# DEPRESSION AND ANXIETY IN ADOLESCENTS AND ADULTS WITH CYSTIC FIBROSIS IN THE UK: A CROSS-SECTIONAL STUDY

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**ABSTRACT**

**Background**: The International Depression/anxiety Epidemiological Study (TIDES) in the UK aimed to establish: (i) the prevalence of anxiety and depression amongst people with CF compared to a normative sample, (ii) the association between mood, demographic and clinical variables and, (iii) guidance for specialist-referral decision-making.

**Methods**: Patients (≥12 years) completed the Hospital Anxiety and Depression Scale (HADS). CF-HADS scores, expressed as percentiles, were compared with a normative sample. Multiple-regression analysis explored associations between demographic, clinical and mood variables.

**Results**: Thirty-nine CF Centres recruited 2065 patients. Adults with CF were similar in terms of anxiety and depression to the general population. Adolescents with CF were less anxious and depressed. For adult patients, older age, unemployment for health reasons and poor lung function were associated with disordered mood. Gender-specific CF-percentile scores were calculated.

**Conclusion**: Surveillance, with attention to gender and risk factors is advocated. This work provides unique benchmark scores to aid referral decision-making.

**Key words**; anxiety, depression, HADS, cystic fibrosis, prevalence, management

**Background**

Advances in the diagnosis and treatment of cystic fibrosis (CF) have led to dramatic improvements in prognosis [1,2]. However, arduous treatment regimens [3], considerable morbidity and early mortality [1] impact on psychological health which remains a critical target for assessment and intervention.

There is a complex relationship between psychological and physical health [4]. Those with respiratory disease have an increased risk for co-morbid anxiety and depression [5-7], with routine assessment recommended [8]. However, the findings in CF are inconsistent, as there are difficulties interpreting and comparing results across studies because of different sampling approaches, measurement instruments and a lack of consensus on clinical cut-off scores. Single-centre reports of adult patients cite depression rates of 17-30%, linking depression with worse adherence, poorer lung-function and quality of life (QoL) [9-11]. Lower and elevated rates of depression have been reported in children, adolescents and young adults who have CF compared with healthy controls [12,13]. Normal [12-14] and elevated levels of anxiety [15,16] have been reported in adult and adolescent patients.

To address the limitations of previous studies The International Depression/anxiety Epidemiology Study (TIDES) aimed to conduct rigorous evaluation of depression and anxiety in CF patients and parent-caregivers in eight European countries and the US. Although some preliminary TIDES findings have been presented in abstract form, to date only one national patient data-set has been published (TIDES-Germany). In this study, patients were no more or less depressed that the general population, however, adults with CF had greater elevated symptoms of anxiety than healthy controls. Younger patients reported fewer symptoms of both depression and anxiety than older ones [17].

This paper presents TIDES-UK patient data, which aimed to estimate; (i) prevalence of depression and anxiety amongst adolescents and adults with CF in the UK in comparison to

a normative, adult UK sample, (ii) associations between mood, demographic and clinical variables and, (iii) provide guidance for specialist referral decision-making. Rates of depression and anxiety were expected to be higher in those with CF than in the general population and elevated symptoms were expected to be associated with worse health status.

## Materials and methods

### *Study design*

A cross-sectional study involving paediatric and adult UK CF centres was undertaken. National Research Ethics Service approval was granted (NRES 07/Q1205) with site-specific approval being obtained from local Research and Development units. All participants provided written consent. Parental consent and child assent were given for those under 16 years. Final consent was taken in April 2012.

### *Subjects and procedure*

All patients (≥12 years) except for transplant-recipients were asked to participate in the study during routine out-patient appointments between October 2009 and April 2012. Demographic, clinical, and mood variables were collected and the Hospital Anxiety and Depression Scale (HADS) [18] was completed immediately prior to consultations. The HADS was scored within a week with referral pathways in place (referral to CF psychosocial professional or liaison with external mental health services).

### *Measures*

*Demographic and clinical variables*

Demographic and clinical data were obtained from participants and verified by medical records where appropriate. Not all clinics collected every variable but when possible, the following data were obtained: age, gender, height, weight, $FEV_1$% predicted, education-level, employment status, diabetes, current IV-antibiotics, nutritional supplements, enteral tube

feeds, intravenous access device and whether the person was diagnosed with diabetes, haemoptysis or pneumothorax in the past six months. Whether the participant was listed for transplant, had a current prescription for anti-depressants or anxiolytics or was engaged in counselling for depression or anxiety, were documented.

*Hospital Anxiety and Depression Scale (HADS)*

The HADS was indentified as the most appropriate TIDES measure because of its extensive reliability and validity data [19], good sensitivity and specificity [20] and international translations. It is a 14-item (7 depression, 7 anxiety), self-report scale that evaluates and quantifies anxiety and depression in hospital settings without somatic items. Respondents consider how they have been feeling over the past 7 days and answer on 4-point Likert scaling (scored '0' - '3'), yielding a total anxiety or depression score of between 0 and 21. Depression and anxiety are categorised according to published thresholds [21] ('none': raw scores <7; 'mild': 8-10; 'moderate': 11-15; 'severe': ≥16) however, there is little agreement about the clinical value of these which makes it difficult to interpret data and establish referral pathways for specialist assessment [22].

An alternative approach of using a HADS centile-structure was proposed in a large study of non-clinical UK adults (978 women, 810 men) in community settings. This sample was deemed representative of the UK population in terms of age, gender and occupational status [23]. Using these normative data, gender-specific tables converted raw HADS scores to percentiles which establish the comparative scarcity of a person's depression or anxiety score and augment management decisions based on comparative severity.

***Statistical analysis***

To provide contextual information about the estimated prevalence of depression and anxiety in CF, the categorised prevalence of anxiety and depression ('none', 'mild', 'moderate' or 'severe') was compared between the UK normative adult sample and the adult CF sample,

and between the latter and the adolescent CF sample, using chi-squared or Fisher's exact tests (there are no UK normative data for adolescents) and independent samples t-tests. Graphical comparisons were made between samples by comparing the percentile plots of the empirical cumulative distribution functions.

Regression analysis was used to explore the influence of demographic and clinical variables on depression and anxiety. Preliminary regressions using the total depression and anxiety scores showed highly skewed residuals and heterogeneity in the residual variance. Therefore, these scores were transformed firstly to the percentile of the empirical cumulative distribution of the observed score and secondly, using the logistic transformation. The empirical cumulative distribution function used was the one appropriate to the gender and the set of data, CF adult or CF adolescent. These transformations achieved homogeneity of variance and satisfactory approximation to the normal distribution, thus, supporting valid *P*-values with which to assess significant associations.

The following strategy was used to identify variables associated with depression and anxiety. Variables were divided into two groups for both adults and adolescents; the core group of variables which were available for most individuals and the secondary group of variables, which were available for a reduced subset of individuals (not all variables were collected in every clinic). Regressions were undertaken that included both core and secondary variables using the reduced sample size of individuals who had all variables available. These regressions tested the associations between depression and anxiety with the secondary variables. Regressions were then repeated using only core variables, but utilising the larger sample size. These regressions tested the associations between depression and anxiety with the core variables.

## RESULTS

### *Study population*

The 39 study sites (25 adult, 14 paediatric) included 23/48 CF centres registered with the UK CF Trust and 16 regional clinics. The smallest site had 8 patients; the largest, 530. Twenty-three sites (59%) recruited >70% of their clinic population, with a further 6 (15%) recruiting >60%. A total of 1780 adults and 285 adolescents with CF were included in the study (total n=2065). This represented 45.2% of the total UK adult CF population and 18.3% of adolescents (12-17 years), based on UK CF Trust Registry data [1], having similar age and $FEV_1$ distributions and median BMI. Demographic and clinical characteristics are shown in Table 1.

Direct or indirect access to a clinical psychologist was available in 28 of the 39 (72%) participating sites. Of the 23 participating major centres, integrated clinical psychology posts were established in 18 (78%) with indirect access via a generic hospital clinical psychologist being available in a further 3 (13%). In the 16 participating regional clinics whilst there was no direct access, support was available indirectly in 7 (44%), via network centres or community services.

Internal reliability of the HADS was robust with satisfactory Cronbach alpha coefficients for depression (0.82 and 0.72) and anxiety (0.80 and 0.85) for adults and adolescents, respectively.

### *Estimated prevalence of depression and anxiety*

Table 2 shows the estimated prevalence of depression and anxiety in men and women with CF, adolescent boys and girls with CF and UK normative data together with mean scores.

In terms of prevalence, men with CF were significantly more depressed ($X^2$ = 10.4; P=0.014) and anxious ($X^2$ = 24.3; P<0.001) than men from the general population, but the differences

were small. However, although mean depression score was lower (3.4 for men with CF; 3.6 for UK men) and was not significantly different (P=0.200), mean anxiety score was the same for both groups at 5.7. Adolescent boys with CF were less depressed ($X^2$ = 19.0; P<0.001) and anxious ($X^2$ = 12.5; P=0.006) than adult CF men. Mean depression and anxiety scores for adolescent boys with CF were significantly lower than that for men with CF (depression 1.9 P<0.001; anxiety 4.3 P<0.001).

Women with CF were not significantly different to adult women from the general population for both depression ($X^2$ = 2.38; P=0.50) and anxiety ($X^2$ = 1.03; P=0.79). In fact mean depression score was significantly lower for CF women at 3.4 compared to 4.0 for UK adult women (P<0.001) and mean anxiety score was also lower but not significantly so (6.6 versus 6.8, P=0.311). Adolescent girls with CF were not significantly different to women with CF for both depression ($X^2$ = 5.10; P=0.15) and anxiety ($X^2$ = 5.53; P=0.14) but this is likely the result of a small sample size for adolescents, since the P-values are close to 15%. Mean depression score was significantly lower at 2.4 for girls with CF compared to 3.4 for women with CF (P<0.001). Mean anxiety score was significantly lower at 5.7 for girls with CF compared to 6.6 for women with CF (P=0.011).

In summary, adults with CF were similar in terms of depression and anxiety to the general population, any differences being small. However, adolescent boys and girls with CF were less depressed and anxious than their adult counterparts. This is demonstrated graphically in Figures 1 and 2.

***Associations between mood, demographic and clinical variables***

*Adults with CF*

The core variables comprised: BMI, $FEV_1$% predicted, age, education, employment status, routine/unwell visit and current use of intravenous antibiotics. Secondary variables were: diabetic condition, development of diabetes and haemoptysis in previous 6 months, listed for

transplant, nutritional supplements, enteral tube feeding and a port-a-cath *in situ*. Pneumothorax was excluded because only 4 individuals had experienced this in the past 6 months.

*Depression*: In the regressions with core and secondary variables (292 men, 261 women), the percentage variance accounted for ($R^2$) was 21% for men and 27.5% for women. For men, no secondary variable showed any association with level of depression. For women, only recent haemoptysis was associated with increased depression. In the regressions with only core variables (885 men, 811 women), $R^2$ was 15.5% for men and 15.9% for women; again a poor level of explanation. Generally, for men and women, increasing age, not working due to health reasons, decreasing FEV1% predicted and a clinic visit whilst unwell were associated with increased depression scores. BMI, level of educational attainment and current IVs showed no association with depression.

*Anxiety:* In the regressions with core and secondary variables (292 men, 261 women), $R^2$ was 8.7% for men and 16.6% for women. For men, no secondary variable was associated with level of anxiety. For women, only recent haemoptysis predicted higher levels of anxiety. In the regressions with only core variables (885 men, 811 women) $R^2$ was 4.4% for men and 7.0% for women; a poor level of explanation. For both men and women, age group and employment status were both significant. Generally, increasing age predicted increased anxiety scores. Typically, those in full-time employment reported the least anxiety, whereas those not working due to health reasons reported the highest levels. For women, an 'unwell' visit was associated with heightened anxiety and the use of IVs was related to lower anxiety. $FEV_1$% predicted, BMI and level of educational attainment showed no association with anxiety.

For the demographic and clinical variables that demonstrated a statistically significant association with depression or anxiety, Table 3 shows unadjusted mean values of

depression and anxiety together with the *P*-values from the regressions. The means are for the individuals who were included in the appropriate regression which generated the *P*-value. Unadjusted means are given because adjusted values would be difficult to interpret following the data transformations. Although some variables were shown to be statistically significant, the means in Table 3 indicate that they were not always clinically relevant.

*Adolescents with CF*

Core variables included: BMI, $FEV_1$% predicted, routine/unwell visit and current intravenous antibiotics. Secondary variables comprised: diabetes, nutritional supplements, enteral tube feeding and a port-a-cath *in situ*. Other variables were excluded because too few individuals were involved. In the regression analyses of core and secondary variables, 71 boys and 77 girls were included; $R^2$ was 4.6% for boys and 24.3% for girls for depression and 8.4% for boys and 11.8% for girls for anxiety. For both boys and girls, no secondary variable showed any association with anxiety. For boys, none of the secondary variables showed any association with depression, but for girls, a port-a-cath *in situ* was associated with elevated levels of depression and diabetes with reduced depression. Table 3 also includes unadjusted means and *P*-values for diabetes and port-a-cath *in situ* for depression in girls. In regressions with core variables, 114 boys and 139 girls were included and $R^2$ was 3.1% of boys and 4.6% of girls for depression and 1.6% of boys and 4.4% of girls for anxiety; a negligible level of explanation. For both boys and girls, no core variable showed any association with anxiety.

**Specialist referral threshold scores**

Table 4 shows the depression and anxiety scores for referral based on the top 20%, 10%, 5% and 1% of patients with CF. If referral decisions are based on raw HADS scores (e.g., a score of 11 for 'moderate' anxiety) then men would be referred if they were in the top 10% of the anxiety distribution for men with CF. Women would be referred in the top 20% of the anxiety distribution for CF women. For boys with CF, referral would be only in the top 5%

and for girls in the top 10%. Therefore, clinicians may want to refer patients for depression and anxiety based on the same top percentile for all groups. If referral for anxiety was based on a score placing a patient in the top 5% of the anxiety distribution, then men with CF would be referred at score 13, women at score 14, boys at 10 and girls at 12. For depression the analogous scores are 10, 10, 6 and 8 respectively.

**DISCUSSION**

TIDES-UK is the first study to investigate rates of depression and anxiety in a large, multi-centred, UK sample of people with CF. Adults with CF had a similar estimated prevalence of depression and anxiety as the general population. This was contrary to expectations [24] and cannot be explained by the decade time-difference between the normative and CF samples, as more recent normative data established virtually identical means and standard deviations [25]. Moreover, the estimated prevalence of depression reported by TIDES-Germany was also similar to that of a normative sample [17], albeit that estimated UK anxiety was higher than that reported in Germany, which in turn was higher than the respective normative group. Comparison with single-centre studies or narrative reviews which report variable rates of depression and anxiety are not particularly useful given the methodological limitations and varying results of such reports.

Adolescents with CF were less depressed and anxious than their adult counterparts, with elevated depression scores being minimal in adolescent boys. Adherence problems in this group are frequently noted and together with a decline in lung-function between the ages of 12 and 16 years [1], there remains a clinically compelling case for maintaining close observation.

The importance of evaluating and attending to, patients' and relatives' emotional well-being is gaining worldwide support. In the UK psychological provision is well-established as part of CF management, with centres mandated to provide integrated clinical psychological care as

part of the service specification [26]. It is plausible that low rates of depression and anxiety were detected in this study as a result of there being direct or indirect access to a clinical psychologist in 91% of participating major centres and 44% of regional clinics, (72% access overall).

Surveillance with special attention to gender and the risk factors $FEV_1$% predicted, age and work status, is advocated given that 'moderate/severe' depression was reported by 3.1% of men and 4.6% of women and 'moderate/severe' anxiety was reported by 11.5% of CF men and 17.2% of CF women. Poor lung-function was associated with elevated depression scores in adults, a finding reported by several studies [8,9,17]. The combination of depression and poor lung-function had a greater adverse effect on QoL than poor lung-function alone [10]. Older-age and not working due to health reasons were also associated with higher rates of depressive and anxiety symptoms. These results highlight important psychosocial benefits of living with CF and being in full-time employment [27,28] and a timely reminder that the new era of CF care with mutation-specific treatments, affords greater confidence in psychologically preparing adolescents for the full opportunities of adult life. Additionally, for adult females, psychopathology was associated with haemoptysis and attending clinic when unwell (although lower levels of depression were reported whilst on intravenous [IV] treatment). In adolescent girls, having a port-a-cath *in situ* was associated with higher depression scores and consistent with poor QoL reporting [29].

The HADS is a practical tool for estimating depression and anxiety. It is reliable and valid and remains popular in clinical settings due to its ease of use and the weaknesses of other measures. Whether or not the HADS is the *most* appropriate assessment tool in CF remains to be evaluated. It does not represent the multi-dimensional nature of depression and omits somatic items which can be linked to depression or anxiety but does have advantages over other scales (e.g., the CES-D confounds psychological and somatic symptoms of CF; the

PHQ-9 includes an item on suicidal ideation requiring resource-intensive administration, which is considered in the TIDES-UK pilot data [30]). However, such considerations are tempered by questions over the validity of utilising case-finding or screening questionnaires alone. Systematic review of 16 studies with 7576 patients, suggests that the adoption of screening strategies using standardised questionnaires without organisational enhancements are not justified [31].

TIDES-UK data present a unique opportunity to establish meaningful management of HADS thresholds and clinical responses via the conversion of raw scores into gender-specific, CF-centile scores, which determine who should be kept under a watchful eye, undergo further assessment and be referred for psychosocial and/or mental health intervention (Table 4). Previously this has been a contentious issue. In the original paper [18] of the 18 patients in the 'borderline' range for depression (8+) only 3 presented as definite cases. Of the 20 patients in the same category for anxiety (again 8+), only 1 presented as a definite case. It is wrong to consider these as *diagnostic* of clinical depression and/or anxiety. Instead it is vital that elevated scores are followed by clinical assessment and diagnosis, with referral for psychological intervention when necessary. In accordance with clinical psychology opinion for hospitalised patients, a cut-off at the 90$^{th}$ percentile on the HADS depression scale was deemed the appropriate point for referral for clinical interview with a psychologist [32]. Similarly, in a community sample evaluating the longitudinal effect of anxiety and depression on blood pressure, the 90$^{th}$ percentile of the HADS were also estimated to be the appropriate clinical cut-off points [33]. We advocate 'watchful waiting' at the 80$^{th}$ centile, 'follow-up with clinical discussion in the CF team' at the 90$^{th}$ centile, 'referral to mental health for diagnostic assessment and intervention' at the 95$^{th}$ centile and 'emergency referral' at the 99$^{th}$ centile.

Whilst TIDES-UK was a large study in a comparatively rare disease, with excellent clinical representation of the UK CF population, some sampling bias may still have occurred. There

was a lower response rate for adolescents and this should temper the interpretation of these data. Refusal rates were unavailable and out-patient clinic recruitment possibly excluded poor/non-attendees. The reasons for refusal/poor attendance remain unknown but may have been influenced by psychological symptoms, leading to an under-estimate of psychopathology. The study was cross-sectional but provides robust prevalence estimates, risk factors and critically, threshold referral information. We await longitudinal follow-up to evaluate the trajectory and predictors of depression and anxiety over time.

## Conclusions

Adults with CF in the UK have similar rates of depression and anxiety to the general population. Adolescent patients were less anxious and depressed than their adult counterparts. Older age, not working due to health and poor lung-function were associated with disordered mood. With no consensus on thresholds for specialist assessment or onward referral, converted gender-specific CF percentiles provide unique benchmark profiles that aid clinical management in deciding which patients to 'watch and wait', further assess or refer on.

## Competing interests

The authors have no conflicts of interest to disclose.

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**Table 1. Demographic and clinical characteristics of the CF participants in the HADS study.**

| | Adults (18 years and older) | | | Adolescents (12 to 17 years) | | |
|---|---|---|---|---|---|---|
| | Men | Women | All | Boys | Girls | All |
| Sample size | 929 | 851 | 1780 | 136 | 149 | 285 |
| Age 12-17 | | | | 136(100) | 149(100) | 285(100) |
| 18-23 | 326(35.1) | 315(37.1) | 641(36.0) | | | |
| 24-29 | 268(28.8) | 243(28.6) | 511(28.7) | | | |
| 30-39 | 209(22.5) | 177(20.8) | 386(21.7) | | | |
| 40-49 | 99(10.7) | 79(9.3) | 178(10.0) | | | |
| 50-59 | 17(1.8) | 23(2.7) | 40(2.2) | | | |
| 60+ | 10(1.1) | 13(1.5) | 23(1.3) | | | |
| BMI (kg $m^{-2}$) | | | | | | |
| Mean (SD) | 22.8 (3.7) 12.5- | 21.9 (3.7) | 22.4 (3.7) | 19.9 (3.5) | 20.2 (3.1) | 20.1 (3.3) |
| Range | 42.8 | 12.7-39.7 | 12.5-42.8 | 13.4-36.3 | 13.6-33.2 | 13.4-36.3 |
| $FEV_1$%predicted | | | | | | |
| Mean (SD) | 61.6 (24.8) | 60.1 (23.4) | 60.9 (24.1) | 80.0 (18.7) | 73.6 (21.3) | 76.6 (20.3) |
| Range | 12-135 | 15.132 | 12-135 | 29-129 | 18-122 | 18-129 |
| Education | | | | | | |
| No formal qualns | 97(10.6) | 68(8.1) | 165(9.4) | | | |
| O levels/GCSE | 267(29.1) | 257(30.5) | 524(29.7) | | | |
| A levels /equivalent | 236(25.7) | 240(28.4) | 476(27.0) | | | |
| University degree | 184(20.0) | 137(16.2) | 321(18.2) | | | |
| Postgrad. studies | 40(4.4) | 48(5.7) | 88(5.0) | | | |
| Professional qualns | 95(10.3) | 94(11.1) | 189(10.7) | | | |
| Employment | | | | | | |
| Working full-time | 378(41.1) | 237(28.3) | 615(35.0) | | | |
| Working part-time | 158(17.2) | 205(24.5) | 363(20.7) | | | |
| Not working - health | 211(23.0) | 209(25.0) | 420(23.9) | | | |
| Not working - other | 172(18.7) | 186(22.2) | 358(20.4) | | | |
| Type of visit | | | | | | |
| Routine | 856(92.6) | 773(91.7) | 1629(92.2) | 133(97.8) | 141(95.2) | 274(96.5) |
| Unwell | 68(7.4) | 70(8.3) | 138(7.8) | 3(2.2) | 7(4.7) | 10(3.5) |
| Diabetic | | | | | | |
| No | 225(75.8) | 186(69.4) | 411(72.7) | 78(91.8) | 69(85.2) | 147(88.6) |
| Yes | 72(24.2) | 82(30.6) | 154(27.3) | 7(8.2) | 12(14.8) | 19(11.4) |
| Diabetic in last 6m | | | | | | |
| No | 885(95.9) | 804(94.9) | 1689(95.4) | 131(98.5) | 140(96.6) | 271(97.5) |
| Yes | 38(4.1) | 43(5.1) | 81(4.6) | 2(1.5) | 5(3.4) | 7(2.5) |
| Hemoptysis in last 6m | | | | | | |
| No | 225(75.8) | 196(73.1) | 421(74.5) | 84(98.8) | 75(92.6) | 159(95.8) |
| Yes | 72(24.2) | 72(26.9) | 144(25.5) | 1(1.2) | 6(7.4) | 7(4.2) |
| On IV antibiotics | | | | | | |
| No | 883(95.6) | 772(91.7) | 1655(93.7) | 126(94.7) | 133(91.7) | 259(93.2) |
| Yes | 41(4.4) | 70(8.3) | 111(6.3) | 7(5.3) | 12(8.3) | 19(6.8) |
| Listed for transplant | | | | | | |
| No | 903(97.7) | 821(97.5) | 1724(97.6) | 133(100.0) | 144(99.3) | 277(99.6) |
| Yes | 21(2.3) | 21(2.5) | 42(2.4) | 0(0.0) | 1(0.7) | 1(0.4) |
| Nutritional suppl. | | | | | | |
| No | 166(55.9) | 172(64.2) | 338(59.8) | 53(62.4) | 57(70.4) | 110(66.3) |
| Yes | 131(44.1) | 96(35.8) | 227(40.2) | 32(37.6) | 24(29.6) | 56(33.7) |
| Enteral tube feeds | | | | | | |
| No | 277(93.3) | 253(94.4) | 530(93.8) | 76(89.4) | 67(82.7) | 143(86.1) |
| Yes | 20(6.7) | 15(5.6) | 35(6.2) | 9(10.6) | 14(17.3) | 23(13.9) |
| Portacath insitu | | | | | | |
| No | 239(80.7) | 178(66.4) | 417(73.9) | 61(71.8) | 38(46.9) | 99(59.6) |
| Yes | 57(19.3) | 90(33.6) | 147(26.1) | 24(28.2) | 43(53.1) | 67(40.4) |
| Taking antidepressant | | | | | | |
| No | 864(93.5) | 745(88.6) | 1609(91.2) | 133(100.0) | 141(97.9) | 274(98.9) |
| Yes | 60(6.5) | 96(11.4) | 156(8.8) | 0(0.0) | 3(2.1) | 3(1.1) |
| Counselling for mood | | | | | | |
| No | 862(93.3) | 771(91.7) | 1633(92.5) | 130(97.7) | 133(92.4) | 263(94.9) |
| Yes | 62(6.7) | 70(8.3) | 132(7.5) | 3(2.3) | 11(7.6) | 14(5.1) |

**Table 2. Percentages of samples in each diagnosis group for HADS anxiety and depression score, means and standard deviations (SD).**

| | Men | | | Women | | |
|---|---|---|---|---|---|---|
| | Normative adults | CF adults | CF boys | Normative adults | CF adults | CF girls |
| Sample size | 810 | 929 | 119 | 978 | 850 | 144 |
| **Anxiety score** | | | | | | |
| None(0-7) % | 73.0 | 69.9 | 84.9 | 61.0 | 61.5 | 70.1 |
| Mild (8-10) % | 18.0 | 18.6 | 10.1 | 23.0 | 21.3 | 14.6 |
| Moderate (11-15) % | 8.0 | 9.5 | 5.0 | 13.0 | 14.0 | 13.9 |
| Severe(16-21) % | 1.0 | 2.0 | 0.0 | 3.0 | 3.2 | 1.4 |
| P-value | | <0.001 | 0.006 | | 0.794 | 0.137 |
| Mean | 5.7 | 5.7 | 4.3 | 6.8 | 6.6 | 5.7 |
| SD | 3.7 | 3.9 | 3.2 | 4.1 | 4.3 | 3.8 |
| P-value | | 1.00 | <0.001 | | 0.311 | 0.011 |
| **Depression score** | | | | | | |
| None(0-7) % | 91.0 | 86.9 | 99.2 | 86.0 | 88.1 | 94.4 |
| Mild (8-10) % | 6.0 | 10.0 | 0.8 | 9.0 | 7.3 | 2.8 |
| Moderate (11-15) % | 2.3 | 2.8 | 0.0 | 4.0 | 3.9 | 2.8 |
| Severe(16-21) % | 0.7 | 0.3 | 0.0 | 1.0 | 0.7 | 0.0 |
| P-value | | 0.014 | <0.001 | | 0.498 | 0.146 |
| Mean | 3.6 | 3.4 | 1.9 | 4.0 | 3.4 | 2.4 |
| SD | 3.2 | 3.3 | 2.0 | 3.6 | 3.4 | 2.9 |
| P-value | | 0.200 | <0.001 | | <0.001 | <0.001 |

Based on Snaith and Zigmond (1994) recommended cut-off scores (mild: raw scores between 8 and 10; moderate: 11-15; severe: 16 and above). Normative UK adults from Crawford et al 2001.

**Table 3. Unadjusted mean values and standard errors (SE) of significant predictors of anxiety and depression scores for adults and adolescents with cystic fibrosis together with p-values from regression analyses.**

| | Anxiety | | | | Depression | | | |
|---|---|---|---|---|---|---|---|---|
| | **Men** | **p-value** | **Women** | **p-value** | **Men** | **p-value** | **Women** | **p-value** |
| ***Sample size*** | *885* | | *811* | | *885* | | *811* | |
| **Age** | | | | | | | | |
| 18-23 | 5.0(0.2) | | 6.1(0.3) | | 2.7(0.2) | | 2.9(0.2) | |
| 24-29 | 5.7(0.2) | 0.041 | 6.9(0.3) | 0.048 | 3.1(0.2) | 0.078 | 3.4(0.2) | 0.007 |
| 30-39 | 6.1(0.3) | 0.004 | 6.6(0.3) | 0.390 | 3.7(0.2) | <0.001 | 3.5(0.3) | 0.151 |
| 40-49 | 6.5(0.4) | 0.004 | 6.9(0.5) | 0.504 | 4.7(0.4) | <0.001 | 3.3(0.1) | 0.198 |
| 50+ | 5.5(0.9) | 0.909 | 6.5(0.2) | 0.061 | 4.4(0.8) | 0.066 | 4.7(0.6) | 0.005 |
| **Employment** | | | | | | | | |
| Full-time | 5.2(0.2) | | 5.6(0.3) | | 2.5(0.1) | | 2.3(0.2) | |
| Part-time | 6.0(0.3) | 0.010 | 6.5(0.3) | 0.016 | 3.2(0.2) | 0.008 | 2.8(0.2) | 0.104 |
| Not working - health | 6.6(0.3) | <0.001 | 8.0(0.3) | <0.001 | 5.1(0.3) | <0.001 | 5.2(0.3) | <0.001 |
| Not working - other | 5.2(0.3) | 0.278 | 6.3(0.3) | 0.024 | 3.0(0.3) | 0.002 | 3.1(0.2) | 0.006 |
| **On IV antibiotics** | | | | | | | | |
| No | | | 6.6(0.2) | | | | | |
| Yes | | | 6.3(0.5) | 0.024 | | | | |
| **Type of visit** | | | | | | | | |
| Routine | | | 6.5(0.2) | | 3.2(0.1) | | 3.2(0.1) | |
| Unwell | | | 7.9(0.6) | 0.010 | 4.7(0.4) | 0.035 | 5.0(0.5) | <0.001 |
| **$FEV_1$%predicted** | | | | | | | | |
| Normal (>100%) | | | | | 2.3(0.4) | | 2.4(0.4) | |
| Mild (70-100%) | | | | | 2.7(0.2) | 0.399 | 2.5(0.2) | 0.612 |
| Moderate (40-69%) | | | | | 3.3(0.2) | 0.283 | 3.6(0.2) | 0.038 |
| Severe (<40%) | | | | | 4.5(0.2) | 0.019 | 4.1(0.3) | 0.036 |
| ***Sample size*** | | | *261* | | | | *261* | |
| **Hemoptysis in last 6m** | | | | | | | | |
| No | | | 6.3(0.3) | | | | 2.8(0.2) | |
| Yes | | | 8.8(0.6) | 0.001 | | | 5.5(0.5) | <0.001 |

| | **Girls** | **p-value** |
|---|---|---|
| ***Sample size*** | *77* | |
| **Diabetes** | | |
| No | 2.8(0.4) | |
| Yes | 1.8(0.8) | 0.027 |
| **Portacath *in situ*** | | |
| No | 1.5(0.3) | |
| Yes | 3.6(0.6) | 0.010 |

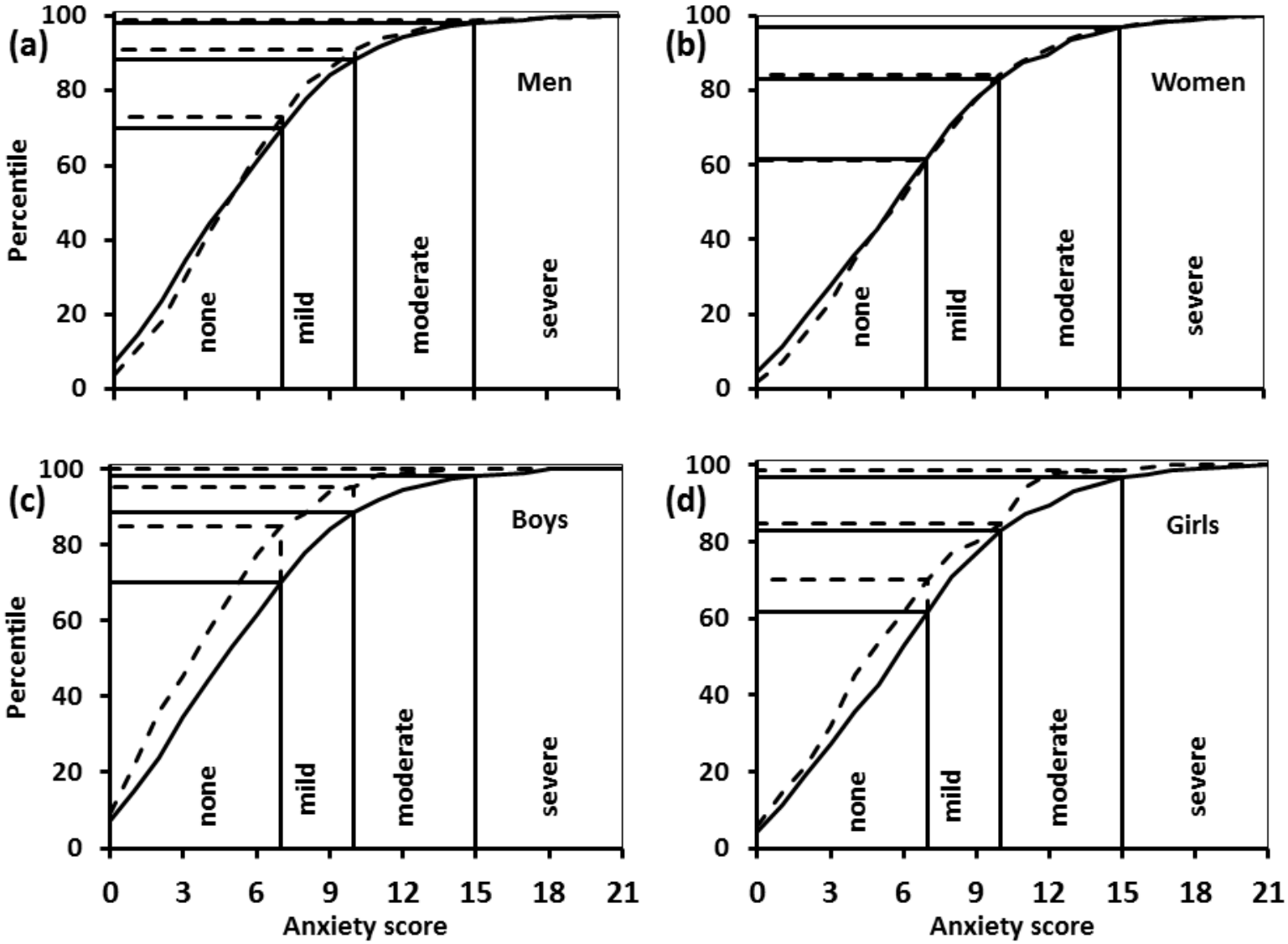
**Table 4. Anxiety and depression scores for referral based on position in top percentage for patients with CF.**

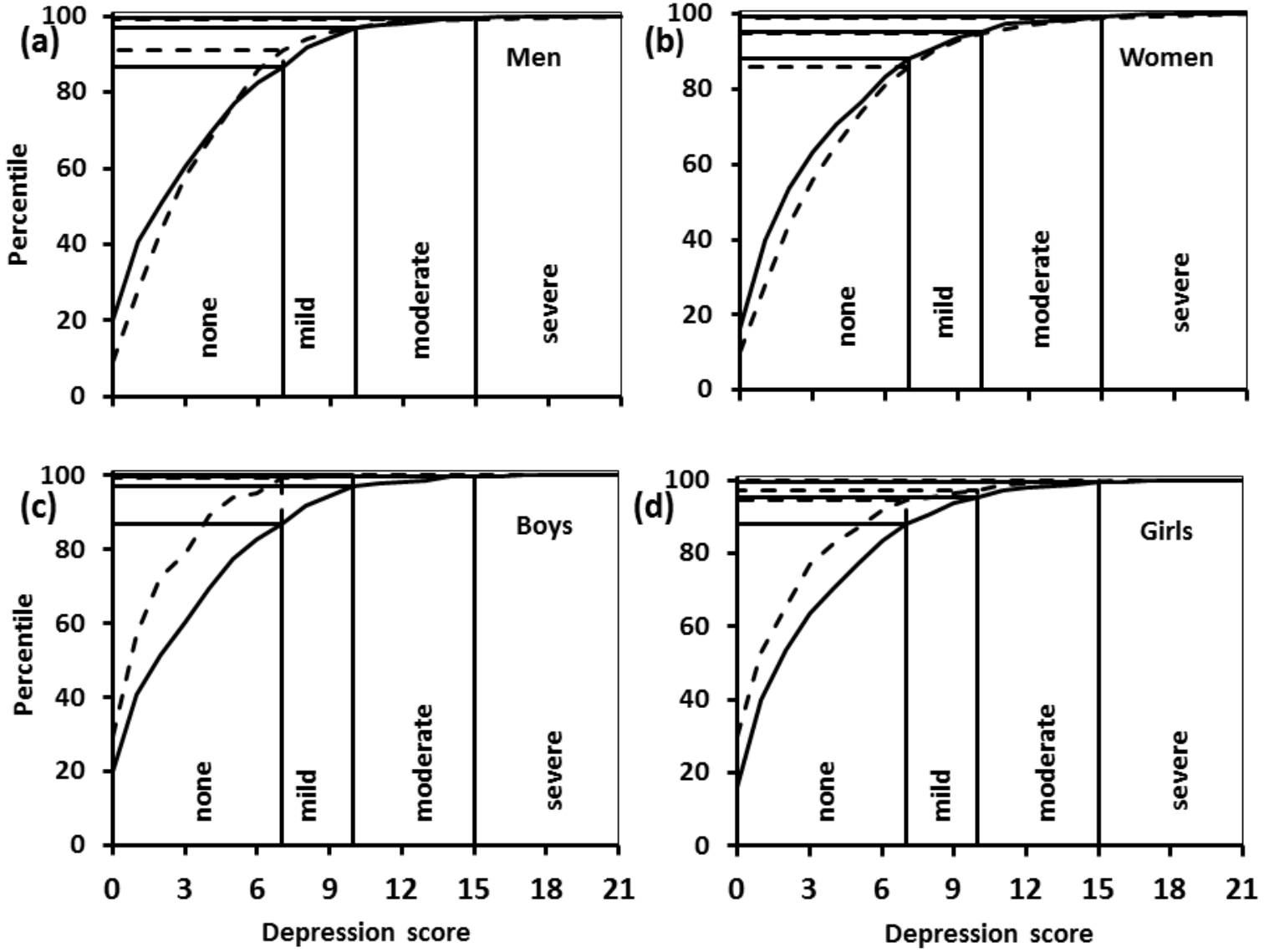
| | Anxiety | | | | Depression | | | |
|---|---|---|---|---|---|---|---|---|
| | **20%** | **10%** | **5%** | **1%** | **20%** | **10%** | **5%** | **1%** |
| **Men:** | | | | | | | | |
| CF adults | 9-10 | 11-12 | 13-16 | 17-21 | 6-7 | 8-9 | 10-13 | 14-21 |
| CF adolescents | 7-8 | 9 | 10-12 | 13-21 | 4 | 5 | 6 | 7-21 |
| **Women:** | | | | | | | | |
| CF adults | 10-12 | 13 | 14-17 | 18-21 | 6-7 | 8-9 | 10-14 | 15-21 |
| CF adolescents | 10 | 11 | 12-14 | 15-21 | 4-5 | 6-7 | 8-11 | 12-21 |

**Figure Legends:**

**Figure 1:** Percentile plots for anxiety scores for (a) adult men with CF (solid line) and normative men (broken line) (b) adult women with CF (solid line) and normative women (broken line) (c) adult men with CF (solid line) and boys with CF (broken line) and (d) adult women with CF (solid line) and girls with CF (broken line). Normative UK adult data from [21].

**Figure 2:** Percentile plots for depression scores for (a) adult men with CF (solid line) and normative men (broken line) (b) adult women with CF (solid line) and normative women (broken line) (c) adult men with CF (solid line) and boys with CF (broken line) and (d) adult women with CF (solid line) and girls with CF (broken line). Normative UK adult data from [21].


(a)
Men
(b)
Women
(c)
Boys
(d)
Girls
Percentile
Anxiety score
none
mild
moderate
severe
0
20
40
60
80
100
0
3
6
9
12
15
18
21


(a)
Men
(b)
Women
(c)
Boys
(d)
Girls
Percentile
Depression score
none
mild
moderate
severe
0
20
40
60
80
100
0
3
6
9
12
15
18
21