Psychometric performance of a new condition-specific preference-weighted measure, Vision Impairment in Low Luminance-Utility Index, and EQ-5D-5L in patients with age-related macular degeneration: a MACUSTAR Study report

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Patient-Reported Outcomes

Psychometric Performance of a New Condition-Specific Preference-Weighted Measure, Vision Impairment in Low Luminance-Utility Index, and EQ-5D-5L in Patients With Age-Related Macular Degeneration: A MACUSTAR Study Report

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ABSTRACT

Objectives: The Vision Impairment in Low Luminance-Utility Index (VILL-UI) is a novel preference-weighted measure for use in patients with age-related macular degeneration (AMD). No evidence exists on its psychometric performance nor its performance in comparison with the generic preference-weighted measure, EQ-5D-5L, commonly used in economic evaluation. This study compares the psychometric performance of VILL-UI with EQ-5D-5L in patients with AMD.

Methods: Assessments of feasibility, convergent/divergent validity, and known-group validity of VILL-UI and EQ-5D-5L are undertaken using MACUSTAR data at baseline, 12, 24, and 36 months. Analyses are undertaken separately using UK and German preference weights for both measures.

Results: The sample with complete responses (n = 586) had mean age 71.9 years (standard deviation 6.9), 65.2% women, with predominantly intermediate AMD (87.2%). VILL-UI and EQ-5D-5L are feasible for completion, although VILL-UI has fewer usable responses due to its response options (baseline 89% vs 100%). EQ-5D-5L has high ceiling effects, with around one-third of participants reporting the best health state compared with under 8% for VILL-UI. Convergent validity between EQ-5D-5L and VILL-UI utilities and dimensions in which a relationship is expected is low, with divergent validity demonstrated where expected. VILL-UI detected statistically significant differences in known groups for visual acuity, visual function, and AMD stage across most time points, with little evidence of known-group validity for EQ-5D-5L.

Conclusions: VILL-UI is appropriate for use in future AMD studies to inform economic evaluation. VILL-UI has superior performance to EQ-5D-5L for known-group validity and has fewer ceiling effects but has fewer usable responses.

Keywords: age-related macular degeneration, EQ-5D-5L, psychometrics, VILL-UI.

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Highlights

- The Vision Impairment in Low Luminance-Utility Index (VILL-UI) is a newly developed condition-specific preference-weighted measure for use in patients with age-related macular degeneration (AMD), but its psychometric performance is unknown.
- To our knowledge, this study is the first to assess the psychometric performance of VILL-UI, also in comparison with generic EQ-5D-5L, using a large multicountry sample of patients with AMD.
- This study generates new knowledge about the performance of VILL-UI and EQ-5D-5L in patients with AMD to inform the use and interpretation of these measures in economic evaluation in AMD.

Introduction

Many international reimbursement agencies and decision-making bodies recommend the use of a generic preference-weighted measure (PWM) to assess benefits of healthcare and treatments using economic evaluation.[1] A PWM consists of a classification system used to assign a participant to a health state and corresponding preference weights that generate utility values for all health states.[2] Utilities reflect how good or bad health states are on a scale in which 1 equals full health, 0 reflects a health state deemed equivalent to being dead, and values below 0 indicate that the health state is considered worse than being dead. A generic PWM measures generic health-related quality of life (HRQoL) and can be used across all patient groups and conditions, enabling comparability and consistency in evaluations and decisions across different conditions. The National Institute for Health and Care Excellence (NICE) in England and Wales recommends the use of generic EQ-5D,[3] a widely used generic PWM that has both a 3-level version (EQ-5D-3L)[4] and a newer 5-level version (EQ-5D-5L).[5] EQ-5D-5L is often specifically named for use by international reimbursement agencies.[1]

Although generic PWMs are recommended for use in all patient groups, they are not necessarily appropriate for use in people with all health conditions, because their generic content may not reflect all that is important to people with a certain condition.[6] For instance, the 5 dimensions covered by EQ-5D-5L do not cover the impact of sensory perception other than pain. Generic PWMs may also not capture improvements or deteriorations in health that have been demonstrated clinically (see, for example, a recent review assessing meaningful change[7]). This can mean that they do not detect change where it has occurred or detect a lower change than suggested clinically. This affects the results of cost-effectiveness analyses because the smaller change in benefit can make the treatments appear less cost-effective and potentially

more expensive than the cutoff required for funding new treatments.

Age-related macular degeneration (AMD) is a condition of the central, specialized area of the retina responsible for central vision. It is the most common cause of severe visual loss in industrialized countries and affects almost 25% of the 60+ years population in Europe.[8] Early and intermediate AMD are not associated with legal blindness but impair vision in low-luminance and low-contrast situations, whereas late-stage AMD is almost always associated with a severe loss of vision and ultimately blindness. Total annual costs due to AMD are estimated to exceed 2 billion Euros in the European Union alone.[9] Visual impairment is 1 area in which EQ-5D has been found to have poor psychometric performance.[10,11] The performance of EQ-5D-3L in AMD in particular has been assessed previously. Studies have found weak evidence of construct validity,[12,13] and the only study assessing responsiveness found that EQ-5D-3L was responsive to treatment.[14] Although 3 studies found that EQ-5D-3L could distinguish between people with AMD and a control group[15-17] and 3 studies found some evidence of known-group validity,[12,14,18] 6 studies found no evidence of known-group validity, meaning that EQ-5D-3L could not distinguish between different severity groups for which we expected it to be able to distinguish clinically.[13,15-17,19,20] To our knowledge, there have been no published studies assessing the psychometric performance of EQ-5D-5L in people with AMD.

The VILL-UI is a new AMD-specific PWM designed for use in people with AMD that can generate health-state utilities reflecting vision-related quality of life (VRQoL) for use in economic evaluation.[21] The VILL-UI was derived from an existing patient-reported outcome measure (PROM), the VILL-33,[22,23] and has both UK and German preference weights.[21] However, the psychometric performance of VILL-UI has not yet been examined. Because NICE recommends the use of EQ-5D where it is appropriate, comparing the psychometric performance of VILL-UI and EQ-5D-5L in people with AMD is of interest for 2 reasons. First, to determine differences found by the measures and second, to assess whether VILL-UI can detect change or differences in groups of different severity of AMD.

This study assesses and compares the psychometric performance of VILL-UI and EQ-5D-5L in patients with AMD using a large multicountry AMD patient data set, and comparisons are made using both UK and German preference weights for each measure.

Methods

VILL-UI and EQ-5D-5L

The Vision Impairment in Low Luminance (VILL-33) measure is a self-report PROM, which has been recently developed for use in patients with AMD.[22,23] The VILL-33 consists of 33 items that focus on visual impairment and VRQoL under challenging luminance and contrast conditions. The VILL-33 has been shown to be content valid, construct valid, criterion valid, test-retest reliable, internally consistent, and responsive to changes over time.[23-25] The VILL-UI is an AMD-specific PWM derived from the VILL-33 that reflects the 3 domains of the VILL-33: reading and accessing information, mobility and safety, and emotional well-being.[21] Reading and accessing information is assessed using "recognizing small objects in dim lighting (eg, coins)" ("information") and "reading print against a colorful background (eg, a brochure)" ("reading"), and each have 4 severity levels (1 = none, 2 = a little, 3 = a lot, 4 = can't do). Mobility and safety is assessed jointly using the combination of items "seeing steps or curbs in the dark" and "feeling unsafe as a pedestrian or cyclist at dawn or at night" with 8 severity levels. Emotional well-being is assessed using "feel worried that your eyesight might get worse" with 4 severity levels (1 = never, 2 = sometimes, 3 = often, 4 = always). VILL-UI is generated from VILL-33 data, but all VILL-33 items have a response option "Don't do this for other reasons," and VILL-UI utilities cannot be generated in cases in which participants select this response for 1 or more items used in the VILL-UI classification system. UK and German preference weights were generated using modeled data from an online discrete choice experiment survey with a duration attribute undertaken with a representative sample of members of the public.[21] The UK preference weights have a utility range of 1 to −0.084 and the German preference weights range from 1 to −0.182.

The EQ-5D-5L is a generic PWM with 5 dimensions of mobility (ie, walking about), self-care (ie, washing or dressing yourself), usual activities, pain/discomfort, and anxiety/depression. Each dimension has 5 levels of severity (1 = none, 2 = slight, 3 = moderate, 4 = severe, 5 = extreme/unable). UK utilities have been generated using the current method recommended by NICE (mapping[26] onto UK EQ-5D-3L utilities[27]), and German utilities have been generated using the German preference weights[28] with a range of 1 to −0.661.

Sample

Analyses are conducted using the MACUSTAR study data set.[29,30] MACUSTAR is a longitudinal, prospective cohort study on AMD, registered on clinicaltrials.gov under NCT03349801. The study was conducted at 20 clinical sites across Europe (Denmark, France, Germany, Italy, Netherlands, Portugal, and the United Kingdom) and included patients with early, intermediate, and late AMD. VILL-33 and EQ-5D-5L questionnaires were self-completed unless patients requested interviewer administration, administered in different languages across different countries with the translation following a standardized protocol described previously.[23] In several scientific advice procedures conducted by the MACUSTAR consortium with the European Medicine Agency (EMA), EMA concluded that the MACUSTAR sample is representative of the general European AMD population; thus, results can be generalized (see respective EMA letters of support available at www.ema.eu). MACUSTAR data of 4 years of follow-up were collected from April 2018 to April 2023 and accessed 8th November 2023. Four time points are used in cases in which both VILL-UI and EQ-5D-5L data are available: baseline, 12 months, 24 months, and 36 months. Feasibility assessments are conducted on all data (there are missing data for EQ-5D-5L and VILL-UI) because they assess missing data (baseline n = 661; 12 months n = 474; 24 months; n = 428; 36 months n = 422). All remaining analyses use complete data for EQ-5D-5L and VILL-UI, that is, only including cases in which both EQ-5D-5L and VILL-UI were completed at that time point with no missing data (baseline n = 586; 12 months n = 416; 24 months n = 378; 36 months n = 367). This approach is taken to ensure that any differences in results across EQ-5D-5L and VILL-UI across the assessments are not due to differences in samples.

Analyses

The analyses report the sample characteristics and assess the feasibility, convergent validity, and known-group validity of VILL-UI and EQ-5D-5L using both UK and German preference weights to generate utilities for each measure. There is no gold standard PWM for vision or AMD; hence, analyses report comparative performance of these 2 measures. The statistical analysis plan was informed by recent psychometric analyses of preference-weighted measures.[31,32]

Feasibility assessments examine the practicality of the measures for completion by people with AMD. This is assessed using missing data for each EQ-5D-5L and VILL-UI dimension because high levels of missing data indicate a lack of evidence for acceptability and feasibility.

Floor and ceiling effects are examined for each dimension and the utilities of each measure. In cases in which there are large proportions of responses observed at the least severe responses, there is an inability to capture an improvement in health (referred to here as ceiling effects). In cases in which there are large proportions of responses observed at the most severe level, there is an inability to capture a deterioration in health (referred to here as floor effects). For a clinical population, large floor and ceiling effects indicate that the measure is unlikely to fully capture clinical changes in the condition. At the measure level, ceiling and floor effects are flagged in situations in which these are >15% of participants (for all dimensions combined).[33,34] For patients reporting full health in EQ-5D-5L, their responses to VILL-UI are examined to assess the ability of VILL-UI to capture the impact of visual impairment in cases in which no impact was indicated using EQ-5D-5L. It is hypothesized that EQ-5D-5L dimensions have larger ceiling effects than VILL-UI dimensions.

Convergent validity assessments examine the strength of association between EQ-5D-5L and VILL-UI. Evidence of convergent validity is determined by whether moderate (0.41-0.60) or good (0.61-0.80) (see Landis et al[35]) agreement is observed in cases in which these are motivated theoretically (eg, emotional well-being dimension in VILL-UI and anxiety/depression dimension in EQ-5D-5L). Divergent validity is demonstrated in cases in which the measures or dimensions are not correlated in situations in which this is also theoretically motivated (eg, information and reading dimensions in VILL-UI and EQ-5D-5L mobility and pain/discomfort), which is expected to be the case in this instance for several dimensions, given the different content (VRQoL vs generic HRQoL) of the measures. Correlations between VILL-UI and EQ-5D-5L utilities are assessed using Pearson correlation coefficients, and correlations between dimensions are assessed using Spearman rank correlation coefficients. Moderate correlations are hypothesized between VILL-UI mobility and safety and EQ-5D-5L mobility; VILL-UI emotional well-being and EQ-5D-5L anxiety/depression; VILL-UI information, reading, mobility, and safety; and EQ-5D-5L usual activities. It is hypothesized that the other dimensions are not correlated, meaning that there is divergent validity because they capture different aspects.

Known-group validity assessments examine the ability to differentiate between groups of different severity. This is assessed using VILL-UI and EQ-5D-5L utilities and dimensions using the distribution of responses, including mean across subgroups and across different time points, and using effect sizes calculated using Cohen's D. Evidence of known-group validity using effect sizes considers 0.2 to 0.49 as small, 0.5 to 0.79 as moderate, and ≥0.8 to be large effect sizes.[36] For differences in means across groups, known-group validity is determined by whether there is a statistically significance difference at the 5% level across known groups (using the *P* value of a *t* test) and whether the direction of the difference is in accordance with clinical expectation (according to the clinical authors). The known groups that are examined are AMD severity (early/intermediate vs late), visual acuity using best-corrected visual acuity (no impairment vs any impairment),[37] visual function (no dysfunction vs dysfunction[37]), and presence of late AMD in the fellow eye (no presence vs presence). Clinical expectation was that utilities would be higher (ie, indicating lower severity) for the lower severity groups (early/intermediate AMD, no impairment, and no dysfunction) in comparison with the higher severity group (late AMD, any impairment, and dysfunction). Visual dysfunction was defined as a visual acuity below the 5th percentile of healthy control participants in the MACUSTAR study.[37] Analyses are conducted separately for each of the 4 time points for AMD stage, but for other severity groups, analysis is only undertaken at baseline because the severity groupings were not available in later time points. It is hypothesized that VILL-UI has moderate known-group validity and that EQ-5D-5L does not reflect all known-group differences.

Change over time was explored using a subsample of participants with complete VILL-UI and EQ-5D-5L data at all time points, using utility values at each time point for all participants and by AMD severity (early/intermediate vs late).

Analyses were undertaken using Stata version 18.

Results

Table 1 reports sample characteristics. The sample at baseline (n = 586) has mean age 71.9 years (standard deviation 6.9), and 65.2% are female. The sample has predominantly intermediate AMD (87.2% at baseline to 83.3% at 36 months).

Figure 1 and Appendix Figure 1 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2025.04.2155 show the distribution of EQ-5D-5L and VILL-UI utilities by time point. EQ-5D-5L has a narrower range than VILL-UI, particularly when using German weights. Both measures have a right-skewed distribution, although EQ-5D-5L has larger ceiling effects, and VILL-UI is less skewed.

Both VILL-UI and EQ-5D-5L are feasible. In terms of missing data, at baseline, all 661 participants fully completed EQ-5D-5L, whereas 586 completed VILL-UI (see Appendix Table 1 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2025.04.2155). The percentage of participants with missing data (responses are unable to be used to generate utilities) for VILL-UI varies from 10.3% to 13.0% by time point and from 0% to 2.1% for EQ-5D-5L.

Table 2 shows the distribution of dimension responses and mean (standard deviation) utility for each measure at each time point. EQ-5D-5L has high ceiling effects (eg at baseline between 50.9% and 95.4% of observations in contrast to 21.5% to 62.1% for VILL-UI). Because of differences in country preference weights, mean VILL-UI utility per time point is lower using German weights, whereas mean EQ-5D-5L utility is higher using German weights.

Table 3 shows the distribution of VILL-UI dimension responses at each time point when the participant is in EQ-5D-5L full health. The proportion of participants at full health using EQ-5D-5L (ie, ceiling response to all dimensions) varies from 32.3% at 36 months to 37.0% at baseline, with all time points exceeding the 15% cutoff. In contrast, the proportion of participants in the best state using VILL-UI varies from 6.6% at 24 months to 7.3% at baseline (see Appendix Table 2 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2025.04.2155 for EQ-5D-5L responses for participants reporting best state using VILL-UI). Table 3 shows that all VILL-UI dimensions capture VRQoL problems not reflected in EQ-5D-5L when the participant is in good health, with notably only 29.2% to 33.3% of participants at the least severe level for VILL-UI emotional well-being, despite having no problems in the anxiety/depression EQ-5D-5L dimension.

Convergent and divergent validity between EQ-5D-5L dimensions and VILL-UI dimensions is shown in Table 4 at baseline and Appendix Tables 3 to 5 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2025.04.2155 for the other time points. In contrast to our hypotheses, low correlations between dimensions are observed in cases in which moderate correlations

Table 1. The MACUSTAR study sample (with complete EQ-5D-5L and VILL-UI data), by time point.

Characteristic	Level	Baseline, *N* = 586		12 months *N* = 416		24 months *N* = 378		36 months *N* = 367	
		n	%	*n*	%	*n*	%	*n*	%
Sex	Female	382	65.2	263	63.2	248	65.6	246	67.0
	Male	204	34.8	153	36.8	130	34.4	121	33.0
AMD stage	Early AMD	34	5.8	26	6.3	18	4.8	17	4.6
	Intermediate AMD	511	87.2	359	86.3	327	86.5	302	83.3
	Late AMD	41	7.0	31	7.5	33	8.7	48	13.1
Best-corrected visual acuity	No impairment	439	74.9	346	83.2	314	83.1	309	84.2
	Impairment	105	17.9	70	16.8	64	16.9	58	15.8
	Missing	42	7.2	0	0	0	0	0	0
Visual function	No dysfunction	96	16.4	85	20.4	77	20.4	75	20.4
	Dysfunction	364	62.1	265	63.7	235	62.2	233	63.5
	Missing	126	21.5	66	15.9	66	17.5	59	16.1
Presence of late AMD in the fellow eye	No presence	505	86.2	389	93.5	351	92.9	340	92.6
	Presence	39	6.7	26	6.3	26	6.9	27	7.4
	Missing	42	7.2	1	0.2	1	0.3	0	0
Age	Mean (SD)	71.9 (6.92)		71.6 (6.90)		71.2 (6.97)		70.7 (6.89)	

AMD indicates age-related macular degeneration; VILL-UI, Vision Impairment in Low Luminance-Utility Index.

were expected. Divergent validity is observed across the remaining EQ-5D-5L and VILL-UI dimensions as expected, indicating that these dimensions capture different aspects.

Correlations between EQ-5D-5L and VILL-UI utilities are low, and for the 12 month time point only there is moderate correlation.

Known-group validity assessments are shown in Table 5. Known-group validity assessed using AMD stage was significantly demonstrated at baseline and 36 months for VILL-UI (both country weights) using *t* tests and with moderate or large effect sizes. Across all time points, the ordering of mean values across severity groups was in accordance with clinical expectation even when not significant. For EQ-5D-5L, it was only significant using German weights at baseline, although the effect size was small. At the 12 month time point, the mean values for the different AMD stage groups were not in accordance with clinical expectations.

VILL-UI detected a statistically significant difference using *t* tests in known groups for visual function and visual acuity (Table 5). EQ-5D-5L detected a statistically significant difference for visual function but not for visual acuity. All of the effect sizes were small for visual function and visual acuity.

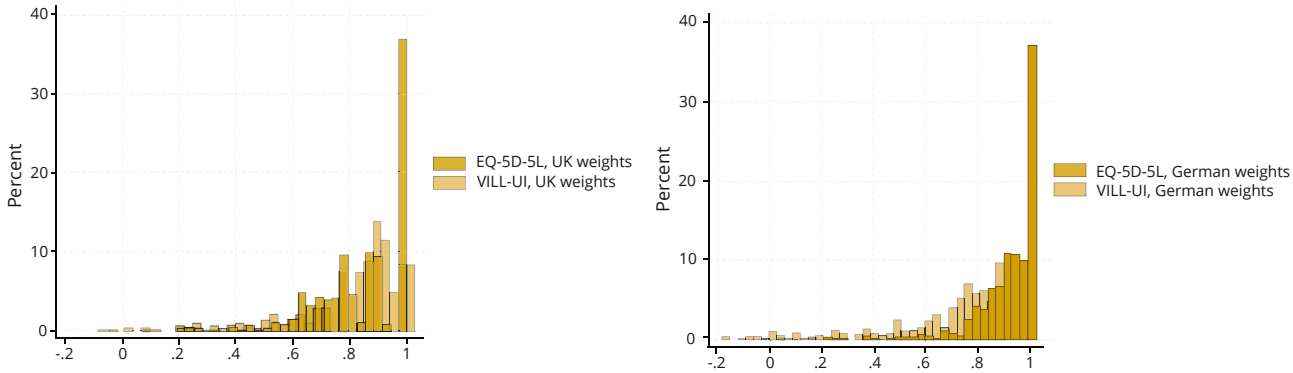
The ordering of VILL-UI utilities across severity groups in the fellow eye (AMD stages according to the Beckman classification) was in accordance with clinical expectations but was not statistically significant. EQ-5D-5L was not in accordance with clinical expectations. All effect sizes were small for presence of late AMD in the fellow eye.

For all participants with utilities at all time points, VILL-UI utilities demonstrate change over time (see Appendix Table 6 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2025.04.2155) that would be expected clinically, in which utilities decrease over time and are lower for participants with more severe AMD. EQ-5D-5L utilities do not decrease as expected at 24 months, and using the German weights do not reflect severity at 24 and 36 months.

Discussion

To our knowledge, this study is the first to assess the psychometric performance of the newly developed VILL-UI PWM derived from the VILL-33 and EQ-5D-5L in patients with AMD

Figure 1. Distribution of EQ-5D-5L and VILL-UI utilities, at baseline.



VILL-UI indicates Vision Impairment in Low Luminance-Utility Index.

Table 2. VILL-UI and EQ-5D-5L dimension responses and utilities, by time point.

VILL-UI dimension	Level	Baseline, %	12 months, %	24 months, %	36 months, %
Information	1	37.5	32.2	28.0	26.7
	2	45.2	50.7	50.5	50.7
	3	14.5	16.1	20.4	20.7
	4	2.7	1.0	1.1	1.9
Reading	1	53.9	48.1	42.3	39.5
	2	34.0	41.8	41.5	45.8
	3	10.4	10.1	15.3	14.4
	4	1.7	0	0.8	0.3
Mobility and safety	1	62.1	61.8	57.4	51.5
	2	26.6	25.7	27.5	33.5
	3	2.7	4.1	4.5	3.3
	4	0.2	1.2	0.5	0.3
	5	5.5	5.5	7.4	6.0
	6	1.5	1.0	2.4	4.1
	7	0.2	0.0	0.0	0.0
	8	1.2	0.7	0.3	1.4
Emotional well-being	1	21.5	24.8	24.6	23.4
	2	41.6	44.5	46.6	45.5
	3	27.0	26.2	22.8	22.6
	4	9.9	4.6	6.1	8.5
EQ-5D-5L dimension					
Mobility	1	72.2	74.8	72.8	70.8
	2	16.6	14.9	16.4	17.2
	3	9.6	8.4	9.0	9.0
	4	1.7	1.9	1.9	3.0
	5	0.0	0.0	0.0	0.0
Self-care	1	95.4	96.2	97.6	96.5
	2	3.2	2.9	1.9	3.3
	3	0.9	0.7	0.3	0.3
	4	0.3	0.2	0.3	0
	5	0.2	0	0	0
Usual activities	1	82.8	86.1	85.7	82.0
	2	12.3	9.6	8.2	11.2
	3	3.8	3.6	5.0	6.0
	4	0.9	0.7	1.1	0.8
	5	0.3	0	0	0
Pain/discomfort	1	50.9	46.2	48.2	46.1
	2	28.8	35.8	32.5	31.9
	3	16.7	13.2	17.2	18.8
	4	3.1	4.8	2.1	3.3
	5	0.5	0	0	0
Anxiety/depression	1	68.6	70.7	71.2	66.2
	2	21.0	18.0	19.8	25.3
	3	8.4	10.1	7.1	6.5
	4	1.5	0.7	1.6	1.6
	5	0.5	0.5	0.3	0.3
VILL-UI, UK weights	Mean (SD)	0.804 (0.191)	0.810 (0.165)	0.783 (0.187)	0.770 (0.195)
VILL-UI, German weights	Mean (SD)	0.756 (0.236)	0.765 (0.211)	0.734 (0.240)	0.715 (0.249)
EQ-5D-5L, UK weights	Mean (SD)	0.836 (0.167)	0.836 (0.160)	0.840 (0.156)	0.828 (0.156)
EQ-5D-5L, German weights	Mean (SD)	0.909 (0.136)	0.910 (0.131)	0.919 (0.114)	0.908 (0.121)

Note. For VILL-UI dimensions of Information and Reading: level 1= none; level 2 = a little; level 3 = a lot; level 4 = can't do. For VILL-UI dimension of mobility and safety (mobility/safety items): level 1 = none/never; level 2 = a little/sometimes; level 3 = a little/often; level 4 = a little/always; level 5 = a lot/often; level 6 = a lot/always; level 7 = can't do/often; level 8 = can't do/always. For VILL-UI dimension of emotional well-being: level 1 = never; level 2 = sometimes; level 3 = often; level 4 = always. For EQ-5D-5L dimensions: level 1 = none; level 2 = slight; level 3 = moderate; level 4 = severe; level 5 = extreme/unable. VILL-UI indicates Vision Impairment in Low Luminance-Utility Index.

and the first to compare the performance of the 2 measures. The study is of international importance and significance because of the use of a multicountry, multicenter data set[29] and the application of different country value sets for each measure. The results provide valuable information to those conducting quality-of-life studies in AMD and undertaking cost-effectiveness analyses of interventions in AMD.

The VILL-UI has superior performance for known-group validity to EQ-5D-5L, with fewer ceiling effects but higher missing data. EQ-5D-5L has little evidence of known-group validity and

Table 3. VILL-UI dimension responses when patients report full health on EQ-5D-5L, by time point.

VILL-UI dimension	Level	Baseline (*n* = 217)		12 months (*n* = 137)		24 months (*n* = 135)		36 months (*n* = 118)	
		n	%	*n*	%	*n*	%	*n*	%
Information	1	94	43.3	54	39.4	48	35.6	40	33.9
	2	99	45.6	72	52.6	70	51.9	56	47.5
	3	21	9.7	10	7.3	14	10.4	21	17.8
	4	3	1.4	1	0.7	3	2.2	1	0.9
Reading	1	138	63.6	78	56.9	74	54.8	57	48.3
	2	57	26.3	53	38.7	46	34.1	46	39.0
	3	18	8.3	6	4.4	14	10.4	15	12.7
	4	4	1.8	0	0	1	0.7	0	0
Mobility and safety	1	166	76.5	103	75.2	100	74.1	79	67.0
	2	40	18.4	24	17.5	28	20.7	29	24.6
	3	3	1.4	5	3.7	2	1.5	4	3.4
	4	1	0.5	2	1.5	0	0	0	0
	5	6	2.8	2	1.5	3	2.2	5	4.2
	6	0	0	1	0.7	2	1.5	0	0
	7	0	0	0	0	0	0	0	0
	8	1	0.5	0	0	0	0	1	0.9
Emotional well-being	1	60	27.7	40	29.2	45	33.3	38	32.2
	2	93	42.9	63	46.0	63	46.7	58	49.2
	3	51	23.5	31	22.6	22	16.3	15	12.7
	4	13	6.0	3	2.2	5	3.7	7	5.9

Note. For VILL-UI dimensions of Information and Reading: level 1= none; level 2 = a little; level 3 = a lot; level 4 = can't do. For VILL-UI dimension of mobility and safety (mobility/safety items): level 1 = none/never; level 2 = a little/sometimes; level 3 = a little/often; level 4 = a little/always; level 5 = a lot/often; level 6 = a lot/always; level 7 = can't do/often; level 8 = can't do/always. For VILL-UI dimension of emotional well-being: level 1 = never; level 2 = sometimes; level 3 = often; level 4 = always. VILL-UI indicates Vision Impairment in Low Luminance-Utility Index.

large ceiling effects, with over one-third of patients reporting full health. There is low correlation between EQ-5D-5L and VILL-UI utilities and dimensions common to each measure for which moderate correlation may be expected. Divergent validity is demonstrated in cases which it is expected between dimensions that would not be expected to be related. Change over time is demonstrated as expected for VILL-UI but is not clearly observed for EQ-5D-5L.

Differences in country preference weights for UK and Germany leads to differences in mean utilities. There are greater similarities between UK utilities than between German utilities, meaning smaller differences between VILL-UI and EQ-5D-5L at the mean level using UK weights than using German weights. This demonstrates the need to understand the implications of specific country preference weights, as well as the performance of the dimensions that generate the utilities.

One limitation of VILL-UI is the large proportion of data regarded as missing/for which a utility score cannot be generated (10.3% to 13.0% across different time points). The missingness mainly occurs (see Appendix Table 1 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2025.04.2155) because of the response option "Don't do this for other reasons," and for participants selecting this response for VILL-UI dimensions, no utility value can be generated. For any data set, this means that some participant data will not be able to be used to generate utilities, and it is more likely that those participants will have

Table 4. Correlations between VILL-UI and EQ-5D-5L dimensions and utilities, reported at baseline.

Instrument and dimension/ preference weights	VILL-UI Information	VILL-UI Reading	VILL-UI Mobility and safety	VILL-UI Emotional well-being	VILL-UI utilities, UK weights	VILL-UI utilities, German weights
EQ-5D-5L mobility	0.12	0.11	0.26	0.09		
EQ-5D-5L Self-care	0.06	0.13	0.16	0.04		
EQ-5D-5L Usual activities	0.20	0.23	0.30	0.14		
EQ-5D-5L Pain/discomfort	0.14	0.11	0.30	0.12		
EQ-5D-5L Anxiety/ depression	0.04	0.09	0.11	0.22		
EQ-5D-5L utilities, UK weights					0.30	
EQ-5D-5L utilities, German weights						0.34

Note. Pearson correlation is reported for dimensions and Spearman rank correlation is reported for utilities. VILL-UI indicates Vision Impairment in Low Luminance-Utility Index.

Table 5. Assessing known-group validity according to age-related macular degeneration (AMD) stage, visual function, visual acuity, and presence of late AMD in fellow eye, by time point.

Time point	Measure	Early/ Intermediate AMD (mean)	*n*	Late AMD (mean)	*n*	Accordance with clinical expectation	*P* value	Effect size
Baseline	VILL-UI, UK weights	0.833	545	0.420	31	Yes	<.001	2.600
	VILL-UI, German weights	0.790		0.304		Yes	<.001	2.418
	EQ-5D-5L, UK weights	0.839		0.790		Yes	.072	0.292
	EQ-5D-5L, German weights	0.913		0.865		Yes	.029	0.354
12 months	VILL-UI, UK weights	0.812	401	0.763	15	Yes	.259	0.297
	VILL-UI, German weights	0.767		0.715		Yes	.349	0.247
	EQ-5D-5L, UK weights	0.835		0.855		No	.647	-0.121
	EQ-5D-5L, German weights	0.910		0.917		No	.826	-0.058
24 months	VILL-UI, UK weights	0.784	345	0.770	33	Yes	.664	0.079
	VILL-UI, German weights	0.736		0.712		Yes	.585	0.100
	EQ-5D-5L, UK weights	0.841		0.828		Yes	.647	0.084
	EQ-5D-5L, German weights	0.919		0.912		Yes	.746	0.059
36 months	VILL-UI, UK weights	0.785	319	0.670	48	Yes	<.001	0.599
	VILL-UI, German weights	0.735		0.585		Yes	<.001	0.612
	EQ-5D-5L, UK weights	0.830		0.815		Yes	.544	0.094
	EQ-5D-5L, German weights	0.909		0.903		Yes	.761	0.047
		Visual function - No dysfunction (mean)	*n*	Visual function - Dysfunction (mean)	*n*			
Baseline	VILL-UI, UK weights	0.883	96	0.816	364	Yes	<.001	0.439
	VILL-UI, German weights	0.854		0.766		Yes	<.001	0.449
	EQ-5D-5L, UK weights	0.879		0.824		Yes	.004	0.329
	EQ-5D-5L, German weights	0.938		0.902		Yes	.023	0.262
		Visual acuity (BCVA)-No impairment (mean)	*n*	Visual acuity (BCVA)-Impairment (mean)	*n*			
Baseline	VILL-UI, UK weights	0.847	439	0.776	105	Yes	<.001	0.484
	VILL-UI, German weights	0.808		0.715		Yes	<.001	0.489
	EQ-5D-5L, UK weights	0.844		0.821		Yes	.190	0.143
	EQ-5D-5L, German weights	0.916		0.898		Yes	.198	0.140
		No presence of late AMD in fellow eye (mean)	*n*	Presence of late AMD in fellow eye (mean)	*n*			
Baseline	VILL-UI, UK weights	0.834	505	0.824	39	Yes	.668	0.071
	VILL-UI, German weights	0.791		0.775		Yes	.619	0.083
	EQ-5D-5L, UK weights	0.838		0.864		No	.331	-0.162
	EQ-5D-5L, German weights	0.911		0.938		No	.218	-0.205

Note. Effect size is calculated using Cohen's D. AMD indicates age-related macular degeneration; BCVA, best-corrected visual acuity; VILL-UI, Vision Impairment in Low Luminance-Utility Index.

comorbidities (because this may mean that they are unable to do things for other reasons) meaning that their responses are not missing at random. This potential level of missing data should be considered in sample size calculations when collecting VILL/VILL-UI data and in subsequent data analyses. It can be considered advantageous that the "Don't do for other reasons" response option acts as a filter in which utilities will only be generated for participants for whom the recorded impacts are due to their eyesight. Therefore, although it is not commonly observed for PROMs to include a response option "Do not do for other reasons," it may be considered advantageous for ensuring that impairment is due to the health condition being assessed, and this is commonly implemented in PROMs for eye conditions.[38,39]

A single vision "bolt-on" dimension to EQ-5D has been explored[40-43] to improve the psychometric performance of EQ-5D-5L in vision. However, 1 additional general dimension on vision is unlikely to reflect all aspects of importance not included in EQ-5D (eg, vision in dark surroundings). EQ-5D with a bolt-on will have different properties and likely different preference weights, reducing comparability of results to other conditions for which EQ-5D or EQ-5D with an alternative bolt-on is used, although this comparability is often the key argument for using a generic PWM.

Study limitations include that the MACUSTAR sample used here contained the sample used to derive the VILL-UI classification system. However, only the baseline sample was used to derive the VILL-UI classification, whereas the analyses undertaken here use 3 additional time points. For the known-group validity assessments of AMD stage, the VILL-UI has much higher effect sizes for baseline than for the other time points, and one possibility is that this is

because these were the data used to select the VILL-UI classification system based on psychometric performance. For the other known-group analyses, severity groups could only be defined at baseline. Therefore, repeating known-group analyses in another data set would be beneficial. The study was unable to assess responsiveness to treatment because the data were from a non-interventional study, and assessment of responsiveness of VILL-UI and EQ-5D-5L to treatment in people with AMD is recommended.

The MACUSTAR data set is a multicountry data set, and in the analyses reported here, the UK and German preference weights are applied to the entire data set, although this includes participant data collected outside of UK and Germany. This increases sample size, enables like-for-like comparisons of the application of the UK and German weights, and relies on the assumption that different language versions of the measures do not affect participant responses. This is often done in multicountry data sets when it is used to inform economic evaluation, in which preference weights for 1 country are applied to the entire sample.

One factor that may have affected results is the different recall period of the measures. EQ-5D-5L has a recall period of "today," whereas VILL-33 asks about your health during the "past month."

The divergent validity between many EQ-5D-5L and VILL-UI dimensions, and low convergent validity in dimensions for which a relationship would be expected, indicate that each measure captures different aspects. VILL-UI focuses on aspects of VRQoL that are affected by AMD to provide utilities that directly and better capture the impact of visual impairment but cannot be used to capture generic HRQoL. In contrast, EQ-5D-5L covers general aspects of HRQoL and does not have a dimension related to vision, meaning that HRQoL impact from visual impairment is captured via its impact on other dimensions. EQ-5D-5L has the benefit of comparability when used across different patient groups and treatments and is able to capture the impact of comorbidities and potentially wider side effects from treatments. However, EQ-5D-5L may underestimate treatment effects in people with AMD because it is not able to reflect known clinical effects.

The evidence provided here demonstrates that EQ-5D-5L is not fully appropriate for use in people with intermediate AMD and details the impact on utilities (and hence quality-adjusted life years) if VILL-UI was used instead of EQ-5D-5L. NICE,[3] for example, allows the use of condition-specific PWMs when evidence shows that EQ-5D is not appropriate. The NICE methods guide[3] suggests that inappropriateness is demonstrated by using evidence of lack of content validity, construct validity, and responsiveness, using a synthesis of peer-reviewed literature. Qualitative work used to develop the VILL-33 identified aspects of importance to patients that are not included in EQ-5D (in particular, reading and accessing information).[22] The evidence presented here shows that EQ-5D-5L performs poorly for convergent validity and known-group validity in AMD, indicating a lack of construct validity in AMD, and, to our knowledge, our study is the first to assess the psychometric performance of EQ-5D-5L in AMD.

Conclusions

The NICE methods guide[3] suggests detailing the methods used to generate utilities from a condition-specific PWM, their validity, and how the methods affect utilities. The details of the validity of VILL-UI and how VILL-UI utilities differ to EQ-5D-5L utilities, using both UK and German preference weights, have been provided here. We have demonstrated that the VILL-UI is appropriate for use in future AMD studies to inform economic evaluation. The results indicate that VILL-UI is more appropriate for use for patients with intermediate AMD than EQ-5D-5L on the grounds of psychometric performance.

Author Disclosures

Author disclosure forms can be accessed below in the Supplemental Material section. The communication reflects the author's view and neither innovative medicines initiative nor the European Union, European Federation of Pharmaceutical Industries and Associations, or any Associated Partners are responsible for any use that may be made of the information contained therein. Dr Rowen is an editor for *Value in Health* and had no role in the peer-review process of this article.

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