

# The Five Senses: A Patient Preference-Based Comparative Analysis

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## ABSTRACT

**Purpose:** The purpose of the study was to quantify and compare the quality of life (QOL) associated with moderate to severe loss of each of the five senses: (1) Visual, (2) hearing, (3) tactile, (4) taste, and (5) smell. **Methods:** A validated, time-trade-off, utility questionnaire was administered through direct interview by the authors in a cross-sectional fashion to quantify the QOL associated with moderate to severe loss of each of the five senses. Each participant personally had, or had experienced, the sensory loss in question. Analysis of variance was utilized to compare the mean utility associated with each of the five sensory losses. Utility anchors were 1.00 (permanently normal for the sense under study) and 0.00 (death). **Results:** Mean time-trade-off utilities for participants who lived with, or had lived with, loss of one of the five senses were as follows: (1) Vision 20/200 in the better-seeing eye, the World Health Organization (WHO) definition of moderate to severe visual loss, utility = 0.62, (2) Karnofsky Performance Status Test moderate to severe tactile sensation loss (Karnofsky 50%–70%), utility = 0.71, (3) the WHO definition of moderate to severe hearing loss in the better-hearing ear, utility = 0.86, (4) moderate to severe taste loss, utility = 0.93, and (5) moderate to severe smell loss, utility = 0.94, ( $P < 0.0001$ ). **Conclusions:** Among people who have lived with moderate to severe loss of one of the five senses, vision loss, and tactile sensation loss caused the greatest diminution in QOL, followed by hearing loss, loss of taste, and loss of smell.

**Key words:** Five senses, quality of life, sensory loss, time-trade-off utility analysis

## INTRODUCTION

Utility analysis is a preference-based, quality of life (QOL) instrument that allows numerical quantification of the QOL associated with health states across health care.<sup>[1]</sup> Time-trade-off utility analysis is a utility variant, with anchors of 1.00 (normal health permanently) and 0.00 (death), demonstrated to have validity,<sup>[1-3]</sup> and both short-term<sup>[4]</sup> and long-term<sup>[5]</sup> reliability. Time-trade-off utilities are typically unaffected by age for cohorts ranging between 20 and 84 years.<sup>[6-14]</sup> They are also

generally unaffected by the level of education and gender,<sup>[6-18]</sup> as well as systemic comorbidities.<sup>[10,19]</sup> Utilities in the United States,<sup>[8,11]</sup> Canada,<sup>[20]</sup> and Europe have been noted to be similar for the same condition of the same severity.<sup>[21]</sup>

Helen Keller, a remarkable woman who lost her vision and hearing at 19 months of age, is quoted, “*After a lifetime in silence and darkness, to be deaf is a greater affliction than to be blind. Hearing is the soul of knowledge and information of a high order. To be cut off from hearing is to be isolated indeed.*”<sup>[22]</sup>

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Two Internet studies<sup>[23,24]</sup> asked the general community which of the five senses (vision, hearing, touch, smell, or taste) was most important. The combined cohorts designated vision in 43%, hearing in 18%, touch in 17%, and smell and taste in 11% each. Nonetheless, these studies were unscientific polls that involved <50 participants and did not list age or gender.

All of the five senses have been individually studied with QOL instruments,<sup>[3-13,25-29]</sup> but the authors found scant, peer-reviewed, literature employing a standardized instrument to quantify and compare QOL loss across the senses. This study was, therefore, undertaken to quantify the QOL associated with moderate to severe loss of each of the five senses using a utility instrument. Uniform utility acquisition was undertaken using: (1) Time-trade-off utility analysis, (2) face-to-face interviews, and (3) a respondent sample of individuals who lived with, or had personally experienced, loss of at least one of the five senses. The QOL associated with visual loss, hearing loss (deafness), tactile loss (numbness, anesthesia, or hypesthesia), loss of taste (ageusia or gustatory loss) and loss of smell (anosmia or olfactory loss) was quantified for each. While standard gamble methodology and rating scales can also be used to acquire utilities, time-trade-off utilities have been shown to have greater construct validity<sup>2</sup> than standard gamble utilities and greater reliability<sup>1</sup> than rating scales.

## METHODS

A time-trade-off utility analysis, QOL questionnaire was administered to consecutive utility participants in New Jersey and Pennsylvania physician offices, as well as Wills Eye Hospital, by the authors. Utility acquisition was approved by the Wills Eye Hospital Institutional Review Board and adhered to the Declaration of Helsinki of 1964 and its amendments. The utilities were acquired by the authors over a 15-year period from 2002 to 2016, during which over 5000 patients were interviewed about conditions associated with specialties across all of medicine. All were interviewed in a cross-sectional fashion using the same instrument, to create a comprehensive time-trade-off utility database. The data in our study herein were utilized when the numbers in each of the five sensory cohorts all reached or exceeded 35. A total of 266 utilities were acquired from 201 participants. The reason for less participants than utilities was due to overlap between the loss of taste and loss of smell cohort participants.

### QOL instrument

Participants in our study underwent a time-trade-off utility instrument consisting of two questions: (1) How much additional time do you theoretically expect to live? then (2) What is the maximum amount of that time - if any - you would be willing to hypothetically trade for return to a normal sensory state (visual, hearing, tactile, gustatory, or olfactory) permanently. The associated utility was calculated

using the formula: Utility = 1.0 – (maximum time of life a person is willing to theoretically trade, if any, for return to a normal sensory state permanently divided by their estimated remaining time of life).<sup>[1]</sup> The utilities are preference-based, meaning that a person can prefer to trade theoretical time of life for a normal health state, or prefer not to trade time of life and remain in their same health state or condition. The closer a utility is to 1.00, the better the associated QOL associated with the health state, while the closer the utility is to 0.00, the poorer the QOL.

### Participant respondents

Utilities can differ markedly for the same health state between respondent cohorts that have, and have not, experienced a health state.<sup>[14-16]</sup> In one analysis<sup>[14]</sup> ophthalmologists underestimated the diminution of patient QOL associated with various degrees of age-related macular degeneration (AMD) by 96%–750%. Utilities from the general public can be even more disparate.<sup>[1,15,16]</sup> A criterion of Value-Based Medicine<sup>®</sup>,<sup>[1]</sup> a standardized methodology of cost-utility analysis, is that utilities employed are obtained from people who have experienced a disease or health state on a firsthand basis,<sup>[1]</sup> as is the case for the study herein.

### Power calculation

A pre-analysis power calculation with Sample Power 2 (SPSS, Chicago), using previous utility data,<sup>[6,8,11]</sup> revealed that, with at least 35 cases in each of the five sensory cohorts, there was an 81% chance of detecting a 10% utility difference among the cohorts. Thus, enrollment was halted when the last of the five sensory category participant numbers reached 35. Sensory cohorts in those categories that reached 35 before the final cohort continued to recruit participants until the final cohort reached 35 participants.

### Utility features

Our time-trade-off utilities have been validated for ophthalmic and non-ophthalmic conditions in peer-reviewed publications.<sup>[1,2,4-20]</sup> Standardization of utility acquisition was considered critical,<sup>[30]</sup> since 27,000,000 different input parameters can be used in a cost-utility analysis,<sup>[31]</sup> with just one (different utility instruments, differing utility respondents, unlike utility collection methodology and questions, and other non-utility related inputs) possibly resulting in disparate outcomes that are not comparable.<sup>[1]</sup>

The vision, hearing, and tactile cohorts mirror the U.S. population in the level of education and ethnicity.<sup>[1,7,8,14]</sup> The tactile utilities presented herein are correlated with other QOL instruments, including the Karnofsky Status Performance Scale, a general medical, QOL instrument.<sup>[32]</sup>

Our ophthalmic utilities have been shown to have an intra-class correlation coefficient of 0.77.<sup>[4]</sup> As per Rosner,<sup>[33]</sup> an intra-class correlation coefficient of >0.75 indicates excellent reliability.

### Inclusion criteria

Best efforts were made to include moderate to severe loss of each of the five senses [Table 1]. All participants in each sensory cohort were interviewed consecutively. Each was asked to assume their respective sensory loss was permanent and could only be improved by trading theoretical time of life.

Visual cohort participants had 20/200 vision in the better-seeing eye, the World Health Organization (WHO) definition of moderate to severe visual loss.<sup>[34]</sup> The hearing loss cohort had WHO moderate to severe hearing loss (mean of 60 dB loss in the better-hearing ear).<sup>[35]</sup>

Loss of tactile sensation was correlated with a Karnofsky 50% level (requires frequent assistance and frequent medical care due to numbness) to a Karnofsky 70% level (unable to carry on normal activity or active work due to numbness).<sup>[32]</sup> The majority of participants in the tactile loss cohort had diabetic neuropathy causing numbness, though Guillain-Barre Syndrome and other neuropathic entities were also encountered. Patients in the tactile cohort generally had neuropathy in both upper and lower limbs, typically more severe in the latter. Neuropathy in the arms and/or hands but not the lower extremities was generally not present.

The utilities associated with the olfactory loss and gustatory loss cohorts were derived from participant cohorts according to their subjective experiences. With an extensive internet search, we were unable to find a WHO or other globally respected organizational definition of either moderate to

severe ageusia or moderate to severe anosmia. Thus, each participant reported their subjective experience with the loss of taste or loss of smell to a subjective moderate to severe degree, such as typically associated with severe upper respiratory infection. The National Anosmia Foundation lists tests for anosmia and ageusia, but none is considered a criterion and thus were not used.<sup>[36]</sup> The Karnofsky Status Performance Scale was not considered by the authors to be sufficiently sensitive for assessing ageusia or anosmia.

### Exclusion criteria

Those with Alzheimer's disease or other dementia variants were excluded. No person with moderate to severe sensory loss since birth, or within the first decade of life, was interviewed since scant utility standards exist for those with life-long diseases.<sup>[1]</sup> Participants <21 years of age were also excluded, as were patients with severe spinal cord injuries or stroke precluding ambulation.

### Dropout rate

Approximately 3.2% of people who initially agreed to participate with utility interviews were unable to answer the utility questions, generally for religious reasons and/or poor conceptualization. This is very similar to the dropout rate in the Beaver Dam Health Outcomes Study<sup>[37]</sup> encompassing 1356 participants evaluated with time-trade-off utility analysis.

### Demographic comparisons

There was a difference in mean age among the 5 cohorts ( $P < 0.001$ ). The visual loss and hearing loss cohorts each had

**Table 1: Sensory parameter inclusion criteria**

Sensory loss	Inclusion parameters	Description
Loss of vision (Legal blindness)	20/200 vision in the better eye 20/200=mean vision associated with the WHO definition of moderate to severe vision loss <sup>[34]</sup> (Visual loss)	Legal blindness in Canada and the United States <sup>[34]</sup>
Loss of tactile sensation (Anesthesia)	Moderate to severe numbness of feet and/or hands (Tactile sensation loss)	Karnofsky Performance Status Scale <sup>[32]</sup> 70% (unable to carry on normal activity or active work) to Karnofsky 50% (requires frequent assistance and frequent medical care) related to the numbness
Loss of hearing (Deafness)	WHO Hearing Loss Grades 2–3 <sup>[35]</sup> Grade 2 (moderate impairment) = 41–60 dB hearing loss Grade 3 (severe impairment) = 61–80 dB hearing loss (Hearing loss)	Hearing in the better ear <sup>[35]</sup> Grade 2 Able to hear and repeat words using raised voice at 1 meter Grade 3 Able to hear some words when shouted into the better ear
Loss of taste (Ageusia)	Moderate to severe loss of taste (Gustatory loss)	Participant had experienced URI resulting in moderate to severe ageusia.
Loss of smell (Anosmia)	Moderate to severe loss of smell (Olfactory loss)	Participant had experienced URI resulting in moderate to severe anosmia

(WHO: World Health Organization, dB: Decibel, URI: Upper respiratory infection)

a mean age of 72 years and the olfactory loss and gustatory loss cohorts a mean age of 46 years. The tactile loss cohort had a mean age of 62 years. A two-tailed Pearson correlation comparing utility and age within each cohort; however, demonstrated no significant relationship within any the 5 individual cohorts (vision loss,  $P = 0.39$ ; hearing loss,  $P = 0.59$ ; tactile loss,  $P = 0.20$ ; olfactory loss,  $P = 0.57$ , and gustatory loss,  $P = 0.83$ ).

Women outnumbered men by a 2:1 ratio in the olfactory loss and gustatory loss cohorts, there was a 60:40 female/male split in the hearing loss cohort, a 50:50 gender split on the vision loss cohort, and 2:1 male/female ratio in the tactile loss cohort ( $P = 0.013$ ). Excluding the tactile cohort, there was no difference in gender among the other cohorts ( $P = 0.49$ ).

Despite demographic differences, it has been consistently demonstrated with multiple regression analysis and other normal-distributive and non-parametric instruments, that age and gender do not typically influence utilities for the same health state.<sup>[1,6-20]</sup> The same is true for systemic comorbidities.<sup>[10,19]</sup> Although more study is needed, depression is a systemic comorbidity that may have a greater tendency to affect non-depression utilities.<sup>[1]</sup> We, therefore, thought it reasonable to include the prevalence of depression, from history, for each sensory loss cohort studied herein.

### Statistics

Continuous utility data were analyzed with one-way analysis of variance (ANOVA) (Analyse-it for Microsoft Excel, Leeds, United Kingdom). The *post hoc*, Tukey honestly significant difference (HSD) Test was next performed to differentiate between the individual cohort pair means (Vassarstats, Poughkeepsie, NY). Two-tailed Pearson correlations were utilized for comparing age with the individual cohort utilities, and categorical data were analyzed with the Chi-square test (Microsoft Excel 2010, Redmond, WA). Since time-trade-off utilities are typically normally distributed but can skew toward 1.0,<sup>[1]</sup> the non-parametric Kruskal–Wallis test for difference in central location (median) among independent samples was also performed. The result was the same as the parametric tests. Significance for all statistical analyses was presumed to occur at  $P < 0.05$ .

## RESULTS

The mean utilities for participants who experienced moderate to severe loss of the five senses are shown in Tables 2-3 and Figure 1. The mean cohort utilities were: (1) Moderate to severe visual loss, utility = 0.62 (95% confidence interval [CI]: 0.56–0.68), (2) moderate to severe tactile loss, utility = 0.71 (95% CI: 0.62–0.80), (3) moderate to severe hearing loss, utility = 0.86 (95% CI: 0.78–0.94), (4) moderate to severe taste loss, utility = 0.93 (95% CI: 0.92–0.94), and (5) moderate to severe smell loss, utility = 0.94 (95%

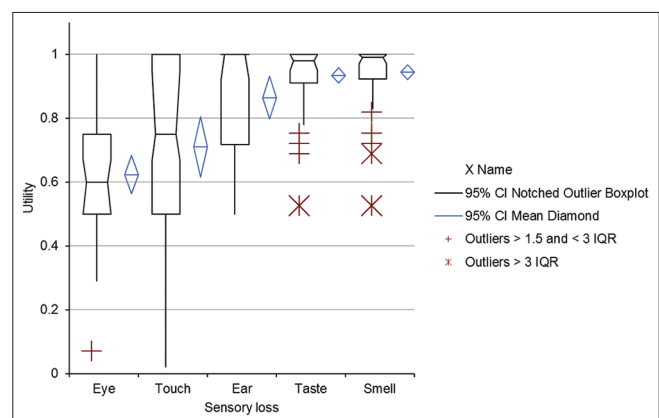
CI: 0.89–0.99). The utility means across the five cohorts differed significantly with both ANOVA ( $P < 0.0001$ ) and the Kruskal–Wallis test ( $P < 0.0001$ ).

The *post hoc* Tukey HSD Test for utility cohort, pair combinations [Table 3] revealed a significantly lower, mean utility in the visual loss cohort referent to the hearing loss, gustatory loss, and olfactory loss cohorts. The tactile loss cohort, the mean utility was also significantly lower than that of the hearing loss, tasting loss, and smelling loss cohorts. The difference between the visual loss and tactile loss, cohort utility means, however, was not significant ( $P = 0.12$ ).

Within the loss of tactile sensation cohort, participants were asked to grade their associated neuropathic pain on a scale of 0 = none, 1 = mild, 2 = moderate, and 3 = severe. When the mean utility of 0.76 of the 21 of 35 participants with no or mild pain was compared with the mean utility of 0.67 for the 14 of 31 participants with moderate to severe pain, there was no significant difference. When the mean utility of 0.76 of participants was compared to the mean utility of 0.62 in the loss of vision cohort; however, there was a significant difference ( $P = 0.02$ ).

### Depression

Participants were considered to have depression if they had the clinical diagnosis, had been an inpatient for depression, or currently took antidepressant medications. The prevalence of depression [Table 4] in the 5 cohorts ranged from 11% in the hearing loss cohort to 39% in the visual loss cohort, bordering on statistical difference (Chi-square,  $P = 0.053$ ) The prevalence of depression was highest in the two cohorts with the lowest mean utility, the visual loss cohort (mean utility = 0.62 and prevalence of depression = 39%) and the tactile loss cohort (mean utility = 0.71 and prevalence of depression = 34%).



**Figure 1:** Box plot demonstrating the distribution of utilities in each of the five sensory loss cohorts. (IQR = Interquartile range, Eye = Visual loss cohort, Touch = Tactile sensation loss cohort, Ear = Hearing loss [deafness] cohort, Taste = Tasting loss cohort, Smell = Smelling loss cohort (ANOVA,  $P < 0.0001$ , Analyse-it for Microsoft Excel, Leeds, UK)

**Table 2: Time-trade-off utilities for moderate to severe loss of the five senses**

Sensory loss	n	Mean utility (P<0.0001)	SD	95% CI	Mean quality of life loss (%)	Participants willing to trade time* (%) (P<0.0001)	Median utility	Utility range
Vision	46	0.62	0.20	0.56–0.68	38	41/46 (89)	0.60	0.05–1.00
Tactile	35	0.71	0.27	0.62–0.80	29	24/35 (69)	0.75	0.02–1.00
Hearing	35	0.86	0.19	0.78–0.94	14	16/35 (46)	1.00	0.50–1.00
Taste	65	0.93	0.11	0.91–0.95	7	33/65 (51)	0.98	0.50–1.00
Smell	65	0.94	0.11	0.89–0.99	6	33/65 (51)	0.99	0.50–1.00

Mean utility  $P<0.0001$  with both ANOVA and the Kruskal–Wallis test. \*Percent willing to trade theoretical time of life in return for a normal sense, utility: Time-trade-off utility, SD: Standard deviation, CI: Confidence interval). ANOVA: Analysis of variance

**Table 3: ANOVA *post hoc* Tukey HSD test results comparing the means of sensory loss cohort pairs**

Comparison of sensory cohort pair (n1n2) utility means	n1 versus n2	Respective utilities	P
Visual loss versus hearing loss	46 versus 35	0.62 versus 0.86	< 0.01
Visual loss versus tactile loss	46 versus 35	0.62 versus 0.71	NS
Visual loss versus smell loss	46 versus 65	0.62 versus 0.94	< 0.01
Visual loss versus taste loss	46 versus 65	0.62 versus 0.93	< 0.01
Tactile loss versus smell loss	35 versus 65	0.71 versus 0.94	< 0.01
Tactile loss versus taste loss	35 versus 65	0.71 versus 0.93	< 0.01
Tactile loss versus hearing loss	35 versus 35	0.86 versus 0.71	< 0.01
Hearing loss versus smell loss	35 versus 65	0.86 versus 0.94	NS
Hearing loss versus taste loss	35 versus 65	0.86 versus 0.93	NS
Smelling loss versus taste loss	65 versus 65	0.94 versus 0.93	NS

ANOVA: Analysis of variance,  $n_1$ : Number of participants in the first cohort of the comparator pair and  $n_2$ : Number of participants in the second cohort of the comparator pair, NS: Not significant

**Table 4: Prevalence of depression in the five sensory loss cohorts**

Sensory cohort	n	Utility	Incidence of depression (%)
Vision loss	46	0.62	18/46 (39)
Tactile loss	35	0.71	12/35 (34)
Hearing loss	35	0.86	4/35 (11)
Taste loss	65	0.93	12/65 (18)
Smell loss	65	0.94	12/65 (18)
Total	246	NA	58/246 (22)

Chi-square,  $P=0.053$ . NA: Not applicable

### Comparators

The QOL associated with virtually all medical conditions can be directly compared to the sensory QOL losses reported herein. A sampling of comparator utilities associated with other systemic and ocular conditions is shown in Table 5. Each comparator utility was obtained with time-trade-off methodology from patients with a specific condition by direct interview. Taste

loss and smell loss were associated with a QOL similar to that associated a previous myocardial infarction without angina or congestive heart failure (utility = 0.94),<sup>[37]</sup> while vision of 20/200 in the better-seeing eye had a QOL similar to that of losing a transplanted kidney (utility = 0.61).<sup>[6]</sup> Moderate to severe hearing loss caused a mean diminution in QOL similar to that associated with diabetes mellitus or a mild stroke.

## DISCUSSION

The data herein demonstrate the greatest diminution in QOL occurring secondary to visual loss (utility = 0.62), though that associated with tactile sensation loss (utility = 0.71) was not statistically different ( $P = 0.12$ ). We believe the tactile loss cohort had a relatively low mean utility due to loss of proprioception, injury to the lower extremities and associated pain in select cases.

There were, however, significant differences in the QOL loss between the visual loss and tactile loss cohorts and each of the hearing loss, taste loss, and smell loss cohorts ( $P < 0.0001$ ).

Visual loss was associated with a 38% diminution in QOL, tactile loss with a 29% loss, and hearing loss with a 14% decrement. Taste loss and smell loss were associated with the smallest losses in QOL, at 7% and 6%, respectively.

### Why people trade

While the utilities presented herein are mean utilities, there is a range of individual utilities [Table 3] that comprise the mean utility in each of the five cohorts. Despite good to excellent reliability for time-trade-off utility analysis,<sup>[4,5]</sup> people trade theoretical time of life for different reasons. A person with vision loss may trade time due to loss of independence, for financial reasons, and/or loss of privacy when unable to handle personal financial affairs. Those with loss of tactile sensation may trade due to the inability to hold a job requiring hand/foot coordination, the onset of foot ulcers,

fear of eventual amputation, and so forth. Nonetheless, when sufficient numbers of patients with a medical condition are polled, the CI for mean utility narrow.<sup>[1,4-6,8,11]</sup> While people trade time for different reasons, the overall proportion traded to ameliorate a medical condition is typically reliable, and likely innate to human nature.<sup>[1,2,4,5,18,20]</sup>

Equally as important as utility instrument standardization, respondent cohorts, and direct interviews versus by mail, are the exact utility questions.<sup>[1]</sup> For example, with diabetic tactile sensation loss there is a distinct difference in mean utility when participants believe they are trading time for a cure of tactile loss from that point forward, versus for a cure for tactile loss and the tactile loss-associated complications that may have already developed (e.g., Charcot joint and so forth).<sup>[1]</sup> We also informed participants herein that the utility

**Table 5: Time-trade-off patient utilities associated with select medical conditions**

Moderate to severe sensory loss (current study)	Sensory loss utility	Medical condition	Utility
Loss of smell (anosmia)	0.94	Treated systemic arterial hypertension with dizziness	0.96 [15]
		Status post myocardial infarction without residual pain or dyspnea	0.94 [39]
		Urinary tract infection, repetitive	0.93*
Loss of taste (ageusia)	0.93	Female baldness	0.93*
		Sinus headaches	0.93*
		Vision of 20/20, <20/40 in the fellow eye	0.92 [1.8]
Loss of hearing (deafness)	0.86	Diabetes mellitus	0.88 [13]
		HIV infection, asymptomatic	0.87 [6]
		Stroke, mild	0.87 [6]
Loss of tactile sensation (anesthesia)	0.71	Renal transplant, 1 year past surgery	0.74 [6]
		Stroke, moderate, Rankin 2, able to look after own affairs, but unable to carry out previous activities	0.73 [6]
		Home dialysis for 8 years	0.72 [6]
Loss of vision (20/200 in better-seeing eye) – (Legal blindness <sup>#</sup> )	0.62	Loss of kidney transplant	0.61 [6]
		Stroke, moderate to severe, Rankin Grade 3–4, needs assistance walking and help with own affairs	0.61 [6]
		Severe angina	0.58 [6]

\*From Center for Value-Based Medicine®, internal time-trade-off utility data, <sup>#</sup>legal blindness in the United States (vision of 20/200 or worse in the better-seeing eye)

questions referred to an immediate cure for their sensory condition (diabetic neuropathy) but not for the underlying disease (diabetes mellitus) that may have caused it and other problems. Though more labor intensive, the benefit of a personal interview to allow a participant to ask such questions, versus a mail questionnaire, is why we undertook the personal interview route.

While some have stated that a well-informed, cognitively robust, general community sample should be used for reference case cost-utility analyses utilized for resource allocation,<sup>[38]</sup> we strongly disagree. In over 90% of cases when time-trade-off utilities from patients have been compared with surrogate respondents (physicians, experts, the general community, and so forth), the surrogate respondents have underestimated the QOL diminution associated with a specific health state referent to patients with that health state.<sup>[1]</sup> Furthermore, ophthalmologists who took care of patients with AMD for years, specialists much more familiar with the disease than anyone in a well-informed, cognitively robust, general community could hope to be about the daily intricacies associated with a serious condition, failed miserably to assess the QOL diminution perceived by patients with vision loss from AMD. With an estimated 20/20-20/25 vision in the better-seeing eye, ophthalmologists were willing to trade a mean 1% of their theoretical remaining time of life for bilateral 20/20 vision, while AMD patients with the same vision were willing to trade 11% of their remaining time, 1000% more. For an estimated vision of 20/200-20/400 in the better-seeing eye, ophthalmologists were willing to trade 23%, versus 48% for AMD patients, 109% more for the patients.

### Strengths of the analysis

Our study uniformly utilized: (1) A validated,<sup>[2,6-20]</sup> reliable,<sup>[4,5]</sup> and utility instrument to measure QOL, (2) patient respondents who had personally experienced health states of interest, (3) standardized, personal interviews, (4) cross-sectional analysis, and (5) consecutive patient data.<sup>[1]</sup> The difference of even one of these parameters can dramatically alter utility outcomes.<sup>[1,14-16]</sup> Standardized, patient preference-based, utilities enhance the validity and reliability of cost-utility analysis, the most sophisticated form of cost-effectiveness analysis.<sup>[1]</sup>

### Potential analysis weaknesses

Participant subjectivity regarding moderate to severe degrees of sensory loss may be a confounding factor, especially in the olfactory loss and gustatory loss cohorts.<sup>[36]</sup> This is less likely for the visual loss, hearing loss, and tactile loss cohorts, each graded according to the WHO<sup>[33,34]</sup> or Karnofsky<sup>[31]</sup> definitions of moderate to severe disease, respectively [Table 1]. We are unaware of a prior QOL, criterion instrument that defines and quantifies QOL across loss of the five senses.

It should be remembered that our analysis addressed moderate to severe loss of each of the five senses. We do not, therefore, know how 100% absolute loss of each sense would compare. Data are available, however, for total vision loss. The utility associated with bilateral loss of light perception has been shown to be 0.26,<sup>[11]</sup> versus 0.62 herein for 20/200 vision bilaterally, a considerable difference.

Age and gender were different among the five the sensory cohorts. Despite this finding, it has consistently been demonstrated that each of these variables does not typically impact time-trade-off utilities.<sup>[1,2,4-19]</sup>

Other than for depression, systemic comorbidities associated with each of the five cohorts were not integrated into this study. It has been shown, however, that utilities are generally not affected by systemic comorbidities.<sup>[10,19]</sup> For example, a person with anosmia alone (utility = 0.94), versus one with anosmia (utility = 0.94), and systemic arterial hypertension (utility = 0.98),<sup>[15]</sup> typically has the same anosmia-related utility of 0.94.<sup>[1,10,19]</sup> There was a higher incidence of depression in our visual loss and tactile sensation loss cohorts, those which also had the lowest mean utilities among the five sensory cohorts. Nonetheless, the cohort utility means for depression demonstrated borderline significance ( $P = 0.053$ ).

In summary, moderate to severe loss of each of the five senses is associated with a reduction in QOL. Moderate to severe visual loss and tactile sensation loss appear to cause the most severe QOL diminution, followed by hearing loss, loss of taste, and loss of smell.

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**How to cite this article:** Brown GC, Brown MM, Sharma S. The Five Senses: A Patient Preference-Based Comparative Analysis. *Clin Res Ophthalmol* 2018;1(1):1-8.