Original Investigation

Bilateral Vestibular Deficiency
Quality of Life and Economic Implications

Daniel Q. Sun, MD; Bryan K. Ward, MD; Yevgeniy R. Semenov, MA; John P. Carey, MD; Charles C. Della Santina, PhD, MD

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

OBJECTIVE To quantify disease-specific and health-related quality of life, health care utilization, and economic impact on individuals with BVD in comparison with those with unilateral vestibular deficiency (UVD).

DESIGN, SETTING, AND PARTICIPANTS Cross-sectional survey study of patients with BVD or UVD and healthy controls at an academic medical center. Vestibular dysfunction was diagnosed by means of caloric nystagmography.

INTERVENTIONS 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.

RESULTS Fifteen patients with BVD, 22 with UVD, and 23 healthy controls participated. In comparison with patients with UVD and controls, patients with BVD had significantly worse DHI ($P < .001$) and HUI3 scores. Statistically significant between-group differences were observed for overall HUI3 score ($P < .001$) and for specific attributes including vision, hearing, ambulation, emotion, and pain ($P < .001$ for all). Generalized linear model analysis of clinical variables associated with HUI3 scores after adjustment for other variables (including sex, race, education, age, and frequency of dizziness-related outpatient clinic visits) showed that the presence of UVD ($P < .001$) or BVD ($P < .001$), increased dizziness-related emergency room visits ($P = .002$), and increased dizziness-related missed work days ($P < .001$) were independently associated with worse HUI3 scores. Patients with BVD and UVD incurred estimated mean (range) annual economic burdens of \$13 019 (\$0-\$48 830) and \$3531 (\$0-\$48 442) per patient, respectively.

CONCLUSIONS AND RELEVANCE Bilateral vestibular deficiency 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.

JAMA Otolaryngol Head Neck Surg. 2014;140(6):527-534. doi:10.1001/jamaoto.2014.490
Published online April 24, 2014.

Supplemental content at jamaotolaryngology.com

Author Affiliations: Department of Otolaryngology–Head and Neck Surgery, Johns Hopkins University School of Medicine, Baltimore, Maryland (Sun, Ward, Semenov, Carey, Della Santina); Department of Biomedical Engineering, Johns Hopkins University School of Medicine, Baltimore, Maryland (Della Santina).

Corresponding Author: Daniel Q. Sun, MD, Johns Hopkins Outpatient Center, Department of Otolaryngology–Head and Neck Surgery, Johns Hopkins University School of Medicine, 601 N Caroline St, Sixth Floor, Baltimore, MD 21287 (dsun8@jhmi.edu).

Copyright 2014 American Medical Association. All rights reserved.

Downloaded From: http://archotol.jamanetwork.com/ by a New York University User on 05/14/2015

Vestibulo-ocular and vestibulospinal reflexes normally maintain stable gaze and posture during head movement. Individuals with bilateral vestibular deficiency (BVD) often experience 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 experience chronic imbalance and instability of vision and posture that render routine daily activities such as walking and driving difficult.

Ototoxic effects due to use of aminoglycosides such as gentamicin sulfate are 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 hinders accrual of information on prevalence, incidence, and health care utilization.[10] However, recent data from the US National Health Interview Survey suggest a severe-to-profound BVD prevalence of 28/100 000 US adults, or 64 046 Americans.[1] Although rare enough to merit designation as an orphan disease[11] in the United States, BVD is a chronic disabling condition that can impose lifelong socioeconomic costs while negatively affecting 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 (MVP).[14] 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 with individuals with UVD and with healthy controls. Using the quality of life data obtained here, we provide a projected cost-utility estimate of an MVP.

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 UVD or BVD 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 participants. Some participants also received an identical paper-based survey, depending on participant preference, and results were then entered electronically by study investigators. Completion of the survey served as informed consent for this study. For UVD and BVD participants, each respondent's medical record was reviewed, and only participants 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 demographic characteristics, 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 Utilities 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.[15] It consists of a 25-item questionnaire that evaluates a respondent's performance along 3 dimensions: physical, emotional, and functional. Participants respond "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. The 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 5 or 6 levels of ability or 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 and/or 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.[16] It has been used extensively in health economic analyses, including studies of cochlear implantation.[17] In the present study, each respondent's overall health utility (total HUI3 score) was calculated using methods prescribed for analysis of HUI3 data.[16]

Economic Burden

The annual, per-patient economic burden for each study group was estimated on the basis of 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 (eg, health care utilization) and indirect costs (eg, lost productivity). Cost of health care utilization was calculated by multiplying self-reported disease-specific annual frequency of clinic and

Copyright 2014 American Medical Association. All rights reserved.

Downloaded From: http://archotol.jamanetwork.com/ by a New York University User on 05/14/2015

Table 1. Demographic and Clinical Characteristics of Study Participants

	BVD (n=15)	UVD (n=22)	Control (n=23)	*P* Value
Age, mean (SD), y	65 (10)	62 (12)	52 (14)	.005
Sex, No. (%)				
Male	11 (73)	9 (41)	10 (44)	.11
Female	4 (27)	13 (59)	13 (56)	
Race, No. (%)				
White	15 (100)	20 (91)	20 (87)	.56
Black	0	0	0	
Asian	0	0	0	
Native American	0	1 (5)	2 (9)	
Hawaiian	0	1 (5)	0	
Other	0	0	1 (4)	
Education, No. (%)				
Less than high school	0	0	1 (4)	.10
High school	7 (47)	3 (14)	4 (17)	
College or higher	8 (53)	19 (86)	18 (78)	
DHI, mean (SD)	62 (31)	27 (23)	0.6 (1.4)	<.001
Physical	17 (10)	7 (7)	0.4 (1.2)	<.001
Emotional	20 (12)	10 (9)	0.1 (0.4)	<.001
Functional	25 (11)	10 (10)	0.1 (0.4)	<.001
Falls, mean (SD)[a]	19 (26)	2 (5)	1 (3)	<.001
Work days missed, mean (SD)[a]	69 (106)	19 (64)	0	.03
Visits, mean (SD)[a]				
Emergency department	0.4 (0.8)	0.1 (0.5)	0	.11
Clinic	1.4 (0.8)	0.6 (1.1)	0	<.001

Abbreviations: BVD, bilateral vestibular deficiency; DHI, Dizziness Handicap Index; UVD, unilateral vestibular deficiency.

[a] Mean number of occurrences attributed to dizziness or imbalance over past 12 mo for each respondent.

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; *Current Procedural Terminology* code 99213). The per-visit cost of ED care for dizziness or balance complaints attributable to otologic and/or vestibular causes was estimated to be $768.33,[18] which represents the national mean aggregate cost of each evaluation of dizziness, after adjustment for inflation. Other potential health care utilization costs such as those related to falls, medication use, vestibular physical therapy, diagnostic testing outside 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 mean hourly wage for US workers in 2012 as estimated by the US Bureau of Labor Statistics.[19] All economic analyses are expressed in 2012 dollars using a discount rate of 3%.[20]

Prospective Cost-Utility Analysis of an MVP

Cost-utility is defined as cost per quality-adjusted life-year (QALY). The projected costs of an MVP can be modeled using estimates derived from the cochlear implant experience (eTable in Supplement)[17,21] because of the similarities in technology, surgical procedure, and postoperative care. Life-years following implantation are calculated by subtracting the mean age of respondents with BVD in this study from the age- and sex-matched life expectancy found in the US Centers for Disease Control and Prevention actuarial life tables.[22] Difference in QALYs between the 2 vestibular deficiency groups is then calculated by annually compounding the difference in health utility between the UVD and BVD groups across the projected mean 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 for continuous variables and the χ^2 test 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 ED 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 sex, race, age, and education status. STATA software, version 12 (StataCorp), was used for all statistical analyses.

Copyright 2014 American Medical Association. All rights reserved.

Downloaded From: http://archotol.jamanetwork.com/ by a New York University User on 05/14/2015

Table 2. Health Utility Index (HUI) and Attribute Scores of Study Participants

	Mean (SD)			
	BVD	UVD	Control	*P* Value
HUI3	0.39 (0.34)	0.63 (0.26)	0.94 (0.09)	<.001
Vision	0.93 (0.05)	0.98 (0.004)	0.99 (0.01)	<.001
Hearing	0.95 (0.08)	0.86 (0.10)	1.00 (0)	<.001
Speech	0.97 (0.05)	0.99 (0.03)	1.00 (0.02)	.09
Ambulation	0.86 (0.09)	0.97 (0.06)	1.00 (0)	<.001
Dexterity	0.99 (0.02)	1.00 (0.01)	1.00 (0)	.09
Emotion	0.87 (0.16)	0.98 (0.05)	0.98 (0.04)	<.001
Cognition	0.92 (0.14)	0.95 (0.12)	1.00 (0.01)	.06
Pain	0.89 (0.12)	0.96 (0.06)	0.99 (0.02)	<.001

Abbreviations: BVD, bilateral vestibular deficiency; HUI3, Health Utility Index Mark 3; UVD, unilateral vestibular deficiency.

Table 3. Estimated Annual Economic Burden[a] of Dizziness or Imbalance Symptoms in Study Participants

	Mean (Range)	
	BVD	UVD
Health care utilization		
ED visits[b]		
No.	0.3 (0-3)	0.1 (0-2.4)
Cost, $	274 (0-2374)	94 (0-1899)
Clinic visits[b]		
No.	1.4 (0-2.4)	0.7 (0-3)
Cost, $	203 (0-348)	92 (0-435)
Lost productivity		
Missed work days[b]		
No.	69 (0-255)	19 (0-255)
Cost, $	12 542 (0-19 159)	3345 (0-46 108)
Total dizziness-related annual economic burden, $	13 019 (0-48 830)	3531 (0-48 442)

Abbreviations: BVD, bilateral vestibular deficiency; ED, emergency department; UVD, unilateral vestibular deficiency.

[a] All data in 2012 US dollars.

[b] Mean number of occurrences attributed to dizziness or imbalance over past 12 mo for each respondent.

Results

Survey response rates for the BVD, UVD, and control groups were 47 of 73 (64%), 24 of 46 (52%), and 23 of 25 (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 controls were recruited. The etiologies of BVD in the study group were as follows: ototoxic effects from intravenous aminoglycoside use (4 [27%]), bilateral chemical labyrinthectomy for Ménière's disease (3 [20%]) (performed elsewhere), Lyme disease (1 [7%]), trauma (1 [7%]), and idiopathic (6 [40%]). For respondents who met inclusion criteria, there was a 100% completion rate for the survey questions analyzed in this study, including DHI, HUI3, health care utilization, and lost productivity. All patients with BVD reported a clinical history consistent with severe-to-profound BVD.

Review of medical records indicated that for patients with UVD, vestibular physical therapy sessions at our institution occurred between 2003 and 2007 (6-9 years prior to survey), with the duration ranging from 1 session to several years. For patients with BVD, 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 participants. In 13 patients with BVD with available audiometric data, 9 showed pure-tone averages within normal range bilaterally whereas 4 showed high-frequency loss consistent with presbycusis. Although audiometric data are not available in the remaining 2 patients with BVD, they both denied substantial hearing loss on the hearing assessment portion of the HUI questionnaire. Patients with UVD demonstrated greater unilateral hearing impairment, with a mean (SD) pure-tone average of 59 (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 participants whereas only 1 patient with BVD had a serious medical comorbidity of cardiac arrhythmia with pacemaker dependence.

The demographic and clinical characteristics of study participants are shown in Table 1. Statistically significant between-group differences were observed for age ($P = .005$), DHI ($P < .001$), number of falls during the previous year ($P < .001$), annual days of work missed because of dizziness ($P = .03$), and annual physician office visits for dizziness ($P < .001$).

Mean HUI3 overall health utility and attribute-specific scores of each study group are shown in **Table 2**. Statistically significant between-group differences were observed for overall score ($P < .001$) and for specific attributes including vision ($P < .001$), hearing ($P < .001$), ambulation ($P < .001$), emotion ($P < .001$), and pain ($P < .001$). Generalized linear model analysis of clinical variables associated with HUI3 scores after adjustment for other variables (including sex, race, education, age, and frequency of dizziness-related visits to an outpatient clinic) showed that the presence of UVD ($P < .001$) or BVD ($P < .001$), increased dizziness-related emergency room visits ($P = .002$), and increased dizziness-related missed work days ($P < .001$) were independently associated with worse HUI3 scores.

Copyright 2014 American Medical Association. All rights reserved.

Downloaded From: http://archotol.jamanetwork.com/ by a New York University User on 05/14/2015

Table 4. Economic Burden, Quality of Life, and Cost-Utility of Treatment for Bilateral Vestibular Deficiency (BVD) in Comparison With Other Conditions

Condition	HUI3, Mean	Annual Cost per Patient, Mean, $[a]	Intervention	Cost-Utility, Mean, $/QALY
Chronic kidney disease necessitating hemodialysis[28]	0.73[27]	83 837	Renal transplantation[29]	35 902
Adult-onset deafness[8]	0.58-0.62[30,b]	15 227	Cochlear implantation[31]	16 061
Heart failure necessitating ICD[3,32]	0.64[26]	83 020	ICD[33]	34 836
Osteoarthritis[34]	0.46[35]	18 171	Knee replacement[36]	59 292
BVD	0.39	13 019	Multichannel vestibular prosthesis[c]	28 490-56 979[c]

Abbreviations: HUI3, Health Utility Index Mark 3; ICD, implantable cardiac defibrillator; QALY, quality-adjusted life-year.

[a] All data in 2012 US dollars.

[b] Health Utility Index Mark 2.

[c] Projected.

The estimated annual per-patient societal economic burden of each study group is shown in **Table 3**. Controls incurred no costs due to dizziness-related problems, whereas patients with BVD and UVD had estimated mean (range) annual, per-patient economic burdens of $13 019 ($0-$48 830) and $3531 ($0-$48 442), respectively.

Discussion

This study investigated the quality of life of individuals lacking vestibular sensation unilaterally or bilaterally using 2 validated instruments. In this study, DHI scores of respondents with BVD indicated a severe handicap, compared with a mild handicap for respondents with UVD.[15] Respondents with BVD 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 data are consistent with DHI scores previously reported for patients with BVD and UVD.[12,23]

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 respondents with BVD rated their general health status. The mean score of 0.39 reported by respondents with BVD is similar to the score of 0.37 reported by a group of similarly aged individuals with profound deafness[24] and those with other debilitating chronic conditions such as untreated rheumatoid arthritis (HUI3, 0.39),[25] whereas the mean HUI3 score of 0.63 reported by respondents with UVD is similar to that reported for patients with congestive heart failure severe enough to have necessitated implantation of a cardiac defibrillator (HUI3, 0.64).[26] In contrast, individuals with chronic kidney disease requiring hemodialysis reported a mean HUI3 score of 0.73, higher (ie, better) than both the BVD and UVD cohorts.[27] **Table 4** shows selected chronic medical conditions and their respective HUI3 scores, economic burden, and cost-utility of intervention in relation to BVD.

The quality of life data for patients with BVD reported herein are consistent with previously published results. Guinand et al[12] used another health-related quality of life instrument on a group of patients with BVD and found impairment in overall health state to a degree similar to those with chronic low back pain,[37] a condition that also carries considerable functional limitations. These findings reveal that although clinicians and third-party payers often consider BVD and UVD to be benign chronic conditions with negligible health impact, individuals 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 patients with BVD occurred not only in the expected attributes of vision and ambulation but also in others such as emotion and pain. This may be due in part to the psychological toll of chronic disequilibrium and difficulty performing routine daily activities. For instance, patients with BVD typically rated their emotional state between “occasionally” and “often” “fretful, angry, irritable, anxious, or depressed” on the HUI3 questionnaire. Moreover, compared with patients with UVD, the overall HUI3 scores of patients with BVD were significantly decreased despite the fact that they actually scored better in the hearing attribute, reflecting both the prevalence of Ménière’s disease-associated hearing loss in individuals with UVD and the overwhelming impact of BVD. Consistent with their poor health status as assessed by HUI3, patients with BVD also reported substantial 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.” Respondents with BVD also reported a mean of approximately 19 falls per 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.[38] 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[39]), may play a confounding role in the self-reported health status of respondents.

Although the controls in the present study had younger mean ages than those in the BVD and UVD groups and had HUI3 scores higher than existing age-adjusted, population-based normative data,[40] 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 workplace absenteeism were all independently associated with worse HUI3 scores. Number of falls was also considered in the statistical model but was found to be collinear with other clinical variables such as the number of ED visits.

Copyright 2014 American Medical Association. All rights reserved.

Downloaded From: http://archotol.jamanetwork.com/ by a New York University User on 05/14/2015

Table 5. Sensitivity Analysis of Cost-Utility

Variable	Base Estimate (Range)[a]	Cost-Utility, Range, $/QALY[b]
Benefit, %[c]	75 (100-50)	28 490-56 979
Discount rate, %	3 (0-6)	15 346-51 201
Annual postoperative admissions, No.	1 (0-2)	36 178-39 742
Device cost, $[d]	35 000 (30 000-40 000)	35 088-41 615
Health utility gain	0.22 (0.4-0.1)	27 540-110 160
Life-years of implant	17.7 (25-12)	36 401-39 662
Annual device failure rate, %	0.2 (0.1-0.5)	37 480-39 504

Abbreviation: QALY, quality-adjusted life-year.

[a] Range is from best to worst.

[b] Base estimate of cost-utility: $37 986/QALY assuming 75% restoration by multichannel vestibular prosthesis.

[c] Percent restoration of function for implanted labyrinth.

[d] Based on mean cochlear implant device cost from Semenov et al.[21]

In estimating the socioeconomic impact of BVD, we found that the annual, per-patient economic burden of BVD is considerably higher than that of UVD and comparable to that of other chronic health conditions such as diabetes mellitus, noncongenital deafness, congestive heart failure, and osteoarthritis (Table 4).[28,34] Most of the increased burden in the BVD cohort can be attributed to higher rates of dizziness-specific workplace 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 an 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 workup typical[18] for inner-ear-related vertigo, which may overestimate costs for patients with BVD who have a known diagnosis and therefore may undergo neuroimaging less frequently. Despite these assumptions, the economic burden reported is likely a conservative estimate because it does not include costs related to medications or other interventions, injuries due to falls, diagnostic testing outside the ED, treatment of secondary conditions that patients with BVD or UVD fail to attribute to their vestibular loss (eg, depression), and inpatient admission, a costly outcome that occurs in approximately 10% of dizziness presentations to the ED.[41]

The large difference in self-reported quality of life between patients with BVD and UVD likely reflects relative inadequacy of vestibular reflexes and vestibular rehabilitation outcomes for those with severe bilateral vestibular loss compared with individuals with a single working labyrinth.[42,43] Restoring the function of 1 labyrinth through gene therapy,[44] stem cell interventions,[45] or prosthetic interventions[14,46-53] could yield substantial benefits. For example, an MVP currently in development may partly restore unilateral semicircular canal function to patients with BVD, thereby improving vestibulo-ocular reflex performance, visual acuity during head movement, and postural stability.[14,46,50-53] An important consideration in its development is the device's cost-utility. On the basis of data presented here, we can estimate the projected cost-utility of MVP implantation.

Because preimplantation health utilities are known, we projected postimplantation 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/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 data compare favorably with the cost-utility of existing interventions[33,36] for other chronic conditions (Table 4) and with the existing standard of economic feasibility in the United States, which considers medical interventions costing no more than $50 000/QALY to be highly cost-effective.[54,55]

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 because 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 individuals with BVD and UVD. 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 affect HUI3 scores.

Conclusions

In comparison with normal controls and with patients with UVD, patients with BVD 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 substantially degrades quality of life for affected individuals, imposes a substantial 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.

Copyright 2014 American Medical Association. All rights reserved.

Downloaded From: http://archotol.jamanetwork.com/ by a New York University User on 05/14/2015

ARTICLE INFORMATION

Submitted for Publication: November 12, 2013; final revision received February 4, 2014; accepted March 2, 2014.

Published Online: April 24, 2014. doi:10.1001/jamaoto.2014.490.

Author Contributions: Dr Sun and Mr Semenov had full access to all of 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, Della Santina.
Acquisition, analysis, or interpretation of data: All authors.
Drafting of the manuscript: Sun, Semenov, Carey, Della Santina.
Critical revision of the manuscript for important intellectual content: Sun, Ward, Semenov, Della Santina.
Statistical analysis: Sun, Semenov.
Administrative, technical, or material support: Della Santina.
Study supervision: Carey, Della Santina.

Conflict of Interest Disclosures: Dr Della Santina holds an equity interest in and is an officer of Labyrinth Devices, LLC. He has been a consultant to Cochlear Corporation and is currently a consultant to MED-EL Gmbh and Novartis. The terms of these arrangements are managed by the Johns Hopkins University Office of Policy Coordination in accordance with University policies on potential conflicts of interest. No other disclosures are reported.

Funding/Support: This work was supported in part by the Johns Hopkins Vestibular NeuroEngineering Laboratory Research Fund. Dr Ward was supported by National Institute on Deafness and Other Communication Disorders (NIDCD) grant T32DC000027 and Dr Della Santina by NIDCD grant R01DC009255.

Role of the Sponsor: The sponsors had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Additional Contributions: David E. Newman-Toker, MD, PhD, Johns Hopkins University School of Medicine, provided helpful input on national health care costs associated with dizziness-related emergency room visits and advice on drafting of the manuscript.

REFERENCES

1. Ward BK, Agrawal Y, Hoffman HJ, Carey JP, Della Santina CC. Prevalence and impact of bilateral vestibular hypofunction: results from the 2008 US National Health Interview Survey. *JAMA Otolaryngol Head Neck Surg*. 2013;139(8):803-810.

2. Minor LB. Gentamicin-induced bilateral vestibular hypofunction. *JAMA*. 1998;279(7):541-544.

3. Brandt T. Bilateral vestibulopathy revisited. *Eur J Med Res*. 1996;1(8):361-368.

4. Verstreken M, Declau F, Wuyts FL, et al. Hereditary otovestibular dysfunction and Ménière's disease in a large Belgian family is caused by a missense mutation in the COCH gene. *Otol Neurotol*. 2001;22(6):874-881.

5. Gillespie MB, Minor LB. Prognosis in bilateral vestibular hypofunction. *Laryngoscope*. 1999;109 (1):35-41.

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.

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.

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.

9. Bourne R, Price H, Taylor H, et al; Global Burden of Disease Vision Loss Expert Group. New systematic review methodology for visual impairment and blindness for the 2010 Global Burden of Disease study. *Ophthalmic Epidemiol*. 2013;20(1):33-39.

10. Vibert D, Liard P, Häusler R. Bilateral idiopathic loss of peripheral vestibular function with normal hearing. *Acta Otolaryngol*. 1995;115(5):611-615.

11. US Food and Drug Administration. Office of Orphan Products Development. http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/OfficeofScienceandHealthCoordination/ucm2018190.htm. Accessed July 28, 2013.

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.

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.

14. Della Santina CC, Migliaccio AA, Patel AH. A multichannel semicircular canal neural prosthesis using electrical stimulation to restore 3-D vestibular sensation. *IEEE Trans Biomed Eng*. 2007;54(6, pt 1): 1016-1030.

15. Jacobson GP, Newman CW. The development of the dizziness handicap inventory. *Arch Otolaryngol Head Neck Surg*. 1990;116(4):424-427.

16. Horsman J, Furlong W, Feeny D, Torrance G. The Health Utilities Index (HUI): concepts, measurement properties and applications. *Health Qual Life Outcomes*. 2003;1(1):54.

17. 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.

18. 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.

19. Bureau of Labor Statistics. Employment, Hours, and Earnings From the Current Employment Statistics Survey (National). http://data.bls.gov/timeseries/CES0500000003?data_tool=XGtable. Accessed February 20, 2013.

20. Gold MR, Siegel JE, Russell LB, Weinstein MC. *Cost-effectiveness in Health and Medicine.* New York, NY: Oxford University Press; 1996.

21. Semenov YR, Yeh ST, Seshamani M, et al; CDaCI Investigative Team. Age-dependent cost-utility of pediatric cochlear implantation. *Ear Hear*. 2013; 34(4):402-412.

22. Arias E. United States life tables, 2008. *Natl Vital Stat Rep*. 2012;61(3):1-64. http://www.cdc.gov/nchs/data/nvsr/nvsr61/nvsr61_03.pdf. Accessed March 1, 2013.

23. 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.

24. 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, pt 1):1482-1488.

25. 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.

26. Noyes K, Corona E, Veazie P, Dick AW, Zhao H, Moss AJ. Examination of the effect of implantable cardioverter-defibrillators on health-related quality of life: based on results from the Multicenter Automatic Defibrillator Trial-II. *Am J Cardiovasc Drugs*. 2009;9(6):393-400.

27. Heidenheim AP, Muirhead N, Moist L, Lindsay RM. Patient quality of life on quotidian hemodialysis. *Am J Kidney Dis*. 2003;42(1)(suppl):36-41.

28. Foley RN, Collins AJ. The growing economic burden of diabetic kidney disease. *Curr Diab Rep*. 2009;9(6):460-465.

29. 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.

30. 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.

31. Semenov YR, Martinez-Monedero R, Niparko JK. Cochlear implants: clinical and societal outcomes. *Otolaryngol Clin North Am*. 2012;45(5): 959-981.

32. 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.

33. 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 Cardiol*. 1992;19(6):1323-1334.

34. Le TK, Montejano LB, Cao Z, Zhao Y, Ang D. Healthcare costs associated with osteoarthritis in US patients. *Pain Pract*. 2012;12(8):633-640.

35. Ruchlin HS, Insinga RP. A review of health-utility data for osteoarthritis: implications for clinical trial-based evaluation. *Pharmacoeconomics*. 2008;26(11):925-935.

36. 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.

Copyright 2014 American Medical Association. All rights reserved.

Downloaded From: http://archotol.jamanetwork.com/ by a New York University User on 05/14/2015

37. 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.

38. Sterling DA, O'Connor JA, Bonadies J. Geriatric falls: injury severity is high and disproportionate to mechanism. *J Trauma*. 2001;50(1):116-119.

39. Hoffman HJ, Li C-M, Losonczy KG, Sklare DA, Cohen H, Della Santina CC. Impact of dizziness and balance problems and other chronic health conditions on falling risk in United States adults. Paper presented at: 141st American Public Health Association Annual Meeting; November 4, 2013; Boston, MA. Abstract 279804.

40. 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.

41. Newman-Toker DE, Camargo CA Jr, 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.

42. Leigh R, Zee D. *The Neurology of Eye Movement*. New York, NY: Oxford University Press; 1999.

43. Herdman SJ. Vestibular rehabilitation. *Curr Opin Neurol*. 2013;26(1):96-101.

44. 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.

45. Ronaghi M, Nasr M, Heller S. Concise review: inner ear stem cells—an oxymoron, but why? *Stem Cells*. 2012;30(1):69-74.

46. Davidovics NS, Rahman MA, Dai C, Ahn J, Fridman GY, Della Santina CC. 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.

47. 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;21(5):830-839.

48. 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.

49. Digiovanna J, Carpaneto J, Micera S, Merfeld DM. Alignment of angular velocity sensors for a vestibular prosthesis. *J Neuroeng Rehabil*. 2012; 9:14.

50. 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.

51. 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.

52. 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; 14(6):863-877.

53. Thompson LA, Haburcakova C, Gong W, et al. Responses evoked by a vestibular implant providing chronic stimulation. *J Vestib Res*. 2012;22(1):11-15.

54. Rohde LE, Bertoldi EG, Goldraich L, Polanczyk CA. Cost-effectiveness of heart failure therapies. *Nat Rev Cardiol*. 2013;10(6):338-354.

55. 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.

Copyright 2014 American Medical Association. All rights reserved.

Downloaded From: http://archotol.jamanetwork.com/ by a New York University User on 05/14/2015