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**Validation of a measure of distress in adults with cystic fibrosis**

**And Clinical Research Portfolio**

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MSc Psychological Therapy in Primary Care

Submitted in partial fulfilment of the requirements for the degree of  
Doctorate in Clinical Psychology

Institute of Health and Wellbeing

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## CHAPTER ONE

### SYSTEMATIC REVIEW

# **A systematic review of factors associated with anxiety and depression in adults with cystic fibrosis.**

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Chapter word count: 6384

Prepared in accordance with the author guidelines for the Journal of Cystic Fibrosis  
(Appendix 1, p.67).

*Submitted in partial fulfilment of the requirements for the degree of Doctorate in  
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## **ABSTRACT**

### **Objectives**

The aim of this systematic review was to identify and synthesise the current research investigating the demographic, clinical and psycho-social factors associated with anxiety and/or depression symptoms in adults with Cystic Fibrosis (CF). Anxiety and depression symptoms are elevated in the adult CF population compared to the general population. An awareness of the factors associated with anxiety/depression would contribute to a better understanding of ‘at-risk’ groups and allow targeted screening and early intervention.

### **Method**

A systematic search was conducted using PsycINFO, Psychology and Behavioural Sciences collection, MEDLINE, EMBASE, and CINAHL. Studies were screened against inclusion/exclusion criteria, with a narrative synthesis of the eligible studies conducted. A study quality tool was adapted for cross-sectional studies and used to evaluate included studies.

### **Results**

Fourteen articles were included in the review. Inconsistent results were found for factors including age, gender, Body Mass Index (BMI), lung functioning, and work status being associated with anxiety/depression. Consistent associations were found between anxiety/depression symptoms and pain and health-related quality of life (HRQoL). Furthermore, depression symptoms were positively associated with anxiety symptoms, and vice versa.

## **Conclusions**

The review identified numerous factors that may be associated with anxiety/depression symptoms in an adult CF population. Consistent associations were found between anxiety and depression symptoms themselves; and also anxiety/depression symptoms and pain and Health Related Quality of Life. However, there were several limitations of the studies including use of cross-sectional designs and limited exploration of interaction effects, which prevented definitive conclusions from being drawn. Future research should address these limitations, seek to replicate findings of single studies and consider the development of a CF specific measure of psychological distress.

**Keywords:** adult, cystic fibrosis, psychological distress, socio-demographic factors, clinical health factors, systematic review

## **INTRODUCTION**

Cystic Fibrosis (CF) is an inherited, progressive and life-limiting condition in which the lungs and digestive system can become obstructed by thick, sticky mucus. Despite advances in diagnosis and treatment, management of CF is complex and individuals can experience frequent infections and progressive failure of most organ systems. Similar to other chronic physical health conditions, adults with CF are at higher risk for experiencing depression and anxiety compared to community samples without chronic health conditions (Quittner et al., 2014). Research has shown that prolonged psychological difficulties in patients with chronic illnesses can be associated with poor treatment adherence (Grenard et al., 2011) and increased healthcare costs (Snell et al., 2014).

Following these findings, recommendations were made to introduce annual screening of patients with CF for symptoms of depression/anxiety, so that those affected received timely further assessment and treatment (Quittner et al., 2014). This was further endorsed by the European Cystic Fibrosis Society's Standards of Care (Smyth et al., 2014), with guidelines being published by the International Committee on Mental Health in Cystic Fibrosis (Quittner et al., 2016) stating that annual screening should be conducted by healthcare professionals, preferably mental health specialists. Although this appears to be reasonable Abbott et al. (2015) had highlighted that limited staff numbers/time were significant barriers to implementing a mental health screening programme.

In order to maximise the potential benefit of a screening programme, with limited resources, it may be beneficial to screen 'at-risk' populations. This would allow early identification of individuals who may be more likely to experience anxiety/depression and allow preventative measures to be implemented to reduce the likelihood of



experiencing anxiety/depression symptoms. Furthermore, it would also allow for early intervention to be provided to those already experiencing anxiety/depression symptoms with the aim of reducing the negative impact of these psychological difficulties. To date, there has been no review of the risk factors associated with anxiety/depression symptoms in an adult CF population. However, risk factors have been identified in other chronic health conditions and reported in a substantial review by Clarke and Currie (2009); for example, risk factors for depression following a stroke included social isolation, functional/cognitive impairment, and past history of depression. In cancer, risk factors for depression included younger age, pain and helpless coping style. It is evident that risk factors for anxiety/depression in chronic health conditions can be categorised under health, demographic and psycho-social factors. As CF is a chronic condition it is likely that some of these factors would also be associated with anxiety/depression in this population.

It is important to highlight that although anxiety/depression are focused upon in the literature it has been argued that the term 'distress' is more favourable as this is considered to be a non-stigmatising term that describes the psychological reaction to broad array of difficulties that individuals with physical health conditions can experience (Holland, 1997). These difficulties can range from physical health symptoms to treatment adherence problems to end of life considerations. Although these difficulties may not map directly onto psychopathology measures, they are important to acknowledge and may have overlap with anxiety/depression symptoms.

To date the majority of research regarding the well-being of individuals with CF has focused on Health Related Quality of Life (HRQoL) which aims to capture a broader conceptualisation of health. A systematic review by Habib et al. (2015) investigated factors associated with HRQoL in CF, reporting that clinical characteristics such as

poorer lung function were negatively associated with HRQoL. Recommendations were made to further investigate/review the relationship of these potential factors on psychological well-being.

Several individual studies have investigated these relationships but, to date, no systematic review has synthesised the available evidence. Such a synthesis has the potential to improve the input of psychological services in adults with CF. Identifying factors associated with anxiety/depression could highlight ‘at-risk’ groups, thereby driving the development of targeted screening tools. This potential facilitation of earlier intervention could limit negative impact on health outcomes. Therefore, this review aimed to identify and synthesise the current research investigating health, demographic and psycho-social factors associated with anxiety and/or depression in an adult CF population.

## **METHODS**

### **Search Strategy**

A search strategy was devised to identify all studies examining anxiety/depression in an adult CF population. Five databases were used in the search (PsycINFO, Psychology and Behavioural Sciences Collection, MEDLINE, EMBASE, and CINAHL) from inception to 26<sup>th</sup> October 2018. Subject headings for each database were identified and combined with keyword text (Appendix 2, p.69). The term ‘distress’ was included in the search terms to ensure that all studies relevant to anxiety/depression were detected. However, only studies specifically measuring anxiety/depression symptoms were included in the current review as these are the most prominently measured constructs in the current CF literature. Reference lists of selected articles were also hand-searched for additional studies.

## Study Selection

All database search results were collated and duplicates removed. Titles and abstracts were screened and selected for full-article review using the criteria in Table 1. The same criteria were used during full-article review. Quantitative data referred to articles presenting original, numerical data. Review papers were excluded to reduce the risk of including the same article twice. The search, screening and extraction of articles were done by one person.

**Table 1.** Inclusion/Exclusion criteria

Inclusion	Exclusion
<ul style="list-style-type: none"><li>• Participant had diagnosis of CF and aged <math>\geq 18</math></li><li>• Specifically measured anxiety and/or depression and reported associations with any of the proposed factors</li><li>• Published in English in a peer-reviewed journal</li><li>• Presented primary quantitative data</li></ul>	<ul style="list-style-type: none"><li>• Focused exclusively on HRQoL</li><li>• Measures anxiety and/or depression in family members/caregivers</li><li>• Review paper</li><li>• Qualitative paper</li></ul>

## Data Extraction and Quality Appraisal

A data extraction table was used to standardise extraction of information across studies, recording information such as study design, data analysis, sample characteristics, measurement tools and relevant results (Appendix 3, p.70).

Study quality was assessed using a quality appraisal tool developed by the researcher based on the Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies (National Heart, Lung and Blood Institute, 2014), the Appraisal Tool for Cross Sectional Studies (AXIS) (Downes et al., 2016), the Cohort Study Checklist by Critical Appraisal Skills Programme (2018) and previous research (Kolte, 2018). A checklist of items was divided into sections including ‘Quality of Reporting’ and three sources of

bias: 'Selection Bias', 'Information Bias', and 'Confounding Bias'. Each domain was rated as 'low', 'moderate' or 'high'. An overall study quality rating was given using the following criteria:

- High quality = low risk of bias in all domains, or moderate risk of bias in only one domain
- Moderate quality = moderate risk of bias in at least two domains
- Low quality = high risk of bias in at least one domain

50% of included papers were also quality assessed by another Trainee Clinical Psychologist. The agreement rate between assessors was 92%, with any disagreements discussed/resolved by consensus.

### **Data Synthesis**

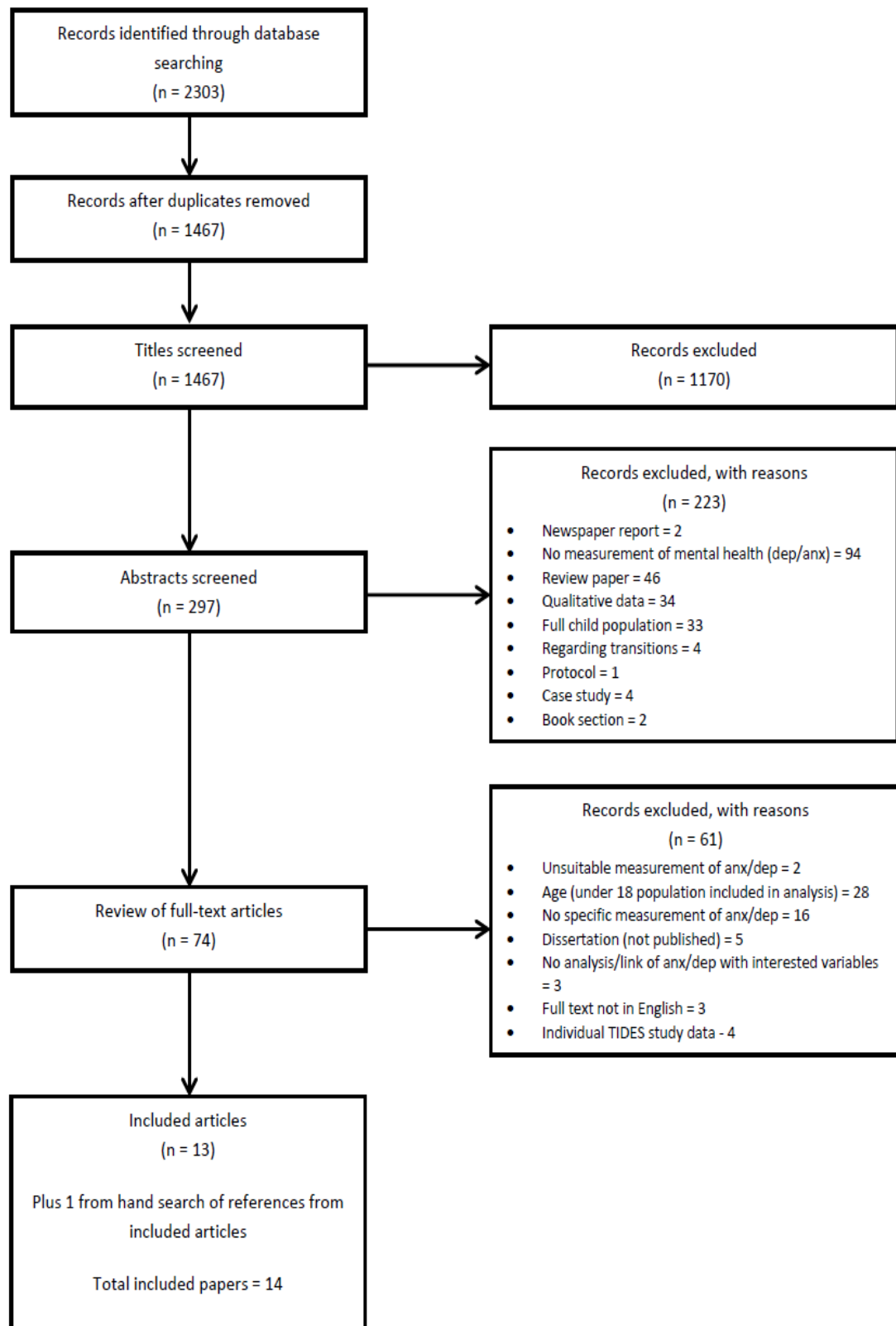
Due to the heterogeneity of the proposed factors associated with psychological distress and the broad nature of the research question, meta-analysis was not appropriate; consequently a narrative synthesis was conducted. To avoid potentially spurious findings from conclusions drawn on examination of single studies, synthesis of results required examined factors to be present in at least two papers. An exception for one paper was retrospectively made as it was deemed important to include due to the substantial international sample population.

## **RESULTS**

### **Study selection**

Figure 1 illustrates the study selection process. The literature search initially yielded 2303 papers, with removal of duplicates leaving 1467 articles. Using the inclusion/exclusion pre-defined criteria, 1393 articles were excluded following screening of the title/abstract. The most common reasons for exclusion were no specific measurement of anxiety/depression and participant age. Of the remaining 74 articles, 13 were eligible for inclusion in the narrative synthesis. One further paper was found through hand-searching of references. The total number of eligible papers included in the narrative synthesis was 14.

**Figure 1.** PRISMA Flow diagram of study selection process



## **Study Characteristics**

Table 2 presents the 14 studies included in the review. Eight studies originated from the USA and Canada (Anderson et al., 2001; Burkner et al., 2004; Hayes et al., 2011; Kopp et al., 2013; Maras et al., 2018; Pakhale et al., 2015; Quon et al., 2015; and Riekert et al., 2007); four from Europe (Delelis et al., 2008; Havermans et al., 2008; Knudsen et al., 2016; and Mengistu et al., 2012) and one from Australia (Burge et al., 2015). One study (Quittner et al., 2014) collated data from nine countries across Europe and USA. All studies presented cross-sectional data. Sample sizes varied from 16 to 183 across 13 of the studies, with one study (Quittner et al., 2014) having a sample size of 4739. Mean ages ranged from 24.1 to 30.7 years, with the majority of studies having a relatively even split in participant gender. One study (Burge et al., 2015) used only male participants. A variety of measures were used to screen for anxiety/depression but all were self-report measures. The percentage of participants scoring above clinical cut-off points on respective measures ranged from 7-50% for depression and 5-31% for anxiety. Studies used a variety of statistical tests depending upon their aims, including correlation, t-test, ANOVA, MANOVA and regression. Effect sizes were reported if available. All studies reported associations between depression and/or anxiety symptoms and a variety of health, demographic or psycho-social factors.

**Table 2.** Summary of studies included in systematic review

Study and Country	Sample Characteristics	Factors Investigated	Relevant Results
Anderson et al. (2001)  USA	N = 34 20 Male, 14 Female Age (M=28.5 ± 8.0)	<u>Psychological</u> BDI STAI MMPI  <u>Other factors</u> Psychosocial support Locus of Control Physical Health Demographic	<u>Age</u> <ul style="list-style-type: none"> <li>No significant difference in BDI (&lt;27age=5.4 v &gt;27age=5.7) or STAI (&lt;27age=33.8 v &gt;27age=35.6)</li> </ul> <u>Gender</u> <ul style="list-style-type: none"> <li>Significant main effect on BDI (Wilks A, 0.66, F=2.95, p&lt;0.05)</li> <li>male gender (M=6.5) associated with higher scores on BDI than female gender (M=4.1) (F=6.16, p&lt;0.05)</li> <li>Trend for STAI score - men (M=37.4) reporting higher levels of anxiety than women (M=31.2) (F=3.50;p=0.07)</li> </ul> <u>Physical Health</u> <ul style="list-style-type: none"> <li>FEV1% and IBW did not predict BDI scores</li> <li>FEV1% predicted STAI scores - individuals with more impaired lung functioning reported increased anxiety (F=6.32, p&lt;0.01)</li> <li>IBW predicted STAI scores - individuals with subnormal body weight reported significantly lower levels of anxiety than those with body weights within normal range (F=17.27, p&lt;0.001)</li> </ul> <u>Psychosocial support</u> <ul style="list-style-type: none"> <li>Increased psychosocial support predicted lower BDI scores (B=-0.47; t=-3.01; p&lt;0.01)</li> </ul> <u>Locus of Control</u> <ul style="list-style-type: none"> <li>No significant findings</li> </ul>
Burge et al. (2015)  Australia	N = 160 (CF=80; Control = 80)  All male Age(CF mean = 30 SD=8; control mean = 31, SD=8)	<u>Psychological</u> HADS  <u>Other factors</u> ICIQ ICIQ-MLUTS	<u>UI</u> <ul style="list-style-type: none"> <li>Men with CF and urinary infection had significantly higher scores for anxiety (p=0.003; <i>d</i>=0.98) and depression (p=0.002; <i>d</i>=1.00) than those without urinary infection.</li> </ul>



Study and Country	Sample Characteristics	Factors Investigated	Relevant Results
Burker et al. (2004)  USA	N=183 91 male 92 female  Age (working M=28.6, SD=7.3; not working M=27.7, SD=8.1)	<u>Psychological</u> STAI BDI  <u>Other factors</u> Type of work/number of hours worked	<u>Work</u> <ul style="list-style-type: none"> <li>Those who were working (M=7.84) had significantly lower BDI scores than those who were not working (M=12.2) (<math>t=3.45</math> (133), <math>p&lt;0.001</math>).</li> <li>No significant difference found for state/trait anxiety.</li> <li>Fewer number of hours worked was associated with higher scores on BDI (<math>r=-0.278</math>, <math>p=0.001</math>), but not with trait/state anxiety.</li> </ul>
Delelis et al. (2008)  France	N = 16 8 male 8 female  Age (M=28 $\pm 4.56$ )	<u>Psychological</u> STAI CES-D  <u>Other factors</u> DAS WCC Disease severity	<u>Marital Adjustment</u> <ul style="list-style-type: none"> <li>Significant negative association with depression (<math>r=-0.62</math>, <math>p&lt;0.01</math>) and anxiety (<math>r=-0.55</math>, <math>p&lt;0.05</math>)</li> </ul> <u>Coping</u> <ul style="list-style-type: none"> <li>Significant positive association between emotion-focused coping and depression (<math>r=0.78</math>, <math>p&lt;0.01</math>) and anxiety (<math>r=0.73</math>, <math>p&lt;0.01</math>).</li> </ul> <u>Disease severity</u> <ul style="list-style-type: none"> <li>No difference in anxiety/depression ratings between those with major v minor rating of disease severity</li> </ul> <u>Anxiety/Depression</u> <ul style="list-style-type: none"> <li>Significant positive correlation between anxiety and depression (<math>r=0.86</math>, <math>p&lt;0.001</math>)</li> </ul>
Havermans et al. (2008)  Belgium	N=57 29 male 28 female Age (M=26.7, SD=8.1)	<u>Psychological</u> HADS  <u>Other</u> CFQ-R Physical Health	<u>Health Related Quality of Life (HRQoL)</u> <ul style="list-style-type: none"> <li>After controlling for lung function, patients with anxiety symptoms had significantly poorer HRQoL scores for variety of domains on the CFQ (F statistic ranges from 4.57 – 8.99).</li> <li>Those with depressive symptoms reported significantly lower HRQoL scores for emotional functioning, eating disturbance and body image on the CFQ-R (F statistic ranges from 5.41 – 11.81)</li> </ul> <u>FEV1%</u> <ul style="list-style-type: none"> <li>No significant association with anxiety/depression.</li> </ul>

Study and Country	Sample Characteristics	Factors Investigated	Relevant Results
Hayes et al. (2011)  USA	N=83 36 Male 47 Female  Age (Median = 29.3, range 19-71)	<u>Psychological</u> HADS  <u>Other</u> BPI PCS CFQ-R Physical Health	<u>Pain</u> <ul style="list-style-type: none"> <li>Significantly higher depression scores in those with pain in the past 7 days (M=6.2) than those with no pain (M=4.9) p=0.03.</li> <li>Significantly higher anxiety scores in patients with pain in the past 7 days (M=8.3) than those with no pain (M=6.9) p=0.04.</li> <li>Increased levels of composite pain score significantly correlated with depression (r=0.43, p=0.0003) and anxiety (r=0.31, p=0.008).</li> </ul>
Knudsen et al. (2016)  Denmark	N=67 29 male 38 females  Age (M=24.1 range:18-30)	<u>Psychological</u> MDI  <u>Other</u> MMAS-8 CFQ-R Socio-demographic	<u>Gender</u> <ul style="list-style-type: none"> <li>Females more likely to report symptoms of depression on the MDI, with a female/male OR of 5:1 (95% CI 1.03-25.3) for moderate-severe depression.</li> </ul> <u>Age/Relationship Status/Education/Work Ability</u> <ul style="list-style-type: none"> <li>Logistic regression results not reported.</li> </ul> <u>Adherence</u> <ul style="list-style-type: none"> <li>Negative association with depression ( r=-0.412, p&lt;0.001)</li> </ul> <u>Health Related Quality of Life</u> <ul style="list-style-type: none"> <li>Significantly higher CFQ-R total scores for those who had ‘no depression’ (MDI &lt;19) v those who ‘mild depression’ (MDI 20&lt;24) on various domains of CFQ-R (Majority of effect sizes, cohen’s d were large ranging from -0.39 to -1.72)</li> </ul>

Study and Country	Sample Characteristics	Factors Investigated	Relevant Results
Kopp et al. (2013)  USA	N=30 19 male 11 females  Age (M=26.1 ± 7.0)	<u>Psychological</u> CES-D  <u>Other</u> Actiwatch 2 memory Physical Health Length of Stay in hospital Quality of Life	<u>Light exposure/ FEV1% / Quality of Life</u> <ul style="list-style-type: none"> <li>No significant difference in cumulative light exposure, FEV1%, or Quality of Life between depressed and non-depressed subjects.</li> </ul> <u>Increase length of stay in hospital</u> <ul style="list-style-type: none"> <li>Significant increase in length of stay for depressed CF patients (15.4 days ) compared to non-depressed CF patient (11.7 days), p=0.032)</li> </ul>
Maras et al. (2018)  Canada	N=45 26 male 19 female  Age (M=30.73 SD=10.80)	<u>Psychological</u> CES-D GAD-7  <u>Other</u> Socio-demographic Physical Health Pains -CFSS BCS CFQ	<u>Age/Sex/FEV1%</u> <ul style="list-style-type: none"> <li>No significant correlation with depression/anxiety</li> </ul> <u>Pain/Breathlessness Catastrophising (BC)</u> <ul style="list-style-type: none"> <li>Significant positive correlation between pain and depression (r=0.454, p=0.002) and pain and anxiety (r=0.406, p0.006).</li> <li>Significant positive correlation between BC and depression (r=0.433, p=0.003) and BC and anxiety (r=0.389, p=0.008)</li> </ul> <u>CFQ</u> <ul style="list-style-type: none"> <li>Significant negative correlation with depression (r=-0.580, p&lt;0.001) and anxiety (r=-0.428, p=0.003)</li> </ul> <u>Anxiety/Depression</u> <ul style="list-style-type: none"> <li>Significant positive correlation between anxiety and depression (r=0.745, p&lt;0.001)</li> </ul>

Study and Country	Sample Characteristics	Factors Investigated	Relevant Results
Mengistu et al. (2012)  UK	N = 121 65 male 46 female  Age (M=30 ±8.8)	<u>Psychological</u> HADS  <u>Other</u> CFQ-R Physical health Socio-demographic	<u>Gender</u> <ul style="list-style-type: none"> <li>Weak positive association between depression and males (r=0.17, p=0.05) but not in regression model</li> </ul> <u>Age</u> <ul style="list-style-type: none"> <li>Weak positive association between depression and older age (r=0.18, p=0.04) but not in regression</li> <li>Significant positive association between anxiety and age (r=0.21, p=0.02), accounting for 2% of variance (<math>\beta=0.20</math>, t=2.22, p=0.03)</li> </ul> <u>BMI</u> <ul style="list-style-type: none"> <li>Significant independent association with depression (<math>\beta=-0.45</math>, t=2.5, p=0.01) accounting for 8% of the variance</li> </ul> <u>FEV1%</u> <ul style="list-style-type: none"> <li>Significant independent association with depression (<math>\beta=-0.49</math>, t=-2.7, p=0.01), accounting for 13% of the variance</li> </ul> <u>CFQ-R</u> <ul style="list-style-type: none"> <li>Significant independent association with depression (<math>\beta=-0.51</math>, t=-3.4, p&lt;0.002), accounting for 23% of the variance</li> <li>Interpersonal Relationships → significant independent association with anxiety score (<math>\beta=-0.42</math>, t=-4.21, p&lt;0.001 accounting for 15% of variance</li> <li>Chest symptoms → significant independent association with anxiety score (<math>\beta=-0.49</math> t=-4.73, p&lt;0.001) accounted for 9% of variance</li> </ul> <u>Hospital Readmission Score</u> <ul style="list-style-type: none"> <li>Significant positive correlation with depression (r=0.40, p&lt;0.001) and anxiety(r=0.25, p=0.01)</li> </ul>
Pakhale et al. (2015)  Canada	N=45 26 male 19 female Age (M=30.7 ±10.8)	<u>Psychological</u> CES-D GAD-7  <u>Other</u> Physical health Psychological Needs	<u>Access to psychological services</u> <ul style="list-style-type: none"> <li>Past access to psychological services in CF care was not significantly related to participants' levels of depression (unadjusted p=0.753, <math>\phi=0.11</math>) and anxiety (unadjusted p=0.325, <math>\phi=0.20</math>)</li> </ul>

Study and Country	Sample Characteristics	Factors Investigated	Relevant Results
Quittner et al.(2014)  Europe and USA	N=4739 2468 male 2271 female  Age (M=28.87 SD=9.5)	<u>Psychological</u> HADS CES-D  <u>Other</u> Demographic Physical health	<u>Age</u> <ul style="list-style-type: none"> <li>Older age significantly associated with depression <math>p&lt;0.001</math> (OR=1.03, 95% CI, 1.02-1.04) and anxiety <math>p&lt;0.001</math> (OR=1.02, 95% CI, 1.01-1.03)</li> </ul> <u>Gender</u> <ul style="list-style-type: none"> <li>Not associated with depression but female gender significantly associated with anxiety <math>p&lt;0.001</math> (OR=1.66, 95% CI, 1.46-1.88)</li> </ul> <u>BMI</u> <ul style="list-style-type: none"> <li>Not associated with depression but lower BMI significantly associated with anxiety <math>p=0.003</math> (OR=1.03 95% CI 1.01-1.05)</li> </ul> <u>FEV1%</u> <ul style="list-style-type: none"> <li>Lower FEV1% significantly associated with depression <math>p&lt;0.001</math> (OR=0.90, 95% CI, 0.88-0.93) and anxiety <math>p=0.002</math> (OR=0.96, 95% CI, 0.93-0.98)</li> </ul> <u>Anxiety/Depression</u> <ul style="list-style-type: none"> <li>Adults reporting anxiety 13.64 times more likely to report elevated depression</li> </ul> <u>Haemoptysis/Pneumothorax</u> <ul style="list-style-type: none"> <li>Significantly associated with depression <math>p&lt;0.001</math> (OR=1.62, 95% CI, 1.33-1.98) and anxiety <math>p&lt;0.001</math> (OR=1.38, 95% CI, 1.15-1.65)</li> </ul> <u>Transplant</u> <ul style="list-style-type: none"> <li>Significantly associated with depression <math>p=0.03</math> (OR=1.39, 95% CI, 1.03-1.87) and anxiety <math>p=0.039</math> (OR=1.34, 95% CI, 1.01-1.77)</li> </ul> <u>Currently on psychiatric medications</u> <ul style="list-style-type: none"> <li>Significantly associated with depression <math>p&lt;0.001</math> (OR=3.56, 95% CI, 2.86-4.42) and anxiety <math>p&lt;0.001</math> (OR=3.37, 95% CI, 2.74-4.14)</li> </ul> <u>Currently receiving psychotherapy</u> <ul style="list-style-type: none"> <li>Significantly associated with depression <math>p&lt;0.001</math> (OR=3.21, 95% CI, 2.54-4.06) and anxiety <math>p&lt;0.001</math> (OR=4.22, 95% CI, 3.37-5.30)</li> </ul> <u>Antibiotics</u> <ul style="list-style-type: none"> <li>Significantly associated with depression <math>p&lt;0.001</math> (OR=1.65, 95% CI, 1.33-2.04) but not anxiety</li> </ul>

Study and Country	Sample Characteristics	Factors Investigated	Relevant Results
Quon et al. (2015)  USA	N=153 77 male 76 female  Age (M=28.6, SD = 8.8)	<u>Psychological</u> GAD-7 PHQ-9  <u>Other</u> Socio-demographic Physical health	<u>Age/Gender/Age of CF diagnosis/BMI/Diabetes/Employment status/Relationship status</u> <ul style="list-style-type: none"> <li>No association with depression/anxiety</li> </ul> <u>FEV1%</u> <ul style="list-style-type: none"> <li>Individuals with higher FEV1% had statistically significant lower depression symptom scores (<math>\beta=-0.04</math>, <math>p=0.04</math>)</li> </ul>
Riekert et al. (2007)  USA	N=76 34 male 42 female  Age (M=30.6 SD=9.6)	<u>Psychological</u> BDI  <u>Other</u> CFQ-R Physical Health	<u>FEV1%</u> <ul style="list-style-type: none"> <li>Significant negative association with higher depressive symptoms (<math>\rho=-0.25</math>, <math>p&lt;0.05</math>)</li> <li>Participants with poor lung function were 3 times more likely (<math>p=0.05</math>, OR=3, 95% CI, 1.0-9.2) to screen positively (<math>BDI\geq 10</math>) for depression than those with better lung function</li> </ul> <u>HRQoL</u> <ul style="list-style-type: none"> <li>Higher depressive symptoms significantly negatively correlated with all CFQ-R subscales (<math>\rho = -0.23</math> to <math>-0.74</math>)</li> <li>Association between depressive symptoms and CFQ scales was maintained regardless of lung function (<math>\rho</math> continues to be within medium to large range)</li> <li>Participants with depressive symptoms had significantly lower HRQoL scores on all CFQ subscales than those participants without depressive symptoms</li> </ul>
<b>Key:</b> BCS = Breathlessness Catastrophising Scale; BDI = Beck Depression Inventory; BPI = Brief Pain Inventory; CES-D = Centre of Epidemiologic Studies – Depression scale; CFQ-R = Cystic Fibrosis Questionnaire – Revised; CFSS = Cystic Fibrosis Stress Scale; DAS = Dyadic Adjustment Scale; FEV1 = Forced Expiratory Volume; GAD-7 = Generalised Anxiety Disorder – scale; HADS = Hospital Anxiety and Depression Scale; IDIQ = International Consultation on Incontinence Questionnaire; IBW = Ideal Body Weight; IDIQ-MLUTS = International Consultation on Incontinence Questionnaire Male Lower Urinary Tract Symptoms; MDI = Major Depression Inventory; MMAS-8 = Morisky Medication Adherence Scale; MMPI = Minnesota Multiphasic Personality Inventory; PCS = Pain Catastrophising Scale; PHQ-8= Personal Health Questionnaire Depression Scale; STAI = State-Trait Anxiety Inventory; WCC = Ways of Coping Checklist			

## **Summary of Study Quality and Risk of Bias**

Quality ratings and risk of bias are summarised in Table 3. Eight studies were deemed ‘high’ quality (Anderson et al., 2001; Delelis et al., 2008; Knudsen et al., 2016; Maras et al., 2018; Mengistu et al., 2012; Pakhale et al., 2015; Quon et al., 2015; Riekert et al., 2007) and six ‘moderate’ quality (Burge et al., 2015; Burker et al., 2004; Havermans et al., 2008; Hayes et al., 2011; Kopp et al., 2013; Quittner et al., 2014).

It is important that findings of the systematic review are interpreted in light of the methodological strengths and weaknesses of the included studies. Only two papers (Burge et al., 2015 and Quon et al., 2015) scored highly on ‘Quality of Reporting’, with the majority rated as ‘moderate’. Strengths included clear reporting of aims/statistical analysis plan and acknowledgement of ethical approval. Studies were penalised for not reporting a power calculation and minimal reporting of limitations. In addition to these problems, three papers (Anderson et al., 2001; Havermans et al., 2008; and Knudsen et al., 2016) also had limited explanation of statistical analysis plan, and/or did not fully report findings, resulting in ‘low’ quality of reporting ratings.

The majority of included studies had a participation rate exceeding 50% of all adults in the CF service that the research was being conducted. However, many did not investigate differences between participants/non-participants. This resulted in ‘moderate’ ‘selection bias’ ratings as it hinders the readers’ assessment of potential sampling bias.

Risk of ‘information bias’ was ‘low’ in all studies as all used valid and reliable measures of anxiety/depression. Although, it is important to acknowledge that these measures are not specific to the CF population but are used widely in services across Europe and USA.

Risk of ‘confounding bias’ was ‘moderate’ in the majority of studies. One common weakness was the use of cross-sectional design which limits conclusions regarding the possible causal influence of factors on anxiety/depression symptoms. Those studies that ‘low’ ‘confounding bias’ (Delelis et al., 2008; Maras et al., 2018; Mengistu et al., 2012; Riekert et al., 2007) acknowledged the possibility of interactions between variables, accounting for this in statistical analyses.



**Table 3.** Summary of Study Quality, Risk of Bias and Overall Quality Ratings

Paper	Quality of Reporting	Risk of Bias			Overall Study Quality Rating
		Selection	Information	Confounding	
Anderson et al. (2001)	Low	Low	Low	Moderate	<u>High</u>
Burge et al. (2015)	High	Moderate	Low	Moderate	<u>Moderate</u>
Burker et al. (2004)	Moderate	Moderate	Low	Moderate	<u>Moderate</u>
Delelis et al. (2008)	Moderate	Moderate	Low	Low	<u>High</u>
Havermans et al. (2008)	Low	Moderate	Low	Moderate	<u>Moderate</u>
Hayes et al. (2011)	Moderate	Moderate	Low	Moderate	<u>Moderate</u>
Knudsen et al. (2016)	Low	Low	Low	Moderate	<u>High</u>
Kopp et al. (2013)	Moderate	Moderate	Low	Moderate	<u>Moderate</u>
Maras et al. (2018)	Moderate	Moderate	Low	Moderate	<u>High</u>
Mengistu et al. (2012)	Moderate	Moderate	Low	Low	<u>High</u>
Pakhale et al. (2015)	Moderate	Low	Low	Moderate	<u>High</u>
Quittner et al. (2014)	Moderate	Moderate	Low	Moderate	<u>Moderate</u>
Quon et al. (2015)	High	Low	Low	Moderate	<u>High</u>
Riekert et al. (2007)	moderate	Moderate	Low	Low	<u>High</u>

## **Demographic Factors**

### Age

Five studies examined the relationship between age and anxiety/depression symptoms (Anderson et al., 2001; Maras et al., 2018; Mengistu et al., 2012; Quittner et al., 2014; Quon et al., 2015), with the majority having a ‘high’ quality rating. One further study (Knudsen et al., 2016) investigated only depressive symptoms but no results were reported. Three studies (Anderson et al., 2001; Maras et al., 2018; Quon et al., 2015) did not find a significant relationship between age and either anxiety or depression symptoms. Mengistu et al. (2012) reported a significant positive association between anxiety and age, with age accounting for 2% of the variance in HADS anxiety scores. However, only a weak positive correlation was found between age and HADS depression scores, which did not contribute to the regression model. The largest study (Quittner et al., 2014) found that older age was significantly associated with higher scores on both depression and anxiety. However, despite regression analyses being used, neither study reported on possible interaction effects of age with other demographic/health variables that may influence anxiety/depression symptoms. In both studies, weak effect sizes were reported therefore although results may be statistically significant, they may not be clinically meaningful results.

### Gender

Six studies examined the relationship between gender and depression symptoms (Anderson et al., 2001; Knudsen et al., 2016; Maras et al., 2018; Mengistu et al., 2012; Quittner et al., 2014; Quon et al., 2015). Four studies (Maras et al., 2018; Mengistu et al., 2012; Quittner et al., 2014; Quon et al., 2015) did not find a significant association, except Mengistu et al. (2012) which reported a weak correlation between male gender and depressive symptoms but this was not maintained in the regression model.

Significant results were reported by Anderson et al. (2001) who found a significant main effect of gender on depressive symptoms, with males reporting higher levels of depression than females. However, the mean difference between BDI scores for males and females was small and therefore the statistically significant difference between male and female depression scores may not be clinically meaningful. Contrastingly, Knudsen et al. (2016) found that females were significantly more likely to report symptoms of depression on the MDI, with a female-male Odds Ratio of 5:1 for moderate-severe depression. However, both papers had ‘moderate’ confounding bias due to possible interaction effects not being reported.

With regards to anxiety, five studies examined the relationship between gender and anxiety symptoms (Anderson et al., 2001; Maras et al., 2018; Mengistu et al., 2012; Quittner et al., 2014; Quon et al., 2015). Two studies (Maras et al., 2018; Quon et al., 2015) found no significant association and no results were reported by Mengistu et al. (2012). Anderson et al. (2001) reported a trend for STAI score with men reporting higher levels of anxiety than women. Contrastingly, Quittner et al. (2014) reported that female gender was significantly associated with higher anxiety. Again, possible confounding and selection biases limit these results. Furthermore, reported effect sizes were small.

### Work

Two studies (Burker et al., 2004; Quon et al., 2015) investigated the relationship between work status and anxiety, with both finding no significant association. With regards to depression, Quon et al. (2015) found no significant results but Burker et al. (2004) found that those who were working had significantly lower BDI scores than those who were not working and this difference was clinically meaningful as the two groups fell into different classifications based on the BDI cut-off scores. Furthermore,

higher scores on BDI were significantly associated with fewer number of hours worked per week, but this was a small effect. However Burker et al. (2004) paper was rated as 'moderate' quality, with issues relating to selection and confounding bias, compared to the 'high' quality paper of Quon et al. (2015). A further paper by Knudsen et al. (2016) did not report results of a regression model investigating effect of work status on depression symptoms.

## **Health Factors**

### Lung Functioning

Eight studies (Anderson et al., 2001; Havermans et al., 2008; Kopp et al., 2013; Maras et al., 2018; Mengistu et al., 2012; Quittner et al., 2014; Quon et al., 2015; Riekert et al., 2007) investigated the association between lung functioning (measured by FEV1% predicted) and depression symptoms. Four researchers (Mengistu et al., 2012; Quittner et al., 2014; Quon et al., 2015; Riekert et al., 2007) found significant associations relating lower lung functioning to higher levels of depressive symptoms. Mengistu et al. (2012) reported that lung functioning accounted for 13% of the variance in depression scores, whilst Riekert et al. (2007) reported that participants with poor lung function were three times more likely to screen positively for depression than those with better lung function. These are reasonable effect sizes and the majority of these studies were of high quality.

Six studies (Anderson et al., 2001; Havermans et al., 2008; Maras et al., 2018; Mengistu et al., 2012; Quittner et al., 2014; Quon et al., 2015) investigated the association between lung functioning and anxiety symptoms. Two studies (Anderson et al., 2001; Quittner et al., 2014) found significant associations relating lower lung functioning with higher levels of anxiety symptoms. However, reported effect sizes were small.

## BMI

Four studies (Anderson et al., 2001; Mengistu et al., 2012; Quittner et al., 2014; Quon et al., 2015) investigated the association between BMI and anxiety/depression symptoms. Anderson et al. (2001) used a different measurement (Ideal Body Weight) finding no association with depression scores, but significant association with lower STAI scores in those with sub-normal body weight. For the remaining three articles, only Mengistu et al. (2012) found a significant association between BMI and depression, accounting for 8% of the variance in depression scores. With regards to anxiety, only Quittner et al. (2014) reported significant results, with lower BMI being significantly associated with anxiety. However, there were concerns regarding selection and confounding bias in this paper and the reported odds ratio was close to the null.

## Pain

Two studies (Hayes et al., 2011; Maras et al., 2018) investigated the relationship between pain presence and anxiety/depression symptoms. Both reported significant positive associations but reported effect sizes were small. Furthermore, there was possible selection bias in both papers and confounding bias in Hayes et al. (2011).

## Other Health Factors

Quittner et al. (2014) investigated the association between several health factors and anxiety/depression symptoms. Significant positive associations were found between anxiety/depression scores and having a haemoptysis/pneumothorax in the past six months, recent intravenous antibiotics and listed for transplant but all with small effect sizes. Further significant positive associations were found between anxiety/depression and taking psychiatric medications/receiving psychotherapy, both with higher effect sizes. However, no confounding variables or interaction effects between variables were considered resulting in a 'moderate' quality rating.

## **Psycho-Social Factors**

### Health-Related Quality of Life

Six studies (Havermans et al., 2008; Knudsen et al., 2016; Kopp et al., 2013; Maras et al., 2018; Mengistu et al., 2012; Riekert et al., 2007) investigated the relationship between HRQoL and depression symptoms. All studies, except Kopp et al. (2013), found significant associations, with poor HRQoL being associated with more depressive symptoms. The majority of these papers were 'high' quality, with medium to large effect sizes reported. Mengistu et al. (2012) found that HRQoL accounted for 23% of the variance in depressive symptoms. Riekert et al. (2007) reported that the association between depressive symptoms and HRQoL scales was maintained regardless of lung functioning. This was replicated by Havermans et al. (2008) who reported that after controlling for lung function those with depressive symptoms reported significantly lower HRQoL scores for emotional functioning, eating disturbance and body image.

With regards to anxiety, three studies (Havermans et al., 2008; Maras et al., 2018; Mengistu et al., 2012) found a significant association, with poorer HRQoL being associated with higher levels of anxiety symptoms. Reported effect sizes ranged from small to large across studies. Specifically, Havermans et al. (2008) reported that after controlling for lung function, those patients who reported symptoms of anxiety had significantly poorer HRQoL scores on a variety of domains. Furthermore, Mengistu et al. (2012) found that interpersonal relationships domain accounted for 15% of variance and chest symptoms domain accounted for 9% of variance in anxiety scores.

### Anxiety/Depression

Three studies (Delelis et al., 2008, Maras et al., 2018; Quittner et al., 2014) investigated the association between anxiety and depression symptoms themselves, with all studies finding significant positive associations with large effect sizes. Quittner et al. (2014)

found that adults reporting anxiety were 13.64 times more likely to report elevated depression than those not elevated on anxiety.

### Relationship Status

Two studies (Knudsen et al., 2016; Quon et al., 2015) investigated the association between relationship status (defined as either single or with partner/married) and anxiety/depression symptoms. No significant association was found by Quon et al. (2015) and no data was reported by Knudsen et al. (2016). Interaction effects were not explored or discussed by either study.

## **DISCUSSION**

To the author's knowledge this is the first systematic review that has examined and synthesised factors associated with anxiety/depression in adults with CF. This review established nine demographic, health or psycho-social factors that had been investigated by at least two studies. A further five health factors investigated by only one study (Quittner et al., 2014) were retrospectively deemed important to include due to the substantial international sample population. Of the principal nine factors, anxiety/depression symptoms were consistently associated with each other and with HRQoL. Large effect sizes were reported from high quality papers, suggesting confidence in the results and demonstrating the clinical relevance of the findings. Further consistent positive associations were found between anxiety/depression symptoms and pain in studies that were of reasonable quality. Effect sizes were, however, small and the differences in anxiety/depression symptom scores between 'pain' and 'no pain' group were not considered to be clinically significant. Relationship status was not associated with anxiety/depression. The remaining five factors (age, gender, work status, lung functioning, BMI) had variable results across studies with some finding significant associations with anxiety/depression symptoms

and others finding no associations. Again there was variability in reported effect sizes and therefore some statistically significant results were not deemed clinically relevant. The five additional health factors (haemoptysis/pneumothorax, intravenous antibiotics, transplant, psychiatric medications and psychotherapy) that Quittner et al. (2014) identified were all significantly positively associated with anxiety/depression. However, only the latter two factors had clinically meaningful differences in anxiety/depression symptoms between the groups.

There are many possible reasons why results varied across studies. Firstly, it is important to consider study quality ratings when interpreting and synthesising results. Selection bias issues were frequent due to papers not exploring/reporting differences between participants/non-participants. Furthermore, the majority of studies did not account for confounding variables or investigate potential interaction effects between health, physical or psycho-social factors. It is possible that individually the factors may not be associated with anxiety/depression symptoms, but collectively they are. These are methodological issues that should be addressed in future studies before final conclusions can be made. Next, sample size varied greatly across studies and power calculations were omitted in the majority. Some studies reported trends in associations between factors and anxiety/depression symptoms which suggested that a significant association may be present but the study was under-powered. Furthermore, studies had very low numbers of participants presenting with depression/anxiety symptoms above the relevant clinical cut-off point. Although this may be representative of the general CF population, for research purposes it may be beneficial to have a greater spread of anxiety/depression symptom levels to detect factors associated with higher levels of depression/anxiety. A further consideration is that the cross-sectional nature of all studies prevented causality being determined as it is only possible to conclude that there is an association rather than a causal relationship. Longitudinal designs are better



placed to identify predictors of anxiety/depression. A final issue regarding the variability of results is the variety of measurement tools used which prevents direct comparison across studies. As none of the generic screening tools have been definitively validated in a CF population, it is recognised that current tools may not adequately detect CF-related psychosocial difficulties (Oxley & Webb., 2005).

### **Implications for future research**

It is acknowledged that the prevalence and impact of anxiety/depression in adult CF populations is a relatively new area of interest, with only one major international study being conducted so far. While the studies in this review were early stage explorations, the results indicate the value in continuing with this research. Longitudinal designs would allow for causality to be investigated and take into account possible interaction effects between variables. Larger sample sizes, gained by international collaboration, would promote adequate power to detect significant results. Finally, the development of a CF-specific measure of anxiety/depression would ensure a consistent approach to both research and clinical practice.

### **Limitations**

This systematic review had several limitations. First the exclusion of unpublished studies may have introduced publication bias as three relevant papers were excluded due to being university dissertations. However, the peer-reviewed criteria acted as a filter offering some reassurance about the quality of included articles. Furthermore, the initial decision to only report on factors that had been investigated by two papers may have introduced a selection bias, overlooking important factors that may be associated with anxiety/depression symptoms. However this criterion was incorporated so as to not make conclusions based on single study findings which could potentially be unreliable. A further limitation is that this review focused exclusively on anxiety/depression but as

discussed previously there are reservations about whether this accurately covers all the distress experienced by adults with CF. The inclusion of a wider range of mental health difficulties may have added to a broader understanding of the distress experienced in CF. Other limitations that have been acknowledged relate to the methodological weaknesses of the included studies such as the exclusive use of cross-sectional designs, limited investigation of interaction effects between factors and potential lack of power. Finally, the search, screening and extraction were done by one person, potentially raising the risk of bias.

### **CONCLUSION**

Awareness of factors that may be associated with anxiety/depression can aid the identification of ‘at-risk’ individuals and encourage appropriate support to be provided. This review found both consistent and inconsistent associations between anxiety/depression symptoms and a variety of demographic, health and psycho-social factors in an adult CF population. The papers were of reasonable quality providing a sound basis for this research, but the variability in results prevents definitive conclusions from being drawn at this stage. Furthermore, the reported effect sizes of statistically significant results were frequently small, therefore raising the question of the clinical meaningfulness of the results. Future research should (1) use large scale longitudinal studies to determine causality and explore interaction effects, (2) seek to replicate findings of single studies, and (3) consider the development of a CF specific measure of anxiety/depression.

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## CHAPTER TWO

### MAJOR RESEARCH PROJECT

#### **Validation of a measure of distress in adults with cystic fibrosis**

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*Submitted in partial fulfilment of the requirements for the degree of Doctorate in*

*Clinical Psychology*

## **PLAIN ENGLISH SUMMARY**

### **Background**

Adults with Cystic Fibrosis (CF) are at a higher risk of experiencing anxiety and depression than the general population. It is important that psychological distress is recognised as if left untreated it can lead to poor health-related quality of life, poor treatment adherence, poor health outcomes and increased healthcare costs. There are concerns that the current questionnaires used in CF services are not the best tools to detect the distress that individuals with CF experience. The Distress in Cystic Fibrosis Scale (DCFS) was developed to meet this need.

### **Aims**

This study aimed to explore the DCFS tool in order to support its development as an appropriate measure of distress for adults with CF.

### **Methods**

119 participants were recruited from the West of Scotland Adult Cystic Fibrosis Service (WoSACFS) either through out-patient clinic appointments or in-patient wards. After providing consent, participants completed four different questionnaires looking at their mood, quality of life and current levels of distress. Current physical health measurements were also recorded and participants were given the opportunity to give feedback on the questionnaires. The data was then explored and analysed.

### **Results**

The results suggested that the DCFS is able to detect current difficulties that adults with CF experience, and is able to distinguish between those who are experiencing high levels of distress and those who are experiencing low levels of distress. Additionally,



positive feedback was provided by participants about the DCFS in comparison to existing tools. Further exploratory analyses highlighted improvements that could be made to the instructions and response scale to ensure that individuals were rating both current and potential future distress relating to all items.

## **Conclusions**

The current study provides initial support for the DCFS being used as a measure of distress in an adult CF population. Suggestions were made to improve the wording of the instructions and response scale used in the DCFS. Studies in the future should continue to investigate the revised version of the DCFS using a larger sample.

## **ABSTRACT**

### **Background**

Anxiety and depression are highly prevalent in adults with Cystic Fibrosis (CF) and can lead to numerous negative outcomes including poorer physical health and health related quality of life, reduced treatment adherence and increased healthcare costs. Currently it is recommended that all adults with CF are screened for anxiety and depression on an annual basis. However, there are concerns that these current measures do not adequately detect the range of difficulties that individuals with CF experience. Consequently, the Distress in Cystic Fibrosis Scale (DCFS) was developed to support the detection of distress specifically in an adult CF population. This study was an initial exploration of the structural and psychometric properties of the DCFS in order to support its development as an appropriate screening measure of distress in an adult CF population.

### **Methods**

119 participants were recruited from the West of Scotland Adult Cystic Fibrosis Service (WoSACFS) through inpatient wards and out-patient clinics. Participants completed a battery of questionnaires assessing their mood, quality of life and current distress relating to CF. Psychometric properties of the DCFS were then evaluated with additional exploratory analyses evaluating the structure and practical use of the measure.

### **Results**

The results indicated a 1-component model for the DCFS and provided support for it being an appropriate measure of CF distress, with positive findings relating to internal consistency and criterion validity. However, exploratory analyses highlighted that two response categories (N/A and 0) were used inconsistently by participants particularly for

those items concerning physical health symptoms. It is possible that this was due to the wording of the rating scale and instructions.

## **Conclusions**

The current study provides preliminary support for the DCFS being used as a measure of distress in an adult CF population. Potential improvements to the instructions and response scale were identified and subsequent recommendations made. Future studies should be conducted to further investigate the psychometric properties of the revised tool using a larger sample with a greater range of clinical and demographic characteristics.

## **INTRODUCTION**

Cystic Fibrosis (CF) is an inherited, progressive and life-limiting condition in which the lungs and digestive system can become obstructed by thick, sticky mucus. Despite recent advances in diagnosis and treatment, management of CF requires a complex, time-consuming daily regime taking two to four hours, in addition to over 20 medication tablets a day. Despite this demanding treatment routine, individuals with CF may experience frequent infections and progressive failure of most organ systems (e.g. lungs, pancreas).

Research (Smith and Schmitz, 2014; Yang et al., 2013) has shown that adults with chronic conditions, such as cancer and diabetes, are at higher risk of experiencing depression and anxiety compared to community samples without chronic health conditions. Quittner et al. (2014) conducted an extensive study of 6088 patients with CF (The International Depression Epidemiological Study -TIDES) and found that depression and anxiety rates were 2-3 times higher in individuals with CF than those without CF. Research has shown that prolonged psychological distress, particularly depressive symptoms in patients with CF, is associated with poor Health-Related Quality of Life (HRQoL) and poor health outcomes (Riekert et al., 2007); increased healthcare utilisation and costs (Snell et al., 2014); and poor treatment adherence (Knudsen et al., 2016). Given these relationships between psychological distress and key health/quality of life outcomes it is important that screening measures accurately detect psychological distress in individuals with CF.

Due to financial and time constraints it is not possible to offer everyone with CF an annual clinical psychology interview and therefore screening measures are routinely used to detect psychological distress. The International Committee on Mental Health in Cystic Fibrosis (ICMH-CF) (Quittner et al., 2016) advises using the Patient Health Questionnaire (PHQ-9) and Generalised Anxiety Disorder Questionnaire (GAD-7).

However, historical research (Oxley & Webb., 2005) and current professionals working in CF services have raised concerns that these generic screens may not adequately detect psychosocial difficulties in a CF population as clinically ‘normal’ scores may be achieved by patients with CF for whom clinical assessment reveals psychosocial difficulties.

Disease-specific measures of distress exist in other long-term conditions such as the Diabetes Distress Scale (DDS) (Polonsky et al., 2005) and the Distress Thermometer (DT) for cancer services (Hoffman et al., 2004). These measures were developed due to individuals experiencing distress related to their physical health condition. It is important to highlight that the term ‘distress’ is used as this is a non-stigmatizing term that describes the broad array of difficulties that individuals with physical health conditions can experience (Holland, 1997). In relation to CF, Pakhale et al. (2015) found that in addition to general mood and anxiety difficulties, adults were interested in discussing several other issues with a psychologist. These included CF-specific adjustment difficulties, treatment adherence, quality of life concerns, death and difficulties with stigma/disclosure to others. Therefore, the aim of these distress measures is not to identify psychopathology, but to identify areas where further assessment and intervention may be beneficial, ranging from physical problems to practical concerns about their CF condition.

As far as the authors are aware there are no current validated measures of distress in an adult CF population. One of the present study’s authors, Dr Sejal Patel, began developing a measure of distress for an adult CF population and the Distress in Cystic Fibrosis Scale (Patel, 2015) was created. Over a three-year period, 150 adult patient files were audited to ascertain the emotional concerns CF patients presented with to the clinical psychologist in an adult CF service. Thirty themes of psychosocial concerns were identified of which eight were excluded due to being isolated occurrences (e.g.

domestic violence and perceptual disturbance). The remaining 22 themes were included in the developed questionnaire which was constructed by adapting the framework of previously validated measures of distress in long-term conditions. For example, the 0-10 rating scale used in the DT (Hoffman et al., 2004) and the wording of instructions in the DDS (Polonsky et al., 2005). It was presented to clinical psychology CF outpatients during face-to-face contact, and was sent to the CF Multidisciplinary Team to check face validity, with positive feedback received. In 2015 the questionnaire was shown to the UK Psychosocial Professions in CF Group (UKPP-CF) where suggestions for format improvement were made and one further item added.

The final 23-item questionnaire is intended to be a quick, self-report measure that CF patients can complete to highlight the areas in which they are currently experiencing distress and to allow for further assessment and appropriate support to be provided. Formal exploration of the psychometric properties of the DCFS is required before it can be disseminated and used in clinical practice.

### **AIMS**

This project is the first phase to evaluate the structure and psychometric properties of the DCFS, a newly-developed self-report measure of distress in an adult CF population. Principal Component Analysis (PCA), internal consistency, criterion validity and content validity were investigated, in addition to reviewing participants' written feedback regarding the DCFS. This is the first structured exploration of the DCFS and the results will inform recommendations about the future use of the DCFS and any further investigations that should be conducted.

## **METHODS**

### **Ethical approval**

A research protocol was developed (Appendix 4, p.72) with initial and subsequent amendments to the study protocol being granted ethical approval by West of Scotland Rec Four committee and by NHS Greater Glasgow and Clyde R&D (Appendix 5, p.84).

### **Sample size**

There is limited literature guidance on sample size required for validation studies. A review by Anthoine et al. (2014) reported that the sample size determination for psychometric validation studies (using exploratory factor analysis and common validity/reliability analyses) is rarely ever justified *a priori*. They found that approximately 92% of the articles reported a subject-to-item ratio greater than or equal to two, with about 90% of articles having a sample size greater than or equal to 100. The current DCFS tool has 23 items therefore, taking into account the review findings and the scope of the current research project, a subject-to-variable ratio of 5/1 was chosen. Thus, the current study aimed to recruit 115 participants.

### **Participants**

119 participants were recruited from the West of Scotland Adult Cystic Fibrosis Service (WoSACFS). Eligible participants were those who had a diagnosis of CF, aged 18 or over, and fluent in English. Individuals who had a learning disability or who were deemed too physically unwell to participate were excluded from the study. One hundred and thirty seven individuals were invited to participate, with 11 declining and seven not returning questionnaires by post. Overall there was an 87% participation rate.

## Measures

Physical Health information – Recent Body Mass Index (BMI) and lung functioning (using FEV1%) measurements were recorded from participants' medical files if consent was provided.

Distress in Cystic Fibrosis Scale (DCFS; Patel, 2015) is a 23-item questionnaire (Appendix 6, p.92). It has an 11-point range with endpoints labelled 'no problems' (0) and 'worst I've ever felt' (10). Respondents are instructed to write the number (0-10) that best describes how they have been feeling over the past two weeks relating to each of the 23 items. Some items are not relevant to everyone therefore all 'N/A' responses were coded as such in SPSS so as to differentiate from genuine missing data. Furthermore, a mean score was calculated for the purpose of some analyses by summing the distress ratings provided, then dividing this by the number of items answered by the participant.

Patient Health Questionnaire-8 (PHQ-8; Kroenke et al., 2009) is an eight-item self-report measure of depression, using a four-point scale from 'not at all' to 'nearly every day'. Responses are based on how the individual has been feeling over the past two weeks. Evidence supports reliability and validity of PHQ-8 as a measure of depression in the general population (Kroenke et al., 2009).

Generalised Anxiety Disorder Questionnaire-7 (GAD-7; Spitzer et al., 2006) is a seven-item self-reported questionnaire, using a four-point scale from 'not at all' to 'nearly every day'. Responses are based on how the individual has been feeling over the past two weeks. Evidence supports reliability and validity of the GAD-7 as a measure of anxiety in the general population (Lowe et al., 2008).

Cystic Fibrosis Questionnaire – Revised (CFQ-R; Quittner et al., 2000) is a 50-item disease-specific health-related quality of life (HRQOL) measure for adults with CF.



There are nine HRQOL domains; three symptom scales and one overall health perception scale. The CFQ-R demonstrated robust psychometric properties and consistent associations with health outcomes in a large national sample (Quittner et al., 2012).

Evaluation Form – Participants were asked to rate how much each questionnaire covered their current difficulties using a four-point scale from ‘did not cover any of my difficulties’ to ‘covered all of my difficulties’. Participants also rated how easy or difficult each questionnaire was to complete using a five-point scale from ‘very difficult’ to ‘very easy’ (Appendix 7, p.93).

### **Procedure**

Potential participants were informed about the research by a familiar clinician either at their multi-disciplinary clinic appointment or during their in-patient stay. If interested they were provided with a research pack including a participant information sheet (Appendix 8, p.95) and consent form (Appendix 9, p.99). Participants were able to complete the research pack during their visit or post it back using a pre-paid envelope.

### **Data analysis**

Principal Component Analysis - to explore the structure of DCFS; to identify whether there was any evidence of the questionnaire measuring different components; to highlight redundant/unrelated items.

Internal Consistency - refers to how well the items on the DCFS relate to each other. It was tested using Cronbach’s Alpha. An alpha score of >.9 indicates ‘excellent’ internal consistency and an alpha of 0.8-0.9 indicates ‘good’ internal consistency (George & Mallery, 2003).

Criterion Validity - investigated by exploring the extent to which DCFS scores correlated with other validated measures, with additional descriptive analyses exploring

this relationship. A correlation coefficient of  $\pm .3$  represents a medium effect and  $\pm .5$  represents a large effect (Field, 2013). It was also investigated by the ability of the DCFS to discriminate between those experiencing psychological distress and those who are not. A Mann Whitney test compared DCFS scores between participants who scored ten and above, and participants who scored below ten (clinical cut-off point) on GAD-7/PHQ-8.

Content Validity - is the degree to which items are representative and relate to the construct being measured (Haynes et al., 1995). It is determined via expert judgement. During the analyses, the researcher noticed possible inconsistencies regarding participants' use of the response scale. Consequently, further exploratory/descriptive statistics were conducted to investigate the practical usage of the DCFS and the wording of the instructions and response scale.

Participant's feedback - descriptive statistics were used to evaluate participants' ratings of the questionnaires.

Missing data was coded as such in SPSS and all analyses were run with pairwise deletion where possible so as to maximise sample size and power.

## **RESULTS**

### **Participant demographics**

Table 1 provides a summary of participant characteristics. The data are skewed towards Caucasian, out-patient and 'non-cepacia' (classification of bacteria growth in CF) categories. Mean age of participants was 30.7 years. There was a relatively representative spread across other categories of marital status, education and work status.

**Table 1.** Summary of participant demographics and clinical characteristics

<b>Age:</b> Mean (SD)		30.7 (11.1)
<b>Gender:</b> n (%)	Male	68 (57.1)
	Female	51 (42.9)
<b>Marital Status:</b> n (%)	Single	49 (41.2)
	Married	27 (22.7)
	Divorced	2 (1.7)
	Separated	1 (.8)
	With a partner	39 (32.8)
	<i>Missing data</i>	1 (.8)
<b>Education:</b> n (%)	Secondary school or less	25 (21)
	GCSEs level (or equivalent)	15 (12.6)
	A/AS level (or equivalent)	10 (8.4)
	Other higher education	30 (25.2)
	University degree	24 (20.2)
	Professional qualification or post-graduate study	14 (11.8)
	<i>Missing data</i>	1 (.8)
<b>Race:</b> n (%)	White – UK	112 (94.1)
	White – other	3 (2.5)
	Indian/Pakistani	2 (1.7)
	Other	1 (.8)
	<i>Missing data</i>	1 (.8)
<b>Current Work Status:</b> n (%)	Attending school outside of home	8 (6.7)
	Taking education courses at home	1 (.8)
	Seeking work	6 (5)
	Working full or part time	68 (57.1)
	Full time homemaker	1 (.8)
	Not attending school or work due to health	23 (19.3)
	Not working for other reasons	10 (8.4)
	<i>Missing data</i>	2 (1.7)
<b>Pathogen growth:</b> n (%)	Non cepacia	99 (83.2)
	Cepacia	12 (10.1)
	Abscessus	8 (6.7)
<b>Setting:</b> n (%)	Outpatient	92 (77.3)
	Inpatient	27 (22.7)
<b>Clinical Measures:</b> mean, SD	Personal Health Questionnaire Depression Scale (PHQ-8) – <i>total score</i>	5.4 (5.1)
	Generalised Anxiety Disorder Questionnaire (GAD-7) – <i>total score</i>	4.6 (4.5)
	Distress in Cystic Fibrosis Scale (DCFS) – <i>mean score</i>	19.6 (16.3)
	Cystic Fibrosis Questionnaire-Revised (CFQ-R) – <i>(range across twelve domains)</i>	51.4-84.7 (18.3-37.3)

## **Principal Component Analysis**

A Principal Component Analysis (PCA) was run on the 23-item DCFS. The suitability of PCA was assessed prior to analysis. Inspection of the correlation matrix showed that all variables had at least one correlation coefficient greater than 0.3. The overall Kaiser-Meyer-Olkin (KMO) measure was 0.83, with individual KMO measures all greater than 0.6. Bartlett's test of sphericity was statistically significant ( $p < 0.001$ ), indicating that the data was likely factorisable. PCA revealed five components that had eigenvalues greater than one and which explained 37.3%, 7.5%, 7.4%, 6.1%, and 5.3% of the total variance, respectively. The five-component solution explained 63.7% of the total variance but after applying Direct Oblimin rotation the rotated solution did not exhibit a simple or meaningful structure (see Table 2). Subsequent exploratory PCA's were conducted, with the two and four component solutions exhibiting the most simple structure, but meaningful interpretation continued to be difficult. On further inspection of the extraction criteria, the first component had an Eigen value of 8.6, with the remaining four components having Eigen values between 1-1.7. Additionally, the scree plot clearly demonstrated one component before the inflection point. Consequently, a one component solution was extracted, with all items loading strongly, providing support to retain all items (see Table 3). Finally, this one component solution could be meaningfully interpreted as measuring the construct 'distress'.

**Table 2.** Pattern and Structure Matrix for 5-component solution

DCFS Item	PATTERN MATRIX				
	Component				
	1	2	3	4	5
DCFS_22	.785	.031	-.061	.073	-.011
DCFS_2	.721	.162	.172	-.137	.118
DCFS_16	.664	-.173	.137	-.020	.061
DCFS_23	.623	-.034	.005	.328	.065
DCFS_1	.480	.328	.001	-.189	.307
DCFS_10	-.138	.700	.101	-.228	.276
DCFS_21	-.206	.674	.207	.307	-.214
DCFS_9	.394	.661	-.053	.042	-.165
DCFS_8	.217	.571	-.279	.075	.275
DCFS_7	.390	.403	.307	.264	-.015
DCFS_6	.311	.352	.221	.269	.062
DCFS_4	.193	.209	.675	.140	-.067
DCFS_5	.307	-.152	.662	.123	.240
DCFS_3	-.098	.123	.603	-.103	.502
DCFS_20	-.153	.078	.276	.738	.003
DCFS_17	.002	-.005	-.023	.668	.242
DCFS_19	.219	-.066	-.085	.628	-.039
DCFS_13	.040	.232	-.397	.460	.419
DCFS_11	.088	-.016	.130	-.086	.739
DCFS_15	.126	-.121	.086	.211	.723
DCFS_12	.008	.151	.001	.364	.492
DCFS_18	.254	.029	.012	.237	.490
DCFS_14	.399	.236	-.124	.193	.419

DCFS Item	STRUCTURE MATRIX				
	Component				
	1	2	3	4	5
DCFS_22	.801	.212	.048	.303	.315
DCFS_2	.785	.346	.295	.151	.440
DCFS_23	.750	.209	.120	.523	.406
DCFS_16	.660	.007	.201	.157	.298
DCFS_14	.658	.455	.043	.447	.658
DCFS_1	.621	.466	.145	.097	.537
DCFS_9	.482	.711	.079	.275	.155
DCFS_10	.075	.699	.217	-.033	.359
DCFS_21	-.024	.681	.279	.379	-.032
DCFS_8	.441	.661	-.114	.312	.476
DCFS_7	.590	.598	.438	.496	.343
DCFS_6	.522	.536	.347	.476	.365
DCFS_4	.340	.376	.734	.287	.194
DCFS_5	.488	.109	.723	.283	.451
DCFS_3	.175	.294	.677	.056	.562
DCFS_20	.116	.264	.329	.735	.164
DCFS_17	.289	.211	.067	.718	.384
DCFS_19	.361	.110	-.023	.661	.156
DCFS_13	.342	.391	-.255	.586	.532
DCFS_15	.458	.148	.210	.383	.802
DCFS_11	.369	.185	.243	.107	.771
DCFS_18	.525	.265	.142	.425	.651
DCFS_12	.344	.361	.130	.510	.612

**Table 3.** One-component solution

<u>DCFS Item</u>	<u>Component 1</u>
DCFS_1	.662
DCFS_2	.704
DCFS_3	.500
DCFS_4	.538
DCFS_5	.618
DCFS_6	.720
DCFS_7	.781
DCFS_8	.638
DCFS_9	.572
DCFS_10	.395
DCFS_11	.575
DCFS_12	.657
DCFS_13	.595
DCFS_14	.808
DCFS_15	.692
DCFS_16	.484
DCFS_17	.556
DCFS_18	.701
DCFS_19	.442
DCFS_20	.462
DCFS_21	.334
DCFS_22	.621
DCFS_23	.718

### **Internal Consistency**

The 23-item DCFS was found to have high internal consistency ( $\alpha=.913$   $n=65$ ), with a range for the total scale, as measured by alpha if item-deleted, between 0.905- 0.914.

However, in this analysis ‘N/A’ responses were considered to be missing data resulting in the analysis using only 50% of the study population. To overcome this, ‘N/A’ responses were re-coded as ‘0’ (given that N/A does mean that there was no distress relating to that item) and the analysis rerun. High internal consistency ( $\alpha=.911$   $n=119$ ) was again demonstrated, with a range for the total scale, as measured by alpha if item-deleted, between 0.902- 0.912.

## Criterion Validity

Based on theoretical and empirical considerations, a series of associations between DCFS items and previously validated measures were chosen a priori. A Spearman correlation analysis was used due to data being ordinal and not all variables being normally distributed, as assessed by Shapiro-Wilk test ( $p < .05$ ). Table 4 illustrates that all correlations were in the predicted direction, and all met statistical significance criteria ( $p < .05$ ), supporting DCFS criterion validity.

**Table 4.** Summary of *a priori* chosen correlations

	DCFS Q1*	DCFS Q2	DCFS Q7	DCFS Q9
<b>FEV 1</b>	Rho = $-.26$ , $p = .007$ N=107			
<b>PHQ-8 Total</b>		Rho = $.73$ , $p < .001$ N=118		
<b>GAD-7 Total</b>		Rho = $.74$ , $p < .001$ N=119		
<b>CFQ-R Physical</b>	Rho = $-.66$ , $p < .001$ N=118			
<b>CFQ-R Emotion</b>		Rho = $-.76$ , $p < .001$ N=118		
<b>CFQ-R Social</b>			Rho = $-.47$ , $p < .001$ , N=118	
<b>CFQ-R Eating</b>				Rho = $-.57$ , $p < .001$ , N=118
<b>Key:</b> CFQ-R = Cystic Fibrosis Questionnaire-Revised; DCFS = Distress in Cystic Fibrosis Scale; FEV1 = Forced Expiratory Volume; GAD-7 = Generalised Anxiety Disorder Questionnaire; PHQ-8 = Personal Health Questionnaire Depression Scale				

\*DCFS Q1 = How have you been feeling physically?

DCFS Q2 = How have you been feeling emotionally?

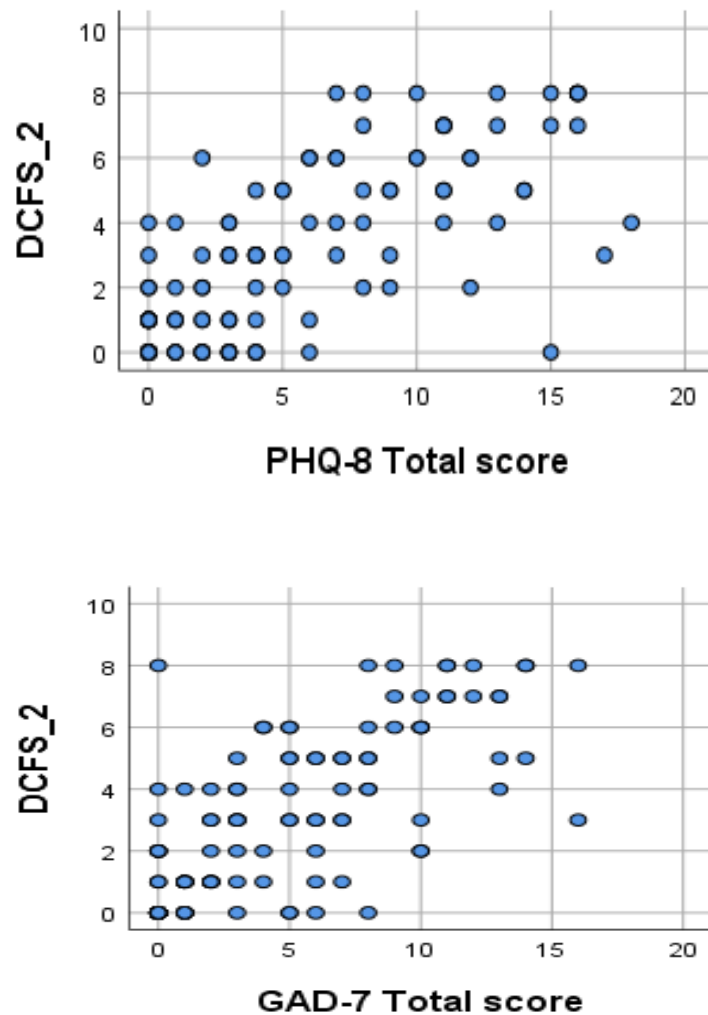
DCFS Q7 = How have you been feeling about your relationships with other people?

DCFS Q9 = How have you been feeling about your body, weight and/or eating?

Large effects were found between DCFS Q2 and already validated measures, with

Figure 1 illustrating scatterplots of these significant positive correlations. However, it also highlights the variation with some participants scoring low (below 10) on PHQ-8/GAD-7 and high (above 5) on DCFS Q2, and vice versa of scoring high on the PHQ-9/GAD-7 but low on the DCFS item 2.

**Figure 1.** Scatterplots of DCFS Q2

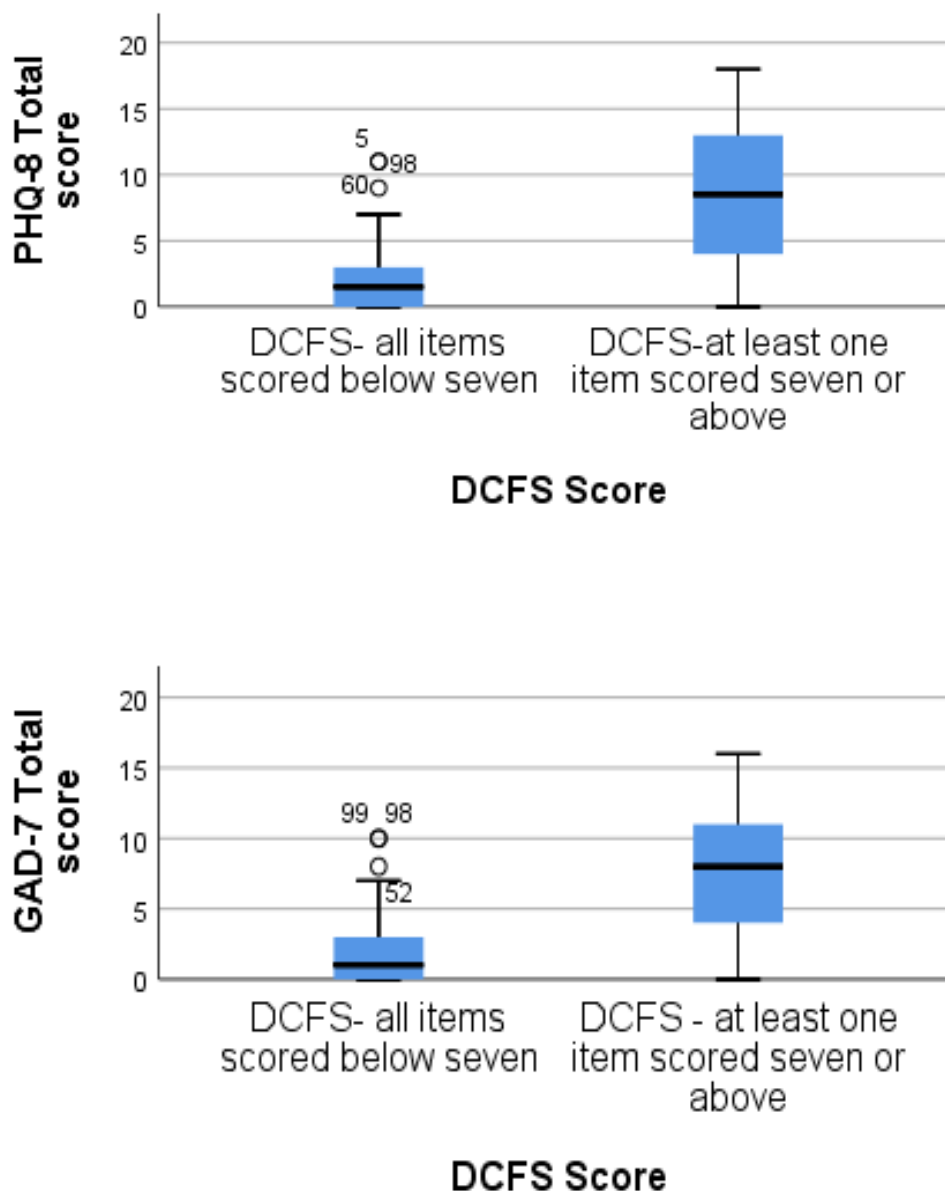


The data were then split into those who scored seven or above on at least one item on the DCFS and those who did not. A cut-off score of seven was selected to ensure that the group represented those who rated themselves as experiencing levels of distress at the higher end of the scale. Differences between the groups on PHQ-8 and GAD-7 total scores were investigated and boxplots presented in Figure 2. As expected, participants who had scored seven or above in at least one item on DCFS had higher PHQ-8 and GAD-7 scores than those who scored below seven on all items. However, the mean PHQ-8 and GAD-7 scores for the group who had scored seven or more on one item were 8.8 and 7.4 respectively which did not meet clinical cut-off point of 10. Overall these analyses suggest that the DCFS is able to pick up difficulties detected by the



PHQ-8 and GAD-7, but it is also able to detect additional distress that is not identified by the PHQ-8 or GAD-7.

**Figure 2.** Boxplots of PHQ-8 and GAD-7 total scores

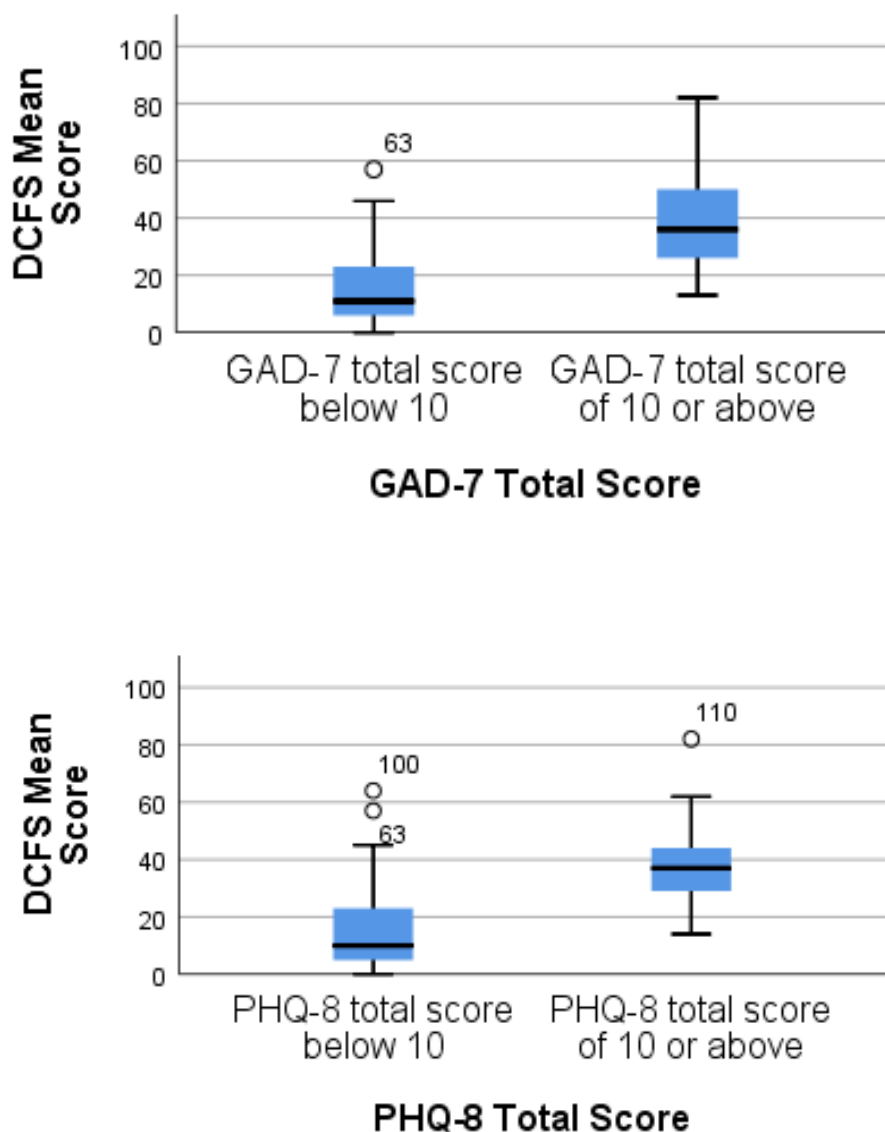


Next, the ability of the DCFS to discriminate between those scoring above and below clinical cut-off point (10) on PHQ-8 and GAD-7 was evaluated (see Figure 3 for boxplots). Distributions of the DCFS mean score for ‘depressed’ and ‘non-depressed’ groups were not similar, as assessed by visual inspection. A Mann Whitney test revealed DCFS total scores for ‘depressed’ group (mean rank = 95.81) were

significantly higher than for ‘non-depressed’ group (mean rank = 49.49),  $U = 275$ ,  $z = -6.12$ ,  $p < .001$ ,  $\eta^2 = 0.32$ .

Similar results were found when comparing ‘anxious’ and ‘non-anxious’ groups, with distributions of the DCFS total score for each group not being similar, as assessed by visual inspection. A Mann Whitney test revealed DCFS total scores for ‘anxious’ group (mean rank = 95.75) were significantly higher than for ‘non-anxious’ group (mean rank = 51.89),  $U = 280.5$ ,  $z = -5.39$ ,  $p < .001$ ,  $\eta^2 = 0.25$ . Therefore, the DCFS is able to discriminate between those scoring above and below the clinical cut-off for GAD-7 and PHQ-8.

**Figure 3.** Boxplots of DCFS Mean Score

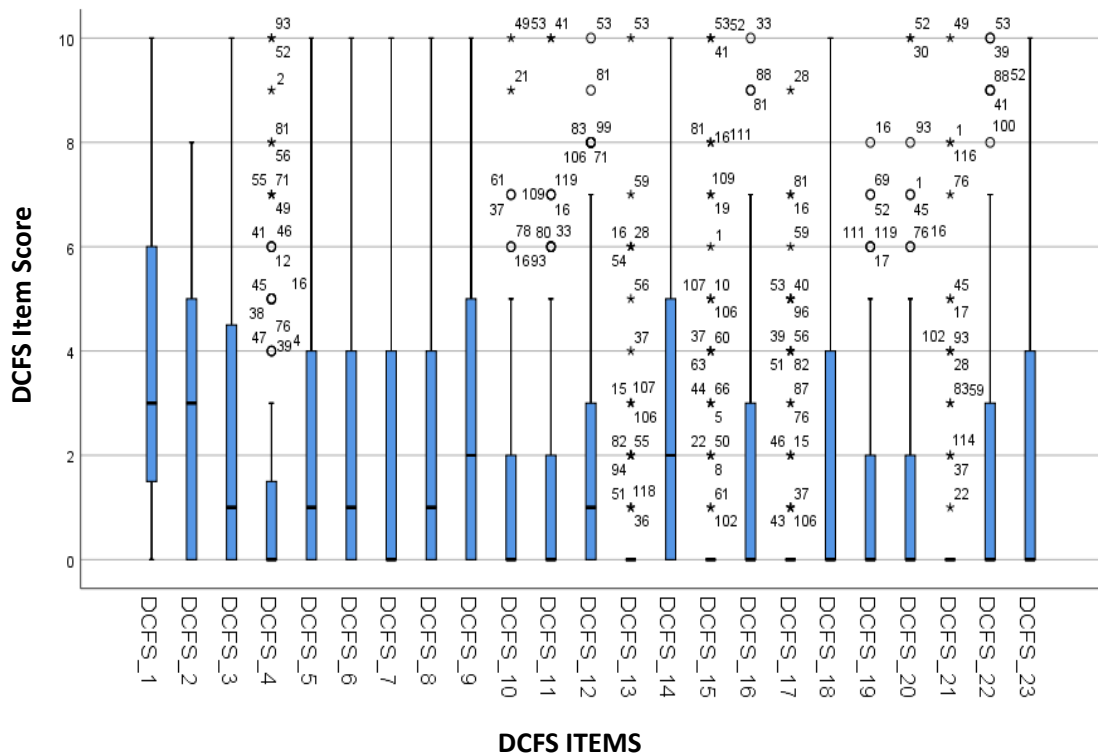


## Content Validity

The method used to create the DCFS supports content validity of the screening tool.

Visual inspection of boxplots (see Figure 4) revealed responses were skewed towards the lower end of the distress scale, with medians for all items being under three. For four items (13, 15, 17, 21) only outliers were presented as up to 80% of participants responded '0' or 'N/A'. However, for every item, including those with only outliers, the boxplots illustrate a range of distress ratings provided by participants from '0' to at least '8', with the majority of items having scores of '10' by several participants. These descriptive analyses provide support for the '0-10' scale and for all items to be included in the DCFS.

**Figure 4.** Boxplots for all DCFS items



Further exploratory analyses were conducted to investigate the distribution of responses across all items (Appendix 10 p.100) and to consider the wording of the response scale. For items relating to specific physical health symptoms (11, 13, 15, 17), there was a high percentage (60-70%) of participants rating these as '0'. Due to the wording of 'no problems' being associated with the score of '0' on the visual scale at the top of the questionnaire it is unclear whether participants were reporting 'no distress' in that area as intended, or whether they meant that the specific item did not apply to them. Furthermore, Q22 regarding 'upsetting past events' was only recorded by one participant as 'N/A', whilst 73 (61.3%) recorded it as '0'. It would be unlikely that these individuals have all experienced significant previous upsetting events and do not have any current distress in that area. It is more likely that they are using the rating '0' to indicate that the item does not apply to them. Overall these data suggest that participants are possibly interchanging between 'N/A' and '0' responses, particularly on certain physical health items.

### **Questionnaire evaluation**

Tables 5 and 6 illustrate participants' evaluation of the questionnaires, with participants consistently rating the DCFS as better than the PHQ-8 and GAD-7 in relation to how well it covered their difficulties. With regards to ease of completion, all questionnaires were rated the same. This demonstrates that the DCFS is deemed to be comparable, if not better than currently used measures. Of the 32 participants who provided written feedback, at least 50% commented on the usefulness of the questionnaires, with specific positive feedback on the DCFS:

*'CFQ-R is very long-winded and at times hard to follow. DCFS – is the best of the measures. Questions are specific and cover all areas of CF but not so long that you get tired and lose interest. The 1-10 scoring system is also better as it allows more precise and nuanced answers than the other scoring systems.'*

*'I feel the questionnaire covered all aspects of living daily life with CF.... the questionnaire also gives you the opportunity to express any negative feelings you have regarding your CF'*

The most common criticism of the questionnaires was in relation to the rating scales with participants providing mixed opinions about which rating scale was the most helpful. The inclusion of comment boxes was a repeated suggestion by participants as would allow them to expand on their responses.

**Table 5.** N (%) responses to how well questionnaires covered current difficulties

	Did not cover any of my difficulties	Covered some of my difficulties	Covered most of my difficulties	Covered all of my difficulties
<b>DCFS</b>	3 (2%)	18 (15%)	44 (37%)	45 (37%)
<b>PHQ-8</b>	3 (2%)	30 (25%)	41 (34%)	36 (30%)
<b>GAD-7</b>	9 (7%)	28 (23%)	34 (28%)	39 (32%)
<b>CFQ-R</b>	3 (2%)	20 (16%)	36 (30%)	51 (42%)
<b>Key:</b> CFQ-R = Cystic Fibrosis Questionnaire-Revised; DCFS = Distress in Cystic Fibrosis Scale; GAD-7 = Generalised Anxiety Disorder Questionnaire; PHQ-8 = Personal Health Questionnaire Depression Scale				

**Table 6.** N (%) responses to how easy or hard questionnaires were to complete

	Very Difficult	Difficult	OK	Easy	Very Easy
<b>DCFS</b>	0	1 (<1%)	18 (15%)	25 (21%)	59 (49%)
<b>PHQ-8</b>	1 (<1%)	2 (1%)	15 (12%)	24 (20%)	61 (51%)
<b>GAD-7</b>	1 (<1%)	5 (4%)	16 (13%)	26 (21%)	55 (46%)
<b>CFQ-R</b>	0	2 (1%)	18 (15%)	26 (21%)	57 (47%)
<b>Key:</b> CFQ-R = Cystic Fibrosis Questionnaire-Revised; DCFS = Distress in Cystic Fibrosis Scale; GAD-7 = Generalised Anxiety Disorder Questionnaire; PHQ-8 = Personal Health Questionnaire Depression Scale					

## **DISCUSSION**

Overall the results suggested a one-component structure for the DCFS and provided support for it being an appropriate measure of distress in CF. Positive findings relating to internal consistency, criterion validity and participants' feedback were found. However, there were potential changes to be made to improve content validity, specifically regarding the instructions and wording of the response scale.

With regards to the structure, PCA indicated a five-component structure using the traditional Eigen value criteria. Based on the Diabetes Distress Screening scale (Polonsky et al., 2005) it was possible that these components related to different aspects of distress, such as physical health, emotional wellbeing and social aspects. However, the results were difficult to interpret meaningfully. Through further inspection of extraction criteria and exploratory PCA, a one-component solution was deemed most meaningful, with high component loadings for all items. This is consistent with the purpose of the DCFS and provides support that the DCFS was measuring distress as intended.

Due to this result, and the high extent of correlations between items, it could be argued that only one item enquiring about general distress levels is required; similar to the Distress Thermometer used in cancer services (Hoffman et al., 2004). However, descriptive statistics demonstrated that all items were rated by participants using the full breadth of the '0-10' scale and therefore it was deemed appropriate to retain all items. A further possibility was to remove any item in which only outlier data points were presented on the boxplots as it could be interpreted that these items are not common issues associated with significant distress. However, these items were related to specific physical health symptoms and with the current sample being skewed towards a healthy outpatient population the prevalence may have been under-represented. This is supported by the fact that a significant proportion of the outlier data points were

inpatient participants, and it would therefore be expected to see a greater representation of these items in future studies with higher number of inpatients. These results provide support for the '0-10' scale and retaining all 23 items in the DCFS.

The DCFS was able to accurately identify on-going difficulties, similar to previously validated measures, with additional exploratory analyses highlighting a pattern of participants for whom the DCFS picks up additional distress not detected by current measures. This reflects the concerns raised by clinicians in CF services and strengthens the rationale for having a screening tool specific to CF difficulties. Although the DCFS is not intended to be used as a diagnostic tool, results suggested it was able to discriminate between those experiencing significant levels of depression/anxiety symptoms and those who are not (as measured by clinical cut-off points recommended for GAD-7 / PHQ-8). It is worth noting that this difference was found in this relatively healthy sample. It would be beneficial to replicate this finding in future studies with a larger participant pool and greater representation of those individuals experiencing high levels of distress.

With regards to content validity, the development process of the DCFS suggests it should be sufficient, but exploratory analyses raised possible improvements to the wording of the response scale and instructions. It is possible that the wording of '0' as 'no problems' on the visual ruler at the top of the questionnaire was confusing for participants, resulting in '0' responses being used to indicate that that particular issue was not relevant to the individuals. This also raised the possibility that individuals were only rating distress if the item currently applied to them. However, the DCFS aims to detect distress in certain areas even if the individual is not experiencing the difficulty at that time. For example, item 18 asks about an individual's feelings about being in hospital; the DCFS is interested in current distress levels if the individual has been in hospital recently but is also interested in the individual's feelings about potentially

being in hospital in future. It is possible that this intention is not made clear in the instructions, resulting in individuals responding only if the item is relevant to their current situation. In a clinical setting it is beneficial to discuss current difficulties and the distress that can be associated with particular symptoms/situations. However, it is also helpful to consider future problems, particularly in physical health settings such as CF services where there is a high likelihood of inpatient stays and deterioration in physical health. Therefore, it is important to consider the wording used to ensure that all relevant information is being gathered so that appropriate support can be provided.

Finally, participants' feedback about the DCFS was positive, highlighting helpful aspects such as its conciseness and range of emotional difficulties addressed. This provides support that it has the potential to be a clinically useful tool that patients could benefit from. Suggestions were made to include comment boxes to allow individuals to expand on their answers. Although this may be helpful, the purpose of the DCFS is to be a quick screening tool to highlight individuals for whom further assessment may be helpful, during which time individuals would have the opportunity to have a more detailed discussion about their current difficulties.

Overall, the results demonstrated the potential of the DCFS to be an appropriate measure of distress in an adult CF population. However, some changes were proposed, including rephrasing the instructions to emphasise that individuals should rate current and potential future distress in relation to items. The wording of the visual scale was also changed from 'no problems' to 'no concerns' and the 'N/A' option removed in order to further reinforce that the questionnaire is asking about distress and not just presence of difficulties (Appendix 11, p101).



## **Limitations**

The study sample included a higher number of out-patients which may be a naturally healthier population in which patients are coping well with CF and are not requiring hospitalisation. Consequently, this may have led to the overall distress levels in the study sample being skewed towards the lower end and not representative of individuals who experience higher levels of distress. Additionally, the study sample also had a high number of participants in the ‘non-cepacia’ category. Patients who grow cepacia or abscessus pathogens can be more physically unwell and therefore typically met the exclusion criteria of the present study. Due to these difficulties, the generalisability of the study findings must be considered and it would be helpful to have a wider sample in future studies.

## **Clinical Implications and Future Research**

The current study suggests the DCFS is a promising screening tool for detecting distress in an adult CF population. It is able to detect what previously validated measures identify, but also identifies additional difficulties that were undetected by previous measures. Furthermore, it provides helpful detail about the areas of distress specifically relating to CF. Participants’ feedback suggests it is an accessible tool and they value an opportunity to think about the emotional impact of CF. Having a user-friendly, quick tool to detect these difficulties as early as possible would allow timely further assessment and appropriate intervention to be provided. These initial findings of the utility of the DCFS are promising but recommendations have been made regarding possible changes. Future research is needed to further investigate its psychometric properties. Such studies should recruit a larger sample of adults with a wide range of current difficulties, potentially including more in-patients and those with the more serious pathogen growths. Finally, in its current state, it is thought that a score of five or above on any item on the DCFS should prompt further assessment. This is similar to

the cut-off point used in the DT in cancer services (Hoffman et al., 2004). However, research should be conducted to formally explore this cut-off point for the DCFS in an adult CF population.

### **CONCLUSION**

The current study provides support that the DCFS can be a useful measure of distress in an adult CF population, with positive findings related to internal consistency, criterion validity and participant feedback. Potential improvements to the instructions and response scale were identified and subsequent recommendations made. Future studies should be conducted to further investigate the psychometric properties of the revised tool, using a wider population.

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## **APPENDICES**

### **Appendix 1 – Summary of Author Guidelines**

#### **NEW SUBMISSIONS**

Submission to this journal proceeds totally online and you will be guided stepwise through the creation and uploading of your files. The system automatically converts your files to a single PDF file, which is used in the peer-review process.

As part of the Your Paper Your Way service, you may choose to submit your manuscript as a single file to be used in the refereeing process. This can be a PDF file or a Word document, in any format or lay-out that can be used by referees to evaluate your manuscript. It should contain high enough quality figures for refereeing. If you prefer to do so, you may still provide all or some of the source files at the initial submission. Please note that individual figure files larger than 10 MB must be uploaded separately.

#### ***References***

There are no strict requirements on reference formatting at submission. References can be in any style or format as long as the style is consistent. Where applicable, author(s) name(s), journal title/book title, chapter title/article title, year of publication, volume number/book chapter and the article number or pagination must be present. Use of DOI is highly encouraged. The reference style used by the journal will be applied to the accepted article by Elsevier at the proof stage. Note that missing data will be highlighted at proof stage for the author to correct.

#### ***Formatting requirements***

There are no strict formatting requirements but all manuscripts must contain the essential elements needed to convey your manuscript, for example Abstract, Keywords, Introduction, Materials and Methods, Results, Conclusions, Artwork and Tables with Captions.

If your article includes any Videos and/or other Supplementary material, this should be included in your initial submission for peer review purposes.

Divide the article into clearly defined sections.

#### ***Figures and tables embedded in text***

Please ensure the figures and the tables included in the single file are placed next to the relevant text in the manuscript, rather than at the bottom or the top of the file. The corresponding caption should be placed directly below the figure or table.

## **Cover letter**

Corresponding authors must provide a cover letter which includes statements answering the following questions:

- Has the work been seen and approved by all co-authors?
- How is the work clinically relevant, and how does it add to existing research?
- Have papers closely related to the submitted manuscript been published or submitted for publication elsewhere? If so please provide details.

Failure to provide a cover letter addressing each of the questions above will result in the paper being returned to the author. The cover letter must be uploaded as a separate submission item.

## **Appendix 2 – Search terms**

### **EBSCO Host – PsychINFO, CINAHL, Psychology and Behavioural Sciences Collection**

1. Anxiety/Depression
  - a. Subject headings individually per database
  - b. Free text = (emotion\* or wellbeing or “well being” or depress\* or anxi\* or “mental health” or mood or psycho\* or distress) *in title and abstract*
2. Adult
  - a. Subject headings individually per database
  - b. Free text = (adult or aged) *in title and abstract*
3. Cystic Fibrosis
  - a. Subject headings individually per database
  - b. Free text = (cystic fibrosis or CF) *in title and abstract*

### **OVID Host – Medline and Embase**

1. Anxiety/Depression
  - a. Subject headings individually per database
  - b. Free text = (emotion\* or wellbeing or ‘well being’ or depress\* or anxi\* or ‘mental health’ or mood or psycho\* or distress).TW
2. Adult
  - a. Subject headings individually per database
  - b. Free text = (adult or aged).TW
3. CF
  - a. Subject headings individually per database
  - b. Free text = (cystic fibrosis or CF).TW



### **Appendix 3 – Data Extraction and Quality Appraisal Tool**

- Article Info
  - Title, study setting, country, single centre/multicentre, method used to confirm CF diagnosis, sampling method
- Sample
  - Number eligible/recruited/dropout/follow up etc,
  - Mean/SD (median/IQR) of continuous characteristics eg age, BMI, FEV1%
  - Frequency/proportion of categorical characteristics eg gender
- Depression/Anxiety measures
  - What tools were used
  - Mean scores/how many presented with clinical risk
  - Definition of clinical cut off points
- Proposed predictive factors (see list above)
  - Continuous characteristics - Mean, standard deviation (median/IQR)
  - Categorical characteristics – Frequency/proportion
  - Tools used to measure these
- Statistical methods and effect sizes
  - Method → Bivariable or Multivariable
  - Statistical tests (effect estimate recorded):
    - 1. Student's t-test (mean difference, t-statistic)
    - 2. Analysis of Variance (F-statistic)
    - 3. Pearson's or Spearman's correlation test (correlation coefficient)
    - 4. Simple Linear Regression (regression coefficient)
    - 5. Effect size (mean difference divided by pooled standard deviation)
    - 6. Multivariable Linear Regression (regression coefficient, names of variables included in final model)
    - 7. Analysis of Co-variance (F-statistic, name of variable adjusted for in final model)
    - Confounding variables accounted for?
- Statistical significance
  - P value for each statistical test → could group into various levels...

	Question		Yes	Some-what	No	NR, CD*	Quality Rating
Quality of reporting	1.	Were the aims/objective of the study clear?					
	2.	Was ethical approval or consent of participants attained?					
	3.	Were the methods (including statistical methods) sufficiently described to enable them to be repeated?					
	4.	Was a sample size justification, power description, or variance and effect estimates provided?					
	5.	Is it clear what was used to determine statistical significance and/or precision estimates? (eg p-values, confidence intervals)					
	6.	Were the basic data adequately described?					
	7.	Were the limitations of the study discussed?					
Question			Yes	Some-what	No	NRCD	Risk of bias rating
Selection Bias	8.	Was the study population clearly defined (is it clear who the research was about?)					
	9.	Was the selection process likely to select participants that were representative of the target population under investigation? Were inclusion and exclusion criteria applied uniformly to all participants?					
	10.	Was the participation rate of eligible persons at least 50%?					
	11.	Were measures undertaken to address and categorise non-responders?					
Information Bias	12.	Was the target variable measured using instruments/measurements that had been trialled, piloted or published previously? (pain, QoL)					
	13.	Was the depression/anxiety variable measured using instruments/measurements that have been trialled, piloted or published previously?					
	14.	Were measures implemented consistently across all study participants?					
Confoundin g Bias	15.	Was the study design appropriate for the stated aim(s)?					
	16.	Were key potential confounding variables measured and adjusted statistically for the impact on the relationship between target variables and psychological outcomes? Were any interactions between variables investigated?					
Overall Quality:							

\*Not reported or cannot determine

## **Appendix 4 – Major Research Project Protocol** (Version 3, 27/06/18)

### **Abstract**

Cystic Fibrosis is a chronic disease with elevated risk of co-morbid anxiety and depression. Current screening measures may not adequately detect distress that individuals with physical health conditions can experience.

The Distress in Cystic Fibrosis Scale (DCFS) is a newly developed 23-item questionnaire which aims to identify areas of difficulty for adults with Cystic Fibrosis. This study aims to explore psychometric properties of the DCFS in an adult Cystic Fibrosis population.

Approximately 115 patients with Cystic Fibrosis will be recruited. Participants will complete 4 questionnaires and provide demographic information. Analyses will be conducted to evaluate the reliability and validity of the DCFS.

If found to have good psychometric properties, the DCFS could be used as an accurate screening tool of distress relevant to a CF population and as a regular outcome measure for psychological therapies in CF services.

### **Introduction**

#### **Cystic Fibrosis**

Cystic Fibrosis (CF) is an inherited, progressive and life-limiting condition in which the lungs and digestive system can become obstructed by thick, sticky mucus. Despite recent advances in diagnosis and treatment, management of CF requires a complex, time-consuming daily regimen taking two to four hours, in addition to over 20 medication tablets a day. Despite this demanding treatment routine, individuals with CF experience frequent infections and progressive failure of most organ systems (e.g. lungs, pancreas).

#### **Screening of psychological distress in CF**

Various research (Smith & Schmitz, 2014; Yang et al., 2013) has shown that adults with chronic conditions, such as cancer and diabetes, are at higher risk for experiencing depression and anxiety compared to community samples. Quittner et al (2014) conducted an extensive study of 6088 patients with CF (The International Depression Epidemiological Study -TIDES) and found that depression and anxiety rates were 2-3 times higher in individuals with CF than those reported in community samples.

#### Difficulties with Current Screening Measures

Due to financial and time constraints it is not possible to offer everyone with CF an annual clinical interview and therefore screening measures are routinely used to detect psychological distress. The International Committee Mental Health in Cystic Fibrosis (ICMH-CF) advise using the Patient Health Questionnaire (PHQ-9) and Generalised Anxiety Disorder Questionnaire (GAD-7). However, it has been highlighted that these generic screens may not adequately detect psychosocial difficulties in a CF population as clinically 'normal' scores may be achieved by patients with CF for whom clinical assessment reveals psychosocial difficulties. For example, patient anxieties regarding treatment management or attending MDT meetings may not be detected through the GAD-7. Research has shown that prolonged psychological distress in patients with chronic illnesses can be associated with poor treatment adherence (Grenard et al, 2011), poor health outcomes (Riekert, 2007) and increased healthcare costs (Snell et al, 2014). Given these significant effects of psychological distress on quality of life and key health outcomes it is important that screening measures accurately detect psychological distress with specific reference to the physical health condition.

#### Disease Specific Measures

Disease-specific measures of emotional distress exist in other long-term conditions such as the Diabetes Distress Scale (DDS) (Polonsky et al., 2005) and the Distress Thermometer (DT) for cancer services (Hoffman et al., 2004).

These measures were developed due to these populations experiencing specific types of distress relating to their physical health conditions. It is important to highlight that the term ‘distress’ is used as this is a non-stigmatizing term that describes the broad array of difficulties that individuals with physical health conditions can experience. Therefore, the aim of these measures is not to identify psychopathology but to identify areas that further assessment and intervention may be beneficial ranging from physical problems to practical concerns.

### Distress in Cystic Fibrosis Scale (DCFS)

The DCFS has been developed to detect distress in a CF population. 150 adult patient files were audited over a 3-year period to ascertain the emotional concerns CF patients presented with to the clinical psychologist (CP). 30 themes of psychosocial concerns were identified of which 8 were excluded due to being isolated occurrences (e.g. domestic violence and perceptual disturbance). The remaining 22 themes were included in the questionnaire which was constructed by adapting the framework of previously validated measures. It was presented to current Clinical Psychology CF outpatients during face-to-face contact, and was sent to the CF MDT to check face validity, with positive feedback received. In 2015 the questionnaire was shown to the UK Psychosocial Professions in CF Group (UKPP-CF) and the questionnaire format was improved, and one further item added.

The final 23-item questionnaire now requires formal exploration of psychometric properties before the DCFS can be disseminated and used in clinical practice.

### **Aims and hypotheses**

#### Aims

This is the first phase to evaluate the reliability and validity of the newly-developed self-report measure of distress in a CF population – the DCFS.

#### Hypotheses

- The DCFS will have acceptable psychometric properties:
  - Construct Validity: Exploratory factor analysis to determine subscales.
  - Content validity: All 23 items on DCFS will have a score of at least 1 by at least 1 participant.
  - Internal consistency: The DCFS total score and subscales will have a Cronbach's alpha score of above 0.7.
  - Criterion and Discriminant validity: The DCFS total score and subscales will have a correlation coefficient of +/- .3 with:
    - Total scores of PHQ-8,
    - Total scores of GAD-7
    - Total score and sub-scales of Cystic Fibrosis Questionnaire – Revised (CFQ-R).
  - Optimal cut-off score: DCFS total score and sub-scales will have an Area Under the Curve (AUC) above 0.7.
- The DCFS will be deemed most relevant and easiest to complete by participants compared to the other questionnaires.

### **Plan of Investigation**

#### **Participants**

Participants will be recruited from the West of Scotland Adult Cystic Fibrosis Service (WoSACFS). It has been estimated that it would be possible to gather approximately 115 participants from in-patient wards and MDT clinics during the recruitment phase.

#### **Inclusion and Exclusion Criteria**

- Inclusion criteria
  - Diagnosis of CF
  - Patient attending the WoSACFS either as out-patient or in-patient
  - Aged over 18 years
  - Fluent in English
- Exclusion criteria
  - Diagnosis of learning disability

- Any patient that the CF team consider too unwell due to infection control.

### Recruitment Procedures

Information regarding the purpose of the study and inclusion/exclusion criteria will be provided to the WoSACFS. Participants will be recruited through MDT clinics and in-patient ward. A participant information sheet and consent form will be provided.

### Measures

- Demographic information – Range of demographic and physical health measures.
- Distress in Cystic Fibrosis Scale (DCFS) is a 23-item questionnaire. It has an 11-point range with endpoints labelled ‘no problems’ (0) and ‘worst I’ve ever felt’ (10). Respondents are instructed to write the number (0-10) that best describes how they have been feeling over the past two weeks relating to each of the 23 items. It takes approximately 5 minutes to complete.
- Patient Health Questionnaire 8 (PHQ-8; Kroenke & Spitzer, 2002) is an 8-item self-report questionnaire, using a 4-point scale from ‘not at all’ to ‘nearly every day’. Responses are based on how the individual has been feeling over the past two weeks. Evidence supports reliability and validity of PHQ-8 as a measure of depression in the general population (Kroenke & Spitzer, 2002). It takes approximately 3 minutes to complete.
- Generalised Anxiety Disorder Questionnaire -7 (GAD-7; Spitzer et al, 2006) is a 7 item self-reported questionnaire, using a 4-point scale from ‘not at all’ to ‘nearly every day’. Responses are based on how the individual has been feeling over the past two weeks. Evidence supports reliability and validity of the GAD-7 as a measure of anxiety in the general population (Lowe et al, 2008). It takes approximately 3 minutes to complete.

- Cystic Fibrosis Questionnaire – Revised (CFQ-R; Quittner et al, 2000) is a 50-item disease-specific health-related quality of life (HRQOL) measure for adults with CF. There are 9 HRQOL domains; 3 symptom scales and 1 overall health perception scale. The CFQ-R demonstrated robust psychometric properties and consistent associations with health outcomes in a large national sample (Quittner et al, 2012). It takes approximately 10 minutes to complete.
- Evaluation Form – Participants will be asked which questionnaire 1) best described their current difficulties and 2) was the most difficult to complete. This will approximately take 2 minutes to complete.

### Design

A within group design will be employed with all participants completing 4 questionnaires.

### Research Procedures

Potential participants will be informed about the research and given a participant information sheet by a familiar clinician either at their MDT meeting or during in-patient psychology ward round. This will be within the Queen Elizabeth University Hospital or West Ambulatory Care Hospital. The research pack could be completed at the appointment with the researcher or at home and returned via a pre-paid envelope.

### Data Analysis

- **Descriptive stats** to investigate spread of data → assessment of item inter-correlation; mean; SD.
- **Construct Validity** → conduct an exploratory factor analysis to evaluate number of constructs within DCFS and determine sub-scales.
- **Content/Face Validity** → is the degree to which elements of an assessment instrument measure what they intend to measure. It is determined via expert judgement which has already been completed. Current study could comment on



whether all 23 items received a score of at least above 1 – this would suggest that the DCFS items are relevant to the wide range of distress experienced by CF population.

- **Internal Consistency** → refers to how well the items on the DCFS relate to each other. It can be tested using Cronbach's Alpha for total score and sub-scales of DCFS with an alpha score of  $>.9$  indicating 'excellent' internal consistency and an alpha of  $0.8-0.9$  indicating 'good' internal consistency (George & Mallery, 2003).
- **Criterion/Concurrent Validity** → refers to the extent to which the DCFS scores correlate with other validated measures. A correlation coefficient of  $\pm .3$  represents a medium effect and  $\pm .5$  represents a large effect (Field, 2013).
- **Discriminant Validity** → refers to the ability of the DCFS to discriminate between those who experience psychological distress and those who do not. Can be evaluation through correlations between items/sub-scales on DCFS and CFQ-R.
- **Sensitivity** refers to the ability of the DCFS to correctly identify those experiencing psychological distress as having psychological distress; and **specificity** refers to the ability of the DCFS to correctly identify the non-psychological distress as not having psychological distress. Sensitivity and specificity can be investigated using Receiver Operator Characteristic (ROC) curve analysis. Values closer to 100% represent greater sensitivity and specificity. It may also be possible to identify a 'cut off' score using the ROC analysis for DCFS total score and possible sub-scales.
- **Questionnaire Evaluation** → Calculate percentages for which questionnaire was perceived as 1) most relevant to current difficulties and 2) most difficult to complete.

### Justification of sample size

There is limited literature guidance on sample size required for validation studies. A review by Anthoine et al (2014) reported that the sample size determination for psychometric validation studies is rarely ever justified *a priori* and stated that clear and scientifically sound recommendations on the sample size for validation studies remains to be developed. From a brief look at the literature and reviewing previous trainee theses, it appears that the majority of literature suggests a minimum sample size of 100 or 5 times the number of included items. Given this is a doctoral project with limited scope for recruitment, this project followed the less stringent recommendations of a subject-to-variables ratio of 5/1 (Anthoine, 2014). With a 23-item questionnaire, the researcher aimed to recruit 115 participants.

### Settings and Equipment

Research packs will be provided to participants within the WoSACFS as in/out-patient. Research packs can be completed in private rooms within WoSACFS or at home.

### Health and Safety Issues

Infection control is imperative to consider for both researcher and participants due to the risk of cross infection. The researcher will familiarise themselves with relevant health and safety procedures and ensure the NHS LearnPro health and safety/infection control module is up-to-date.

### Ethical Issues

Ethical approval will be sought from NHS ethics and management approval from NHS Greater Glasgow and Clyde Research and Development committee.

The questionnaire scores will be put into an electronic database where it will be used for data analysis. The anonymous data will be stored on an encrypted password protected University and NHS computer. Completed paper research packs will be stored in a secure filing cabinet within West of Scotland Adult Cystic Fibrosis Service. My

supervisors (Psychologists working in West of Scotland Adult Cystic Fibrosis Service and Glasgow University) and I will have access to the data. Additionally, representatives of the study sponsor, NHS Greater Glasgow & Clyde will also require access if they choose to audit the study. Personal identifiable information will be stored for 3 months after the end of the study, and the research data stored for 10 years. Data will only be used for those purposes approved by ethics committees.

It is possible that participants may become upset when discussing distress relating to their CF. If this occurs when researcher is present, the researcher will use their skills as a trainee clinical psychologist to assess risk and contain any such distress. If researcher has significant concerns regarding the well-being of a participant or if they score within clinical range on PHQ-8/GAD-7 (a score of above 10), their consent will be sought to pass this information to CF Team Clinical Psychologist. Furthermore there will be contact information for appropriate services that the participant can utilise should they wish.

All care will be taken to ensure that the potential participant is able to give informed consent to take part in the research. Clear information sheets explaining the purpose and process of participation will be provided with the option of the researcher verbally reading this to the potential participant. It will be made clear that participation is voluntary; participants are free to withdraw from the study at any point; and withdrawal from the study will have no effect on the care they receive from the WoSACFS.

Participants will be asked to consent to a letter being sent to the West of Scotland Adult Cystic Fibrosis Service informing that they have agreed to participate in the study).

### **Financial Issues**

Overall research cost is expected to be £131.61.

### **Timetable**

<b><u>Task</u></b>	<b><u>Estimated Time to Complete</u></b>	<b><u>Estimated Start Date</u></b>	<b><u>Estimated Completion Date</u></b>
<b>MRP Draft</b>	2 months	01/10/17	04/12/17
<b>MRP proposal</b>	1 month	01/01/18	29/01/18
<b>Finalise Proposal and Materials</b>	3 months	February 2018	April 2018
<b>Ethics Submission</b>	3 months	May 2018	August 2018
<b>Recruit and gather data</b>	7 months	August 2018	February 2019
<b>Test psychometric properties</b>	2 months	February 2019	April 2019
<b>Final write up</b>	3 months	April 2019	July 2019

### **Practical Applications**

If the DCFS is found to be reliable and valid it can be used as a regular outcome measure for psychological therapies in CF services both at review meetings and during 1-1 therapy interventions. This will allow accurate screening of psychological distress relevant to their physical health condition, promote quick intervention when required and evaluate progress throughout therapy. If the reliability and validity is found to be poor then subsequent revisions can be made to the tool and further validation studies conducted in the future.

The results of the study will be written in the trainee clinical psychologist's thesis and disseminated to CF centres across the UK through conferences. Results of the study can also be distributed to participants who are interested in receiving them.

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anxiety in patients with cystic fibrosis and parent caregivers: results of the International Depression Epidemiology Study (TIDES) across nine countries. *Thorax*, 69, 1090-1097.

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**Appendix 5: Letters of Approval (REC and R&D) – original and amendment**

**WoSRES**

*West of Scotland Research Ethics Service*



Dr Alison Jackson  
Institute of Health and Wellbeing  
Administration Building  
Gartnavel Royal Hospital  
Glasgow  
G12 0XH

**West of Scotland REC 4**  
Research Ethics  
Clinical Research and Development  
West Glasgow Ambulatory Care Hospital  
Dalnair Street  
Glasgow  
G3 8SJ  
(Formerly Yorkhill Childrens Hospital)

Date 15 October 2018  
Direct line 0141 232 1808  
E-mail WoSREC4@ggc.scot.nhs.uk

Dear Dr Jackson

**Study title:** Validation of a cystic fibrosis-specific measure of distress in an adult population.  
**REC reference:** 18/WS/0184  
**Protocol number:** N/A  
**IRAS project ID:** 246529

The Research Ethics Committee reviewed the above application at the meeting held on 5 October 2018. Thank you for attending to discuss the application.

We plan to publish your research summary wording for the above study on the HRA website, together with your contact details. Publication will be no earlier than three months from the date of this favourable opinion letter. The expectation is that this information will be published for all studies that receive an ethical opinion but should you wish to provide a substitute contact point, wish to make a request to defer, or require further information, please contact [hra.studyregistration@nhs.net](mailto:hra.studyregistration@nhs.net) outlining the reasons for your request. Under very limited circumstances (e.g. for student research which has received an unfavourable opinion), it may be possible to grant an exemption to the publication of the study.

**Ethical opinion**

The members of the Committee present gave a favourable ethical opinion of the above research on the basis described in the application form, protocol and supporting documentation, subject to the conditions specified below.

**Conditions of the favourable opinion**

The REC favourable opinion is subject to the following conditions being met prior to the start of the study.

- 1) Confirm that the ward nurses will make the first approach to potential participants in order to remove any potential for coercion.

- 2) Amend the PIS as follows:-
  - a) Reword the following sentence in the first paragraph to name the person concerned – at present it is not clear who “me” is: *“If there is anything you would like to discuss, please do not hesitate to contact me”*.
  - b) In *“Why am I being asked to take part”*, replace “part of” to “supported by”.
  - c) The first word of the section *“Do I have to take part”* should be “No”.
  - d) In *“What would I have to do”*, replace “demographic information” with “background information” as it is more understandable to a lay reader. Clearly explain terms like “BMI” and “FEV1” in lay language. Give an example of risk which may be identified to make this clearer.
  - e) In *“Who else would know I am doing this”* ensure that the tense is consistent throughout e.g. in some parts the word “would” is used, in others “will” is used. Provide a bit more detail on what the breach of confidentiality might entail e.g. which groups might need to be informed.
- 3) Add a statement to the consent form allowing participants to agree to their GP being informed about their participation in the study.
- 4) Confirm that the study-specific demographic information document will not be used, since demographic information is already being requested in the CFQ, and the duplication could be quite onerous for participants.
- 5) In the Evaluation Form, reword the questions so as to give the participants a chance to assign a numerical rating e.g. from 0 to 5, with a description of what each numerical value represents (such as 0 – very difficult, 5 – very easy).
- 6) Confirm that you will give participants a shorter time period to consider participation – this is so as not to lose participants who may have forgotten about it by July 2019.

You should notify the REC once all conditions have been met (except for site approvals from host organisations) and provide copies of any revised documentation with updated version numbers. Revised documents should be submitted to the REC electronically from IRAS. The REC will acknowledge receipt and provide a final list of the approved documentation for the study, which you can make available to host organisations to facilitate their permission for the study. Failure to provide the final versions to the REC may cause delay in obtaining permissions.

Management permission must be obtained from each host organisation prior to the start of the study at the site concerned.

*Management permission should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements. Each NHS organisation must confirm through the signing of agreements and/or other documents that it has given permission for the research to proceed (except where explicitly specified otherwise).*

*Guidance on applying for HRA and HCRW Approval (England and Wales)/ NHS permission for research is available in the Integrated Research Application System, at [www.hra.nhs.uk](http://www.hra.nhs.uk) or at <http://www.rdforum.nhs.uk>.*



## Approved documents

The documents reviewed and approved at the meeting were:

<i>Document</i>	<i>Version</i>	<i>Date</i>
GP/consultant information sheets or letters [Letter to Service re participation]	1	27 June 2018
IRAS Application Form [IRAS_Form_14092018]		14 September 2018
Non-validated questionnaire [Demographic Information]	3	27 June 2018
Non-validated questionnaire [Evaluation Questionnaire]	3	27 June 2018
Non-validated questionnaire [Distress in Cystic Fibrosis Scale]	1	27 June 2018
Other [Support Services Available]	2	27 June 2018
Participant consent form [Consent Form ]	4	04 September 2018
Participant information sheet (PIS) [PIS]	4	04 September 2018
Research protocol or project proposal [MRP Proposal ]	3	27 June 2018
Summary CV for Chief Investigator (CI) [CI CV Alison Jackson]		
Summary CV for student [Student CV - Caroline Finlay]		
Summary CV for supervisor (student research) [Supervisor CV - Sejal Patel]		
Validated questionnaire [GAD 7 ]		
Validated questionnaire [PHQ 8 ]		
Validated questionnaire [CFQ-UK]		

**Enclosures:** List of names and professions of members who were present at the meeting and those who submitted written comments

“After ethical review – guidance for researchers”

**Copy to:** Ms Emma Jane Gault  
Ms Elaine O'Neill, NHS Greater Glasgow and Clyde  
[nhsg.NRSPCC@nhs.net](mailto:nhsg.NRSPCC@nhs.net)

Administrator: Mrs Elaine O'Neill  
Telephone Number: 0141 232 1815  
E-Mail: [elaine.o'neill2@ggc.scot.nhs.uk](mailto:elaine.o'neill2@ggc.scot.nhs.uk)  
Website: [www.nhsggc.org.uk/r&d](http://www.nhsggc.org.uk/r&d)

R&D Management Office  
West Glasgow ACH  
Dahair Street  
Glasgow G3 8SW

12 November 2018

Miss Caroline Finlay  
University of Glasgow  
Inst of Health and Wellbeing  
Admin Building  
Garthavel Royal Hospital  
Glasgow G12 0XH

### NHS GG&C Board Approval

Dear Miss C Finlay,

Study Title:	Validation of a cystic fibrosis-specific measure of distress in an adult population
Principal Investigator:	Miss Caroline Finlay
GG&C HB site	West of Scotland Adult Cystic Fibrosis Service (QEUH)
Sponsor	NHS Greater Glasgow and Clyde
R&D reference:	GN18RM362
REC reference:	18/WS/0184
Protocol no:	V3.0; 27/06/18

I am pleased to confirm that Greater Glasgow & Clyde Health Board is now able to grant **Approval** for the above study.

#### Conditions of Approval

1. **For Clinical Trials** as defined by the Medicines for Human Use Clinical Trial Regulations, 2004
  - a. During the life span of the study GGHB requires the following information relating to this site
    - i. Notification of any potential serious breaches.
    - ii. Notification of any regulatory inspections.

It is your responsibility to ensure that all staff involved in the study at this site have the appropriate GCP training according to the GGHB GCP policy ([www.nhsggc.org.uk/content/default.asp?page=s1411](http://www.nhsggc.org.uk/content/default.asp?page=s1411)), evidence of such training to be filed in the site file.

2. **For all studies** the following information is required during their lifespan.
  - a. Recruitment Numbers on a monthly basis
  - b. Any change of staff named on the original SSI form
  - c. Any amendments – Substantial or Non Substantial
  - d. Notification of Trial/study end including final recruitment figures
  - e. Final Report & Copies of Publications/Abstracts

**Please add this approval to your study file as this letter may be subject to audit and monitoring.**

Your personal information will be held on a secure national web-based NHS database.

I wish you every success with this research study

Yours sincerely,

Mrs Elaine O'Neill  
**Senior Research Administrator**

Cc: Miss Emma Jane Gault (University of Glasgow)

Miss Caroline Finlay  
Institute of Health and Wellbeing  
Administration Building  
Gartnavel Hospital  
Glasgow  
G12 0XH

**West of Scotland REC 4**  
Research Ethics  
Clinical Research and Development  
West Glasgow Ambulatory Care Hospital  
Dalnair Street  
Glasgow  
G3 8SJ  
(Formerly Yorkhill Childrens Hospital)

Date 5 December 2018  
Direct line 0141 232 1808  
E-mail WoSREC4@ggc.scot.nhs.uk

Dear Miss Finlay

<b>Study title:</b>	Validation of a cystic fibrosis-specific measure of distress in an adult population.
<b>REC reference:</b>	18/WS/0184
<b>Protocol number:</b>	N/A
<b>Amendment number:</b>	Amendment No:1 11/11/18 (REC Ref AM01)
<b>Amendment date:</b>	26 November 2018
<b>IRAS project ID:</b>	246529

#### **Summary of Amendment**

1) Change of CI from Dr Alison Jackson to Professor Jon Evans. The PIS and consent form have been updated to reflect this.

2) Dr Sejal Patel, Clin Psychologist will take consent and give info to participants. This is to improve the likelihood of gaining the required number of participants within the available time frame. Dr Patel is an experienced clinical psychologist and will be able to manage any distress expressed by participants

The above amendment was reviewed by the Sub-Committee in correspondence.

#### **Ethical opinion**

The members of the Committee taking part in the review gave a favourable ethical opinion of the amendment on the basis described in the notice of amendment form and supporting documentation.

□

## Approved documents

The documents reviewed and approved at the meeting were:

<i>Document</i>	<i>Version</i>	<i>Date</i>
Notice of Substantial Amendment (non-CTIMP)	Amendment No:1 11/11/18 (REC Ref AM01)	26 November 2018
Other [Dr Sejal Patel CV]	N/A	
Other [Subcttee query to applicant]	N/A	29 November 2018
Other [Applicant response to subcttee query]	N/A	29 November 2018
Participant consent form [tracked]	6	11 November 2018
Participant information sheet (PIS) [tracked]	6	11 November 2018
Summary CV for Chief Investigator (CI) [Professor J Evans CV (new CI)]	N/A	06 October 2018

## Membership of the Committee

The members of the Committee who took part in the review are listed on the attached sheet.

## Working with NHS Care Organisations

Sponsors should ensure that they notify the R&D office for the relevant NHS care organisation of this amendment in line with the terms detailed in the categorisation email issued by the lead nation for the study.

## Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

We are pleased to welcome researchers and R & D staff at our Research Ethics Committee members' training days – see details at <http://www.hra.nhs.uk/hra-training/>

<b>18/WS/0184:</b>	<b>Please quote this number on all correspondence</b>
--------------------	---

Yours sincerely

✓  
On behalf of  
**Dr Ken James**  
Chair

Dear Miss C Finlay,

**R&D Ref:** GN18RM362 **Ethics Ref:** 18/WS/0184

**Investigator and site(s):** Miss Caroline Finlay

**Project Title:** Validation of a cystic fibrosis-specific measure of distress in an adult population

**Protocol Number:** V3

**Amendment: Substantial** Amendment 1 (26/11/18)

**Sponsor:** NHS Greater Glasgow and Clyde

I am pleased to inform you that R&D have reviewed the above study's Amendment and can confirm that Management Approval is still valid for this study.

Reviewed Documents:	Version	Dated
Ethics Approval Letter		05/12/18
Notice of Substantial Amendment form		26/11/18
Prof Jonathan Evans CV		
Dr Sejal Patel CV		
Participant Information sheet and consent form	6	11/11/18
Updated SSI form		

I wish you every success with this research project.

Kind regards

**NHS GG&C R&D**

West Glasgow Ambulatory Care Hospital

Dalnair Street

Glasgow G3 8SW

Tel: +44 (0)141 232 1815

Generic email for PR team: [RandD.PRTeam@ggc.scot.nhs.uk](mailto:RandD.PRTeam@ggc.scot.nhs.uk)

Web: [www.nhsggc.org.uk/r&d](http://www.nhsggc.org.uk/r&d)

My working days - Mon, Tues, Thurs & Fri 7-2.30 and Wed 7-5

## **Appendix 6: DCFS Original**

### **Distress in Cystic Fibrosis Scale**

Below is a list of common issues affecting people with Cystic Fibrosis.

- ✓ Please read each item carefully, and using the scale at the top as a guide, fill in the box next to each question with the number that comes closest to how you have been feeling about that issue **over the past 2 weeks**.
- ✓ If a question doesn't apply to you (e.g. for Q. 10, if you don't have Diabetes) just write in N/A for 'not applicable'.
- ✓ Please don't think over each question too much; just write the number that first comes to mind.

0	1	2	3	4	5	6	7	8	9	10
No problems										Worst I've ever felt

	<b>Over the PAST 2 WEEKS:</b>	<b>0...10</b>
1.	How have you been feeling <b>physically</b> ? (E.g. feeling tired, in pain, chesty, blocked up or anything else)	
2.	How have you been feeling <b>emotionally</b> ? (E.g. feeling sad, worried, angry, upset or anything else)	
3.	How have you been feeling <b>about your work situation</b> ? (Whether or not you do paid work)	
4.	How have you been feeling <b>about your housing situation</b> ?	
5.	How have you been feeling <b>about your financial situation</b> ? (E.g. debts/ benefits)	
6.	How have you been feeling <b>about going out, socialising, or having things to do in the day</b> ?	
7.	How have you been feeling <b>about your relationships with other people</b> ? (E.g. your partner, friends, family or anyone else)	
8.	How have you been feeling <b>about managing CF treatments</b> ?	
9.	How have you been feeling <b>about your body, weight and/or eating</b> ?	
10.	How have you been feeling <b>about your Diabetes control</b> ?	
11.	How have you been feeling <b>about having a specific procedure or treatment</b> ? (E.g. getting a button, a port, blood tests/ needles, or anything else)	
12.	How have you been feeling <b>about lung function tests and results</b> ?	
13.	How have you been feeling <b>about coughing up blood (haemoptysis)</b> ?	
14.	How have you been feeling <b>about CF getting worse</b> ?	
15.	How have you been feeling <b>about a recent (new) diagnosis or bug</b> ?	
16.	How have you been feeling <b>about fertility, pregnancy or parenting</b> ?	
17.	How have you been feeling <b>about anything to do with transplant</b> ? (E.g. just thinking about it, being on the list, or having had one already)	
18.	How have you been feeling <b>about being in hospital</b> ?	
19.	How have you been feeling <b>about coming to clinic</b> ?	
20.	How have you been feeling <b>about telling other people about CF</b> ? (E.g. at work, school, college or university, or friends & family)	
21.	How have you been feeling <b>about your use of street drugs or alcohol</b> ?	
22.	How have you been feeling <b>about upsetting past events</b> ? (E.g. memories of an accident, experiences as a child, a medical procedure, or anything else)	
23.	How have you been feeling <b>about anything to do with end of life</b> ? (E.g. Someone you know who has died, or concerns about when you die)	

## **Appendix 7: Questionnaire Evaluation**

### **Questionnaire Evaluation**

**Title of Study:** Validation of a cystic fibrosis-specific measure of distress in an adult population

Please answer the following questions about the questionnaires you have just completed.

- For each questionnaire please circle how much it covered your current difficulties using the following scale:

0= did not cover any of my difficulties    1= covered some of my difficulties  
2= covered most of my difficulties        3= covered all of my difficulties

	Did not cover any of my difficulties	Covered some of my difficulties	Covered most of my difficulties	Covered all of my difficulties
<b>Distress in Cystic Fibrosis Scale (DCFS)</b>	0	1	2	3
<b>Patient Health Questionnaire (PHQ-8)</b>	0	1	2	3
<b>Generalised Anxiety Disorder Questionnaire (GAD-7)</b>	0	1	2	3
<b>Cystic Fibrosis Questionnaire-Revised (CFQ-R)</b>	0	1	2	3

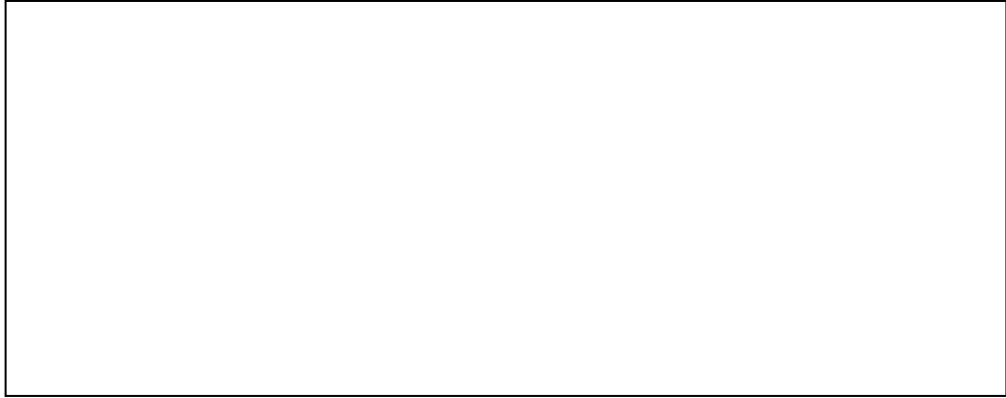
- For each questionnaire please circle how easy or difficult it was to complete with regards to understanding the questions and the layout, using the following scale:

0= very difficult    1= difficult    2= Ok    3= easy    4 = very easy

	Very difficult	Difficult	Ok	Easy	Very easy
<b>Distress in Cystic Fibrosis Scale (DCFS)</b>	0	1	2	3	4
<b>Patient Health Questionnaire (PHQ-8)</b>	0	1	2	3	4
<b>Generalised Anxiety Disorder Questionnaire (GAD-7)</b>	0	1	2	3	4
<b>Cystic Fibrosis Questionnaire-Revised (CFQ-R)</b>	0	1	2	3	4



- Please provide any other comments regarding the questionnaires that you have completed.

A large, empty rectangular box with a thin black border, intended for the respondent to provide any other comments regarding the questionnaires.

*Thank you for taking part in this study.*

## **Appendix 8: Participant Information Sheet**



University  
of Glasgow



### **Participant Information Sheet**

**Study Title:** Validation of a cystic fibrosis-specific measure of distress in an adult population

We would like to invite you to take part in a research study. Before you decide you need to understand why the research is being done and what it would involve for you. Please take time to read the following information carefully. If there is anything you would like to discuss, please do not hesitate to contact Caroline Finlay.

#### **What is the study about?**

A new questionnaire (Distress in Cystic Fibrosis Scale) has been developed to measure distress specific to individuals with Cystic Fibrosis. This study looks at whether this new questionnaire is reliable and valid, before it can be used in an official capacity. This study is being completed in part fulfilment of the Doctorate in Clinical Psychology qualification.

#### **Why am I being asked to take part?**

You have been invited to take part in this study as you are supported by the West of Scotland Adult Cystic Fibrosis Service.

#### **Do I have to take part?**

No, it is up to you to decide. If you decide you do want to take part, you will get a copy of this information to keep and you will be asked to sign a form to show you have agreed to take part. You are free to withdraw at any time, without giving reason. This would not affect the standard of care you receive or your future treatment.

#### **What would I have to do?**

You can take your time to decide about taking part in the research or not. All questionnaires must be completed by March 2019 to be included. If you decide to take part you would be asked to complete 4 questionnaires about your current distress, mood and quality of life. Additionally, you would be asked to complete an evaluation form. These questionnaires could be completed at the West of Scotland Adult Cystic Fibrosis Service, or at home. It is expected to take approximately 25 minutes in total. The questionnaires will be reviewed by Caroline Finlay or Dr Patel as they may indicate some feelings of distress. For your safety, if any risk is identified,

such as high levels of anxiety or low mood, this information will be passed onto Dr Patel, Clinical Psychologist for the West of Scotland Adult Cystic Fibrosis Service.

You will also be asked to give permission for Caroline Finlay to access your medical records within the West of Scotland Adult Cystic Fibrosis Service to gather recent physical health measurements including weight and lung functioning, and classification of CF.

### **Who else would know I am doing this?**

The staff at the West of Scotland Adult Cystic Fibrosis Service will be informed that you are taking part in the study, but all the information that you provide will be kept confidential. All data collected will be anonymised in the research report. Confidentiality will only have to be broken if there were concerns that you or someone else was at risk of harm. If this happened then the information will be passed onto Dr Patel, Clinical Psychologist for the West of Scotland Adult Cystic Fibrosis Service.

### **What happens to the information?**

NHS Greater Glasgow and Clyde (NHS GG&C) is the sponsor for this study based in the United Kingdom. We will be using information from you and your medical records in order to undertake this study and will act as the data controller for this study. This means that we are responsible for looking after your information and using it properly. NHS Greater Glasgow and Clyde will keep identifiable information about you for 3 months after the study has finished.

Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible.

For the current study the questionnaire scores will be put into an electronic database where it will be used for data analysis. The anonymous data will be stored on an encrypted password protected University and NHS computer. Completed paper research packs will be stored in a secure filing cabinet within West of Scotland Adult Cystic Fibrosis Service. My supervisors (Psychologists working in West of Scotland Adult Cystic Fibrosis Service and Glasgow University) and I will have access to the data. The information will be analysed and presented in the form of a report and submitted to the University of Glasgow in part fulfilment of the Doctorate in Clinical Psychology, for publication in a scientific journal, and at relevant conference presentations. All participants will be provided with a summary of results if they would like them.

NHS GG&C will use your name, NHS number and contact details to make sure that relevant information about the study is recorded for your care, and to oversee the quality of the study. Individuals from NHS GG&C and regulatory organisations may

look at your medical and research records to check the accuracy of the research study. The research team will pass these details to NHS GG&C along with the information collected from you and your medical records. The only people in NHS GG&C who will have access to information that identifies you will be the people who need to audit the data collection process. The analysed data will not contain any personal identifiable information.

NHS GG&C will collect information about you for this study from medical records and the questionnaires you complete. This information will include your name, NHS number, contact details and health information, which is regarded as a special category of information. We will use this information to audit the research project.

You can find out more about how we use your information from the contact details below.

### **What are the possible benefits and risks of taking part?**

Current measures of distress do not always identify the specific distress experienced by individuals with Cystic Fibrosis. Specific measures of distress have been developed for other health conditions such as cancer and diabetes. By taking part in this research you will be contributing to the development of a new questionnaire measuring distress specifically related to Cystic Fibrosis.

The questionnaires asking about your distress and mood may highlight that you are having some difficulties with your emotional wellbeing. You are free to withdraw from the research at any time and can access psychological support within the West of Scotland Adult Cystic Fibrosis Service.

### **Who has reviewed the study?**

This study has been approved by the University of Glasgow, the West of Scotland Research Ethics Committee and the NHS Greater Glasgow & Clyde Research and Development Team.

### **Who do I contact for more information?**

You may contact any of the researchers involved in this study if you have further questions about the research. An independent contact person is also available to provide information about taking part in research. Contact details can be found at the end of this leaflet.

### What do I do now?

If you are interested in taking part in the research then please:

- Complete the consent form, the four questionnaires, and the evaluation form in the research pack. The completed research pack can be handed back to Caroline Finlay or Dr Sejal Patel.
- Alternatively, if you would prefer to complete the questionnaires at home, please do so and post the completed research pack using the pre-paid envelope provided.

### What if I have a complaint?

If you have any problems during the study, please do not hesitate to contact any member of the research team (contact information below).

If you wish to make a formal complaint, please contact:

Complaints Department  
West Glasgow Ambulatory Care Hospital  
Dalnair Street  
Glasgow  
G3 8SJ

Phone: 0141 201 4500

Email: [complaints@ggc.scot.nhs.uk](mailto:complaints@ggc.scot.nhs.uk)

*Thank you for taking the time to read this leaflet and for any further input you may wish to have.*

### Contact Information:

Name	Role	Email	Telephone
Caroline Finlay	Researcher	<a href="mailto:c.finlay.2@research.gla.ac.uk">c.finlay.2@research.gla.ac.uk</a>	
Dr Alison Jackson	Academic Supervisor	<a href="mailto:Alison.Jackson@glasgow.ac.uk">Alison.Jackson@glasgow.ac.uk</a>	0141 211 3917
Dr Sejal Patel	Clinical Supervisor	<a href="mailto:sejal.patel@ggc.scot.nhs.uk">sejal.patel@ggc.scot.nhs.uk</a>	
Rory O'Connor	Independent Contact	<a href="mailto:Rory.OConnor@glasgow.ac.uk">Rory.OConnor@glasgow.ac.uk</a>	

## Appendix 9: Participant Consent Form



University  
of Glasgow

### Consent Form



**Participant ID Number:** \_\_\_\_\_

**Title of Study:** Validation of a cystic fibrosis-specific measure of distress in an adult population

**Name of Researcher:** Caroline Finlay (Trainee Clinical Psychologist)

Please initial each box.

I confirm that I have read and understood the *Participant Information Leaflet (Version 5, 17/10/18)* for the above study and have had the opportunity to ask questions.

☐

I understand that my participation is voluntary and that I am free to withdraw at any time and without giving any reason. If I do withdraw from the study my continued care will not be affected.

☐

I understand that my medical care or legal rights will not be affected by taking part.

☐

I understand that Caroline Finlay and supervising Psychologists (Dr Alison Jackson, University of Glasgow and Dr Sejal Patel, West of Scotland Adult Cystic Fibrosis Service) will have access to the information that I provide. My information may also be looked at by representatives of the study Sponsor, NHS GG&C, for audit purposes.

☐

I understand that Caroline Finlay will contact Dr Patel if any risk is identified from the questionnaires.

☐

I give permission for the researcher to inform the West of Scotland Adult Cystic Fibrosis Service of my involvement in this study.

☐

I give permission for the researcher to access my medical records held within the West of Scotland Adult Cystic Fibrosis Service.

☐

I would like to receive a summary of the project findings once it is completed (estimated completion date December 2019). Please send a copy to me at the following address:

☐

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I agree to take part in the above study.

\_\_\_\_\_  
Name of Participant

\_\_\_\_\_  
Date

\_\_\_\_\_  
Signature

\_\_\_\_\_  
Name of Researcher

\_\_\_\_\_  
Date

\_\_\_\_\_  
Signature

**Appendix 10: N (%) of participant responses to DCFS items**

<b>DCFS Question</b>	<b>Median (IQR)</b>	<b>N (%) scoring 'N/A'</b>	<b>N (%) scoring '0'</b>	<b>N (%) scoring 1-4</b>	<b>N (%) scoring 5-10</b>
<b>1</b>	3 (5)	0	19 (16)	54 (45.4)	46 (38.6)
<b>2</b>	3 (5)	0	32 (26.9)	51 (42.9)	36 (30.2)
<b>3</b>	1 (5)	8 (6.7)	44 (37)	39 (32.8)	28 (23.5)
<b>4</b>	0 (2)	0	81 (68.1)	23 (19.3)	15 (12.6)
<b>5</b>	1 (4)	0	58 (48.7)	35 (29.4)	26 (21.9)
<b>6</b>	1 (4)	0	56 (47.1)	35 (29.4)	28 (23.5)
<b>7</b>	0 (4)	0	62 (52.1)	31 (26)	26 (21.9)
<b>8</b>	1 (4)	0	49 (41.2)	44 (37)	26 (21.8)
<b>9</b>	2 (5)	0	42 (35.3)	40 (33.6)	37 (31.1)
<b>10</b>	0 (2)	44 (37)	50 (42)	14 (11.8)	11 (9.2)
<b>11</b>	0 (2)	13 (10.9)	74 (62.2)	16 (13.5)	16 (13.4)
<b>12</b>	1 (3)	1 (.8)	58 (48.7)	41 (34.5)	19 (16)
<b>13</b>	0 (0)	22 (18.5)	77 (64.7)	13 (10.9)	7 (5.9)
<b>14</b>	2 (5)	1 (.8)	42 (35.3)	44 (37)	32 (26.9)
<b>15</b>	0 (0)	15 (12.6)	80 (67.2)	12 (10.1)	12 (10.1)
<b>16</b>	0 (3)	8 (6.7)	63 (52.9)	31 (26.1)	17 (14.3)
<b>17</b>	0 (0)	13 (10.9)	82 (68.9)	14 (11.8)	10 (8.4)
<b>18</b>	0 (4)	8 (6.7)	60 (50.4)	25 (21)	26 (21.9)
<b>19</b>	0 (2)	1 (.8)	70 (58.8)	34 (28.6)	14 (11.8)
<b>20</b>	0 (2)	0	76 (63.9)	23 (19.3)	20 (16.8)
<b>21</b>	0 (0)	13 (10.9)	92 (77.3)	8 (6.7)	6 (5.1)
<b>22</b>	0 (3)	1 (.8)	73 (61.3)	21 (17.7)	24 (20.2)
<b>23</b>	0 (4)	0	68 (57.1)	23 (19.3)	28 (23.6)

## **Appendix 11: Proposed Revised DCFS**

### **Distress in Cystic Fibrosis Scale (DCFS)**

Below is a list of common issues that affect many people with CF. They may or may not all affect you now, or in the future. We are still interested in how you feel about them.

- ✓ Please read each item carefully, and using the scale at the top as a guide, fill in the box next to each question with the number that comes closest to how you have been *feeling* about that issue *over the past 2 weeks*.
- ✓ Please don't think over each question for more than a few seconds; just write in the first number that comes to mind.

<b>0</b>	<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>	<b>6</b>	<b>7</b>	<b>8</b>	<b>9</b>	<b>10</b>
<b>No concerns</b>									<b>Worst I've ever felt</b>	

	<b>Over the PAST 2 WEEKS:</b>	<b>0...10</b>
1.	How have you been feeling <b>physically</b> ? (E.g. feeling tired, in pain, chesty, blocked up or anything else)	
2.	How have you been feeling <b>emotionally</b> ? (E.g. feeling sad, worried, angry, upset or anything else)	
3.	How have you been feeling <b>about your work situation</b> ? (Whether or not you do paid work)	
4.	How have you been feeling <b>about your housing situation</b> ?	
5.	How have you been feeling <b>about your financial situation</b> ? (E.g. debts/ benefits)	
6.	How have you been feeling <b>about going out, socialising, or having things to do in the day</b> ?	
7.	How have you been feeling <b>about your relationships with other people</b> ? (E.g. your partner, friends, family or anyone else)	
8.	How have you been feeling <b>about managing CF treatments</b> ?	
9.	How have you been feeling <b>about your body, weight and/or eating</b> ?	
10.	How have you been feeling <b>about CF-related diabetes (CFRD)</b> ? (Either now, or as a potential future possibility)	
11.	How have you been feeling <b>about having a specific procedure or treatment</b> ? (E.g. getting a button, a port, blood tests/ needles, or anything else)	
12.	How have you been feeling <b>about lung function tests and results</b> ?	
13.	How have you been feeling <b>about coughing up blood (haemoptysis)</b> ? (Either now, or as a potential future possibility)	
14.	How have you been feeling <b>about CF getting worse</b> ?	
15.	How have you been feeling <b>about a recent (new) diagnosis or bug</b> ?	
16.	How have you been feeling <b>about fertility, pregnancy or parenting</b> ?	
17.	How have you been feeling <b>about anything to do with transplant</b> ? (E.g. just thinking about it, being on the list, or having had one already)	
18.	How have you been feeling <b>about being in hospital</b> ? (Either now, or as a potential future possibility)	
19.	How have you been feeling <b>about coming to clinic</b> ?	
20.	How have you been feeling <b>about telling other people about CF</b> ? (E.g. at work, school, college or university, or friends & family)	
21.	How have you been feeling <b>about using street drugs or alcohol</b> ?	
22.	How have you been feeling <b>about upsetting past events</b> ? (E.g. memories of an accident, experiences as a child, a medical procedure, or anything else)	
23.	How have you been feeling <b>about anything to do with end of life</b> ? (E.g. Someone you know who has died, or concerns about when you die)	