ORIGINAL PAPER



Health-related quality of life measured with the EQ-5D-5L: estimation of normative index values based on a representative German population sample and value set

Thomas Grochtdreis¹ · Judith Dams¹ · Hans-Helmut König¹ · Alexander Konnopka¹

Received: 8 February 2019 / Accepted: 23 April 2019 / Published online: 27 April 2019 © Springer-Verlag GmbH Germany, part of Springer Nature 2019

Abstract

Background The generic and preference-based instrument EQ-5D is available in a five-response levels version (EQ-5D-5L). A value set for the EQ-5D-5L based on a representative sample of the German population has recently been developed. The aim of this study was to estimate normative values of the EQ-5D-5L index for Germany, and to examine associations between the EQ-5D-5L and selected sociodemographic factors.

Methods The analysis was based on a representative sample (n = 4998) of the German general adult population in 2014. Participants had to rate their health-related quality of life on the EQ-5D-5L descriptive system as well as on a visual analogue scale (EQ-VAS). Normative values of the EQ-5D-5L index were estimated for selected sociodemographic characteristics. For the examination of associations between EQ-5D-5L index scores and selected sociodemographic factors, multivariate regression analyses were used.

Results The mean EQ-5D-5L index score of the total sample was 0.88 (SD 0.18), corresponding to an overall mean EQ-VAS score of 71.59 (SD 21.36). Female gender and increasing age were associated with a lower EQ-5D-5L index score (p < 0.001). Higher education, full-time employment and private health insurance were associated with a higher EQ-5D-5L index score (p < 0.001).

Conclusion This was the first study to estimate normative values of the EQ-5D-5L index for Germany based on a representative sample. The German normative values of the EQ-5D-5L are comparable to those reported for other countries. However, the mean EQ-5D-5L index score of the total sample was worse than those of the samples of studies from other countries.

Keywords EQ-5D · Population norms · Quality of life · Cost-utility analysis

JEL Classification $I10 \cdot I30 \cdot J11$

Background

Health economic evaluation is nowadays a central component of health technology assessments for supporting reimbursement decisions throughout Europe. The health economic perspective is a key to health technology assessments, as healthcare expenditure is believed to increase while there is a trend towards budgetary constraints in healthcare [1]. The majority of European countries recommend cost-utility analyses in methodological guidelines as preferred analysis type for health economic evaluations [2].

In cost-utility analyses, health-related quality of life (HrQoL) is usually combined with a specific amount of time spent in a given health state into a single measure of effectiveness, namely quality-adjusted life years (QALYs). HrQoL is represented by utilities measured on a theoretical scale from 0 to 1, with 0 being defined as a health state corresponding to death and 1 being defined as full health [3]. One widely used generic instrument for estimating utilities is the EQ-5D that recently has been revised from a three-response levels version (EQ-5D-3L) to a five-response levels version (EQ-5D-3L) to a five-response levels version (EQ-5D-5L) to increase sensitivity for detecting clinically important differences in HrQoL and to reduce

Thomas Grochtdreis t.grochtdreis@uke.de

¹ Department of Health Economics and Health Services Research, Hamburg Center for Health Economics, University Medical Center Hamburg-Eppendorf, Martinistr. 52, 20246 Hamburg, Germany

potential ceiling effects [4]. Besides other questionnairebased instruments for the derivation of HrQoL, the EQ-5D is the majorly recommended instrument throughout European countries [2].

The EQ-5D-5L consists of the five dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/ depression. The dimensions are divided into the five ordinal levels 'no problems', 'slight problems', 'moderate problems', 'severe problems' and 'extreme problems' [4]. Based on these five dimensions and five levels, the EQ-5D-5L is able to describe $5^5 = 3125$ different health states. To link the 3125 possible unique health states derived from the EQ-5D-5L with utilities, a set of preference valuations of the general population regarding different health states was derived and used to predict EQ-5D-5L index scores [5]. Recently, such a value set for EQ-5D-5L has been developed for Germany [6]. The German value set allows to assign EQ-5D-5L index scores to each of the health states ranging from -0.661(extreme problems in all 5 dimensions) to 1 (no problems in any dimension). As the German value set allows assigning negative EQ-5D-5L index scores, utilities that represent HrQoL worse than death are possible.

So far, certain studies are planned that intend to use the EQ-5D-5L for the economic analysis as measure of effectiveness (e.g., [7–9]). Yet, to be able to compare HrQoL of patients with a specific disorder or disease, e.g., derived from cost-utility analyses, with the HrQoL of the general population, normative values need to be derived and presented for different subgroups based on sociodemographic characteristics. Furthermore, German normative values of the EQ-5D-5L index are needed to adapt model-based economic evaluations to better reflect the German population and its characteristics and ultimately inform policy to improve health resources allocation [10–12].

To date, no normative values of the EQ-5D-5L based on societal preferences in a representative German sample have been published. Earlier publications focused on psychometric properties and normative values of the EQ-5D-5L in a representative German sample based on crude sum scores of the EQ-5D-5L response levels, or the visual analog scale of the EQ-5D (EQ-VAS) only [13, 14], or on normative values in representative samples of other countries, such as South Australia [15], Spain [11] or Poland [10]. Other publications focused on normative values of the EQ-5D-5L in samples of patients, such as asthma patients [16] or patients with chronic obstructive pulmonary disease [17].

Therefore, the primary aim of this study was to estimate normative values of the EQ-5D-5L for Germany based on a representative population sample and the recently developed societal preferences. A secondary aim of this study was to examine associations between HrQoL, represented by EQ-5D-5L utility scores and EQ-VAS scores, and selected sociodemographic factors.

Methods

Sample

The study is based on a cross-sectional phone survey conducted among 5005 participants of the German general adult population [18]. To select telephone numbers of households randomly and to ensure representativeness, they were drawn from an existing telephone sample comprising of registered and generated telephone numbers [19] proportional to the federal state residential structure, stratified by community size. Data collection took place from March to April 2014. Of the total 5005 participants, 4998 participants that had complete data for the EQ-5D-5L were included in this study. Observations were weighted according to age, gender, education and state of residence to increase representativeness of the results for the German general adult population. The German micro-census was used to generate a design weight that compensates underrepresented and overrepresented observations regarding the respective characteristics. Due to weighing, the total sample included in this study augmented to n = 5001. A more detailed description of the sample and the weighting can be found elsewhere [18].

Measures

The generic EQ-5D-5L was used to assess HrQoL [4]. The EQ-5D-5L consists of five questions (items) for selfclassification of current problems in health by five ordinal levels. Furthermore, it consists of a visual analogue scale (EQ-VAS) that assesses subjective HrQoL on a scale ranging from 0 (worst imaginable health state) to 100 (best imaginable health state) [20].

Sociodemographic characteristics collected in the survey were age, gender, marital status, educational attainment, employment status, type of health insurance, area of residence and size of municipality. Age was categorized into the seven categories 18-24, 25-34, 35-44, 45-54, 55-64, 65–74 and \geq 75 years. Furthermore, the number of medical conditions was calculated. For this purpose, participants were asked whether a doctor has ever diagnosed one of the following diseases: lung diseases, diabetes, other metabolic diseases, chronic pain, diseases of the digestive tract, cancer, cardiac and circulatory diseases, skin diseases, osteoporosis, mental disorders, joint diseases, injuries and intoxications, flu, urogenital diseases, neurological diseases, dental diseases or eye diseases. To maintain practicability of the survey, diagnoses were restricted to the most frequent (chronic) conditions or disease groups reported in common German surveys [18, 21–23].

Statistical analysis

Descriptive statistics were estimated for sociodemographic characteristics and number of medical conditions. Furthermore, descriptive statistics were estimated for item responses in EQ-5D-5L dimensions, the top 75% most frequently reported EQ-5D-5L health states and mean EQ-5D-5L index scores by sociodemographic characteristics and by gender. Correlation between EQ-5D-5L index score and the EQ-VAS score was evaluated with Spearman's rank correlation coefficient (ρ). A weak correlation was defined by $\rho < 0.30$, a moderate correlation by $0.30 \ge \rho < 0.50$ and a strong correlation by $\rho \ge 0.50$ [24].

To examine associations between EQ-5D-5L index scores, EQ-VAS scores and selected sociodemographic factors, a generalized linear model (GLM) with a Poisson family and log link function was used [25]. This model takes into account the skewed distribution and the heteroscedasticity of EO-5D-5L index scores and EO-VAS scores [26, 27]. As the Poisson family of the GLM is only defined for non-negative integers in the dependent variable, the EQ-5D-5L disutility score (1-EQ-5D-5L index score) was used as dependent variable [15]. Following an earlier study that focused on normative values in representative samples of South Australia, the variables gender, categorized age and education attainment were entered into Model 1 [15]. In Model 2, the variables number of medical conditions, type of health insurance, employment status, and marital status were further added based on a backward stepwise multivariate analysis. From a model with a full set of potential explanatory variables, variables were manually considered for subtraction by a sequence of GLMs based on p values (deleted variables: smoking status, federal state and community size). For the Models 3 and 4, the EQ-VAS score was used as dependent variable, the regression model and the independent variables were chosen according to the Models 1 and 2, respectively.

All analyses were performed using Stata/SE 15.0 (Stata-Corp, TX, USA). All applied statistics were two-sided. In total, 32 tests for statistical significance of group differences in sociodemographic characteristics and mean EQ-5D-5L index scores, and one Spearman's rank correlation were conducted. Therefore, all tests were assessed at the 0.0016 (0.05/32) alpha level, following Bonferroni's correction for multiple significance tests to avoid a type I error [28].

Results

In the total weighted sample (n = 5001), 52% were female and the mean age was 51 years. Female participants were slightly older than males (52 vs. 49 years, p < 0.001). Of all participants, 49% were married or in a partnership, whereas 29% were never married. Furthermore, 39% of all participants reported a low level of qualification and 42% reported that they were not employed or retired. One or two medical conditions were reported by 29% and 17% of the participants, respectively, whereas three or more medical conditions were reported by 18% of the participants. Characteristics of the total sample are presented in Table 1.

The most frequent item response for all EQ-5D-5L dimensions was 'No problems' in the total sample. Frequencies of item responses in each EQ-5D-5L dimension by age categories are presented in Table 5 ("Appendix 1"). The most frequently reported EQ-5D-5L health states were '11111' (n=1530; 31%), '11121' (n=715; 14%) and '21121' (281; 6%). Those health states corresponded to a mean EQ-5D-5L index score of 1.00, 0.94 and 0.92 and were associated with a mean EQ-VAS score of 84.54, 78.10 and 72.98, respectively. In total, 371 individual health states of 3125 possible patterns (12%) were reported by the participants. The majority of the sample (75%) was represented by 23 out of all possible health states (Table 2).

Both, the EQ-5D-5L index scores and the EQ-VAS scores were left-skewed with a clustering at 1.00 (n = 1530; 31%) and 80 (n = 944; 19%), respectively. Furthermore, the EQ-VAS scores clustered at 90 (n = 711; 14%), 70 (n = 579; 12%) and 50 (n = 552; 11%; Fig. 1). The mean EQ-5D-5L index score of the total sample was 0.88 (SD 0.18), corresponding to an overall mean EQ-VAS score of 71.59 (SD 21.36). The EQ-5D-5L index scores and the EQ-VAS scores were strongly positively correlated (ρ = 0.60, p < 0.001).

Females had a statistically significantly lower mean EQ-5D-5L index score than men [0.86 (SD 0.16) vs. 0.90 (SD 0.20); p < 0.001]. There was no difference in mean EQ-VAS scores between genders. The mean EQ-5D-5L index scores were statistically significantly different for participants in different age categories (p < 0.001) and dropped from 0.94 (SD 0.08) for participants aged 18–24 to 0.80 (0.28) for participants aged 75 years and older. Mean EQ-5D-5L index scores differed statistically significantly in subsamples with different marital statuses, levels of education and employment statuses (all with p < 0.001). The mean EQ-5D-5L index scores by sociodemographic characteristics and by gender and the mean EQ-5D-5L index scores by age categories and by number of medical conditions are reported in Table 3 and in Table 6 ("Appendix 2"), respectively.

In Model 1, female gender was statistically significantly associated with a higher EQ-5D-5L disutility score (and, therefore, a lower EQ-5D-5L index score). The age categories from 35 to 44 years onwards were statistically significantly associated with increasingly higher EQ-5D-5L disutility scores (p < 0.001). Compared with low education, middle and high educations were statistically significantly associated with decreasingly lower EQ-5D-5L disutility scores (p < 0.001). By entering further variables in Model

Table 1 Characteristics of the sample

	Total sample ($n = 4998$)	Total sample (weighted; $n = 5001$)	Male gender (weighted; $n = 2417$)	Female gen- der (weighted; n=2584)
Gender, female: <i>n</i> (%)	2660 (53.22)	2584 (51.67)		
Age: mean (SD)	54.73 (18.52)	50.70 (18.54)	49.42 (17.82)**	51.90 (19.11)**
18–24: <i>n</i> (%)	380 (7.60)	474 (9.47)	244 (10.08)*	230 (8.90)*
25–34: <i>n</i> (%)	516 (10.32)	722 (14.43)	359 (14.86)	363 (14.03)
35–44: <i>n</i> (%)	626 (12.53)	776 (15.51)	389 (16.10)	386 (14.95)
45–54: <i>n</i> (%)	876 (17.53)	996 (19.92)	502 (20.79)	494 (19.10)
55–64: <i>n</i> (%)	920 (18.41)	787 (15.73)	388 (16.04)	399 (15.45)
65–74: <i>n</i> (%)	891 (17.83)	654 (13.08)	308 (12.74)	346 (13.39)
≥75: <i>n</i> (%)	789 (15.79)	593 (11.86)	227 (9.37)	366 (14.18)
Marital status				
Never married: <i>n</i> (%)	1377 (27.77)	1449 (29.21)	767 (31.93)**	683 (26.66)**
Married/in partnership: n (%)	2088 (42.11)	2442 (49.21)	1341 (55.86)	1101 (42.98)
Separated/divorced: n (%)	725 (14.62)	544 (10.97)	185 (7.70)	359 (14.03)
Widowed: n (%)	768 (15.4)	527 (10.61)	108 (4.51)	418 (16.33)
Education				
Low qualification: <i>n</i> (%)	1361 (27.28)	1947 (39.02)	951 (39.41)	996 (38.65)
Middle qualification: n (%)	1621 (32.49)	1461 (29.28)	640 (26.54)	821 (31.86)
High qualification: n (%)	1959 (39.27)	1481 (29.69)	769 (31.89)	712 (27.63)
No graduation/other: n (%)	48 (0.96)	100 (2.01)	52 (2.16)	48 (1.86)
Employment				
Full-time employed: n (%)	1733 (34.70)	1892 (37.86)	1264 (52.29)**	628 (24.34)**
Part-time employed: n (%)	506 (10.13)	566 (11.33)	101 (4.20)	465 (18.01)
Marginally employed: n (%)	185 (3.70)	230 (4.61)	68 (2.83)	162 (6.28)
Not employed: n (%)	484 (9.69)	578 (11.57)	242 (10.02)	336 (13.02)
Retired: n (%)	1913 (38.31)	1517 (30.36)	650 (26.90)	867 (33.60)
Apprenticeship/other: n (%)	173 (3.46)	213 (4.27)	91 (3.76)	122 (4.74)
Federal states				
Old federal states: n (%)	3935 (78.73)	3981 (79.61)	1930 (79.84)	2052 (79.40)
New federal states and Berlin: n (%)	1063 (21.27)	1019 (20.39)	487 (20.16)	532 (20.60)
Size of municipality				
<2000: <i>n</i> (%)	303 (6.06)	322 (6.44)	166 (6.88)	156 (6.03)
2000 to < 5000: <i>n</i> (%)	397 (7.94)	451 (9.02)	219 (9.05)	232 (8.99)
5000 to < 20,000: <i>n</i> (%)	1345 (26.91)	1422 (28.44)	689 (28.52)	733 (28.38)
20,000 to < 50,000: <i>n</i> (%)	886 (17.73)	895 (17.89)	420 (17.37)	475 (18.37)
50,000 to < 100,000: n (%)	458 (9.16)	438 (8.75)	208 (8.60)	230 (8.90)
100,000 to < 500,000: n (%)	750 (15.01)	712 (14.25)	351 (14.52)	361 (13.99)
\geq 500,000: <i>n</i> (%)	859 (17.19)	761 (15.21)	364 (15.0)	397 (15.35)
Medical conditions: mean (SD)	1.38 (1.52)	1.31 (1.49)	1.16 (1.37)**	1.45 (1.58)**
0 medical conditions: n (%)	1735 (34.91)	1842 (37.09)	964 (40.18)**	878 (34.20)**
1 medical condition: n (%)	1449 (29.15)	1432 (28.85)	737 (30.72)	695 (27.10)
2 medical conditions: n (%)	823 (16.56)	821 (16.53)	361 (15.05)	460 (17.92)
3 + medical conditions: n (%)	963 (19.38)	871 (17.53)	337 (14.05)	533 (20.79)

Some numbers do not sum up to the total number of observations or total number of weighted population due to missing answers

SD standard deviation; comparisons of mean age and mean number of medical conditions by gender were analyzed using the survey designadjusted Wald test; comparisons of categorical characteristics by gender were analyzed using the Pearson Chi² statistic corrected for the survey design

 $^*p\!\le\!0.0016$

 $**p \le 0.001$

Table 2 Most frequently reported EQ-5D-5L health states with index scores and EQ-VAS scores (weighted sample; n = 5001)

EQ-5D-5L health state	n	%	Cumu- lative %	Mean EQ- 5D-5L index score	Mean EQ- VAS score
11111	1530	30.60	30.60	1.00	84.52
11121	715	14.29	44.89	0.94	78.10
21121	281	5.62	50.51	0.92	72.98
11112	214	4.27	54.78	0.97	81.27
11122	132	2.64	57.42	0.91	74.18
21111	107	2.14	59.57	0.97	75.21
11131	98	1.96	61.53	0.89	67.97
11221	76	1.51	63.04	0.91	71.04
21221	69	1.39	64.43	0.88	66.32
11211	67	1.34	65.77	0.96	81.93
31121	62	1.24	67.01	0.90	69.71
21122	52	1.04	68.05	0.89	68.78
31221	50	0.99	69.05	0.87	62.23
31231	48	0.96	70.01	0.81	55.70
21131	43	0.85	70.86	0.87	68.22
21231	34	0.68	71.55	0.83	54.81
31131	33	0.66	72.21	0.85	62.04
11113	32	0.64	72.84	0.92	74.09
11222	28	0.55	73.40	0.88	70.63
11123	26	0.53	73.92	0.86	69.55
11223	25	0.50	74.43	0.83	64.54
21211	25	0.50	74.92	0.94	75.20
21222	24	0.49	75.41	0.85	63.97

2, the association between female gender and increased EQ-5D-5L disutility score became statistically insignificant. However, number of medical conditions was statistically significantly associated with increasingly higher EQ-5D-5L disutility scores (p < 0.001). Furthermore, the EQ-5D-5L disutility scores were statistically significantly lower in participants with private health insurance or private supplementary insurance(s) (p < 0.001). Not employed participants had statistically significantly higher EQ-5D-5L disutility scores than full-time employed participants (p < 0.001). In the Models 3 and 4, using the EQ-VAS score as dependent variable, the associations were in correspondence with the Models 1 and 2, respectively (Table 4).

Discussion

The aims of this study were to estimate normative values for the EQ-5D-5L for Germany and to examine associations between the EQ-5D-5L and selected sociodemographic factors. This was the first study that reported normative values based on a representative German population sample and the recently developed German value set [6].

The overall mean EO-5D-5L index score of the representative German population sample was 0.88. This score was slightly worse than EQ-5D-5L index scores for representative population samples in South Australia (0.91) [15], Spain (0.90) [11] and Poland (0.89) [10]. The EQ-5D-5L index scores for both, the Spanish and Polish population were estimated by use of an interim value set, based on a mapping algorithm. According to Eurostat, in 2013, self-perceived health and overall life satisfaction were higher in Spain and lower in Poland when compared to Germany [29]. One earlier study calculated a crude overall mean EQ-5D-5L sum score of 91.5 based on equally weighted EQ-5D-5L health states with presumed equal widths of the response levels of a representative German population sample [13]. Another study reported an overall mean EQ-VAS score of 85.1, also based on a representative German population sample. Compared with the overall mean EQ-VAS score of the current study (71.6), the HrQoL in the other study seems to be considerably better [14]. However, the sample of the study by Hinz et al. [13] was younger (47 years vs. 51 years); yet, both samples were comparable with respect to gender, education and employment. The samples of those studies consisted of 2555 participants surveyed in 2011 [13] and 2040 participants surveyed in 2015 [14], respectively, and thus, not more than half the size compared to the current study.

In the sample of this study, almost one-third of the respondents (31%) reported an EQ-5D-5L health state with no problems across all dimensions. Such a ceiling effect of the EQ-5D-5L has already been reported elsewhere for German population samples. In two of those studies, even more than half to almost two-thirds of the respondents (60-64%) reported an EQ-5D-5L health state with no problems across all dimensions [13, 14]. According to an earlier study, a ceiling effect of 15% or higher of the population analyzed should be considered as serious [30]. Yet, based on the current representative German population sample, Konnopka and König [31] ascertained that the occurrence of a ceiling effect of the EQ-5D-5L is strongly related to morbidity. Accordingly, it was implied that EQ-5D-5L health states with no problems across all dimensions observed in population samples resulted from a correct measurement of good health rather than from a measurement limitation. For example, two-thirds of the German adult population did not report limitations in activities of daily living in the national health interview survey in 2014/2015 [32]. The EQ-VAS score of the respondents that reported an EQ-5D-5L health state with no problems across all dimensions in the current study was above 90.00 in more than half of the cases (mean EQ-VAS score 84.52).

Another 14% and 6% of the respondents reported having slight pain or discomfort only (health state '11121') or both, having slight pain or discomfort and slight problems in walking about (health state '21121'), respectively. Thus, in



Fig. 1 Scatterplot of EQ-5D-5L index scores and EQ-VAS scores (n=4997; weighted sample), histograms of EQ-5D-5L index scores (n=5001, weighted sample) and EQ-VAS scores (n=4997; weighted sample)

more than half of the current population sample, HrQoL was explained by just three health states. In total, HrQoL was explained by 12% of all possible EQ-5D-5L health states. Two earlier studies were able to explain HrQoL using 50 and 63 different EQ-5D-3L health states in representative German population samples. In contrast, in the sample of this study, 370 different EQ-5D-5L health states have been used to explain HrQoL. Therefore, it is assumed that the discriminatory power of the EQ-5D-5L descriptive system has improved compared with the EQ-5D-3L [33, 34].

Female participants from the new German Federal States and Berlin had statistically significantly lower EQ-5D-5L index scores than females from old German Federal States (-0.04; p < 0.001). Yet, female participants from the new German Federal States and Berlin were statistically significantly older (+6.44 years; p < 0.001) and had statistically significantly more medical conditions (+19.28%; p=0.0016). Furthermore, female participants from new and old German Federal States differed statistically significantly in educational and employment status (data not shown). Notwithstanding, results of the German Federal Health Surveys show that middle-aged to old-aged females from old German Federal States stated good to very good subjective health more often compared with females from new German Federal States throughout all three surveys [35].

The multivariate regression analyses were able to reproduce findings from other studies regarding associations of the EQ-5D-5L index and sociodemographic factors [15, 36]. Older age, female gender and low level of educational status were independently associated with a lower EQ-5D-5L index score. The association between age and EQ-5D-5L index score diminished after additionally controlling for medical conditions.

Strengths and limitations

The first strength of this study was a large sample size and the weighting of the observations to ensure representativeness of the results. Second, this study was able to examine associations between HrQoL, selected sociodemographic Health-related quality of life measured with the EQ-5D-5L: estimation of normative index values...

Table 3Mean EQ-5D-5L indexscores by sociodemographiccharacteristics by gender(weighted sample)

	Total		Male g	gender	Femal	e gender
	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)
Total sample	5001	0.88 (0.18)	2417	0.90 (0.16)**	2584	0.86 (0.20)**
Age category, years						
18–24	474	0.94 (0.08)**	244	0.94 (0.09)**	230	0.94 (0.08)**
25–34	722	0.92 (0.11)	359	0.93 (0.12)	363	0.92 (0.10)
35–44	776	0.90 (0.14)	389	0.92 (0.11)	386	0.88 (0.17)
45–54	996	0.87 (0.17)	502	0.89 (0.15)	494	0.86 (0.19)
55–64	787	0.87 (0.20)	388	0.87 (0.19)	399	0.86 (0.20)
65–74	654	0.85 (0.24)	308	0.86 (0.22)	346	0.85 (0.25)
≥75	593	0.80 (0.28)	227	0.84 (0.23)	366	0.77 (0.31)
Marital status						
Never married	1449	0.90 (0.16)**	767	0.90 (0.16)**	683	0.90 (0.17)**
Married/in partnership	2442	0.89 (0.15)	1341	0.90 (0.14)	1101	0.88 (0.15)
Separated/divorced	544	0.84 (0.26)	185	0.85 (0.24)	359	0.83 (0.27)
Widowed	527	0.82 (0.29)	108	0.84 (0.24)	418	0.81 (0.30)
Education						
Low qualification	1947	0.84 (0.18)**	951	0.86 (0.16)**	996	0.82 (0.20)**
Middle qualification	1461	0.89 (0.18)	640	0.90 (0.15)	821	0.88 (0.20)
High qualification	1481	0.93 (0.15)	769	0.93 (0.13)	712	0.92 (0.16)
No graduation/other	100	0.88 (0.17)	52	0.92 (0.09)	48	0.84 (0.13)
Employment						
Full-time employed	1892	0.92 (0.13)**	1264	0.92 (0.11)**	628	0.90 (0.16)**
Part-time employed	566	0.90 (0.15)	101	0.91 (0.16)	465	0.90 (0.14)
Marginally employed	230	0.91 (0.11)	68	0.89 (0.11)	162	0.92 (0.11)
Not employed	578	0.89 (0.16)	242	0.88 (0.18)	336	0.89 (0.15)
Retired	1517	0.82 (0.27)	650	0.84 (0.24)	867	0.80 (0.29)
Apprenticeship/other	213	0.91 (0.13)	91	0.91 (0.14)	122	0.91 (0.12)
Federal states						
Old federal states	3981	0.88 (0.18)**	1930	0.90 (0.16)	2052	0.87 (0.19)**
New federal states and Berlin	1019	0.86 (0.20)	487	0.89 (0.16)	532	0.83 (0.23)
Size of municipality						
<2000	322	0.89 (0.18)	166	0.90 (0.14)	156	0.87 (0.21)
2000 to < 5000	451	0.89 (0.15)	219	0.91 (0.12)	232	0.87 (0.18)
5000 to < 20,000	1422	0.88 (0.17)	689	0.90 (0.15)	733	0.87 (0.19)
20,000 to < 50,000	895	0.87 (0.20)	420	0.89 (0.17)	475	0.85 (0.22)
50,000 to < 100,000	438	0.90 (0.15)	208	0.91 (0.12)	230	0.88 (0.18)
100,000 to < 500,000	712	0.87 (0.19)	351	0.88 (0.18)	361	0.86 (0.20)
≥500,000	761	0.87 (0.21)	364	0.89 (0.19)	397	0.86 (0.23)
Medical conditions						
0 medical conditions	1823	0.95 (0.08)**	964	0.95 (0.08)**	878	0.95 (0.07)**
1 medical condition	1432	0.90 (0.15)	737	0.91 (0.13)	695	0.89 (0.17)
2 medical conditions	821	0.85 (0.18)	361	0.86 (0.18)	460	0.85 (0.19)
3 or more medical conditions	871	0.72 (0.28)	337	0.74 (0.26)	533	0.71 (0.29)

SD standard deviation; comparisons of mean EQ-5D-5L index scores by gender and by categorical characteristics were analyzed using the survey design-adjusted Wald test

 $*p \le 0.0016$

 $**p \le 0.001$

	,		,			•) ,	•			
Variable	EQ-5D-	5L disutility scores	~				EQ-VAS	scores				
	Model 1	(n = 4989)		Model 2	(n = 4920)		Model 1	(n = 4984)		Model 2	(n = 4915)	
	Beta	95% CI	<i>p</i> value	Beta	95% CI	<i>p</i> value	Beta	95% CI	<i>p</i> value	Beta	95% CI	<i>p</i> value
Gender (ref. male)												
Female	0.20	0.11; 0.30	< 0.001	0.06	-0.03; 0.16	0.150	-0.00	-0.02;0.01	0.621	0.02	0.01; 0.04	0.009
Age category (ref. 18-24)												
25-34	0.30	0.03; 0.58	0.032	0.41	0.15; 0.66	0.002	-0.05	-0.08; -0.01	0.005	-0.08	-0.11; -0.04	< 0.001
35-44	0.49	0.24; 0.75	< 0.001	0.62	0.34; 0.90	< 0.001	- 0.06	-0.10; -0.03	< 0.001	-0.10	-0.14; -0.06	< 0.001
45-54	0.71	0.48; 0.95	< 0.001	0.62	0.39; 0.85	< 0.001	- 0.12	-0.15; -0.08	< 0.001	-0.12	-0.16; -0.08	< 0.001
55-64	0.71	0.47; 0.95	< 0.001	0.43	0.19; 0.67	< 0.001	-0.16	-0.19; -0.12	< 0.001	-0.12	-0.16; -0.07	< 0.001
65-74	0.76	0.52; 1.00	< 0.001	0.25	-0.03; 0.52	0.080	-0.17	-0.21; -0.14	< 0.001	-0.07	-0.13; -0.01	0.020
\geq 75	1.03	0.80; 1.26	< 0.001	0.42	0.14; 0.70	0.003	-0.25	-0.29; -0.21	< 0.001	-0.12	-0.18; -0.06	< 0.001
Education (ref. low qualification)												
Middle qualification	-0.25	-0.37; -0.14	< 0.001	-0.18	-0.28; -0.08	< 0.001	0.04	0.02; 0.07	0.001	0.03	0.00; 0.05	0.020
High qualification	-0.59	-0.72; -0.47	< 0.001	- 0.39	-0.51; -0.28	< 0.001	0.12	0.09; 0.14	< 0.001	0.08	0.06; 0.10	< 0.001
No graduation/other	0.16	-0.16; 0.48	0.335	-0.01	-0.26; 0.27	0.970	0.07	0.00; 0.14	0.045	0.09	0.01; 0.16	0.021
Medical conditions (ref. 0 medical c	conditions											
1 medical condition				0.68	0.55; 0.80	< 0.001				- 0.09	-0.10; -0.07	< 0.001
2 medical conditions				0.98	0.85; 1.11	< 0.001				-0.18	-0.21; -0.15	< 0.001
3 or more medical conditions				1.57	1.45; 1.69	< 0.001				-0.32	-0.36; -0.29	< 0.001
Health insurance (ref. statutory heal	lth insurar	ice)										
Statutory health insurance plus private supplementary insurance(s)				- 0.23	-0.33; -0.13	< 0.001				0.04	0.02, 0.06	< 0.001
Private health insurance				-0.30	-0.45; -0.16	< 0.001				0.04	0.02, 0.07	< 0.001
No health insurance/other				0.41	-0.11; 0.92	0.120				- 0.02	-0.10; 0.07	0.650
Employment (ref. full-time employe	(pe											
Part-time employed				0.00	-0.16; 0.16	0.999				- 0.02	-0.04; 0.02	0.330
Marginally employed				- 0.06	-0.30; 0.19	0.650				-0.01	-0.05; 0.03	0.710
Not employed				0.31	0.13; 0.50	0.001				-0.05	-0.07; -0.02	0.005
Retired				0.42	0.26; 0.58	< 0.001				-0.10	-0.15; -0.06	< 0.001
Apprenticeship/other				0.28	0.04; 0.51	0.021				- 0.03	-0.08; 0.01	0.120
Marital status (ref. never married)												
Married/in partnership				- 0.25	-0.37; -0.13	< 0.001				0.05	0.03; 0.08	< 0.001
Separated/divorced				- 0.04	-0.18; 0.10	0.580				0.03	- 0.01; 0.06	0.140

Table 4 Generalized linear models of EQ-5D-5L disutility scores and EQ-VAS scores and selected sociodemographic characteristics (weighted sample)

Variable	EQ-5D	-5L disutility score	s				EQ-VAS	scores				
	Model	1 (<i>n</i> =4989)		Model 2	(n = 4920)		Model 1	(n = 4984)		Model 2	(n=4915)	
	Beta	95% CI	<i>p</i> value	Beta	95% CI	<i>p</i> value	Beta	95% CI	<i>p</i> value	Beta	95% CI	<i>p</i> value
Widowed				- 0.17	-0.32; -0.01	0.033				0.04	- 0.00; 0.08	0.068
Constant	-2.66	-2.89; -2.43	< 0.001	-3.25	-3.49; -3.01	< 0.001	4.34	4.30; 4.37	< 0.001	4.41	4.37; 4.45	< 0.001
CI confidence interval												
301d indicates statistically sign	nificant coeffic	ient $(p < 0.05)$										

Table 4 (continued)

factors and especially number of medical conditions by multivariate analyses. However, some limitations of the study have to be mentioned. First, there is a noteworthy chance of selection bias and recall bias due to the phone surveyapproach. Despite weighting of the observations, there is some evidence for reduced representativeness of participants aged 65–74 years. Second, the enquiry of medical conditions was restricted to the most frequent, mainly chronic conditions or disease groups. It is possible that medical conditions not enquired in the survey used for this study introduced measurement error to the multivariate regression analyses and skewed the results. Yet, the association between HrQoL and the number of medical conditions in the multivariate analyses was statistically significant.

Conclusion

This study was able to provide normative values of the EQ-5D-5L based on societal preferences in a representative German sample. The normative values of the EQ-5D-5L can be used for model-based economic evaluations for the estimation of QALYs and for comparison of specific patient groups with the German general population. Further research is needed to investigate the association between HrQoL derived from the EQ-5D-5L and medical conditions using medical diagnoses of more chronic conditions and disease groups.

Acknowledgements We thank Maria Meyer for her support in visualization and data presentation as well as two anonymous referees for their helpful comments.

Funding This study was funded by the German Federal Ministry of Education and Research (BMBF; Grant number: 01EH1101B).

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Appendix 1

See Table 5.

 Table 5
 Frequencies of item responses in each EQ-5D-5L dimension by age category in percent (%; weighted sample)

	Total (<i>n</i> =5001)	18–24 (<i>n</i> =474)	25–34 (<i>n</i> =722)	35–44 (<i>n</i> =776)	45–54 (<i>n</i> =996)	55–64 (<i>n</i> =787)	65–74 (<i>n</i> =654)	≥ 75 (n=593)
Mobility								
No problems	64.57	87.86	84.56	76.00	65.03	56.06	50.47	32.78
Slight problems	17.67	10.14	9.50	14.41	18.43	21.30	22.67	26.31
Moderate prob- lems	10.86	1.58	3.51	6.37	10.99	13.75	16.08	23.25
Severe problems	6.32	0.43	2.29	3.22	5.34	7.95	9.46	16.01
Extreme problems	0.58	0	0.14	0	0.21	0.94	1.32	1.66
Self-care								
No problems	92.80	99.01	97.30	97.11	91.83	93.34	89.52	81.28
Slight problems	4.29	0.78	1.81	2.54	5.13	4.27	5.93	9.20
Moderate prob- lems	1.92	0.21	0.79	0.28	2.36	1.88	2.68	5.25
Severe problems	0.74	0	0.10	0.08	0.54	0.29	1.67	2.87
Extreme problems	0.25	0	0	0	0.14	0.22	0.20	1.41
Usual activities								
No problems	71.67	79.23	79.01	78.06	70.80	71.09	69.78	52.65
Slight problems	15.79	14.71	14.05	12.42	15.16	14.64	18.75	22.47
Moderate prob- lems	8.71	4.80	4.79	6.95	9.60	10.80	7.71	15.73
Severe problems	2.91	0.53	1.70	1.63	3.87	3.12	3.06	5.87
Extreme problems	0.93	0.74	0.46	0.93	0.57	0.34	0.70	3.29
Pain/discomfort								
No problems	43.08	54.57	54.70	46.89	40.72	39.93	37.09	29.52
Slight problems	35.78	41.68	32.56	35.76	35.46	34.15	36.99	36.37
Moderate prob- lems	14.74	2.24	10.48	11.61	16.64	18.74	16.95	23.06
Severe problems	5.72	1.52	2.26	5.47	6.25	6.56	7.44	9.70
Extreme problems	0.69	0	0	0.28	0.93	0.62	1.53	1.35
Anxiety/depression								
No problems	74.89	74.61	73.33	76.60	74.20	76.31	75.82	72.99
Slight problems	16.22	20.83	18.53	14.55	15.85	15.24	14.87	15.31
Moderate prob- lems	6.54	3.31	5.60	6.39	7.82	5.22	7.74	8.74
Severe problems	1.72	0.60	1.95	1.91	1.31	2.86	1.05	2.00
Extreme problems	0.64	0.65	0.59	0.55	0.82	0.36	0.53	0.97

Appendix 2

See Table 6.

Tuble of medical by 5D 5D match beores by age categories by number of medical conditions (weighted same	npie
---	------

	Total		0 medi	cal conditions	1 medi	cal condition	2 mec	lical conditions	3 or more medical conditions	
	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)
Total sample	5001	0.88 (0.18)	1842	0.95 (0.08)**	1432	0.90 (0.15)**	821	0.85 (0.18)**	871	0.72 (0.28)**
Age category,	years									
18–24	474	0.94 (0.08)**	259	0.96 (0.06) **	135	0.94 (0.09)**	63	0.89 (0.10)	10	0.76 (0.19)
25-34	722	0.92 (0.11)	375	0.96 (0.05)	217	0.91 (0.09)	83	0.87 (0.15)	45	0.74 (0.20)
35–44	776	0.90 (0.14)	372	0.96 (0.07)	239	0.89 (0.16)	87	0.84 (0.16)	77	0.77 (0.20)
45-54	996	0.87 (0.17)	378	0.95 (0.07)	275	0.91 (0.12)	166	0.85 (0.13)	165	0.67 (0.26)
55-64	787	0.87 (0.20)	211	0.95 (0.09)	227	0.90 (0.16)	154	0.88 (0.14)	191	0.74 (0.27)
65–74	654	0.85 (0.24)	157	0.95 (0.10)	178	0.88 (0.21)	125	0.87 (0.20)	190	0.73 (0.29)
≥ 75	593	0.80 (0.28)	90	0.89 (0.16)	161	0.86 (0.21)	143	0.80 (0.30)	193	0.70 (0.32)

SD standard deviation; comparisons of mean EQ-5D-5L index scores by medical conditions and by age categories were analyzed using the survey design-adjusted Wald test

 $*p \le 0.0016$

 $**p \le 0.001$

References

- European Commission: Strengthening of the EU Cooperation on Health Technology Assessment (HTA). http://ec.europa.eu/smart -regulation/roadmaps/docs/2016_sante_144_health_technology _assessments_en.pdf (2016). Accessed 12 Sep 2018
- Heintz, E., Gerber-Grote, A., Ghabri, S., Hamers, F.F., Rupel, V.P., Slabe-Erker, R., Davidson, T.: Is there a European view on health economic evaluations? Results from a synopsis of methodological guidelines used in the EUnetHTA partner countries. Pharmacoeconomics (2016). https://doi.org/10.1007/s4027 3-015-0328-1
- Drummond, M.F., Sculpher, M.J., Torrance, G.W., O'Brien, B.J., Stoddard, G.L.: Methods for the Economic Evaluation of Health Care Programmes. Oxford University Press, Oxford (2005)
- Herdman, M., Gudex, C., Lloyd, A., Janssen, M., Kind, P., Parkin, D., Bonsel, G., Badia, X.: Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). Qual. Life Res. (2011). https://doi.org/10.1007/s11136-011-9903-x
- Devlin, N.J., Shah, K.K., Feng, Y., Mulhern, B., van Hout, B.: Valuing health-related quality of life: an EQ-5D-5L value set for England. Health Econ. (2018). https://doi.org/10.1002/hec.3564
- Ludwig, K., Graf von der Schulenburg, J.-M., Greiner, W.: German value set for the EQ-5D-5L. Pharmacoeconomics (2018). https://doi.org/10.1007/s40273-018-0615-8
- Watzke, B., Haller, E., Steinmann, M., Heddaeus, D., Härter, M., König, H.-H., Wegscheider, K., Rosemann, T.: Effectiveness and cost-effectiveness of telephone-based cognitive-behavioural therapy in primary care: study protocol of TIDe—telephone intervention for depression. BMC Psychiatry (2017). https://doi. org/10.1186/s12888-017-1429-5
- Gensichen, J., Schultz, S., Adrion, C., Schmidt, K., Schauer, M., Lindemann, D., Unruh, N., Kosilek, R.P., Schneider, A., Scherer, M., Bergmann, A., Heintze, C., Joos, S., Briegel, J., Scherag, A., König, H.-H., Brettschneider, C., Schulze, T.G., Mansmann, U., Linde, K., Lühmann, D., Voigt, K., Gehrke-Beck, S., Koch, R., Zwissler, B., Schneider, G., Gerlach, H., Kluge, S., Koch, T., Walther, A., Atmann, O., Oltrogge, J., Sauer, M., Schnurr, J., Elbert, T.: Effect of a combined brief narrative exposure therapy with case management versus treatment as usual in primary care

for patients with traumatic stress sequelae following intensive care medicine: study protocol for a multicenter randomized controlled trial (PICTURE). Trials (2018). https://doi.org/10.1186/s1306 3-018-2853-7

- Schultz, K., Seidl, H., Jelusic, D., Wagner, R., Wittmann, M., Faller, H., Nowak, D., Schuler, M.: Effectiveness of pulmonary rehabilitation for patients with asthma: study protocol of a randomized controlled trial (EPRA). BMC Pulm. Med. (2017). https ://doi.org/10.1186/s12890-017-0389-3
- Golicki, D., Niewada, M.: EQ-5D-5L Polish population norms. Arch. Med. Sci. (2017). https://doi.org/10.5114/aoms.2015.52126
- Garcia-Gordillo, M.A., Adsuar, J.C., Olivares, P.R.: Normative values of EQ-5D-5L: in a Spanish representative population sample from Spanish Health Survey, 2011. Qual. Life Res. (2016). https://doi.org/10.1007/s11136-015-1164-7
- van den Berg, B.: SF-6D population norms. Health Econ. (2012). https://doi.org/10.1002/hec.1823
- Hinz, A., Kohlmann, T., Stöbel-Richter, Y., Zenger, M., Brähler, E.: The quality of life questionnaire EQ-5D-5L: psychometric properties and normative values for the general German population. Qual. Life Res. (2014). https://doi.org/10.1007/s1113 6-013-0498-2
- Huber, M.B., Felix, J., Vogelmann, M., Leidl, R.: Health-related quality of life of the general German population in 2015: results from the EQ-5D-5L. Int. J. Environ. Res. Public Health (2017). https://doi.org/10.3390/ijerph14040426
- McCaffrey, N., Kaambwa, B., Currow, D.C., Ratcliffe, J.: Healthrelated quality of life measured using the EQ-5D-5L: South Australian population norms. Health Qual. Life Outcomes (2016). https://doi.org/10.1186/s12955-016-0537-0
- Collado Mateo, D., García Gordillo, M.A., Olivares, P.R., Adsuar, J.C.: Normative values of EQ-5D-5L for diabetes patients from Spain. Nutr. Hosp. (2015). https://doi.org/10.3305/ nh.2015.32.4.9605
- Garcia-Gordillo, M.Á., Collado-Mateo, D., Olivares, P.R., Adsuar, J.C., Merellano-Navarro, E.: A cross-sectional assessment of health-related quality of life among patients with chronic obstructive pulmonary disease. Iran. J. Public Health 46, 1046–1053 (2017)

- Grupp, H., König, H.-H., Konnopka, A.: Health care utilisation and costs in the general population in Germany. Health Policy (2016). https://doi.org/10.1016/j.healthpol.2015.11.005
- Arbeitskreis Deutscher Markt- und Sozialforschungsinstitute e.V. (ADM): Die ADM Stichproben f
 ür Telefonbefragungen. ADM, Frankfurt am Main
- 20. The EuroQol Group: EuroQol—a new facility for the measurement of health-related quality of life. Health Policy (1990). https ://doi.org/10.1016/0168-8510(90)90421-9
- Ellert, U., Kurth, B.M.: Gesundheitsbezogene Lebensqualität bei Erwachsenen in Deutschland. Bundesgesundheitsblatt, Gesundheitsforschung, Gesundheitsschutz (2013). https://doi. org/10.1007/s00103-013-1700-y
- 22. Koch-Institut, Robert: Ergebnisse der Studie » Gesundheit in Deutschland aktuell 2010«. Beiträge zur Gesundheitsberichterstattung des Bundes. Robert Koch-Institut, Berlin (2012)
- TNS Infratest Sozialforschung: SOEP 2013—Erhebungsinstrumente 2013 (Welle 30) des Sozio-oekonomischen Panels: Personenfragebogen, Altstichproben. SOEP Survey Papers 180: Series A. DIW/SOEP, Berlin (2014)
- 24. Cohen, J.: Statistical Power Analysis for the Behavioral Sciences. L. Erlbaum Associates, Hillsdale (1988)
- 25. McCullagh, P., Nelder, J.A.: Generalized Linear Models. Chapman and Hall, London (1989)
- de Jong, P., Heller, G.Z.: Generalized Linear Models for Insurance Data. Cambridge University Press, Cambridge (2008)
- Manning, W.G., Basu, A., Mullahy, J.: Generalized modeling approaches to risk adjustment of skewed outcomes data. J. Health Econ. (2005). https://doi.org/10.1016/j.jhealeco.2004.09.011
- Dickhaus, T.: Classes of multiple test procedures. In: Dickhaus, T. (ed.) Simultaneous Statistical Inference: With Applications in the Life Sciences, pp. 29–45. Springer, Berlin (2014)
- 29. Eurostat: Quality of Life. Facts and Reviews. https:// ec.europa.eu/eurostat/documents/3217494/6856423/

KS-05-14-073-EN-N/742aee45-4085-4dac-9e2e-9ed7e9501f23 (2015). Accessed 18 Jan 2019

- McHorney, C.A., Tarlov, A.R.: Individual-patient monitoring in clinical practice: are available health status surveys adequate? Qual. Life Res. 4, 293–307 (1995)
- Konnopka, A., König, H.-H.: The "no problems"-problem: an empirical analysis of ceiling effects on the EQ-5D 5L. Qual. Life Res. (2017). https://doi.org/10.1007/s11136-017-1551-3
- von der Lippe, E., Fehr, A., Lange, C.: Gesundheitsbedingte Einschränkungen bei alltäglichen Aktivitäten in Deutschland. J. Health Monit. (2017). https://doi.org/10.17886/ RKI-GBE-2017-059
- König, H.-H., Bernert, S., Angermeyer, M.C.: Gesundheitszustand der deutschen Bevölkerung: Ergebnisse einer repräsentativen Befragung mit dem EuroQol-Instrument. Gesundheitswesen (2005). https://doi.org/10.1055/s-2005-857991
- Hinz, A., Klaiberg, A., Brähler, E., König, H.-H.: Der Lebensqualitatsfragebogen EQ-5D: Modelle und Normwerte fur die Allgemeinbevölkerung. Psychother. Psychosom. Med. Psychol. (2006). https://doi.org/10.1055/s-2005-867061
- 35. Atzpodien, K., Bergmann, E., Bertz, J., Busch, M., Eis, D., Ellert, U., Fuchs, J., Gaber, E., Gutsche, J., Haberland, J., Hagen, C., Hapke, U.: Beiträge zur Gesundheitsberichterstattung des Bundes. 20 Jahre nach dem Fall der Mauer: Wie hat sich die Gesundheit in Deutschland entwickelt? Robert Koch-Institut, Berlin (2009)
- 36. Feng, Y., Devlin, N., Herdman, M.: Assessing the health of the general population in England: how do the three- and five-level versions of EQ-5D compare? Health Qual. Life Outcomes (2015). https://doi.org/10.1186/s12955-015-0356-8

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.