285]
41. Guyot J-P, Sigrist A, Pelizzone M, Kos MI. Adaptation to steady-state electrical stimulation of the vestibular system in humans. Ann Otol Rhinol Laryngol. 2011; 120(3):143–149. [PubMed: 21510138]
42. Digiovanna J, Carpaneto J, Micera S, Merfeld DM. Alignment of angular velocity sensors for a vestibular prosthesis. J Neuroeng Rehabil. 2012; 9:14. [PubMed: 22329908]
43. Phillips C, DeFrancisci C, Ling L, et al. Postural responses to electrical stimulation of the vestibular end organs in human subjects. Exp Brain Res. 2013; 229(2):181–195. [PubMed: 23771587]
44. Rubinstein JT, Bierer S, Kaneko C, et al. Implantation of the semicircular canals with preservation of hearing and rotational sensitivity: a vestibular neurostimulator suitable for clinical research. Otol Neurotol. 2012; 33(5):789–796. [PubMed: 22699989]
45. Dai C, Fridman GY, Chiang B, et al. Directional plasticity rapidly improves 3D vestibulo-ocular reflex alignment in monkeys using a multichannel vestibular prosthesis. J Assoc Res Otolaryngol. 2013:1–15.
46. Thompson LA, Haburcakova C, Gong W, et al. Responses evoked by a vestibular implant providing chronic stimulation. J Vest Res. 2012; 22(1):11–15.
47. Larsen GC, Manolis AS, Sonnenberg FA, Beshansky JR, Estes NAM, Pauker SG. Cost-effectiveness of the implantable cardioverter-defibrillator: Effect of improved battery life and comparison with amiodarone therapy. J Am Coll Card. 1992; 19(6):1323–1334.
48. Drewett RF, Minns RJ, Sibly TF. Measuring outcome of total knee replacement using quality of life indices. Ann R Coll Surg Engl. 1992; 74(4):286–290. [PubMed: 1416685]
49. Rohde LE, Bertoldi EG, Goldraich L, Polanczyk CA. Cost-effectiveness of heart failure therapies. Nat Rev Cardiol. 2013; 10(6):338–354. [PubMed: 23609174]
50. Chambers JD, Lord J, Cohen JT, Neumann PJ, Buxton MJ. Illustrating potential efficiency gains from using cost-effectiveness evidence to reallocate medicare expenditures. Value Health. 2013; 16(4):629–638. [PubMed: 23796298]
51. Wong G, Howard K, Chapman JR, et al. Comparative survival and economic benefits of deceased donor kidney transplantation and dialysis in people with varying ages and co-morbidities. PLoS One. 2012; 7(1):e29591. [PubMed: 22279541]
52. Klop WM, Boermans PP, Ferrier MB, van den Hout WB, Stiggelbout AM, Frijns JH. Clinical relevance of quality of life outcome in cochlear implantation in postlingually deafened adults. Otol Neurotol. 2008; 29(5):615–621. [PubMed: 18451751]
53. Semenov YR, Martinez-Monedero R, Niparko JK. Cochlear Implants: Clinical and Societal Outcomes. Otolaryngol Clin N Am. 2012; 45(5):959–981.
54. Dunlay SM, Shah ND, Shi Q, et al. Lifetime costs of medical care after heart failure diagnosis. Circ Cardiovasc Qual Outcomes. 2011; 4(1):68–75. [PubMed: 21139091]
55. Ruchlin HS, Insinga RP. A review of health-utility data for osteoarthritis: implications for clinical trial-based evaluation. Pharmacoeconomics. 2008; 26(11):925–935. [PubMed: 18850762]

Table 1

Demographic and clinical characteristics of study subjects

	BVD[1] (N=15)	UVD[2] (N=22)	Normal (N=23)	P value
Mean Age (SD[3])	65 (10)	62 (12)	52 (14)	0.005
Gender (%)				
Male	73	41	44	0.1
Female	27	59	56	
Race (%)				
White	100	91	87	0.6
Black	0	0	0	
Asian	0	0	0	
Native American	0	5	9	
Hawaiian	0	5	0	
Other	0	0	4	
Education (%)				
Less than HS[4]	0	0	5	0.1
HS	47	14	17	
College or higher	53	86	78	
Mean DHI[5] (SD)	62 (31)	27 (23)	0.6 (1.4)	<0.001
Physical (SD)	17 (10)	7 (7)	0.4 (1.2)	<0.001
Emotional (SD)	20 (12)	10 (9)	0.1 (0.4)	<0.001
Functional (SD)	25 (11)	10 (10)	0.1 (0.4)	<0.001
Falls (SD)*	19 (26)	2 (5)	1 (3)	<0.001
Work days missed (SD)*	69 (106)	19 (64)	0 (0)	0.03
ED[6] visits (SD)*	0.4 (0.8)	0.1 (0.5)	0 (0)	0.1
Clinic visits (SD)*	1.4 (0.8)	0.6 (1.1)	0 (0)	<0.001

*Mean number of occurrences attributed to dizziness or imbalance over past 12 months for each respondent

[1]Bilateral vestibular deficiency

[2]Unilateral vestibular deficiency

[3]Standard deviation

[4]High school

[5]Dizziness Handicap Index

[6]Emergency department

Table 2

Health Utility Index (HUI) and attribute scores of study subjects

	Mean (SD[1])			P value
	BVD[2]	UVD[3]	Normal	
HUI3[4]	0.39 (0.34)	0.63 (0.26)	0.94 (0.09)	<0.0001
Vision	0.93 (0.05)	0.98 (0.004)	0.99 (0.01)	<0.0001
Hearing	0.95 (0.08)	0.86 (0.1)	1.00 (0)	<0.0001
Speech	0.97 (0.05)	0.99 (0.03)	1.00 (0.02)	0.09
Ambulation	0.86 (0.09)	0.97 (0.06)	1.00 (0)	<0.0001
Dexterity	0.99 (0.02)	1.00 (0.01)	1.00 (0)	0.09
Emotion	0.87 (0.2)	0.98 (0.05)	0.98 (0.04)	<0.0001
Cognition	0.92 (0.1)	0.95 (0.1)	1.00 (0.01)	0.06
Pain	0.89 (0.1)	0.96 (0.06)	0.99 (0.02)	<0.0001

[1]Standard deviation

[2]Bilateral vestibular deficiency

[3]Unilateral vestibular deficiency

[4]Health Utility Index Mark 3

Table 3

Estimated annual economic burden† of dizziness or imbalance complaints in study subjects

	BVD[1]	UVD[2]	Normal
Health care utilization			
Mean ED[3] visits (range)*	**0.3** (0 – 3)	**0.1** (0 – 2.4)	**0** (0–0)
Cost† (range)	**$274** (0 – 2,374)	**$94** (0–1,899)	**0** (0–0)
Mean clinic visits (range)*	**1.4** (0 – 2.4)	**0.7** (0 – 3)	**0** (0–0)
Cost† (range)	**$203** (0 – 348)	**$92** (0 – 435)	**0** (0–0)
Lost productivity			
Mean missed work days (range)*	**69** (0 – 255)	**19** (0 – 255)	**0** (0–0)
Cost† (range)	**$12,542** (0 – 19,159)	**$3,345** (0 – 46,108)	**0** (0–0)
Total dizziness-related annual economic burden (range) †	**$13,019** (0 – 48,830)	**$3,531** (0 – 48,442)	**$0** (0–0)

*Mean number of occurrences attributed to dizziness or imbalance over past 12 months for each respondent

†all figures in 2012 dollars

[1]Bilateral vestibular deficiency

[2]Unilateral vestibular deficiency

[3]Emergency department

Table 4

Economic burden, quality of life, and cost utility of treatment for bilateral vestibular deficiency (BVD) in comparison to other conditions

Condition (Ref)	HUI3[1] (Ref)	Annual cost per patient (2012 USD)	Intervention (Ref)	Cost-utility ($/QALY[2])
Chronic kidney disease requiring hemodialysis ([31])	0.73 ([26])	83,837	Renal transplantation ([51])	35,902
Adult-onset deafness ([8])	0.58–0.62[*] ([52])	15,227	Cochlear implantation ([53])	16,061
Heart failure requiring ICD([3,54])	0.64 ([25])	83,020	ICD ([47])	34,836
Osteoarthritis ([32])	0.46 ([55])	18,171	Knee replacement ([48])	59,292
BVD	0.39	13,019	Multi-channel Vestibular Prosthesis[†]	28,490 – 56,979[†]

[*]HUI Mark 2

[†]Projected

[1]Health Utility Index Mark 3

[2]Quality-adjusted life-year

[3]Implantable cardiac defibrillator

Table 5

Cost-Utility and Sensitivity Analysis

Cost-Utility Ratios	Total Lifetime Cost	QALYs Gained	Cost/QALY
100% Benefit	$60,386	2.1	$28,490
75% Benefit	$60,386	1.6	$37,986
50% Benefit	$60,386	1.1	$56,979

Sensitivity Analysis

Variables	Base Estimate[1]	Range of Estimate (Best to Worst)	Cost-Utility Cost per QALY (Base $31,737)
Discount Rate	3%	0 – 6	$15,346–$51,201
No. of Post-operative Admissions	1/year	0 to 2	$36,178–$39,742
Device Cost[2]	$35,000	$30,000–$40,000	$35,088–$41,615
Health Utility Gain	0.22	0.1 – 0.4	$27,540–$110,160
Life-years of Implant	17.7	12–25	$36,401–$39,662
Annual Device Failure Rate	0.2%	0.1–0.5	$37,480–$39,504

[1]Assuming 75% benefit from implantation.

[2]Based on average cochlear implant device cost from Semenov et al., 2013 [20].