Health and Quality of Life Outcomes

REVIEW

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Tools used to measure quality of life in adults with cystic fibrosis– a systematic review

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Abstract

Background Measuring the quality of life in patients with cystic fibrosis is important, both in terms of assessing the implementation of new therapies and monitoring their effects, as well as the ongoing evaluation of patients' condition. The objective of this study is to present tools for measuring the quality of life in adult patients with cystic fibrosis, along with their characteristics and measurement properties.

Methods The systematic review was performed according to the PRISMA guidelines based on a previously prepared research protocol (PROSPERO: CRD42023491030). Searches were performed in Medline (via PubMed), Embase (via OVID), and Cochrane Library databases. In addition, manual searches of bibliographies from the studies included in the analysis and grey literature were performed. Quality assessment of the included studies was performed according to the guidelines of COnsensus-based Standards for the selection of health Measurement INstruments (COSMIN).

Results The systematic search identified 3,359 studies, of which 26 met the inclusion criteria for the analysis. Two publications were additionally included as a result of the manual search. A total of 16 tools for measuring the quality of life in adults with cystic fibrosis were identified, the measurement properties of which were presented in the included studies. Among these tools, the Cystic Fibrosis Questionnaire-Revised (CFQ-R) and the Cystic Fibrosis Quality of Life Questionnaire (CFQoL) were most frequently analyzed. There were also other new, promising tools.

Conclusion Most studies reported acceptable measurement properties of tools used to measure quality of life in adult patients with cystic fibrosis. In many cases, however, significant limitations were observed related to the lack of comprehensive analysis of the factor structure and other aspects related to validation and responsiveness. There have also been problems with the reliability of some tool scales (including the CFQ-R 14+). The small number of studies makes it difficult to present clear conclusions regarding the usefulness of existing tools. In turn, new tools that may be used in economic analyses (CFQ-R-8 dimensions) or in individualized assessment of quality of life using a mobile application (Q-Life) seem promising. However, further research on large patient populations is necessary to analyze the measurement properties of all tools.

Keywords Cystic fibrosis, Quality of life, Adult, Surveys and questionnaires, Systematic review

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Background

Cystic fibrosis (CF) is a genetic disease that may significantly affects patients' quality of life [1]. They have to face many challenges that affect both their physical and mental health [2].

The quality of life of patients with cystic fibrosis is influenced by, among others, factors related to physical health (including breathing difficulties, digestive problems or frequent infections), mental health (depression, stress, anxiety) or treatment received (frequent inhalations, taking medications) [3, 4]. It is worth emphasizing the role of social and psychological support in improving the quality of life of patients [5]. Educational programs, support groups and close cooperation with the treatment team can help patients cope with the disease and improve their well-being [6].

Moreover, the quality of life is conditioned by the availability of medical care (including modern therapies and efficient specialist care) [7]. Despite the challenges posed by cystic fibrosis, increasingly effective treatment strategies and growing awareness of the disease may contribute to further improvement of the quality of life of patients affected by this disease [8–10].

In order to measure the quality of life in patients with cystic fibrosis, various types of questionnaires are used, starting from general questionnaires (e.g. SF-36), through to specialized questionnaires created to measure the quality of life only in patients with cystic fibrosis (CFQ-R, CFQoL) [11, 12]. New, dedicated tools are also being created, which are not yet widely known or widespread, and their value for measuring the quality of life may be important. This may be significant, especially in the situation of the increasing availability of modern therapies, such as cystic fibrosis transmembrane conductance regulator (CFTR) modulators, which have had a positive impact on patients' functioning [13–15].

The objective of the study is to present tools for measuring the quality of life in adults with cystic fibrosis, along with their characteristics and measurement properties (reliability, content validity, construct validity, criterion validity and responsiveness).

Methods

Search strategy

To identify studies, a systematic search was performed based on the PRISMA guidelines [16]. The search was based on a protocol developed prior to the study. The protocol was registered on PROSPERO (CRD42023491030) [17]. The following sources of medical information were searched: Medline (via PubMed), Embase (via Ovid), Cochrane Library. The databases were searched on November 1, 2023 in accordance with the search strategies available in the supplementary material (table S1-S3). In addition, manual searches of bibliographies from the studies included in the analysis and grey literature were performed (searches included TRIP Database and Google Scholar). Articles published at any time and in any country were considered.

Inclusion and exclusion criteria

The review included publications in English or Polish. Its aim was to present the measurement properties of questionnaires for measuring the quality of life of adults suffering from cystic fibrosis. Some tools were designed to measure the quality of life of adolescents (from 14 years of age) and adults together, and such publications were also included in the analysis.

Publications relating exclusively to children and letters to editors, conference abstracts and review publications were excluded. Publications that analysed the results jointly for groups of children under 14 years of age and adults were not included in the analysis. Validation studies that did not separately analyse the population of patients with cystic fibrosis, but included a broader population, e.g. people with lung diseases, were also not included. Studies in which only translation and linguistic validation were performed without further testing of the tool and statistical analysis of the results were not included in the analysis.

Study selection

Studies were selected by two authors working independently (J.Ś. and K.W.). Disagreements were resolved by consensus, with the participation of a third author (D.S.P.). At the first stage, duplicates were deleted. Then, the titles and abstracts of the publications were screened. As a result, publications eligible for full-text analysis were identified. Finally, those that met all inclusion criteria for the analysis were selected.

Data extraction and analysis

As part of the analysis, the following elements were extracted and presented for each of the found questionnaires/studies: the first author of the study; year of publication; language version of the questionnaire the measurement properties of which were calculated in the study; characteristics of the tool (including an approximation of the number of domains, individual items and the range of possible scores; time taken to perform the test); description and construct of the study along with the presentation of the population, sample size, mode of administration of the tool, time of repeating the study (in the case of test-retest); and also measurement properties.

The following parameters were searched for in the publications: reliability (including internal consistency and test-retest), content validity, construct validity (including structural validity, convergent and discriminant performance of the test), criterion validity and responsiveness.

Definitions for these measurement properties were based on those provided by the COnsensus-based Standards for the selection of health Measurement INstruments [18].

Risk of bias and quality assessment

The COSMIN Risk of Bias Checklist [19–21] was used to assess risk of bias (RoB) of the included studies. The tool was created for use in systematic reviews to assess the quality of studies that analyze Patient-Reported Outcome Measures (PROMs) - PROMs also include measuring the quality of life. The tool consists of 10 boxes in which standards are verified for: PROM development (box 1), content validity (box 2), structural validity (box 3), internal consistency (box 4), cross-cultural validity\measurement invariance (box 5), reliability (box 6), measurement error (box 7), criterion validity (box 8), construct validity (box 9), and responsiveness (box 10).

Each parameter could receive one of four ratings: very good, adequate, doubtful or inadequate. According to the tool's methodology, only those elements that were described in a given study were assessed. We assessed PROM development (box 1) only in the case of studies describing tools for the first time.

We also assessed individual studies in terms of criteria for good measurement properties and overall quality of evidence in accordance with the COSMIN methodology for systematic reviews of PROMs [22]. Based on the criteria contained therein, each of the measurement properties included in a given study was assessed separately and could receive a rating of sufficient (+), insufficient (-) or indeterminate (?). In the case of content validity, an inconsistent (±) rating was also possible. The quality of evidence for individual measurement properties was assessed for a specific tool, after analysing the results of all studies in which it was used (possible ratings: high, moderate, low, very low).

The assessment was performed by two authors working independently (D.S.P. and J.Ś.). Disagreements were resolved by consensus, with the participation of a third independent author (K.W.).

Results

Search results

The systematic search identified 3,359 studies, of which 26 met the inclusion criteria for the analysis. The stages of study selection are presented in Fig. 1. The list of publications included and excluded from the review based on the analysis of full texts can be found in the supplementary material (table S4). Two publications were additionally included as a result of manual search.

The most frequently analysed tool was CFQ-R 14+– Cystic Fibrosis Questionnaire-Revised ($n = 9$; Quittner 2005 [23], Bregnballe 2008 [24], Rozov 2006 [25], Sands 2009 [26], Olveira 2010 [27], Quittner 2012 [28], Hochwälder 2017 [29], Solé 2018 [30], Navarro 2022 [31]) and its original version, i.e. CFQ 14+– Cystic Fibrosis Questionnaire ($n = 3$; Henry 2003 [32], Klijn 2004 [33], Wenninger 2003 [34]). One publication aimed to create a shortened tool based on CFQ-R 14+, intended for use in economic analyses. After the analyses, it was named CFQ-R-8 dimensions (Acaster 2023 [35]).

Other tools were:

- CFQoL– Cystic Fibrosis Quality of Life Questionnaire ($n = 5$; Gee 2000 [36], Dębska 2007 [37], Monti 2008 [38], Salek 2012 [39], Stofa 2016 [40]),
- SF-36– The 36-Item Short Form Health Survey ($n = 2$; Goldbeck 2001 [41], Gee 2002 [42]),
- FLZ^M– Questions on Life Satisfaction ($n = 2$; Goldbeck 2001 [41], Goldbeck 2003 [43]–FLZ^M-CF),
- UKSIP– United Kingdom Sickness Impact Profile ($n = 1$; Salek 2012 [39]),
- CRDQ– Chronic Respiratory Disease Questionnaire ($n = 1$; Bradley 1999 [44]),
- PLC– Quality of Life Profile for the Chronically Ill ($n = 1$; Goldbeck 2001 [41]),
- SGRQ– St. George's Respiratory Questionnaire ($n = 1$; Padilla 2007 [45]),
- PQLS– The Pulmonary-specific Quality-of-Life Scale ($n = 1$; Hoffman 2015 [46]),
- SIG scale– Single Item Global scale ($n = 1$; Yohannes 2011 [47]),
- CAT– Chronic Obstructive Pulmonary Disease Assessment Test ($n = 1$; Pott 2020 [48]),
- AWESCORE ($n = 1$; Button 2021 [49]),
- Q-Life ($n = 1$; Muilwijk 2023 [50]).

Tools created specifically to assess the quality of life of patients with cystic fibrosis include: CFQ-R 14+, CFQ 14+, CFQoL, FLZ^M-CF, AWESCORE and Q-Life. The characteristics of all tools are presented in supplementary material (table S5). In turn, the characteristics of the studies found, along with information on the study population and content validity, are presented in the supplementary material (table S6).

It should be emphasized that the process of implementing new tools is poorly described in the publications found. Detailed information is missing, including in terms of how to generate items or consult the tool with patients and experts before moving on to using the tool on a wider scale. The descriptions of these activities are very general, which reduces the rating in the COSMIN Risk of Bias Checklist to the level of doubtful or inadequate. It should be emphasized, however, that the requirements for the above-mentioned tool are highly demanding and, for example, the lack of information about recording meetings with patients during group

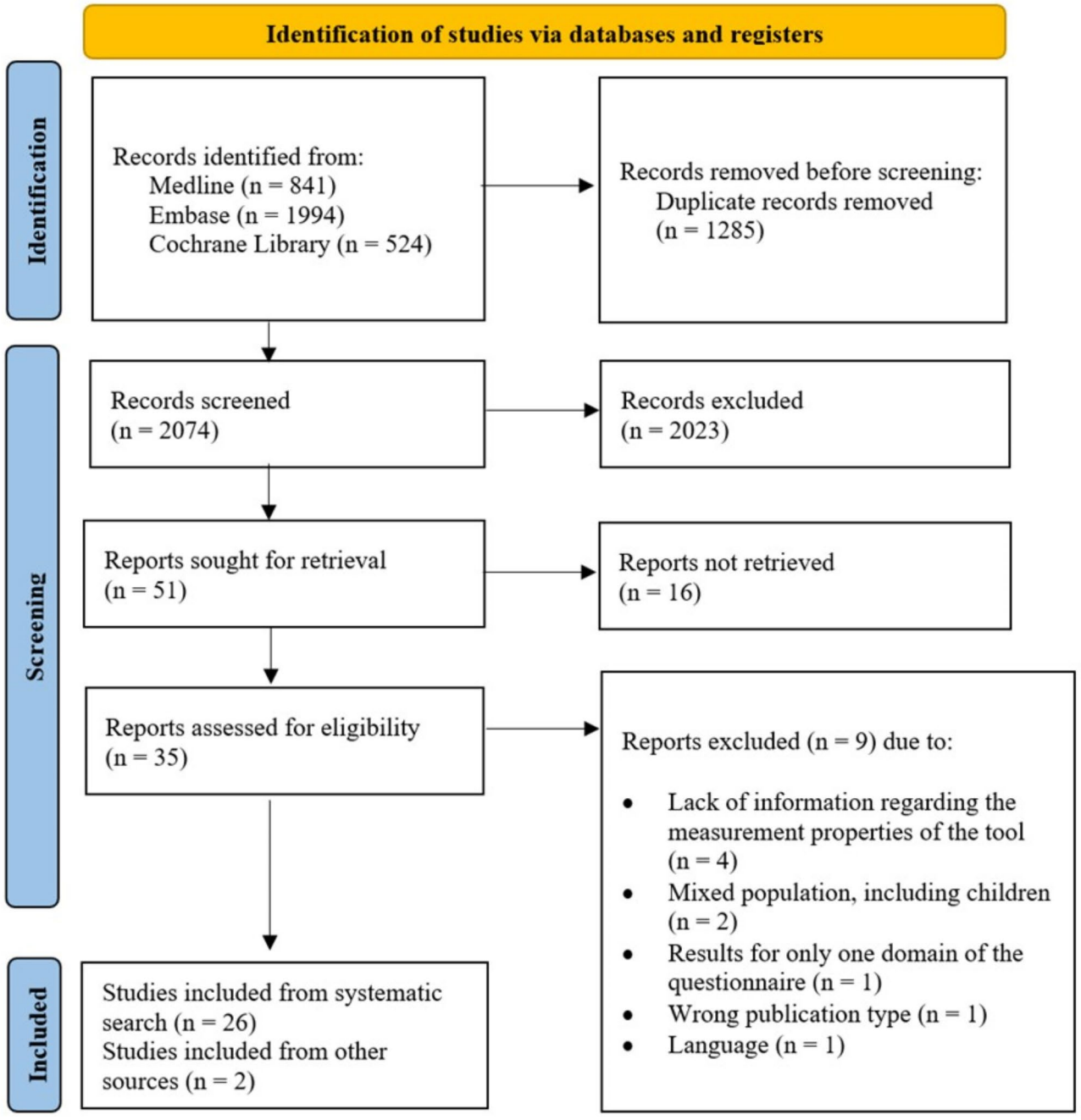

Fig. 1 PRISMA flow diagram

meetings or interviews, during which relevance, comprehensiveness and comprehensibility of the PROM were discussed, causes the rating to be lowered to the doubtful level. Moreover, too few evaluators of the relevance, comprehensiveness and comprehensibility of the PROM were also the reason for the lower rating. After analysing the studies, it can also be concluded that there is a lack of information on the number of patients and experts who were involved in the PROM assessment, the method of analysing the obtained data and the number of people who performed this analysis. The inability to assess individual elements of the analysed tools due to their sparse description results in the general conclusion that the RoB was moderate or high, and the way of implementing and describing new tools in scientific publications was not optimal. This applies to all found publications that described PROM design and/or content validity [31, 32, 34, 43, 49, 50], except for the publication Acaster 2023 [35] where the RoB can be considered low.

In many studies, content validity analysis was not performed at all, even though it was justified, e.g. in the case of using tools created to assess the quality of life used in diseases other than cystic fibrosis.

The most frequently analysed parameter, which in the found publications was internal consistency (23 out of 28 studies analysing this parameter), usually received a very good rating in the RoB assessment. The five studies received a doubtful rating for this parameter [39, 40, 43, 48, 50]. The ratings awarded in other parameters varied significantly and were not as good. In the case of publications in which at least three measurement properties were analysed, only one of them received the maximum score. It was the publication by Klijn 2004 [33], which determined reliability (internal consistency and test-retest) and construct validity (known groups validity) of CFQ 14+. Several publications in the scope of at least one of the analysed elements received an inadequate rating [37, 39, 44, 46, 47, 49]. Detailed RoB analysis results can be found in supplementary material (table S9).

Measurement properties

CFQ-R 14+ was analysed in nine studies [23–31]. Reliability (internal consistency) was acceptable (Cronbach's alpha ≥ 0.70) for most domains. However, in several studies the results for some domains were unsatisfactory. Treatment burden, digestive symptoms and social functioning domains were most often indicated as the subscales with poor reliability [23, 24, 26–29]. Physical functioning in 8/9 studies assessing CFQ-R 14 + had the highest internal consistency value ($\alpha > 0.90$). Two studies indicated strong and moderate correlations of the CFQ-R 14 + domains with the domains of the SF-36 and SGRQ questionnaires [23, 27]. Construct validity analyses also showed that CFQ-R 14 + scores were statistically significantly different when compared in the following groups: disease severity groups (mild group had higher scores than severe group) [23, 24, 27–29], nutritional status groups (nourished group had higher scores than malnourished group) [24, 29], gender groups (male had better HRQoL than female) [27–29], and age groups (younger adults had better HRQoL than older adults [23, 24].

Of all the tools found, CFQoL had the most favorable psychometric properties. All studies ($n = 5$) assessing CFQoL showed good reliability (internal consistency and test-retest) for all CFQoL domains [36–40]. As in the case of CFQ-R 14+, CFQoL moderately to strongly correlated with SF-36 [36, 38] and SGRQ [37] and additionally correlated well with UKSIP [39]. Moreover, CFQoL discriminated between: disease severity, nutritional status and age groups [36, 38, 39]. In the context of responsiveness, moderate to large effect sizes across the nine domains were found - statistically significantly increased scores for these domains after 2 weeks of antibiotic therapy [36].

Within the search studies were also found assessing the psychometric properties of the electronic version of CFQ-R [50], as well as tools that were not originally intended for CF patients [39, 41, 42, 44–48]. All tools were characterized by good reliability (internal consistency). In turn, based on test-retest, good reliability was found in all domains in the case of Q-life [50], AWESCORE [49], UKSIP [39], SIG scale [47], PQLS [46], and CRDQ [44]. Based on the results of four studies, correlations were indicated between CFQ-R and Q-life [50], AWESCORE [49] and CAT [48] and between CFQoL and SIG scale [47].

Table 1 presents selected, most important results from the studies found. In the case of two parameters (internal consistency and test-retest), it was decided to present the results of research analysing these parameters separately. For each of them, ranges are indicated from the domain that performed the worst to the domain that performed most favorably. Detailed results of each study are presented in the supplementary material (table S6).

Discussion

There are only a few systematic reviews on the measurement properties of tools intended for people with cystic fibrosis [11, 51, 52]. Not all of them focused exclusively on the measurement properties of tools intended to assess the quality of life. Individual reviews also described not all the tools available and found by us. In addition, they included tools intended to be completed by children (under 14 years of age) and adults. The way the data was presented made it impossible to easily and quickly read detailed data separately for these two groups. Our systematic review focused on tools designed to be completed by adults. Due to the fact that some of the tools are intended for people starting from 14 years of age, in many cases it was not possible to isolate a subpopulation of people only over 18 years of age.

An important problem that should be emphasized was the small sample size in most of the studies. In as many as 15 studies (out of 28), the studied population was less than 100 people, of which in 10 it did not exceed 50 people [25–27, 30, 37, 39, 40, 44, 45, 48]. Naturally, one must be aware that the number of adult patients with cystic fibrosis varies in different countries (the differences result, among others, from the size of the country and the availability of modern therapies) [7], and conducting research on validity and reliability on such a small population is fraught with the risk of error from a statistical point of view.

The most frequently used tool to measure quality of life in adults is the CFQ-R [23–30, 53–63]. It should be emphasized, however, that the studies found analysing

Table 1 Summary of measurement properties of tools for measuring the quality of life used in the identified studies

PROM	Number of studies included	Measurement properties
CFQ-R 14+	9 [23–31]	Internal consistency: α = 0.18 (treatment burden)– 0.94 (physical functioning) [23]; α = 0.54 (social functioning)– 0.95 (physical functioning) [24]; α = 0.29 (social functioning)– 0.86 (respiratory symptoms) [26]; α = 0.31 (digestive symptoms)– 0.96 (physical functioning) [27]; α = 0.51 (treatment burden)– 0.94 (physical functioning) [28]; α = 0.53 (social functioning)– 0.93 (physical functioning) [29]; α = 0.47 (social functioning)– 0.90 (physical functioning) [31]. Reliability– test-retest: ICC = 0.45 (social functioning/ treatment burden)– 0.90 (respiratory symptoms) [23]; ICC = -0.19 (social functioning)– 0.99 (physical functioning) [25]; ICC = 0.47 (digestive symptoms)– 0.95 (physical functioning) [27]; ICC = 0.71 (treatment burden)– 0.96 (physical functioning) [29]. Construct validity (comparison between other instruments): the tool had satisfactory results of convergent validity with SF-36 [23] and SGRQ [27]. Construct validity (comparison between subgroups): CFQ-R 14 + discriminate between different levels of disease severity (determined by FEV_1%) [23, 24, 27–29].
CFQ 14+	3 [32–34]	Structural validity: nine domains relating to HRQoL, 3 symptom scales and 1 health perception scale were separated [32, 34]. Internal consistency: α = 0.66 (body image)– 0.93 (physical functioning) [32]; α = 0.45 (body image)– 0.92 (physical functioning) [33]; α = 0.71 (eating disturbances)– 0.94 (physical functioning) [34]. Reliability– test-retest: ICC = 0.72 (energy)– 0.97 (role limitations, perception of health) [32]; ICC = 0.72 (digestive symptoms)– 0.98 (physical functioning, role limitations) [33]. Construct validity (comparison between other instruments): the tool had satisfactory results of convergent validity with NHP [32]. Construct validity (comparison between subgroups): CFQ 14 + does not discriminate between different levels of disease severity (determined by FEV_1%) in the case of several domains (energy, emotional state, role limitations, embarrassment and digestive symptoms) [33, 34]. Responsiveness (comparison before and after rehabilitation): difference was observed between the results before and after rehabilitation in terms of physical functioning, energy, emotional state, body image, respiratory symptoms and weight problem [34]. Responsiveness (comparison before and after antibiotic treatment for exacerbation): results of 4 domains changed before and after antibiotic therapy for exacerbation (physical functioning (ES = 0.38), energy (ES = 0.68), emotions (ES = 0.26), and respiratory symptoms (ES = 0.63)) [32].
CFQ-R-8D	1 [35]	Structural validity: eight domains were separated (physical functioning, vitality, emotional functioning, role functioning, respiratory symptoms, body image, digestive symptoms, and treatment burden).
CFQoL	5 [36–40]	Structural validity: nine domains were separated: physical functioning, social functioning, treatment issues, chest symptoms, emotional functioning, concerns for the future, interpersonal relationships, body image, and career concerns [36, 38]. Internal consistency: α = 0.72 (body image)– 0.92 (physical functioning) [36]; α = 0.73 (body image)– 0.92 (physical functioning) [37]; α = 0.73 (body image)– 0.91 (chest symptoms) [38]; α = 0.82 (treatment issues)– 0.96 (physical functioning, career concerns) [40]. Reliability– test-retest: all domains had good reliability [36, 37, 39]. This is confirmed by the results of another study, which calculated intraclass correlation coefficients (ICC = 0.83 [95%CI (0.74; 0.88)] (social functioning)– 0.98 [95%CI (0.96; 0.98)] (interpersonal relationships)) [38]. Construct validity (comparison between other instruments): the tool had satisfactory results of convergent validity with SF-36 [36, 38], SGRQ [37], UKSIP [39]. No statistically significant correlations were found between CFQoL and most of WHOQoL-BREF [37]. Construct validity (comparison between subgroups): CFQoL discriminates between different levels of disease severity (determined by FEV_1%) [36, 38, 39]. Responsiveness (comparison before and after antibiotic therapy lasting 2 weeks): several significant differences with large effect sizes across the 7 out of 9 domains (d > 0.80). Moderate effect sizes were across the treatment burden (d = 0.56) and career (d = 0.59) [36].
Q-Life	1 [50]	Internal consistency: reliability of individual Q-Life scores was high (at least 3 personal items were described, $N = 223$)– α = 0.83. Reliability– test-retest: ICC = 0.90 [95%CI (0.65; 0.92)]. Construct validity (comparison between other instruments): overall Q-Life scores were positively correlated with CFQ-R respiratory domain score ($r = 0.57$, $p < 0.001$) and overall CFQ-R scores ($r = 0.71$, $p < 0.001$). Responsiveness (comparison after treatment with a product containing elexacaftor/tezacaftor/ivacaftor): Q-life scores ($N = 123$)– MD = 20.8 [95%CI: (17.5; 25.0) $p < 0.001$]. Median overall Q-life scores at baseline, 3 and 6 months were 65.0, 84.2 and 87.5, respectively.

Table 1 (continued)

PROM	Number of studies included	Measurement properties
AWESCORE	1 [49]	Reliability– test-retest: ICC (for total score) = 0.989 [95%CI (0.979; 0.994)], ICC (for individual domains) = 0.87 [95%CI (0.775; 0.931)] (mood)– 0.97 [95%CI (0.947; 0.985)] (weight). Construct validity (comparison between other instruments): the tool had satisfactory results of convergent validity with CFQ-R 14+. Construct validity (comparison between subgroups): total score was significantly higher (MD = 25 [95%CI: (22; 28)]) for the 183 clinically stable participants ($N = 183$) compared to the participants with an exacerbation ($N = 63$). Responsiveness (comparison between clinical stable vs. exacerbation groups): a significant reduction in AWESCORE total score was indicated between clinical stability and exacerbation groups– MD = -30 [95%CI: (-32; -25)]. Significant reductions were observed in all domains ($p < 0.001$).
CAT	1 [48]	Internal consistency: α = 0.89 (total score). Construct validity (comparison between other instruments): the tool had satisfactory results of convergent validity with other tools (SGRQ, CFQ-R 14+).
UKSIP	1 [39]	Internal consistency: α = 0.87 (total score). Reliability– test-retest: the Spearman's rank correlation coefficients ranged from 0.57 to 0.84 (all domains had acceptable level of reproducibility). Construct validity (comparison between subgroups): limited ability to observe differences between disease severity groups (no significant differences were found between severe and moderate groups).
SIG scale	1 [47]	Reliability (test-retest): ICC = 0.78 [95%CI (0.59; 0.88)]. Criterion validity: sensitivity and specificity of a SIG compared to a 50% threshold for CFQoL was 93% [95%CI (87; 97)] n/N = 100/107)] and 64% [95%CI (39; 84) n/N = 9/14] (for SIG score ≥ 5). The area under the ROC curve was 0.84. Increasing the threshold of a SIG scale to ≥ 6 reduced the sensitivity to 82% and increased the specificity to 78% (11/14). Construct validity (comparison between subgroups): SIG scale was weakly correlated with FEV_1% ($r = 0.21$).
PQLS	1 [46]	Structural validity: three domains were separated (task interference, psychological, physical function). Internal consistency: α = 0.82 (physical domain)– 0.83 (psychological/task interference domains). Reliability– test-retest: the Pearson correlation coefficients ranged from 0.52 to 0.78 (all domains had acceptable level of reproducibility). Construct validity (comparison between other instruments): the tool had satisfactory results of convergent validity with other tools (SOBQ, SF-36). Construct validity (comparison between subgroups): PQLS total score was correlated with disease severity (6MWT distance and FEV_1%)– worse PQLS score associated with shorter 6MWT distance and lower FEV_1%.
SGRQ	1 [45]	Internal consistency: α = 0.49 (impact subscale)– α = 0.87 (activity subscale). Construct validity (comparison between subgroups): SGRQ discriminates between different degrees of disease severity (determined by FEV_1%).
FLZ^M	2 [41, 43]	Structural validity: 18 questions were separated (in a modified version of the questionnaire intended for patients with cystic fibrosis FLZ^M-CF) [43]. Internal consistency: FLZ^M total score of general life satisfaction– α = 0.72, FLZ^M total score of satisfaction with health– α = 0.77 [41]. FLZ^M-CF total score of general life satisfaction– α = 0.73, FLZ^M-CF total score of general health satisfaction– α = 0.85 [43]. Construct validity (comparison between subgroups): low correlation between FLZ^M-CF and FEV_1%. Limited ability to observe differences between subgroups [41, 43].
SF-36	2 [41, 42]	Structural validity: eight domains were separated, in accordance with the original design of the tool [41]. Internal consistency: α = 0.78 (general health)– 0.93 (physical functioning) [41]; α = 0.82 (social functioning)– 0.91 (physical functioning) [42]. Construct validity (comparison between subgroups): SF-36 does not discriminate between different levels of disease severity (determined by FEV_1%) sufficiently enough to detect progressive changes present in CF [41, 42].

Table 1 (continued)

PROM	Number of studies included	Measurement properties
PLC	1 [41]	Internal consistency: α = 0.72 (sense of belonging to others)– 0.93 (capacity). Construct validity (comparison between other instruments): in comparison to SF-36 and FLZ^M the tool achieved the most favorable results in psychosocial domains. Construct validity (comparison between subgroups): significant correlations were found between absence of pulmonary symptoms and all PLC domains. Significant correlations were also found between FEV_1% and capacity domain (rs = 0.50).
CRDQ	1 [44]	Structural validity: three domains were separated (in the final version of the questionnaire, it was decided to exclude the fourth domain: dyspnoea). Internal consistency: α = 0.78 (dyspnoea)– 0.93 (fatigue). Reliability (test-retest): correlations were good for most of all (14/15) items.

6MWT– 6 min Walk Test; AWESCORE– Alfred Wellness Score; CAT– COPD [Chronic Obstructive Pulmonary Disease] Assessment Test; CF– Cystic Fibrosis; CFQ 14+– Cystic Fibrosis Questionnaire for adolescents and adults; CFQoL– Cystic Fibrosis Quality of Life Questionnaire; CFQ-R-8D– Cystic Fibrosis Questionnaire Revised 8 Dimensions; CFQ-R 14+– Cystic Fibrosis Questionnaire-Revised for adolescent and adults; CI– confidence interval; CRDQ– Chronic Respiratory Disease Questionnaire; FEV_1%– forced expiratory volume in one second; FLZ^M– Questions on life satisfaction specific module; FLZ^M-CF– Questions on life satisfaction for adolescents and adults with cystic fibrosis– specific module; HRQoL– health-related quality of life; ICC– Intraclass Correlation Coefficient; MD– mean difference; N– number of participants; NHP– Nottingham Health Profile; PLC– Quality of Life Profile for the Chronically Ill; PQLS– Pulmonary-specific Quality-of-Life; SF-36–36-Item Short Form Survey; SGRQ– St George's Respiratory Questionnaire; SIG– Single-item global; SOBQ– Shortness of Breath Questionnaire; UKSIP– UK Sickness Impact profile; WHOQoL-BREF– World Health Organization Quality of Life Brief Version

individual measurement properties of given language versions lack the assessment of many aspects related to, among others, validity or responsiveness. The results also suggest medium or poor internal consistency of some domains of the questionnaire (the social functioning and treatment burden scales are the weakest).

CFQoL was also a frequently used tool [4, 36–40, 64–69]. Internal consistency of individual domains was at a good level in all analysed studies. The results of the remaining parameters were also at a satisfactory level.

The remaining tools were usually analysed in one study, which does not allow for a clear statement of their usefulness or lack of usefulness in assessing the quality of life of patients with cystic fibrosis. However, what deserves attention is a tool created by modifying and shortening CFQ-R 14+, which is intended to be used in economic analyses (CFQ-R-8D). As the authors of the tool note in the case of cost-effectiveness analyses, some agencies evaluating new drugs require "measures of HRQOL in the form of health state utilities to generate quality-adjusted life-years, which combine the value of HRQOL with the length of life into a single index number" [35]. A tool that is often used in economic analyses, i.e. EQ-5D, does not have an appropriate level of sensitivity in assessing lung function in the population of people with cystic fibrosis [35, 70, 71]. Therefore, it was decided to create a tool based on CFQ-R that could be widely used in the future (in addition to those currently available and used) during economic analyses when introducing new therapies. CFQ-R-8D is a new tool and requires further research to fully establish its usefulness.

A trend that is becoming more and more common is the use of online tools instead of traditional (paper) ones. One of the studies found compared the electronic version of CFQ-R 14 + with the traditional version. Based on the results, it can be concluded that the tool turned out to be reliable and valid, and can be used instead of the paper version [30]. The use of the electronic version significantly speeds up the assessment of quality of life because the results can be generated automatically, without the need to manually, tediously calculate them for each domain.

In terms of electronic tools, it is worth paying attention to the new and innovative tool, i.e. Q-Life. It is a mobile application that allows you to describe 3–5 items that patients indicate as important for their personal quality of life in an open text field, and rank these items in order of importance. Then, the indicated item is assigned to the domains defined in the application – 16 domains [50]. The above personalized approach allows for a complete change in the way of assessing the quality of life by isolating the most important elements from the point of view of individual patients. However, further research on a larger and more diverse group of people is necessary.

The above examples show that the development of new tools to assess the quality of life in patients with cystic fibrosis is possible. All the more so because the situation of patients after the increasing implementation of modern therapies has resulted in a significant extension of life and a reduction in respiratory symptoms [7, 72]. In some studies, a significant ceiling effects were observed (many study participants achieving the maximum result) [23, 24, 27, 28, 31, 42]. This results in a situation in which the results exceed the measurement capabilities of the tool. This is also one of the arguments justifying the creation of new tools and changes in the approach to assessing the quality of life of patients with cystic fibrosis.

The strengths of our review include the systematic approach and analysis of full texts, assessment of the risk of bias and study quality by three independently working

analysts. Our systematic review included all types of tools, also electronic ones. A comprehensive assessment of the risk of error and the quality of each study also allows you to quickly find out which tool has been well researched and which requires further research and observation. In turn, the limitations of our systematic review include the lack of analysis of publications in languages other than English or Polish. We identified several studies that were discussed in other languages, but due to our team's limitations, we were unable to translate them. The inability to assess the quality of life separately for the population of people aged 14 to 18 and adults may be considered a limitation. The above applies to most studies analysing tools to be completed for people aged 14 and older, which did not analyse the adolescent and adult populations separately. In our opinion, however, this should not affect the assessment of the psychometric properties of the analysed tools. A significant limitation that affects the possibility of unambiguous interpretation of the results is the small number of studies that met the inclusion criteria in the review and the various parameters that were analyzed in them. Various statistical methods were also frequently used. At the same time, our RoB and quality of studies analysis, as well as the data synthesis presented in Table 1, may facilitate the interpretation of the results. Analysis of the available studies does not allow us to identify a clear advantage of one tool over another. We believe that it is necessary to conduct further studies, using the tools described in our article, to be able to clearly assess their usefulness in the analyzed patient population.

Conclusion

Generally, the tools for measuring the quality of life analyzed in the article, with a few exceptions, are characterized by acceptable measurement properties. At the same time, many tools lack sufficient research to clearly determine their usefulness in the population of cystic fibrosis patients. Key analyses that would confirm the factor structure of the tools were often not conducted. The vast majority of studies also did not assess responsiveness. This also applies to the most widely used tools around the world (including the CFQ-R 14 + and CFQoL). Shortcomings and sometimes divergent research results in the field of measurement properties create a kind of gap that newly created tools try to fill. These include, among others: Q-Life, which completely changes the way of analyzing the quality of life of patients by using an individualized approach and a different form of filling out (mobile application). A tool that may be helpful in conducting economic analyses (CFQ-R-8D) has also been created. All tools require further, reliable research on large patient populations to determine their real value. However, based on the collected data, it can be seen that there is an opportunity to develop new tools, adapted to the current health situation of patients with cystic fibrosis.

Abbreviations

6MWT	6 min Walk Test
AWESCORE	Alfred Wellness Score
CAT	COPD [Chronic Obstructive Pulmonary Disease] Assessment Test
CF	Cystic Fibrosis
CFQ 14+	Cystic Fibrosis Questionnaire for adolescents and adults
CFQoL	Cystic Fibrosis Quality of Life Questionnaire
CFQ	R–8D–Cystic Fibrosis Questionnaire Revised 8 Dimensions
CFQ	R 14+–Cystic Fibrosis Questionnaire–Revised for adolescent and adults
CFTR	Cystic fibrosis transmembrane conductance regulator
CI	Confidence interval
COSMIN	COnsensus–based Standards for the selection of health Measurement Instruments
CRDQ	Chronic Respiratory Disease Questionnaire
FEV1%	Forced expiratory volume in one second
FLZM	Questions on life satisfaction specific module
FLZM	CF–Questions on life satisfaction for adolescents and adults with cystic fibrosis–specific module
HRQoL	Health–related quality of life
ICC	Intraclass Correlation Coefficient
MD	Mean difference
N	Number of participants
NHP	Nottingham Health Profile
PLC	Quality of Life Profile for the Chronically Ill
PQLS	Pulmonary–specific Quality–of–Life
PROM	Patient–Reported Outcome Measures
RoB	Risk of bias
SF	36–36–Item Short Form Survey
SGRQ	St George's Respiratory Questionnaire
SIG	Single–item global
SOBQ	Shortness of Breath Questionnaire
UKSIP	UK Sickness Impact profile
WHOQoL	BREF–World Health Organization Quality of Life Brief Version

Supplementary Information

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Supplementary Material 1

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Author contributions

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Data availability

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Declarations

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