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Original Article

"Il faut continuer à poser des questions" patient reported outcome measures in cystic fibrosis: An anthropological perspective

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ABSTRACT

Background: People with cystic fibrosis (pwCF) are central in the development of patient-led assessment tools. Qualitative analysis of a frequently used CF-specific patient-reported outcome measure (PROM) sought patient recommendations for development of a new quality of life (QoL) tool.

Methods: We performed an inventory of PROMs, symptom-report and QoL tools used in clinical trials within the European Cystic Fibrosis Society Clinical Trial Network (ECFS-CTN) and in routine clinical practice among Cystic Fibrosis Europe and ECFS members. A qualitative study using cognitive interviews with pwCF and their caregivers reviewed the Cystic Fibrosis Questionnaire (CFQ), the French initial form of the Cystic Fibrosis Questionnaire-Revised (CFQ-R).

Results: Survey results from 33 countries revealed over 70 tools used in routine clinical practice, utilized by clinical specialists (n=124), pwCF/parents/carers (n=49) and other allied health professionals (n=60). The CFQ-R was the main PROM used in clinical trials. The qualitative study enrolled 99 pwCF, 6 to 11 years (n=31); 12 to 18 years (n=38); >18 years (n=30) and 26 parents. Inductive thematic analysis based on the CFQ, revealed 19 key themes. Themes common across all cohorts included burden of treatment, impact of disease on day-to-day life, relationships/family, stress/mood, and nutrition. Themes unique to individual groups included, treatment when not symptomatic for the paediatric group; education/studies and planning for the future for adolescents, impact of anxiety and depression on day-to-day life for adults, and for parents, questions addressing anxiety and their role as carers.

Conclusions: Patient-centeredness is paramount in development of an up-to-date PROM in the era of novel therapies.

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1. Introduction

Cystic fibrosis (CF) is the most common life-limiting, autosomal recessive disease, affecting approximately 48,000 people in Europe. Symptoms include a build-up of mucus in the lungs, digestive tract and other organs resulting in lifelong complex medical management and wide-ranging challenges for pwCF and their families [1]. In recent years, there has been growing interest amongst regulatory bodies and research regarding integration of patient perspective of their illness and treatment options into the wider healthcare scene [2–4]. This can be facilitated through use of PROMs which enable assessment of patients' perception of health status and quality of life [5]. These tools are varied, based on questionnaires, interviews or scales and focus on physical, mental, emotional and social functioning. International regulatory agencies, such as the European Medicines Agency (EMA) and Food and Drug Administration (FDA), acknowledge that PROMs are an accurate measurement of patient experience and should be linked to existing safety and efficacy measurements in regulatory decisions for drug development, especially for orphan drugs such as cystic fibrosis transmembrane conductance regulator (CFTR) modulators [6,7]. Importantly, in the field of CF, PROMs are valued as a vital element of capturing patient-focused perspective on the impact of CF on daily life, including under-reported areas such as potential treatment burden [8]. Indeed, the use of PROMs to focus patient-centred care can not only empower patients and their healthcare providers but can also increase treatment adherence and patient self-management [9].

CF-specific PROMs were implemented over twenty years ago in the context of more severe disease [10,11]. This questions their current ability to capture subtle modifications in patients' health, many of whom now present with milder symptomatic disease. This collaborative study, led by the ECFS-CTN and CF Europe (the federation of European CF patient associations), aims to improve and harmonize clinical research for CF-specific PROMs throughout Europe.

The ECFS-CTN and CF Europe conducted a survey of ECFS-CTN centres, and ECFS and CF Europe members to make an inventory of PROMs used in routine clinical practice and in clinical trials. An in-depth qualitative study of patients' perspectives of a CF-specific PROM, the CFQ, was then performed using a qualitative research method based on patient interviews, to gather opinion from the life experience of pwCF and their parents (for children under 14 years), to determine patient-centred priorities.

2. Methods

2.1. Online survey

The ECFS-CTN and CF Europe undertook an initial electronic survey, using a popular web-based survey platform, from March to November 2019 to make an inventory of PROMs/symptom report and QoL tools used during routine CF clinical practice. The survey targeted all CTN clinical sites (43 CF centres, located in 15 European countries), and ECFS and CF Europe members.

2.2. Cognitive interviews: patient recruitment

An in-depth qualitative study was then conducted in France focusing on the most widely used French CF-specific PROM, the CFQ, the precursor to the CFQ-R [10,12] utilizing the Consolidated Criteria for Reporting Qualitative Research Guidelines (COREQ) [13] to inform the methodological approach. This French PROM was specifically developed to assess improvement of QoL by Pulmozyme in patients aged 8 years and above and was then translated into English with an additional 8 questions to become the CFQ-R (see Supplemental Table 1) [11].

A cross-sectional qualitative design using purposive sampling across different age cohorts [14] was used to recruit pwCF and their carers from four Paris-based hospitals (paediatric Necker Enfants Malades, and three adult CF centres Foch, Cochin and Créteil Hospitals). Participants were invited to take part in the study following a routine clinical visit. An interpretative description approach was used to conduct an initial patient review and evaluation of the CFQ. This in turn facilitated identification of key domains and recommendations for refinement of any future tool [15–17].

2.3. Data collection: interviews and interview guide

A semi-structured interview schedule (see Supplemental Table 2) was iteratively developed using the study objectives to critique the CFQ content and structure, by the study team (RC, IS and KH) and an external anthropological research expert (VBontemps). This schedule was piloted and refined within the team prior to study recruitment. Systematic questions included themes considered by the patients as (i) the most important to ask and mandatory to include within the questionnaire, (ii) those themes which were deemed to be missing, (iii) themes not fully addressed by the current content and structure of the questionnaire (iv) themes deemed irrelevant and (v) 'new' or 'reworded' questions for inclusion in a future tool.

2.4. Data capture, coding and analysis

One-to-one, face-to-face interviews were conducted in French, using the CFQ: the French-language questionnaire, by the principal researcher (RC), with parents present during paediatric interviews. Data saturation was achieved when no further new themes were elicited in the interview process. The interviews lasted between 24 and 65 minutes (mean 30 minutes), with transcription following each interview. Three co-authors (IS, RC, KH) assisted in manual systematic text condensation, distilling themes to elicit key areas identified by respondents [13]. A consensus-based approach was used, with two separate coders working independently to ensure the quality and trustworthiness of the initial analysis. Subsequent monitoring of coding was initially conducted independently, and then collectively by three further members of the research team to arbitrate any discrepancies. Quotations in this text are translated from the original French transcription into English. Statistical analysis included descriptive statistics and Fisher exact analysis for qualitative variables. Statistical significance level was accepted for $p<0.05$.

3. Results

3.1. Online survey

The online survey of PROMs/symptom report/QoL tools used in routine clinical practice elicited a total of 233 responses from 19

Abbreviations: CF, cystic fibrosis; CF Europe, Cystic Fibrosis Europe; CFQ, Cystic Fibrosis Questionnaire; CFTR, cystic fibrosis transmembrane conductance regulator; CRISS, Chronic Respiratory Infection Symptom Scale (CRISS); DASS, the Depression Anxiety Stress Scales questionnaire; ECFS-CTN, European Cystic Fibrosis Society-Clinical Trial Network; EQ5D5L, EuroQoL-5 dimension-5 level scale; FDA, Food and Drug Administration; EMA, European Medicines Agency; HRQoL, health-related quality of life; HSD, the Health Service Diary; PRO, patient reported outcome; PROMs, patient reported outcome measures; pwCF, people with cystic fibrosis; SF12, the short-form 12; TSQM, the Treatment Satisfaction Questionnaire for Medication; QoL, quality of life.

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CTN sites, and ECFS and CF Europe members from 33 respondent countries (see Supplemental Figure 1).

Respondents included clinical specialists (54%), pwCF/parents (26%), nursing staff (5%), physiotherapists (4%), clinical psychologists (4%), research coordinators (3%), dietitians (1%) and other allied health professionals (3%). Over 70 tools were identified, including both CF specific (n=7) and generic tools (n=65). The 6 tools most frequently used included the Cystic Fibrosis Questionnaire-Revised (CFQ-R), General Anxiety Disorder-7 (GAD-7), Patient Health Questionnaire-9 (PHQ9), Hospital Anxiety and Depression Scale (HADS), the Cystic Fibrosis Questionnaire (CFQ) and the Patient Symptom Diary. Use of tools varied geographically across Europe, with greater frequency of use in western Europe, focused on Germany, France and the UK (see supplemental Figure 2).

Out of the 19 CTN centres, 50% used these tools during routine clinical care, larger centres (>100 patients) more frequently. Significantly more adult centres (n=11) used PROMs than combined centres (n=6) or paediatric centres alone (n=2) (p=0.05). Lack of time during clinical assessments and lack of staff to implement these tools were the main reasons cited for non-use of these tools. These results identified the heterogeneity of tools used in clinical practice. France preferentially used the Cystic Fibrosis Questionnaire (CFQ).

A separate analysis of use of PROMs/symptom report/QoL tools within CTN *clinical trials* (n=31 trials) was conducted during the same time period. Trials utilizing these tools assessed modulator therapies (71%), anti-inflammatory treatments (10%), anti-infectives (10%), airway surface liquid osmotic therapies (7%) and physiotherapy-based conditioning programmes (2%). The CFQ-R was the most widely utilised trial tool (42%), with 32% of trials using tools such as the CFQ, Chronic Respiratory Infection Symptom Scale (CRISS), the Health Service Diary (HSD), the Treatment Satisfaction Questionnaire for Medication (TSQM), the Short-Form 12 (SF12), the EQ5D5L (EuroQoL 5 domain-5 level scale) and the Depression Anxiety Stress Scales Questionnaire (DASS). 26% of trials did not use any tool, the majority of these being paediatric trials.

3.2. Patient evaluation of the CFQ: cognitive interviews: theme identification and common themes

Considering most of the widely used questionnaires were created almost twenty years ago, and in light of the changing clinical status and QoL of many CF patients, we performed cognitive interviews to assess if they felt the CFQ questionnaire was still accurate and reflective of their QoL. 125 study participants (61 male and 64 female) were enrolled and age-stratified: 6-11 years (n=31); 12-18 years (n=38); >18 years (n=30) and parents (n=26). Inductive thematic analysis of interview transcripts revealed 19 key themes which respondents felt mandatory for inclusion in a CF-specific PROM (see Fig. 1).

Themes common across all age cohorts included burden of treatment (22%), impact of disease on day-to-day life (15%), relationships/family (12%), stress/mood (11%), and nutrition (relating to CF-specific dietary needs, and additional time needed to prepare/self-monitor nutrition) (5%).

The paediatric group identified a significantly lower number of themes, listing 6 out of 19 themes. Those included burden of treatment (39% of all paediatric responses; e.g. time needed to perform treatments, activities missed because of treatments); relationships/family (22% e.g. how to discuss CF with family/friends); impact of disease (20% e.g. practical impact of CF on holidays/school trips), on-going treatments when not presenting with symptoms (10%), stress/mood (6%), and nutrition (3%).

Adolescents outlined 8 preferential themes: impact of disease (27% e.g. the practical challenges presented by CF in their day-to-day routines, missed social or leisure activities due to CF); stress/mood (18%); burden of treatment (16% e.g. practical challenges of time needed for treatment); relationships/family (16% e.g. regarding when/how to disclose CF to peers); education/studies (9%); sport (7%); planning for the future (7% e.g. plans for future studies/careers); and nutrition (5%). Many adolescents identified the need for more questions to address indicators of the impact of CF upon quality of sleep, mood and most importantly how their disease impacted upon future life plans. Treatment 'burden' was identified as a key area for 'future improvement in any new tool' focusing on the need for more questions by specific treatment type e.g. physiotherapy, medication intake, and aerosol therapies. Importantly, a common adolescent critique of the CFQ was the pervading 'negative' tone of many questions, identifying a systemic focus on emotional and functional limitations in the existing tool, rather than a preferred focus on functional *abilities*:

Teenager C: «Il y a trop de questions me demandant ce que je ne peux pas faire, pourquoi ne pas me demander ce que je peux faire?»

"There are too many questions asking me about what I can't do, what about asking me what I can do?"

Adolescents also highlighted the need to remove and replace irrelevant and outdated questions and those suggesting negative emotions, for example, *"I felt useless". (Teenager A)*

Adults with CF reported the widest range of themes of all respondent cohorts, identifying 17 out of 19 themes. Burden of treatment (16%), education/studies (14%), stress/mood (13%), sport (11%) and impact of disease (8%) were identified as the most frequently cited themes. Adults with CF expressed a desire for more questions on the impact of cough, pain, breathlessness, gastro-intestinal symptoms and anxiety and depression on their day-to-day life. They also expressed a desire for more focus on treatments, and the time burden of their therapies considering each treatment type. Importantly, adult patients wanted more questions regarding 'future plans' e.g. family planning and the impact of CF on future relationships and career and on 'normal' life despite CF, specifically addressing significant improvement in quality of life since starting modulator therapies.

Parents reported 13 out of the 19 themes. The top five themes identified by this cohort included: burden of treatment (17%); reformat the tool (15% e.g. relating to a request to shorten the lengthy CFQ); education/studies (12% e.g. the impact of CF upon their children's studies and amount of schooling missed secondary to their CF); day-to-day planning (7%) and issues specific to parents (7% e.g. relating to a request for more questions addressing issues such as parental anxiety and guilt parenting a child with a chronic illness).

Parent A: «Nous avons besoin de plus de questions sur la colère de nos enfants et notre sentiment de culpabilité (de nous parents).»

"We need more questions about our children's anger and our (parents') sense of guilt."

Parents identified the need to discuss their role as carers adapting to the unique challenges of CF:

Parent H: «Je veux être le même parent pour tous mes enfants.»

"I want to be the same parent for all my children." (Parent C)

3.3. Theme grouping

To optimize understanding of the impact of CF across age cohorts, the themes identified were in turn, grouped into 6 key domains (Fig. 2).

The 'Disease' domain included the following themes: impact of disease; 'normal' life despite CF; talking about CF; and pain. The 'Treatment' domain included reference to burden of treatment/disease and on-going treatment when not symptomatic. The 'Social functioning' domain incorporated the themes of relationships/family; issues specific to parents and intimate relation-

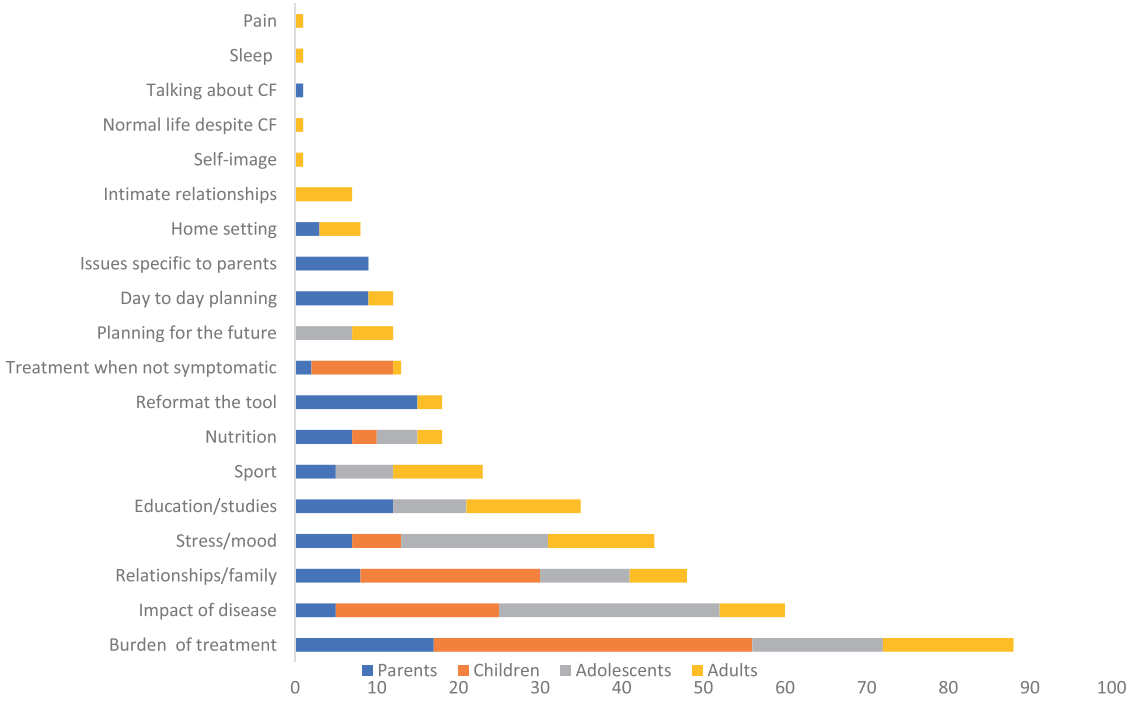

Fig. 1. Themes by respondent age cohort (%).

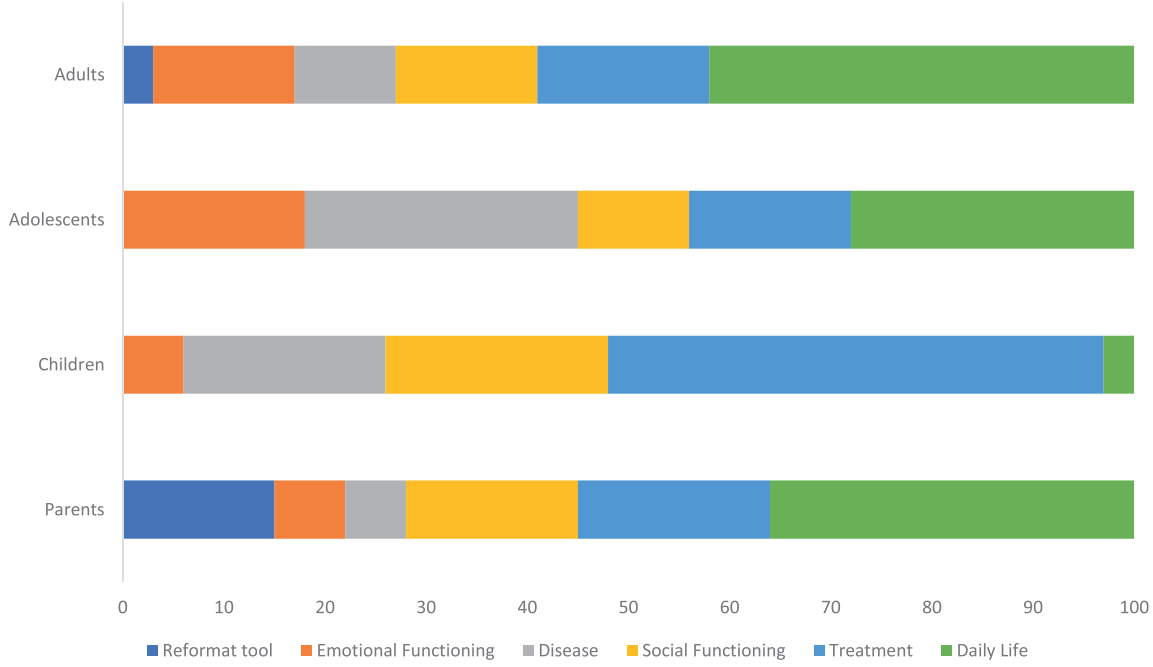

Fig. 2. Domains by respondent age cohort (%).

ships. The 'Emotional functioning' domain included reference to stress/mood and self-image, whilst the 'Daily life' domain included reference to education/studies; planning for the future; the respondent's home setting (living with parents, independently); day-to-day planning; nutrition; sport and sleep. The domain relating to 'Reformat Tool' included respondent comments regarding the structure of any future PROMs, creating a shorter, accessible format and wording in a positive tone.

The 'Daily life' domain was prioritized by the adolescent, adult, and parent cohorts, whilst the 'treatment' domain was prioritized by the paediatric cohort (49% of all paediatric respondents) (Fig. 2). Parents and adults were the only two groups to identify the need to 'reformat' the questionnaire.

4. Discussion

This qualitative study based on cognitive interviews assessing a CF-specific PROM, allowed identification of 19 key themes considered essential by pwCF and their caregivers in a CF PROM. The 5 themes shared across all cohorts included burden of treatment, impact of disease on day-to-day life, relationships/family, stress/mood and nutrition. Themes unique to individual age groups included,

treatment when not symptomatic for the paediatric group; education/studies and planning for the future for adolescents, impact of anxiety and depression on day-to-day life for adults, and for parents, questions addressing anxiety, guilt and their role of carers. Importantly, parents, adolescents and adults outlined the need for a shorter tool and criticized the negative tone and focus on limitations imposed by CF in many of the existing questions, rather than their preferred focus on functional abilities.

5. Development of a new PROM tool

The need to assess the impact of CF upon quality of life, adapt therapeutic strategies and incorporate patient perspective in clinical trials is widely recognized [8,18–20]. Our survey revealed over 70 tools reported in current clinical practice, emphasising the need for an up-to-date, accessible, and standardised CF-specific PROM.

The most widely used validated tool, the CFQ-R, covers general health-related QoL (HRQoL) themes alongside CF-specific ones. CFTR modulator trials utilize the CFQ-R as a secondary outcome measure and have demonstrated respiratory domain improvement over a 24-week period [21]. However, other domains addressing areas such as impact of CF on daily life or anxiety and future planning, which are meaningful for patients, are not included. Both the CFQ and subsequent CFQ-R were developed almost 2 decades ago. Advances in therapies and improvements in the symptomatic profile of the CF population, coupled with the era of new modulator therapies, necessitate a tool sensitive enough to detect potentially wider-ranging treatment effects in patients who are increasingly less symptomatic. Indeed, common interviewee critiques of the CFQ were the 'irrelevant' and 'outdated' questions. A new approach is required, to develop a tool which is both valid and sensitive to detect treatment effect whilst also being accessible to as many patients as possible. Provision in many European language translations and an accessible electronic format would facilitate access. Any new tool must also account for the fact that many pwCF and their carers adopt coping mechanisms for this chronic condition which may make it difficult to create a tool sensitive enough to detect treatment effect, particularly in regard to psychosocial benefits of treatment with new modulator therapies [14,22].

6. Key parameters of a new PROM

This study directly assessed personal insights of pwCF and their families, enrolling more than 20 subjects per cohort and evaluating their opinion of an existing disease-specific PROM. Respondents highlighted the need to remove and replace outdated questions such as those relating to the 'negative' impact of CF treatments upon their daily activities, preferring a more structured approach to assess type and frequency of daily treatments and therapies. They also highlighted the need for a tool focusing on their abilities rather than inabilities, and the importance of a positive tone in the formulation of questions in a future PROM, for example, removing existing words and phrases such as 'useless' and 'my CF prevents me from…' in relation to their CF.

All cohorts prioritized treatment burden and impact of disease on day-to-day life as key parameters for focus in a CF-specific PROM. The impact of treatment burden has long been acknowledged in CF and other chronic disease areas [23,24]. Similar to other chronic disease areas such as cancer and HIV, CF patients share concerns about the impact of their condition and consequent functional limitations, for example, at school or work and in regard to missed or cancelled social or leisure opportunities [25,26].

Most importantly, this study highlighted the significance of domains often overlooked in existing PROMs, namely relationships/family and stress/mood, identified as key themes by all study cohorts. This emphasized the pivotal role of family dynamics and emotional well-being which do not seem to be adequately addressed in current tools [27]. Future life, in a landscape of improved prognosis brought about by CFTR modulators also needs to be addressed. Adolescents and adults emphasized the need for questions about future plans, 'becoming an adult' for adolescents and fulfilling a 'normal' life in relationships and careers for adults. Parental concern about their children's future was a key theme, acknowledging the struggles that parents face throughout their child's CF journey [28,29].

6.1. Strengths and limitations

To our knowledge, this is the first study of its kind to utilize patients as the 'experts' to critique an existing PROM rather than conventional studies which have interviewed clinicians and allied health carers of pwCF to develop a critical framework for tool development [30]. This is different from previous methodologies based on opinions of CF experts and then assessed by the patients. We strongly advocate here that future studies must allow patients to build *their own* tool. Indeed, the use of a semi-structured interview format allowed unexpected themes arising during interviews to be developed in more detail [31]. To avoid potential interviewer bias, and minimize interviewer reflexivity, the interviewer was not a member of the healthcare team at any of the participating centres. The sample size by cohort (n=20 to 30) ensured a comprehensive sample across groups. Selection bias of the centres' healthcare staff may have led to inconsistency in patient selection, however, we attempted to avoid this by enrollment of consecutive patients at routine clinical assessment. The use of software regarding the coding and analysis of the qualitative data would enhance future studies of this nature, increasing confidence in dependability and trustworthiness of the large qualitative data set and intercoder reliability could be enhanced through the use of statistical measures of concordance [32].

7. Conclusion

This study highlights the need for new, sensitive, standardised PROMs particularly in the current context of new generation modulator therapies. Our observations have identified new areas that are considered mandatory by patients and parents, highlighting the necessity for development of a novel patient-informed questionnaire which could be used by the CF community. A quote from a teenage respondent aptly summarizes the need for this type of in-depth qualitative, patient-centric PROM research:

«Il faut continuer à poser des questions.»
"We must continue to ask questions."
Considerations for future interventions

- Qualitative research strategies, such as semi-structured interviews or focus groups, engaging pwCF, their families and their healthcare teams should be used to inform and develop new outcome measures in the field of CF research
- PROM development should be collaborative, blending clinical trial network and patient expertise

Declaration of Competing Interest

RC, AC, VBontemps, EL, EB, VB, MK, FC, MB, HdeK, PdeC, KH and IH have no conflicts of interest. ISG has received grants and personal fees from Vertex Pharmaceuticals, personal fees from Eloxx, and non-financial support from PTC Therapeutics; P-RB has received personal fees from Astra Zeneca, Boehringer-Ingelheim, Chiesi, GSK, Insmed, Novartis and Pfizer and grant from GSK; DH has received personal fees from Vertex; CM personal fees from Chiesi and Zambon.

CRediT authorship contribution statement

Rosa Coucke: Conceptualization, Methodology, Formal analysis, Writing – original draft, Writing – review & editing, Project administration, Supervision. **Audrey Chansard:** Conceptualization, Methodology, Writing – review & editing. **Véronique Bontemps:** Conceptualization, Methodology, Formal analysis, Investigation, Writing – review & editing. **Dominique Grenet:** Investigation, Writing – review & editing. **Dominique Hubert:** Investigation, Writing – review & editing. **Clémence Martin:** Investigation, Writing – review & editing. **Elise Lammertyn:** Writing – original draft, Writing – review & editing. **Emmanuelle Bardin:** Writing – review & editing. **Veerle Bulteel:** Writing – review & editing. **Frédérique Chedevergne:** Investigation, Writing – review & editing. **Muriel Le Bourgeois:** Investigation, Writing – review & editing. **Pierre-Régis Burgel:** Investigation, Writing – review & editing. **Isabelle Honore:** Investigation, Writing – review & editing. **Hilde de Keyser:** Writing – review & editing. **Maya Kirszenbaum:** Investigation, Writing – original draft, Writing – review & editing. **Paola de Carli:** Writing – review & editing. **Isabelle Sermet-Gaudelus:** Conceptualization, Methodology, Formal analysis, Investigation, Writing – original draft, Writing – review & editing, Project administration, Supervision. **Kate Hayes:** Conceptualization, Methodology, Formal analysis, Writing – original draft, Writing – review & editing, Project administration, Supervision.

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Supplementary materials

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References

[1] Sawicki GS, Goss CH. Tackling the increasing complexity of CF care. Ped Pulmnol 2015;50(suppl 40):S74–9.
[2] Slattery P, Saeri AK, Bragge P. Research co-design in health: a rapid overview of reviews. Health Res Policy Syst 2020;18:17. doi:10.1186/s12961-020-0528-9.
[3] . EMA report of the workshop on endpoints for cystic fibrosis clinical trials. European Medicines Agency London; September 2012. p. 27–8.
[4] Rowbotham NJ, Smith SJ, Elliott ZC, Leighton PA, Rayner OC, Morley R, et al. Adapting the James Lind Alliance priority setting process to better support patient participation: an example from cystic fibrosis. Res Involv Engagem 2019;5:24. doi:10.1186/s40900-019-0159-x.
[5] Marquis P, Arnould B, Acquadro C, Roberts WM. Patient-reported outcomes and health-related quality of life in effectiveness studies: pros and cons. Drug Dev Res 2006;67:193–201.
[6] U.S Department of Health and Human services food and drug administration guidance for industry: patient-reported outcome measures: use in medical product development to support labeling claims. US FDA, Clinical/Medical; 2009. [http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM193282.pdf].
[7] EMA (Committee for medicinal products for human use (CMHP)) Reflection paper on the regulatory guidance for the use of health-related quality of life (HRQL) measures in the evaluation of medicinal products; 2005. Doc. Ref. EMA/CHMP/EWP/139391/2004London.
[8] Goss CH, Quittner AL. Patient-reported outcomes in cystic fibrosis. Proc Am Thorac Soc 2007;4(4):378–86.
[9] Lakshminarayana R, Wang D, Burn D, Chaudhuri KR, Galtrey C, Guzman NV, et al. Using a smartphone-based self-management platform to support medication adherence and clinical consultation in Parkinson's disease. NPJ Parkinsons Dis. 2017 Jan 9;3:2. doi:10.1038/s41531-016-0003-z.
[10] Henry B, Grosskopf C, Aussage P, Goehrs JM, Launois Rthe French CFQOL Study Group. Construction of a disease specific quality of life questionnaire for cystic fibrosis. [Abstract]. Pediatr Pulmonol 1996(13):337–8 10.
[11] Quittner AL, Sweeny S, Watrous M, Munzenberger P, Bearss K, Nitza AG, et al. Translation and linguistic validation of a disease-specific quality of life measure for cystic fibrosis. J Pediatr Psychol 2000;25(6):403–14.
[12] Henry B, Aussage P, Grosskopf C, Goehrs JM. Development of the CFQ for assessing quality of life in paediatric and adult patients. Qual Life Res 2003;12(1):63–76.
[13] Tong A, Sainsbury P, Craig J. Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. Int J Qual Health Care 2007;19(6):349–57.
[14] Williams B, Corlett J, Dowell JS, Coyle J, Mukhopadhyay S. I've never not had it so I don't really know what it's like not to": nondifference and biological disruption among children and young people with cystic fibrosis. Qual Health Res 2009;19(10):1443–55.
[15] Murray J, Craig CL, Honey S, House A. A systematic review of patient-reported factors associated with uptake and completion of cardiovascular lifestyle behaviour change. BMC Cardiovasc Disord 2012;12:120.
[16] Spencer L, Ritchie J, Lewis J, Dillon L. Quality in qualitative evaluation: a framework for assessing research evidence. Natl Centre Soc Res 2003 ISBN 07115 04465 8.
[17] Mejdahl CT, Schougaard Hjollund N, Riskjaer E, Lomborg K. Patient-reported measures in the interaction between patient ad clinician – a multi-perspective qualitative study. J Patient Rep Outcomes 2020 Jan 9;4(1):3. doi:10.1186/s41687-019-0170-x.
[18] Kyte D, Duffy H, Fletcher B, Gheorghe A, Mercieca-Bebber R, King M, et al. Systematic evaluation of the patient-reported outcome (PRO) content of clinical trial protocols. PLoS ONE 2014;9(10). doi:10.1371/journal.pone.0110229.
[19] Abbott JA, Hart A, Havermans T, Matossian A, Goldbeck L, Bareto C, et al. Measuring health-related quality of life in clinical trials in cystic fibrosis. J Cystic Fibros 2011;10(Suppl 2):S82–5.
[20] Modi AC, Lim CS, Driscoll KA, Piazza-Waggoner C, Quittner AL, Woolridge J. Changes in pediatric health-related quality of life in cystic fibrosis after IV antibiotic treatment for pulmonary exacerbations. J Clin Psychol Med Settings 2010;17:49–55.
[21] Middleton PG, Mall MA, Drevínek P, Lands EF, McKone EF, Polieni D, et al. Elexacaftor-texacaftor-ivacaftor for cystic fibrosis with a single Phe508del allele. NEJM 2019;381:1809–19. doi:10.1056/NEJMoa1908639.
[22] Bell SC, Mainz JG, MacGregor G, Madge S, Macey J, Fridman M, et al. Patient-reported outcomes in patients with a G155D mutation on ivacaftor treatment: results from a cross-sectional study. BMC Pulm Med 2019;19:146. doi:10.1186/s12890-019-0887-6.
[23] Calthorpe R, Smith SJ, Rowbotham NJ, Leighton PA, Davies G, Daniels T, et al. What effective ways of motivation, support and technologies help people with cystic fibrosis improve and sustain adherence to treatment? BMJ Open Respir Res 2020;7:e000601 101136/bmjresp-2020-000601.
[24] Kyle J, Skleparis D;, Mair FS, Gallacher KI. What helps and hinders the provision of healthcare that minimises treatment burden and maximises patient capacity? A qualitative study of stroke health professional perspectives. BMJ Open 2020 Mar 18;10(3):e034113.
[25] Bhatti ZU, Salek MS, Finlay AY. Chronic diseases influence life changing decisions: a new domain in quality of life research. J R Soc Med 2011;104:241–50.
[26] Cooper V, Clatworthy J, Harding R, Whetham JEmerge Consortium. Measuring quality of life among people living with HIV: a systematic review of reviews. Health Qual Life Outcomes 2017;15:220. doi:10.1186/s12955-017-0778-6.
[27] Leeman J, Crandell JL, Lee A, Bai J, Sandelowski M, Knafl K. Family functioning and the well-being of children with chronic conditions: a meta-analysis. Res Nurs Health 2016;39:229–43.
[28] Moola FJ. This is the best fatal illness that you can have": contrasting and comparing the experiences of parenting youth with cystic fibrosis and congenital heart disease. Qual Health Res 2012;22(2):212–25.
[29] Waldboth V, Patch C, Mahrer-Imhof R, Metcalfe A. Living a normal life in an extraordinary way: a systematic review investigating experiences of families of young people's transition into adulthood when affected by a genetic and chronic childhood condition. Int J Nurs Stud 2016;62:44–59.
[30] McCarrier KP, Hassan M, Hodgkins P, Suthoff E, McGarry LJ, Martin ML. The cystic fibrosis impact questionnaire: qualitative development and cognitive evaluation of a new patient-reported outcome instrument to assess the life impacts of cystic fibrosis. J Patient Rep Outcomes 2020;4:36. doi:10.1186/s41687-020-00199-5.
[31] Ponto J. Understanding and evaluating survey research. J Adv Pract Oncol 2015;6(2):168–71 Mar-Apr.
[32] Cascio MA, Lee E, Vaudrin N, Freedman DA. A team-based approach to open coding: considerations for creating intercoder consensus. Field Methods 2019;31(2):116–30.