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Original article

Evaluating the correspondence between the EQ-5D-5L and disease severity and quality of life in adults and adolescents with cystic fibrosis

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ABSTRACT

Background: The EQ-5D is the recommended measure to capture health-related quality of life (HRQoL), recognised for use in health technology appraisal bodies. In order to assess whether it is appropriate to use the EQ-5D for making decisions about the cost-utility of treatments in cystic fibrosis (CF), this study assesses the performance of the EQ-5D-5L in adults and adolescents with CF.
Method: This was a cross-sectional observational survey study of patients with CF attending a single large CF centre. Participants were asked to complete a survey that included two HRQoL measures; the EQ-5D-5L and CF Quality of Life (CFQoL) questionnaires.
Results: Among 213 participants, the median EQ-5D-5L index score was 0.76 (IQR 0.66 – 0.84) and the visual analogue (EQ-VAS) was 70 (60 – 80). Both the EQ-5D index and EQ-VAS discriminated between disease severity based on lung function ($p = 0.01$ and $p < 0.01$, respectively) and pulmonary exacerbation ($p = 0.02$ and $p < 0.01$, respectively); however, EQ-VAS differentiated between more lung function severity groups compared to EQ-5D index. The EQ-5D-5L demonstrated convergent validity as its dimensions, index score, and EQ-VAS had significant correlations with most CFQoL domains. Though, EQ-VAS significantly predicted more domains of CFQoL (4 domains) compared to EQ-5D index (only 1 domain).
Conclusion: The generic EQ-5D-5L performed adequately in discriminating between CF disease severity, and its index score and EQ-VAS had moderate correlations with CFQoL. However, using a complementary condition-specific measure alongside the EQ-5D-5L can provide better insight of HRQoL in CF and benefit the process of cost-utility analysis.

1. Introduction

Cystic Fibrosis (CF) is a multi-system chronic condition that progressively worsens over time. Despite this, the survival rate has improved over the past decade for people with CF (pwCF) due to the improvement of treatments that prevent disease progression and maintain patient health [1]. The UK CF Registry currently includes 10,908 pwCF, and predicted that 50 % of pwCF born today will live to at least 53.3 years [2]. With continuous enhancements being made in the area of CF treatments, the CF population is expected to rise by 50 % in 2025 compared to 2010, owing to improved life expectancy [3]. Along with the constant rise in CF survival and the introduction of new, very high-cost treatments over the upcoming years, the healthcare system will face a substantial economic burden.

Healthcare resources are finite and there is a growing recognition that economic justifications are often required to support the allocation of healthcare interventions [4], as providing extra resources to one area means fewer resources available elsewhere [5]. Indeed cost-utility analysis is used by many decision-making bodies (e.g. National Institute for Health and Care Excellence (NICE) in the UK and Haute Autorité de Santé (HAS) in France) to inform decisions about the

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provision of new treatments [6,7]. Health-related quality of life (HRQoL) captured via a utility measure enables the benefits of diverse interventions to be compared on a common (utility) scale [5]. Utility values are commonly derived from preference-based generic HRQoL questionnaires like EQ-5D, which employs different dimensions to describe health states that can then be assigned values on a utility scale [8]. However, generic HRQoL measures like EQ-5D may have limited sensitivity in capturing small changes in a specific disease compared to condition-specific measures due to their generic nature [9,10]. Therefore, it is essential to evaluate the performance of generic measures to ensure their suitability for use in cost-utility analysis in this population [7].

There is a limited literature evaluating the appropriateness of EQ-5D to, for example, capture HRQoL changes in different health states for pwCF. While some studies have reported EQ-5D's (mostly 3L version) ability to discriminate pulmonary exacerbation (PEx) disease severity [11-13], concerns remain about its sensitivity toward lung disease severity and fully capturing health dimensions relevant to pwCF [12-15]. As the EQ-5D-5L's performance, which is supposedly more sensitive to changes in health than 3L [16], has not yet been properly evaluated in CF; this study aims to assess EQ-5D-5L validity in terms of discriminating between disease severities and its convergent validity with the condition-specific CF quality of life questionnaire (CFQoL) in pwCF.

2. Methods

2.1. Study population

This is a cross-sectional observational survey study pwCF aged 16 years and older who were registered in the UK CF Registry. The sample was recruited between July 2020 to March 2021 from a single large CF centre. The data for this study came from the Living with CF (LwCF) study which is part of an RfPB study funded by NIHR Grant (PB-PG-1217−20,018). It aimed to collect information about the quality of life for pwCF registered in the UK CF Registry and link it to the CF Trust Data Registry. The participants completed a survey that included two measures of HRQoL: a generic (EQ-5D-5L) and condition-specific (CFQoL) measure [16,17]. Candidates were invited to participate in the study when they were sent their annual routine clinical visit invitation. Several methods to fill the survey were available for the outpatient clinic and inpatient participants (online, PDF, and paper versions). A £10 financial incentive was offered to the participants for completing the survey. Ethical approval was gained for the LwCF study (REC: 16/NW/0514), and an informed consent (online or paper version) was sought from participants before filling in the survey.

2.2. Measures

2.2.1. Demographic and clinical variables

For those who consented, demographic (age, gender, ethnicity, education level, marital status, employment status) and clinical (height, weight, body mass index (BMI), forced expired volume in 1 second (FEV1), percent predicted FEV1 (ppFEV1), CF-related diabetes (CFRD), and number of IV antibiotic courses and days) variables were extracted from the closest encounter data within the UK CF Registry and/or their CF centre's electronic medical record.

2.2.2. Quality of life measures

2.2.2.1. EQ-5D-5L

The EQ-5D-5L is a generic preference-based HRQoL measure [18]. Participants are asked to describe their health on five dimensions; mobility, self-care, usual activity, pain/discomfort, anxiety/depression, where each dimension has five levels. A health state description is thereby provided e.g. 11111 would denote no problems on all five dimensions [19]. Utility values (referred to as the EQ-5D index score) were then assigned to these EQ-5D-5L health states through mapping to the 3L version of the EQ-5D [20], as per NICE latest recommendation at the time the analysis began [21]. EQ-5D index scores generated as such range between − 0.59 to 1, where 1 is (full health) and 0 is (death) [22], and provide a common scale on which to assess health states, and compare the benefits of different treatments [22].

As part of the EQ-5D-5L, respondents are also asked to complete the EQ-VAS, a visual analogue scale that enables a visual reporting of health state on the day the measure is completed [19]. The EQ-VAS uses a 0 to 100 scale to evaluate the quality of life, were 100 is "The best health you can imagine" and 0 is "The worst health you can imagine" [22].

2.2.2.2. Cystic fibrosis quality of life questionnaire

The CFQoL is a validated condition-specific HRQoL measure for adults and adolescents with CF [17]. It contains 9 domains (physical functioning, social functioning, treatment issues, chest symptoms, emotional functioning, concerns for the future, interpersonal relationships, body image, career concerns) and each of their items have 6 levels. Each domain provides a single score to assess HRQoL areas related to pwCF. Each domain consists of items that evaluate specific issues associated with that domain; therefore, CFQoL can assess HRQoL on a domain-by-domain and item-by-item basis offering more specificity and comparability. CFQoL uses a 0 to 100 scale system for each domain, where a high score indicates better quality of life in each domain [17]. No overall score was generated for CFQoL in this study.

2.3. Statistical analysis

SPSS version 25 was used to assign the scores for the measures and for data analysis. All available cases i.e. those which had complete data on the specific variables in question were included in the analysis. Descriptive statistics were derived for demographic, clinical, and HRQoL variables. Shapiro-Wilk tests were carried out to determine the normality of the data distribution of all the variables.

We generated two sets of disease severity groups. One set with three groups based on the severity of lung function (*mild*: ppFEV1 ≥70 %, *moderate*: ppFEV1 40 − 69 %, and *severe*: ppFEV1 <40 %) [23]; the other set with two groups based on the occurrence of PEx in the year prior to enrolment (*No PEx*: no IV antibiotic courses, and *PEx*: ≥1 IV antibiotic courses). Kruskal-Wallis test was used to assess the variance in EQ-5D index score and EQ-VAS between lung function severity groups; significance achieved if p-value <0.05. When a significant difference existed, multiple Mann-Whitney tests with Bonferroni correction (significance achieved if p-value <0.01) were carried out to determine which groups had significant differences. The variance in EQ-5D index score and EQ-VAS between PEx disease severity groups was assessed using Mann-Whitney test; significance achieved if p-value <0.05.

To assess convergent validity, we ran Spearman's Rank correlation tests on the EQ-5D-5L (index score, EQ-VAS, and dimensions) and CFQoL domains. We considered correlation coefficient strong >0.7, moderate between 0.7 and 0.3, and weak <0.3 [24]. Before running the correlational tests between the EQ-5D-5L and CFQoL domains, we hypothesised the domains that would have significant (strong to moderate) correlations based on the similarity of concepts covered by the domains' items, and assumed that the rest of the domains would show weak to no correlation. This facilitated the evaluation of the association between like and unlike domains of both HRQoL measures.

The relationship between EQ-5D-5L and CFQoL domains was also assessed using multiple linear regression models, after testing the assumptions underlying the models. Two models were used; the first model had the EQ-5D index score as the dependent variable, while the second model had the EQ-VAS as the dependent variable. Both

Table 1
Demographic and clinical data.

	Total		*Total*
Age (*n* = 213)		**Height (cm) (*n* = 213)**	
Mean (SD)	36.5 (12.1)	Mean (SD)	167.7 (10)
Median (IQR)	35 (26.6 – 43.9)	Median (IQR)	168 (160–176)
Range	18 – 77.7	Range	143 – 193
Gender, n (%), (*n* = 213)		**Weight (kg) (*n* = 212)** *	
Female	113 (53.1 %)	Mean (SD)	64.4 (13.7)
Male	100 (46.9 %)	Median (IQR)	62 (55 – 72.5)
Ethnicity, n (%), (*n* = 213)		Range	38 – 123
White	202 (94.8 %)	**BMI (kg/m2) (*n* = 212)** *	
Other	11 (5.1 %)	Mean (SD)	22.8 (3.8)
Education level, n (%), (*n* = 213)		Median (IQR)	22.2 (20.5 – 24.5)
University	92 (42.5 %)	Range	15.7 – 39.7
College	66 (31 %)	**ppFEV1 (*n* = 206)** **	
High school	14 (6.6 %)	Mean (SD)	66.5 (22.9)
Less than high school	12 (5.6 %)	Median (IQR)	66 (47.9 – 79.8)
Not known	29 (13.6 %)	Range	19.6 – 134.8
Marital status, n (%), (*n* = 213)		**FEV1 in litres (*n* = 206)** **	
Married	84 (39.4 %)	Mean (SD)	2.3 (0.9)
Single	84 (39.4 %)	Median (IQR)	2.2 (1.6 – 2.9)
Long-term partner	25 (11.7 %)	Range	0.6 – 6.20
Divorced	3 (1.4 %)	**Number of IV abx course (*n* = 213)**	
Separated	2 (0.9 %)	Mean (SD)	0.83 (1.2)
Widowed	2 (0.9 %)	Median (IQR)	0 (0 - 1)
Not known	13 (6.1 %)	Range	0 – 7
Employment status, n (%), (*n* = 213)		**Number of IV abx days (*n* = 213)**	
Full-time	101 (47.4 %)	Mean (SD)	15.1 (26.4)
Part-time	43 (20.2 %)	Median (IQR)	0 (0 - 17)
Student	30 (14.1 %)	Range	0 – 191
Unemployed	17 (8 %)	**CFRD, n (%), (*n* = 212)** ***	
Homemaker	4 (1.9 %)	CFRD	64 (30.2 %)
Retired	5 (2.3 %)		
Disabled	1 (0.5 %)	No CFRD	148 (69.8 %)
Not known	12 (5.6 %)		

* One participant did not have a reported weight and BMI.
** Seven participants did not have a reported ppFEV1 and FEV1 in litres.
*** One participant had missing data in CFRD diagnosis.
Abbreviation: BMI = body mass index, ppFEV1 = precent predicted forced expired volume in 1 second, I V = intravenous, abx = antibiotic, CFRD = CF-related diabetes.

models had the nine CFQoL domains as the predictor variables, and controlled for age and gender.

3. Results

3.1. Descriptive statistics

A total of 213 responses were received. Table 1 illustrates the sample's demographic and clinical data. Shapiro-Wilk test showed that all the variables did not follow a normal distribution except for height. Table 2 illustrates descriptive analysis for HRQoL measures. The distribution of all the HRQoL measures (EQ-5D index score, EQ-VAS and the CFQoL domains) is shown in the supplementary material (Figs. 1 and 2).

3.2. Quality of life and disease severity

Between the lung severity groups, we found significant difference in both EQ-5D index score and EQ-VAS ($p = 0.01$ and $p < 0.01$, respectively). Pairwise comparisons with a Bonferroni correction showed that the index score was only significantly different between mild and moderate groups ($p = 0.01$), while EQ-VAS was significantly different between mild and severe groups ($p < 0.01$) and moderate and severe groups ($p = 0.01$). We found significant difference in both the index score and EQ-VAS between the PEx severity groups ($U = 4229.5$, $p = 0.02$), and ($U = 4092.5$, $p < 0.01$), respectively. Table 3 shows descriptive statistics for the index score and EQ-VAS across the lung function and PEx disease severity groups.

Table 2
HRQoL descriptive statistics.

	Total (*n* = 213)
EQ-5D-5L (index score)	
Mean (SD)	0.74 (0.17)
Median (IQR)	0.76 (0.66 – 0.84)
Range	0.03 – 1.00
EQ-VAS	
Mean (SD)	69.8 (16.9)
Median (IQR)	70 (60 – 80)
Range	10 – 100
CFQoL domains	
Physical Functioning	
Mean (SD)	70.9 (24.4)
Median (IQR)	78 (54.7 – 90)
Range	0 – 100
Social Functioning	
Mean (SD)	49.4 (32.4)
Median (IQR)	40 (22.5 – 80)
Range	0 – 100
Treatment Issues	
Mean (SD)	62.6 (28.1)
Median (IQR)	66.6 (46.6 – 86.6)
Range	0 – 100
Chest Symptoms	
Mean (SD)	69.9 (27.3)
Median (IQR)	75 (55 – 92.5)
Range	0 – 100
Emotional Functioning	
Mean (SD)	70.3 (25)
Median (IQR)	77 (56.2 – 90)
Range	0 – 100
Concerns for the future	
Mean (SD)	48.1 (24.1)
Median (IQR)	46.6 (30 – 63.3)
Range	0 – 100
Interpersonal Relationship	
Mean (SD)	50.8 (24.5)
Median (IQR)	50 (34 – 70)
Range	0 – 100
Body Image	
Mean (SD)	66.3 (26.7)
Median (IQR)	73.3 (46.6 – 86.6)
Range	0 – 100
Career concerns	
Mean (SD)	57.4 (30)
Median (IQR)	60 (35 – 80)
Range	0 – 100

3.3. Convergent validity

Table 4 shows the correlation coefficients between EQ-5D-5L and CFQoL domains. Among EQ-5D-5L dimensions, usual activity and anxiety/depression had significant correlations with all CFQoL domains; however, the correlations were moderate to weak. EQ-5D-5L's self-care dimension had significant correlations with only 7 CFQoL domains. As for CFQoL, the physical functioning domain demonstrated the highest (moderate) correlations with 4 dimensions of the EQ-5D-5L, the index score, and EQ-VAS compared to the other CFQoL domains. Concerns of the future domain exhibited the least significant correlations with EQ-5D-5L dimensions, showing correlation only with anxiety/depression ($r_s = -0.36$, $p < 0.01$) and usual activity ($r_s = -0.15$, $p = 0.02$).

Most of the correlations showed significance, but no strong correlations ($r_s > 0.7$) were detected. All hypothesised strong correlations had moderate strength ($r_s = 0.3 - 0.7$). Most of the domains that we predicted to have moderate correlation met the hypotheses except for anxiety/depression and treatment issues ($r_s = -0.20$, $p < 0.001$); mobility and social functioning ($r_s = -0.24$, $p < 0.01$); and anxiety/depression and social functioning ($r_s = -0.23$, $p < 0.01$) which were weak.

Table 3
descriptive statistics for the EQ-5D-5L across the lung function and pulmonary exacerbation severity groups.

Disease severity	Number in group	Index score median (IQR)	p-value	EQ-VAS median (IQR)	p-value
Lung function					
Mild severity (ppFEV1 ≥70 %)	98	0.76 (0.72 – 0.87)	0.01*	75 (65 – 85)	<0.01*
Moderate severity (ppFEV1 40 - 69 %)	87	0.74 (0.62 – 0.83)		72 (55 – 80)	
Severe severity (ppFEV1 <40 %)	21	0.73 (0.60 – 0.81)		60 (50 – 70)	
Pulmonary exacerbation					
No PEx (0 courses)	116	0.76 (0.72 – 0.87)	0.02**	75 (65 – 85)	<0.01**
PEx (1 course or more)	97	0.72 (0.62 – 0.83)		70 (52.5 – 78.5)	

A total of 206 participants in the lung function groups – seven participants were not included in these groups due to the unavailability of their ppFEV1.
* Kruskal-Wallis tests' p-value. Post-hoc results for lung function groups: (utility value; mild vs. moderate "$p = 0.01$", EQ-VAS; mild vs. severe "$p < 0.01$" and moderate vs. severe "$p = 0.01$").

Table 4
Spearman's Rank correlation test results for EQ-5D-5L and CFQoL domains.

	Mobility	Self-care	Usual activity	Pain/ discomfort	Anxiety/ depression	Index score	EQ-VAS
Physical functioning	**−0.55****	**−0.42****	**−0.61****	**−0.45****	−0.17**	0.58**	0.50**
Social functioning	**−0.24****	−0.24**	−0.27**	−0.22**	**−0.23****	0.31**	0.30**
Treatment issues	−0.34**	−0.30**	−0.39**	−0.40**	**−0.20****	0.46**	0.41**
Chest symptom	−0.40**	−0.28**	**−0.35****	**−0.33****	−0.19**	0.41**,**	0.48**
Emotional functioning	−0.21**	−0.24**	−0.34**	**−0.38****	**−0.46****	0.50**	0.34**
Concerns for the future	−0.09	−0.12	−0.15*	−0.07	**−0.36****	0.20**	0.14*
Interpersonal relationships	−0.24**	−0.27**	−0.29**	−0.27**	**−0.40****	0.41**	0.24**
Body image	−0.18**	−0.13	−0.22**	−0.15*	−0.14*	0.21**	0.20**
Career concerns	−0.40**	−0.28**	−0.45**	−0.31**	**−0.30****	0.45**	0.29**

Bold values are those pairs of domains where we hypothesised strong correlations.
All correlations were negative due to the method each measure captures HEQoL (higher domain scores in CFQoL mean better HRQoL while lower domain scores in EQ-5D-5L mean better HRQoL), expect for utility value and EQ-VAS (higher score means better HRQoL).
* Correlation is significant at the 0.05 level (2-tailed).
** Correlation is significant at the 0.01 level (2-tailed).

Some associations that we did not predict to have correlations showed otherwise. Mobility had moderate correlations with treatment issue, chest symptoms, and career concerns ($r_s = -0.34$, $p < 0.01$; $r_s = -0.40$, $p < 0.01$; and $r_s = -0.40$, $p < 0.01$, respectively). Self-care was associated with treatment issues ($r_s = -0.30$, $p < 0.01$). Usual activity was correlated moderately with treatment issues, emotional functioning, and career concerns ($r_s = -0.39$, $p < 0.01$; $r_s = -0.34$, $p < 0.01$; and $r_s = -0.45$, $p < 0.01$, respectively). Pain/discomfort was associated with treatment issues and career concerns ($r_s = -0.40$, $p < 0.01$ and $r_s = -0.31$, $p < 0.01$, respectively). The rest of the correlations were significant but weak in strength.

3.4. *The relationship between EQ-5D-5L and CFQOL*

The results of the regression analysis carried out are presented in Table 5. Model 1 (index score as the outcome variable) demonstrated that using the CFQoL 9-domains would provide good estimates of index score ($F_{11,201} = 9.612$, $p < 0.01$), though, only physical functioning ($t = 3.7856$, $p < 0.01$) was a significant predictor of index score. A one unit increase in physical functioning was estimated to increase the EQ-5D index score by 0.003. In total, CFQoL domains explained 34.5 % of the variability in the index score.

Model 2 (EQ-VAS as the outcome variable) demonstrated that using the CFQoL 9-domains would provide good estimates of EQ-VAS ($F_{11,201} = 9.748$, $p < 0.01$), and that physical functioning ($t = 3.243$, $p < 0.01$), treatment issues ($t = 2.099$, $p = 0.03$), chest symptoms ($t = 2.680$, $p < 0.01$), and emotional functioning ($t = -2.675$, $p < 0.01$) were significant predictors of EQ-VAS. With one unit increase in physical functioning, EQ-VAS was estimated to increase by 0.237. With one unit increase in treatment issues, EQ-VAS was estimated to increase by 0.106 points. With one unit increase in chest symptoms, EQ-VAS was estimated to increase by 0.163 points. Also, with one unit increased in emotional functioning, EQ-VAS was estimated to decrease by 0.180 points. In total, CFQoL domains explain 34.8 % of the variability in the EQ-VAS.

4. Discussion

This study provides evidence that the EQ-5D-5L (index score and EQ-VAS) can discriminate between disease severity based on lung function and PEx. Also, it demonstrated convergent validity when its correlation with the CFQoL was tested. This study sample was representative of the population in the UK CF Registry (N = 10,908) in ppFEV1 (sample median; 66 %, population median; 76.4 %), BMI (sample median; 22.2, population median; 23.9), ethnicity (white ratio in sample; 94.8 %, white ratio in population; 92.1 %), and CFRD (sample ratio; 30.2 %, population ratio; 31 %) [2]. The UK CF Registry includes over 92 % of the CF population in the UK; therefore, strengthening the current study generalisability.

In spite of their generic nature, EQ-5D index score and EQ-VAS were able to discriminate between disease severities in CF. Both the index score and EQ-VAS declined with more exacerbation events, which concur with the current literature [11-13]. Most studies reported that the index score and EQ-VAS decline as the severity of lung function worsens (lower ppFEV1) [13,25]. However, Gold et al. [12] did not identify this association between the index score and

Table 5
the EQ-5D-5L and CFQoL regression model.

	Index score (Model 1)			EQ-VAS (Model 2)		
	Coefficient	95 % CI [lower, upper]	p-value	Coefficient	95 % CI [lower, upper]	p-value
Constant	0.424	[0.331, 0.518]	<0.001	41.953	[33.014, 50.893]	<0.001
Physical functioning	0.003	[0.001, 0.004]	**<0.001**	0.237	[0.093, 0.380]	**0.001**
Social functioning	0.000	[0.000, 0.001]	0.506	0.058	[−0.012, 0.128]	0.105
Treatment issues	0.001	[0.000, 0.002]	0.184	0.106	[0.006, 0.206]	**0.037**
Chest symptoms	−0.000	[−0.001, 0.001]	0.968	0.163	[0.043, 0.283]	**0.008**
Emotional functioning	−0.000	[−0.001, 0.001]	0.946	−0.180	[−0.313, - 0.047]	**0.008**
Concerns for the future	0.000	[−0.001, 0.001]	0.509	0.033	[−0.067, 0.133]	0.520
Interpersonal relationship	0.001	[−0.001, 0.002]	0.305	0.049	[−0.065, 0.164]	0.399
Body image	0.000	[−0.001, 0.001]	0.499	0.039	[−0.043, 0.121]	0.344
Career concerns	0.000	[−0.001, 0.001]	0.408	−0.065	[−0.161, 0.031]	0.184
Age	0.000	[−0.001, 0.002]	0.666	−0.029	[−0.194, 0.136]	0.731
Gender (female)	−0.004	[−0.046, 0.039]	0.865	2.077	[−1.996, 6.1469]	0.316
R^2	0.345			0.348		
Observation number	213			213		

Scoring guide: EQ-5D "Index score" (0−1 for death to full health), EQ-VAS (0 to 100 for worst to best imaginable health states).

ppFEV1, and their subsequent generalised linear regression model also supported this finding. In our study, EQ-VAS discriminated between more lung function severity groups (mild vs. severe; and moderate vs. severe) compared to the index score (mild vs. moderate), which agrees with Solem et al. [13] observations.

Our analysis showed that the index score correlated significantly with all the CFQoL domains; though, the correlations were moderate to weak (r_s<0.7). Bradley et al. [11] also found moderate to weak correlations between the index score (via EQ-5D-3L) and the condition-specific CFQ-R measure. In domain-by-domain analysis, most of EQ-5D-5L dimensions demonstrated significant correlations with CFQoL domains; concerns of the future and body image domains had the least significant associations with EQ-5D-5L dimensions. This is expected given that none of EQ-5D dimensions fall under these two domains' concepts. The physical functioning domain had the highest (but moderate) correlations with EQ-5D-5L dimensions (except for anxiety/depression), index score, and EQ-VAS compared to CFQoL other domains. This concur with Eidt-Koch et al. [26] findings as physical functioning domain of the CFQ had the highest correlations with most of EQ-5D-Y (youth version) dimensions compared to CFQ other domains. Moreover, CFQoL's social functioning domain had unanticipated weak correlations with EQ-5D-5L dimensions, which could be due to the unexpectedly low score on that domain. Our study was conducted during the COVID-19 pandemic outbreak, and everyone had to self-isolate especially high-risk group like CF; this likely explains the unusually low score of social functioning domain.

Similar to the index score, EQ-VAS had significantly moderate to weak correlations with all CFQoL domains. This agrees with Eidt-Koch et al. [26] findings about the correlation between EQ-VAS and the CFQ. In the multivariate analysis, more domains of CFQoL (physical functioning, treatment issues, chest symptoms, and emotional functioning) predicted EQ-VAS compared to the index score (only physical functioning). This indicates that the index score is not fully inclusive of some aspects of HRQoL, conversely more domains of the CFQoL predicted EQ-VAS (a scale of general health). Though, the negative direction of EQ-VAS and CFQoL's emotional functioning domain relationship was counter-intuitive to the expected finding in the model; this could be due to chance, given that the correlational test direction between them was the opposite (Table 4).

Physical functioning domain of CFQoL was the only domain that had a significant relationship with both the index score and EQ-VAS in both models. This is likely due to the concepts covered under the domain which resemble most of EQ-5D-5L dimensions. As shown in the correlational tests between EQ-5D-5L and CFQoL domains; mobility, usual activity, self-care, and pain/discomfort had moderate correlations with physical functioning, as all involve activity in some aspect. These findings indicate the impact of physical activity on quality of life in pwCF, which has been recognised previously [27]. The physical functioning domain of the CFQoL has been acknowledged as an independent predictor of survival in pwCF [28].

The generic EQ-5D-5L is part of the reference case developed by NICE i.e. a favoured method for estimating clinical effectiveness and monetary value [7]. It is able to generate a utility value, which is needed for cost-utility analysis / to inform decisions about the provision of new treatments. Our study showed that EQ-5D-5L index score was adequately able to discriminate between different CF disease severities and had moderate correlations with CFQoL domains. However, given its limited performance in differentiating between lung disease severities and estimating CFQoL domains (compared to EQ-VAS), it would be complementary to use it with a condition-specific measure (e.g. CFQoL and/or CFQ-R). With the EQ-5D as the primary economic outcome measure, the addition of a secondary condition-specific measure in clinical trials or economic evaluation of new interventions can ensure that potential benefits that may be missed when using the EQ-5D alone would be captured.

Our study is limited by its cross-sectional nature which prevented us from capturing HRQoL changes over time. Since this is the first study to compare EQ-5D-5L and CFQoL performances, it was hard to relate our findings to other studies. On the other hand, our study's demographics and clinical data were not very different from the data reported by the UK CF Registry, which strengthens the study's external validity. In future studies, it will be interesting to follow the changes of EQ-5D-5L over time and see whether it can capture changes in disease severity. The inclusion of a CF-specific measure like CFQoL can also provide a good reference to EQ-5D-5L to compare its performance.

5. Conclusions

The generic EQ-5D-5L performed adequately in capturing HRQoL in pwCF. It was able to discriminate between CF disease severity and had moderate associations with CFQoL. The addition of a CF-specific HRQoL measure in cost-utility analysis is recommended to provide a detailed assessment. Further longitudinal studies are needed to evaluate the ability of the EQ-5D-5L to capture changes in health states over time in pwCF.

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Declaration of competing interest

RA, JA, DO, RC, SC, NS, JW, DT, and GB have no direct conflicts of interest to declare in relation to this study. Outside of the submitted work, SC has served on advisory boards and/or given educational lectures for which she or her institution have received fees for (Vertex, Chiesi, and Profile Pharma). NS has served on advisory boards and/or given educational lectures for which he has received consultancy fees (Vertex, Gilead, Chiesi, Zambon, Roche, and Menarini).

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Supplementary materials

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