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Patient-Reported Outcomes

Distribution of the EQ-5D-5L Profiles and Values in Three Patient Groups

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ABSTRACT

Background: The distribution of EQ-5D-3L values (health state profiles, weighted by value sets) often shows two distinct groups, arising from both the distribution of profiles and the characteristics of value sets. To date, there is little evidence about the distribution of EQ-5D-5L values. **Objectives:** To explore the distribution of EQ-5D-5L profiles; to compare the distributions of EQ-5D-5L values arising from the English value set (EVS) and a 'mapped' value set (MVS); and to develop further the methods used to investigate clustering within EQ-5D data. **Methods:** We obtained data from Cambridgeshire Community Services NHS Trust containing EQ-5D-5L profiles before treatment for three patient groups: community rehabilitation (N=6919); musculoskeletal physiotherapy (N=19999); and specialist nursing services (N=3366). Values were calculated using the EVS and MVS. Clusters were examined using the k-means method and Calinski–Harabasz pseudo-F index stopping rule. **Results:** We found no evidence for clustering of EQ-5D-5L values arising from the classification system and no strong or consistent evidence of clustering arising from the EVS. There was clearer evidence of clustering using the MVS, with two being the optimal number of clusters. The clusters that were found for the EVS were very different from the MVS clusters. **Conclusions:** Unlike the EQ-5D-3L, clustering of EQ-5D-5L values does not seem to be driven by clustering of its profile. This suggests the EQ-5D-5L is superior in that it is less likely to generate artefactual clusters – however, clusters may still result from using value sets such as MVS that have the tendency to generate them.

Introduction

Health status or health-related quality of life (HRQOL) measures, such as the EQ-5D,[1] are often summarized by a single number, which is calculated by summation of scores attached to questionnaire item responses. The distribution of the total score within a population or sample will depend both on participants' responses and the scoring system applied to them. It is therefore valuable to examine whether and how the characteristics of the measurement instrument and its scoring system affect the distributions of these observed scores. Parkin et al[2] showed that a commonly found feature of the distribution of values[a] data from the 3-level version of the EQ-5D (the EQ-5D-3L), 2 distinctive but overlapping groups, results from the interaction between the classification system used in the questionnaire and the scoring system in the form of "value sets." It is essential to be aware of such patterns in interpreting distributions of HRQOL data because, for example, it might be concluded that a patient population contains groups with different underlying levels of ill health, when that is simply an artifact of the measurement instrument. There are also potential issues when undertaking statistical modeling of values data, such as assumptions of normality of residuals in regression analysis. It is therefore important to examine this issue for the 5-level version of the EQ-5D, the EQ-5D-5L.[3]

The EQ-5D-5L describes HRQOL in terms of 5 dimensions (mobility; self-care; usual activities; pain and discomfort; and anxiety and depression), each of which has 5 levels (no, slight, moderate, severe, or extreme problems). This permits creation of a health state *profile* for each respondent, consisting of the

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[a] In this paper, we refer to the scores attached to EQ-5D health states as 'values', because of their origins in studies of peoples' preferences for different health states.

combination of levels within dimensions. In the EQ-5D-5L, the 5 dimensions and 5 levels define 3125 (= 5^5) profiles. Values are attached to these profiles using value sets,[4] usually obtained from stated preference surveys of the general public. These values are anchored at 1, representing full health, and 0, meaning a health state as bad as being dead, with the possibility of having negative numbers representing even worse health states.

There has been little work to explore the characteristics of distributions of EQ-5D-5L data. There are relatively few EQ-5D-5L data currently accessible to researchers, and EQ-5D-5L value sets are only now becoming available.[5–10] Until recently, the EQ-5D-5L index could only be calculated using a mapping (sometimes called a "crosswalk") algorithm derived from the EQ-5D-3L descriptive system and value sets.[11] Increasing use of the EQ-5D-5L, for which requests for licenses now exceed those for the EQ-5D-3L,[1] means that understanding the characteristics of these distributions is timely.

In this article, we examine the EQ-5D-5L using 2 value sets, the English value set (EVS) resulting from the study by Devlin et al[5] and a mapped value set (MVS) resulting from the van Hout et al[11] study, which was intended to provide an interim means of valuing EQ-5D-5L states while studies to produce value sets were being completed. The MVS used in our analyses is derived from the UK EQ-5D-3L value set generated by the Measurement and Valuation of Health (MVH) study.[12,13] At the time of writing, the MVS is recommended by the United Kingdom's National Institute for Health and Care Excellence (NICE) for use in valuing EQ-5D-5L data in evidence submitted to them,[14] although this is under review. Because the MVS might inherit the known characteristics of the EQ-5D-3L value set, it forms a useful comparator with the main focus of this article, the EVS. This is also relevant to health technology assessments undertaken elsewhere if local equivalents of the MVS are used instead of value sets derived from direct valuation of EQ-5D-5L profiles.

There are grounds for hypothesizing that EQ-5D-5L values data (ie, patients' EQ-5D-5L profile data, summarized using a value set) might *not* have the 2-group distribution commonly observed for the EQ-5D-3L. First, a study comparing the distributions of data from the 2 EQ-5D versions in a general population sample in England found a wider spread of profiles reported for the EQ-5D-5L, including a larger proportion who reported severe problems (levels 4 and 5 in the 5L version; level 3 in the 3L version) and fewer who reported no problems in any dimension.[15] Craig et al[16] reported similar findings using data from a US general population sample. Second, as Figure 1 shows, the distributions of EQ-5D-5L values over all possible profiles, for both the EVS and the MVS, do not have the 2-group shape of the EQ-5D-3L value set.

The study reported in this article had 2 main aims and 1 secondary aim: to explore the distribution of EQ-5D-5L profile data; to compare the EVS-based and MVS-based distributions of values; and to develop further the methods used by Parkin et al[2] to investigate clustering within EQ-5D datasets.

Data and Methods

The data were collected as part of routine clinical practice in Cambridgeshire Community Services, part of the English National

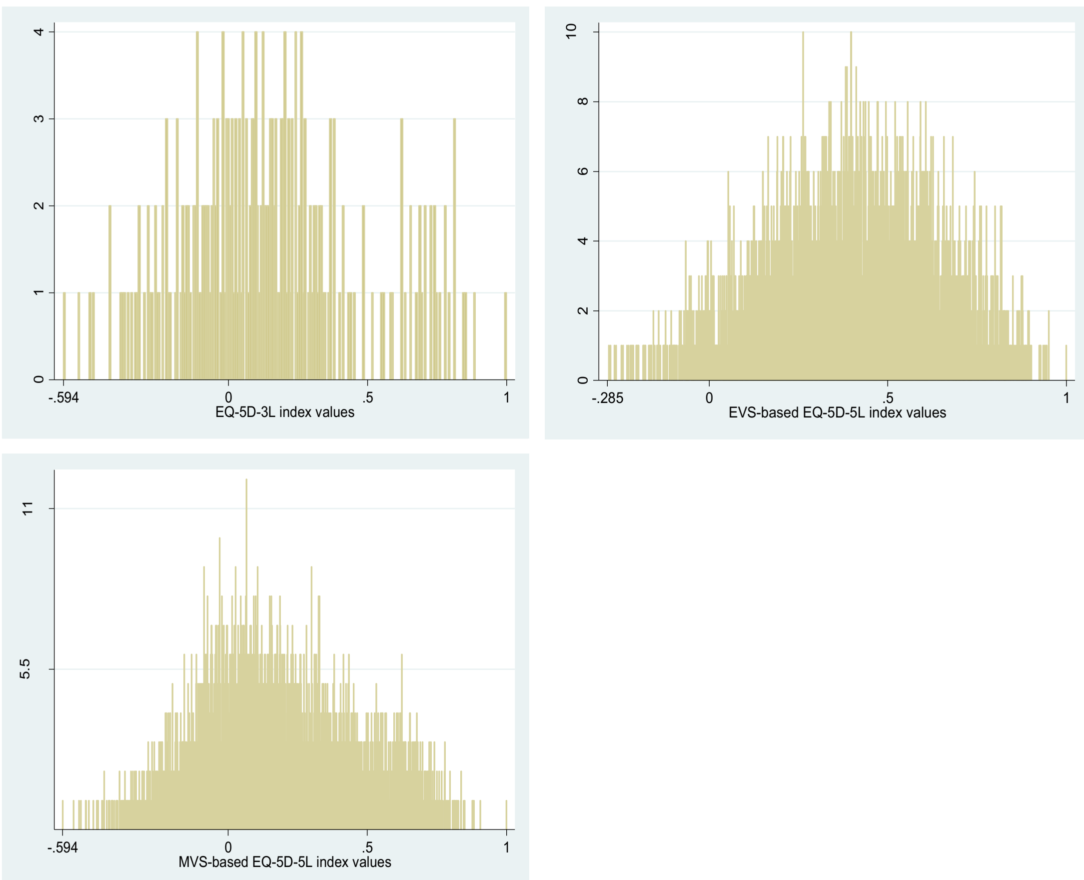

Fig. 1 – Frequency of values in the EQ-5D-3L and the EVS- and MVS-based EQ-5D-5L index over all possible profiles. EVS, English value set; MVS, mapped value set.

Table 1 – Impact of presence of worse levels on the distribution of 3125 EQ-5D-5L values.

Levels	Value set	Lowest value without levels	Highest value with levels	Number ≤ lowest without	Number between lowest without and highest		Number ≥ highest with	Mean value with levels	Mean value without levels
					With level	Without level			
5	EVS	−0.094	0.816	56	2045	965	59	0.302	0.550
	MVS	0.036	0.556	1003	1099	654	369	0.037	0.484
4, 5	EVS	0.593	0.838	2543	340	198	44	0.351	0.764
	MVS	0.516	0.813	2665	217	225	18	0.142	0.676
3, 4, 5	EVS	0.701	0.937	2871	223	27	4	0.378	0.851
	MVS	0.592	0.883	2820	272	30	3	0.178	0.762

EVS, English value set; MVS, mapped value set.

Health Service (NHS). Clinicians provide a paper copy of the EQ-5D-5L to patients as part of their assessment and intervention planning. The individual responses are copied to the patient's electronic patient record. The Trust's data warehouse team extracts and collates the data along with basic demographic information.

The clinical teams collecting the data provide services to distinctive patient groups. Rehabilitation services are provided by Occupational Therapists and Physiotherapists to people characterized broadly as frail elderly and people managing conditions such as stroke. Home visits are geared toward improving participation in treatment through interventions such as providing mobility and self-care advice, assistive technology, and housing adaptations. Specialist nurses work in small disease-specific teams helping patients to manage their long-term chronic conditions such as diabetes, Parkinson's disease, multiple sclerosis, and chronic respiratory diseases. They see patients in clinic settings and in their own homes. In contrast the musculoskeletal (MSK) physiotherapy services are provided to service users across the life span with acute injuries and long-term MSK chronic conditions covering rheumatology, orthopedic, and persistent pain. The clinical team mainly comprises physiotherapists and clinical specialists whose focus is on spinal and peripheral joint pain and dysfunction. Patients attend outpatient clinics based in hospitals, medical centers, and bespoke departments within primary care. Together the data collected represent a reasonably comprehensive survey of these service users over the months from January 2013 to March 2015.

Forty-six patients are excluded from the analysis because they were under 13 years old. There were therefore 30 284 patient observations across 3 patient groups: MSK physiotherapy services (MSK) (N = 19 999), specialist nursing services (SNS) (N = 3366), and community rehabilitation services (CRS) (N = 6919).

We explored in 2 ways that clusters of values can be generated by EQ-5D-5L profiles alone, using the full EQ-5D-5L set of 3125 profiles and both the EVS and the MVS. First, we divided profiles into 2 groups according to whether they had level 5 in any dimension or no level 5 in any dimension, and similarly for levels 4 and 5 and levels 3, 4, and 5. This follows the method used by Parkin et al[2] for the EQ-5D-3L, although it is more complicated because of the greater number of levels. Second, we examined the differences between consecutive EQ-5D-5L values ordered by size to see whether we could identify any notable gaps in the distribution.

In the article by Parkin et al,[2] a k-means clustering procedure[17] was used to search for clusters in EQ-5D-3L data. In this study, we extended this using a procedure that applied 2 search methods to determine the optimal number of clusters in EQ-5D-5L data. Technical details of this are given in the Appendix (see Supplemental Materials found at https://doi.org/10.1016/j.jval.2018.08.012).

Results

Table 1 analyzes the EVS and MVS value sets; that is, the values that are attached to each of the possible EQ-5D-5L profiles. It

Table 2 – Patients' demographic characteristics and self-reported health.

	All patients	MSK	Specialist nursing	Community rehabilitation
% of male	40.4	40.2	47.9	37.5
Mean age (SD), years	59.1 (18.9)	52.5 (17.3)	67 (15.2)	74.4 (14.1)
Age range, years	13-104	13-96	17-104	18-103
Mean EQ-VAS	65.5	68.2	64.6	60.9
Mean MVS index	0.550	0.572	0.614	0.455
Mean EVS index	0.653	0.671	0.692	0.582
1st frequently reported profile (%)	11121 (4.0)	11121 (5.0)	11111 (13.2)	11111 (1.9)
2nd frequently reported profile (%)	11111 (3.2)	11221 (4.5)	11121 (4.0)	21221 (1.2)
3rd frequently reported profile (%)	11221 (3.2)	21221 (3.3)	11112 (3.4)	11121 (1.1)
4th frequently reported profile (%)	21221 (2.6)	21231 (3.2)	11122 (1.6)	32331 (1.0)
5th frequently reported profile (%)	21231 (2.3)	11231 (2.7)	21121 (1.5)	33331 (1.0)
N of unique profiles reported by patients	1730	1141	732	1240
N	30 284	19 999	3366	6919

EVS, English value set; MSK, musculoskeletal; MVS, mapped value set.

shows how the presence of more severe levels within dimensions affects the values that profiles have. Profiles were partitioned according to the presence or absence in any dimension of level 5, levels 4 and 5, and levels 3, 4, and 5. In each line of the table, we report in the third and fourth columns the lowest value taken by a profile that does not contain the level or levels and the highest value taken by a profile that does. The fifth column shows the number of profiles that take a value below the lowest for those that do not contain the level or levels. The eighth column similarly shows the number of profiles that take a value above the highest for those that contain the level or levels, all of which do not. Columns 6 and 7 show the extent of overlap, the number of profiles whose values lie within these lowest and highest values, for those that do and do not contain the level or levels. The final columns show the mean values for profiles according to whether they do or do not contain the level or levels.

To illustrate our method, examine row 2, which applies the EVS to generate the values. The smallest value from health profiles without level 5 is −0.094 (column 3), and the highest value from those with level 5 is 0.816 (column 4). The mean value for profiles with level 5 is 0.302 (column 9), and the mean value for those without level 5 is 0.550 (column 10). The profiles are divided into 4 mutually exclusive groups, reported in columns 5 to 8. Column 5 shows that there are 56 profiles with values no larger than −0.094. Column 8 shows that there are 59 profiles with values no smaller than 0.816. There are 3010 profiles (= 3125 − 56 − 59) with values in a range of −0.094 to 0.816, with 2045 profiles with level 5 (column 6) and 965 health profiles without (column 7). The overlap between the 2 groups of profiles with values sitting between −0.094 and 0.816 suggests that whether there is a level 5 in profiles is not a clear criterion for identifying high and low clusters.

The extent of the overlaps between profiles that do or do not contain worse levels does not suggest any obvious clustering. For profiles that do not have worse levels, many more have values that are within the range of values taken by profiles that do have them, rather than are above that range. Profiles that contain worse levels also form the large majority of those whose values lie in the range taken by profiles that do not.

We ranked profiles by their values and calculated the difference between adjacent profiles to see whether there are any obvious gaps in the distribution of values. Most differences are small; we use a search for differences >0.01 as an illustration. For the EVS, there are 7 differences >0.01. Using the standard 5-digit notation for profiles, in which each digit represents the level for a dimension in the order described earlier, the biggest difference (0.050) is between health states 11111 (value = 1) and 12111 (value = 0.950). Note that health state 11211 has the same value as health state 12111. Another 2 are close to the highest value, and 4 are close to the lowest. For the MVS, there are 9 of these, the largest of which (0.094) is between health states 11111 (value = 1) and 11211 (value = 0.906). Of the others, 2 are also close to the highest value, and 6 are close to the lowest value. Again, these data do not suggest any obvious clusters, just a slight spreading out of the distribution at the extremes.

Table 3 – Number of patients at each level of each EQ-5D dimension.

	All patients	MSK	Specialist nursing	Community rehabilitation
Mobility				
Level 1	9463 (31.25%)	7413 (37.07%)	1114 (33.10%)	936 (13.53%)
Level 2	7735 (25.54%)	5392 (26.96%)	669 (19.88%)	1674 (24.19%)
Level 3	8321 (27.48%)	4887 (24.44%)	835 (24.81%)	2 599 (37.56%)
Level 4	4064 (13.42%)	2165 (10.83%)	599 (17.80%)	1300 (18.79%)
Level 5	701 (2.31%)	142 (0.71%)	149 (4.43%)	410 (5.93%)
Self-care				
Level 1	16 517 (54.54%)	12 337 (61.69%)	1932 (57.40%)	2248 (32.49%)
Level 2	7227 (23.86%)	4599 (23.00%)	590 (17.53%)	2038 (29.46%)
Level 3	4631 (15.29%)	2446 (12.23%)	482 (14.32%)	1703 (24.61%)
Level 4	1302 (4.30%)	527 (2.64%)	210 (6.24%)	565 (8.17%)
Level 5	607 (2.00%)	90 (0.45%)	152 (4.52%)	365 (5.28%)
Usual activities				
Level 1	5321 (17.57%)	3209 (16.05%)	1201 (35.68%)	911 (13.17%)
Level 2	8733 (28.84%)	6663 (33.32%)	741 (22.01%)	1329 (19.21%)
Level 3	9277 (30.63%)	6562 (32.81%)	760 (22.58%)	1955 (28.26%)
Level 4	4025 (13.29%)	2591 (12.96%)	405 (12.03%)	1029 (14.87%)
Level 5	2928 (9.67%)	974 (4.87%)	259 (7.69%)	1695 (24.50%)
Pain and discomfort				
Level 1	3290 (10.86%)	725 (3.63%)	1259 (37.40%)	1306 (18.88%)
Level 2	8159 (26.94%)	5348 (26.74%)	961 (28.55%)	1850 (26.74%)
Level 3	11 918 (39.35%)	8739 (43.70%)	763 (22.67%)	2416 (34.92%)
Level 4	5736 (18.94%)	4340 (21.70%)	312 (9.27%)	1084 (15.67%)
Level 5	1181 (3.90%)	847 (4.24%)	71 (2.11%)	263 (3.80%)
Anxiety and depression				
Level 1	15 968 (52.73%)	11 231 (56.16%)	1575 (46.79%)	3162 (45.70%)
Level 2	7783 (25.70%)	4880 (24.40%)	964 (28.64%)	1939 (28.02%)
Level 3	4707 (15.54%)	2802 (14.01%)	599 (17.80%)	1306 (18.88%)
Level 4	1272 (4.20%)	778 (3.89%)	156 (4.63%)	338 (4.89%)
Level 5	554 (1.83%)	308 (1.54%)	72 (2.14%)	174 (2.51%)
N	30 284	19 999	3366	6919

MSK, musculoskeletal.

Table 2 reports summary statistics of the patients' characteristics and self-reported health for all patients and the 3 groups. CRS patients report the oldest average age (74.4 years, 37.5% male), followed by SNS (67.0 years, 47.9% male) and MSK (52.5 years old, 40.2% male). MSK patients reported the highest EQ-VAS score, with a mean of 68.2, followed by SNS. CRS patients reported the lowest EQ-VAS score with a mean of 60.9. Using both the EVS and the MVS, the values showed a different level of severity between the 3 groups. SNS patients reported the highest mean, followed by MSK patients. For all 3 groups, the mean is higher using the EVS. Table 2 also presents the top 5 most frequently reported profiles by group. The most frequently reported profile was 11121 for MSK patients (5.0% of observed profiles) and 11111 for both SNS and CRS patients (13.2% and 1.9%, respectively). CRS patients reported 1240 unique profiles, MSK patients 1141, and SNS patients 732; for all patients there were 1730.

Table 3 shows the number of patients in each level of each of the 5 dimensions for all patients and the 3 treatment groups. They differ considerably across different dimensions and groups. For MSK, the dimension that had the largest proportion of no problems (level 1) was self-care (61.7%), whereas the smallest proportion was in pain and discomfort (3.6%). For SNS, the largest proportion was again self-care (57.4%), but the smallest was in mobility (33.1%). For CRS, the largest proportion was anxiety and depression (45.7%) and the smallest usual activities (13.2%). The largest difference between the groups in the number reporting no problems was for pain and discomfort (33.8%) between MSK and SNS, and the smallest was for anxiety and depression (10.5%) between MSK and CRS. The proportion of patients reporting level 5 is noticeably high among the CRS patients for usual activities (24.5%). This is because these patients attend that clinic because of difficulties in carrying out their usual activities, suggesting good face validity for the EQ-5D-5L.

Figures 2 and 3 show the distributions of values for all patients and the 3 treatment groups, with imposed kernel estimates. The null hypothesis of no skewness and kurtosis for each distribution is rejected at the 1% level; all of the distributions are negatively skewed. The MVS data, unlike the EVS data, exhibit a noticeable gap between the values for 11111 and the next highest value profile. For CRS patients only, the kernel estimates based on the MVS data suggest a possible 2-group distribution, like that found in EQ-5D-3L data. Although there is no observable gap between these groups, there is also a noticeable change in the slope of the estimated probability density function of the distribution at around 0.5. These

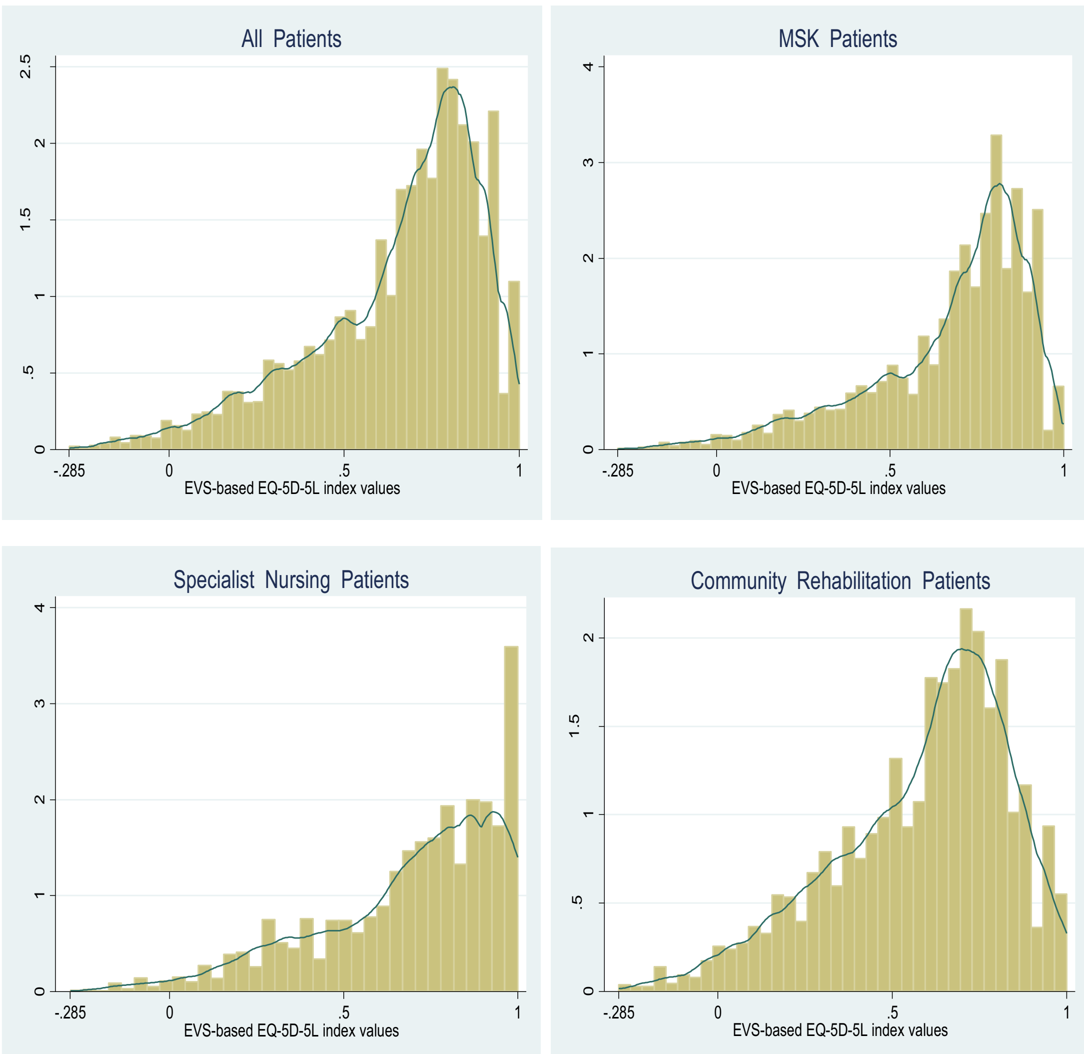

Fig. 2 – Distributions of EVS-based EQ-5D-5L values for all patients and 3 treatment groups. EVS, English value set.

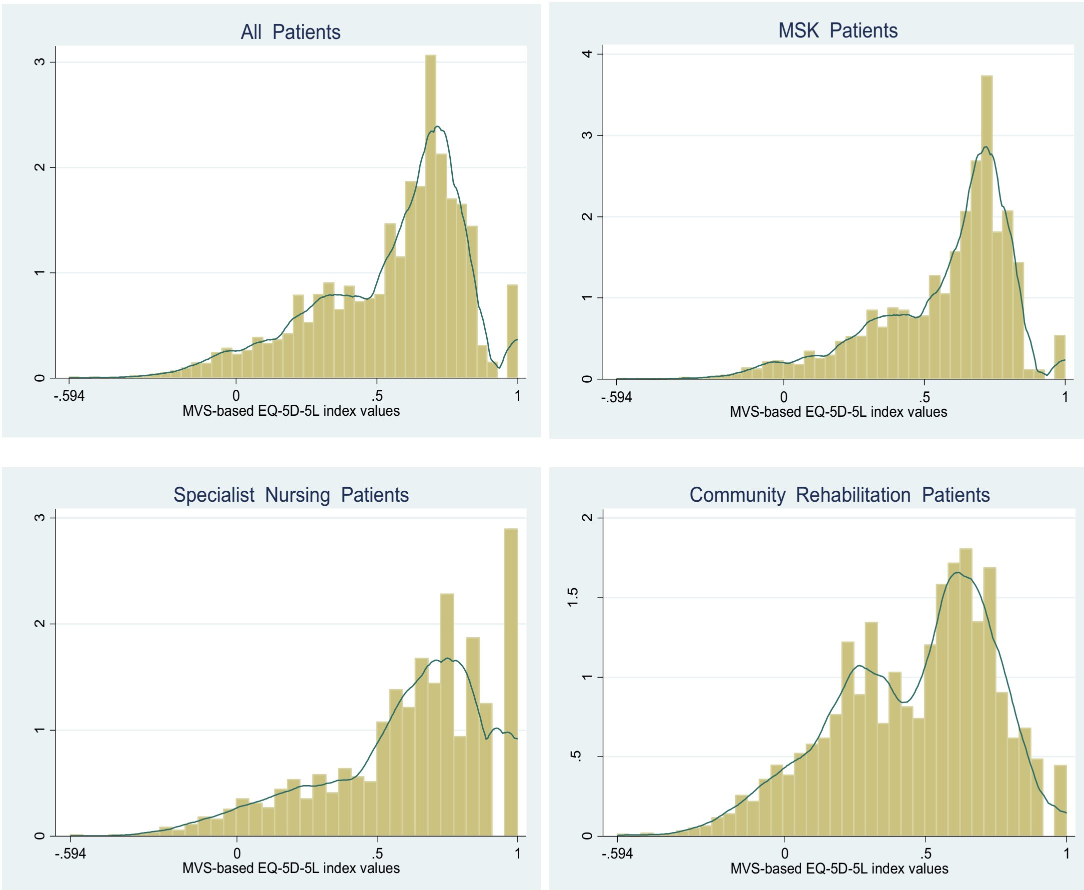

Fig. 3 – Distributions of MVS-based EQ-5D-5L values for all patients and 3 treatment groups. MVS, mapped value set.

suggest that the MVS values may inherit some of the characteristics of the EQ-5D-3L values on which they are based.

The results from the cluster analyses are given in the Appendix (see Supplemental Materials found at https://doi.org/10.1016/j.jval.2018.08.012). They were not conclusive and contained some inconsistencies, and they were very dependent on judgments made by analysts rather than clear and specific criteria. There was again some evidence that the MVS may generate 2 clusters, as with the EQ-5D-3L. The results also suggested that the EVS might generate clusters, although the number of clusters differed between patient groups.

Discussion

The overall conclusions are that, unlike for the EQ-5D-3L, we found no evidence for clustering of EQ-5D-5L values arising from the classification system and no strong or consistent evidence of clustering arising from a directly estimated value set, the EVS. The conclusion about the impact of the classification system is based on the results of analyzing the 3125 profiles data (Table 1) and the profiles used by the 3 patients' groups (Tables 2 and 3). The conclusion about the impact of the value set is based on the distributions of values (Figs. 2 and 3) and results of the cluster analysis on 3 patients' groups (see Appendix in Supplemental Materials found at https://doi.org/10.1016/j.jval.2018.08.012). There was clearer evidence of clustering using the MVS, 2 being the optimal number of clusters as with the EQ-5D-3L, suggesting that the MVS inherits some of the characteristics of the 3L value set from which it is derived. The clusters that were found for the EVS were very different from the MVS clusters. This suggests that although the EQ-5D-5L classification system is superior, in that it is less likely to generate artifactual clusters, clusters may still result from using value sets that have built-in tendencies to generate them.

Cluster analysis proved to be a useful exploratory tool, but a limitation of its use in our study is that judgments, rather than exact criteria, are involved in deciding the robust number of clusters. The evidence that it offers about whether value sets generate clusters is extremely weak; the methods appear to be more suited to specifying more exactly known clusters than detecting unknown clusters.

The data source limits the generalizability of our findings, being restricted to 3 specific patient samples. The characteristic 2-group distribution for EQ-5D-3L values has been found in a wide range of populations, but the evidence about the 5L values distribution is at its early stage, and the patient groups analyzed in this study are quite different from those analyzed by Parkin et al[2] for the EQ-5D-3L. More empirical evidence is needed with data from different population groups before generalizable conclusions about the distribution of the EQ-5D-5L values can be drawn.

This study demonstrates the importance of undertaking careful exploratory analysis of EQ-5D data before its use in different applications, such as health technology assessment and healthcare management processes involving patient-reported outcome measurement.[18] Any statistical techniques used should take account of features of the distribution of the data, such as clustering, to ensure that inferences drawn are valid and reliable.

More empirical research about the distributions of the EQ-5D-5L profiles and values in different patient and population groups is needed.

Heterogeneity of patient response is observed in many situations.[19–21] Individual patients might self-select into specific treatments based on observed and unobserved characteristics that cause patients to respond to the same treatment differently.[22] Potential uses of the methods described in this study are to provide a means of identifying the characteristics of different groups of patients pre-treatment and post-treatment, to use that information to predict which patients might benefit the most from treatment, and to investigate whether there are groups of patients where it appears treatment is less successful.

Supplemental Materials

Supplementary data associated with this article can be found in the online version at https://doi.org/10.1016/j.jval.2018.08.012.

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