Title: Relationship between depression and exacerbations in chronic obstructive pulmonary disease

Authors: Jennifer K Quint, Ramin Baghai-Ravary, Gavin C Donaldson, Jadwiga A Wedzicha.

    Academic Unit of Respiratory Medicine
    University College London, London UK

Corresponding Author: Prof. J A Wedzicha
    Academic Unit of Respiratory Medicine
    University College London
    Hampstead Campus
    Rowland Hill Street
    London NW3 2PF
    UK
    Tel: +44 207 317 7510
    Fax: +44 207 472 6141
    Email: j.a.wedzicha@medsch.ucl.ac.uk

Short title: Depression and exacerbations in COPD

Funding was provided for this study by a grant from the National Institute of Health, USA; RO1 HL082578-01.

Word count: 3,285

Key words: COPD, depression, exacerbations, exacerbation frequency, SGRQ
Abstract

Background: Chronic obstructive pulmonary disease is associated with exacerbations. Some patients are prone to frequent exacerbations and these individuals have worse quality of life, greater limitation of their daily activity and faster disease progression than patients with less frequent exacerbations.

Methods: We performed a prospective study in a well characterised cohort and assessed whether depression, as assessed by the Centre for Epidemiologic Studies Depression Scale was related to exacerbation frequency, systemic inflammation and various social factors. We also investigated the associations of any increase in depressive symptoms at exacerbation.

Results: Frequent exacerbators had a significantly higher baseline depression score than infrequent exacerbators (17.7 (12.4) and 13.6 (10.0) respectively); p = 0.03. Depressed patients spend less time outdoors; r = - 0.34, p = 0.001 and had worse quality of life as measured by the SGRQ; r = 0.47, p < 0.001. Depression increased significantly in patients from baseline to exacerbation; 14.6 (11.8) and 20.3 (10.4) respectively; p < 0.001.

Conclusions: This is the first study to show a relationship between depression and exacerbation frequency in patients with COPD. The finding that frequent exacerbators are more depressed than infrequent exacerbators is relevant, as exacerbation frequency is an important outcome measure in COPD.

Abstract word count: 199
INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is characterized by chronic airflow limitation that is not fully reversible, progressive and associated with a range of pathological changes in the lung, significant co-morbidities and extra-pulmonary manifestations including physical factors and psychological factors such as anxiety and depression (1). The disease is interspersed with exacerbations; periods of acute symptomatic, physiologic and functional deterioration. At exacerbation pulmonary symptoms worsen, six minute walking distance decreases (2), peripheral muscle weakness worsens (3), and there is a fall in outdoor activity for up to 5 weeks after the onset of the exacerbation (4).

Exacerbations have important consequences for patients and health care providers; a negative impact on health related quality of life (5,6), pulmonary function (7), utilisation of health care resources (8) and survival (9). Some patients are prone to frequent exacerbations and these individuals have worse quality of life (5), greater limitation of their daily activity (4), spend less time outdoors, and have faster disease progression (10,7) than patients with less frequent exacerbations.

Depression is a recognised complication of many chronic diseases, and COPD is no exception (11-13). Some studies have suggested depression is more common in COPD, with the prevalence increasing with increasing severity of disease from 19.6% in mild to moderate disease, to 25% in severe disease (11). Other studies have found a much lower prevalence of depression, similar to that of the general population (14). Recognition of depression is important as it affects quality of life, and identification and intervention in these cases with antidepressants may improve functional capacity
and quality of life (15). However, there is a need for better understanding of the factors associated with depression.

We performed a prospective study in a well characterised cohort and for the first time assessed whether depression was related to exacerbation frequency. We also assessed the relationship between depression and systemic inflammation, various social factors and the associations of any increases in depressive symptoms at exacerbation to see if we could predict which patients become more depressed at the time of an exacerbation.

METHODS

Patient recruitment

One hundred and sixty nine patients from the London COPD study were included over a one year period, (May 2006 to 2007). The recruitment and monitoring of patients in the London COPD study has previously been described, however, this data set has not been previously reported. All patients had COPD as defined by a post-bronchodilator forced expiratory volume in one second (FEV$_1$) to forced vital capacity (FVC) ratio below 70% and a $\beta_2$ agonist reversibility of less than 15% or 200 ml. Patients were excluded if they had other significant respiratory or inflammatory diseases.

Patients were recruited when stable, with no exacerbations in the preceding month. At recruitment daily respiratory symptoms, smoking history, exacerbation history, and drug history were recorded. Information was collected regarding social contacts. Height and weight were measured along with baseline lung function using a
volumetric storage spirometer (Vitalograph 2160). Blood was collected for C-Reactive protein (CRP) and Interleukin-6 (IL-6). This study was approved by the Royal Free Hospital Research Ethics Committee and patients gave written informed consent.

Patients completed a St. George’s Respiratory Questionnaire (SGRQ), an MRC dyspnoea score (16) and a Center for Epidemiologic Studies Depression Scale (CES-D). The SGRQ is designed to measure health impairment in patients with COPD (17). There are several questionnaires validated to assess depressive symptoms; HAD, SDS, MMPI, BDI, most of which also include symptoms of anxiety. Anxiety has been shown to be linked to COPD and as we particularly wanted to concentrate on depression, we chose to use the CES-D. The CES-D is a 20 question questionnaire which assesses the frequency and duration of symptoms associated with depression (18). This score has been validated to measure change and improvements in depressive symptoms. A score of 16 or higher classifies a person as having depressive symptoms, validated with DSM-IV criteria for clinical depression (19). This questionnaire has been used to investigate depressive symptoms in chronic diseases, including COPD (11). The maximum score attainable is 60.

**Exacerbations**

Patients completed daily diary cards, recording any increase in daily respiratory symptoms and hours spent outside the home. They contacted the study team if they experienced an increase in their daily respiratory symptoms and were usually reviewed within 24 hours.
Exacerbations were defined according to our usual definition of two symptoms (one of which must be major), on two consecutive days, or if in the opinion of the attending clinician, the patient had an exacerbation (20). Major symptoms were increased dyspnoea, sputum volume or sputum purulence and minor symptoms increased cough, wheeze, sore throat or coroyzal symptoms. Our definition reflects changes in quality of life (5), inflammation (21), and FEV₁ decline (7).

At an exacerbation visit information was collected on symptom type, duration of symptoms and social contacts. Spirometry was performed and blood taken for IL-6 and CRP. Patients also completed a CES-D. All exacerbations were treated with bronchodilators, antibiotics and / or oral steroids as judged by the clinician. Questionnaires were administered or blood samples taken prior to the initiation of treatment.

**Exacerbation frequency**

Exacerbation frequency was based on the median exacerbation frequency in the cohort (20). Patients were defined as “frequent exacerbators” if they had three or more exacerbations in the preceding year, and “infrequent exacerbators” if they had less than three exacerbations in the previous year. The number of exacerbations was obtained by counting the number of exacerbations in the preceding year recorded on the diary card.

**Time outdoors**

The time outdoors for baseline and exacerbation visits was calculated as the average time spent outdoors from three days before the day the patient attended the clinic, to
three days after. A seven day period was chosen to eliminate any variation due to specific days of the week.

**Patient blood sampling and measurement of inflammatory markers**

Seven millilitres of venous blood was collected and centrifuged at 2000rpm for 10 minutes at 4°C within two hours of collection. The serum was then separated and stored at -80°C until later analysis.

Serum IL-6 was quantified using commercial sandwich ELISA (Enzyme-linked immunosorbent assay) kits (R&D Systems, Abingdon, UK). Serum CRP was measured in our hospital laboratory using an Olympus luminometric analyser. The limit of detection for serum IL-6 was 0.7 pg/ml and for CRP was 0.3 mg/l.

**Statistical analysis**

Data were analysed using SPSS version 11. The Kolmogorov-Smirnov test of normality was applied. Normally distributed data were expressed as mean and standard deviation (SD), skewed data as median and interquartile range (IQR). Skewed data were log transformed to obtain a normal distribution. Comparisons between baseline and exacerbation and between frequent and infrequent exacerbators were made by paired and unpaired t test as appropriate. Pearson correlation was used to assess parametric data, and Spearman rank was used to assess non-parametric correlations. The Chi-Square test was used to assess the relationship between exacerbation frequency and depression. A one way ANOVA was used to look at the relationship between MRC score and hours outdoors. Linear regression analysis was
used to look at confounding factors affecting depression scores. For all statistical tests, \( p \leq 0.05 \) was taken as significant.

To identify the features of depression that changed at exacerbation, we used baseline depression scores and principal component analysis (SPSS 14.0; varimax rotation with Kaiser normalization) to identify five summary groupings that explained the pattern of correlations within the 20 question dataset. The five factors explained 61% of the variance. Questions whose rotated component were >0.5 were considered sufficiently similar to be grouped together. Changes in patient scores between baseline and exacerbation, in these five groups, were averaged and compared by paired t-test. We termed these groups: “depressive feelings” (questions 3,6,10,17,18), “activity” (questions 2,7,11,20), “feelings of self-hatred” (questions 15,19), “reflective feelings” (questions 1,13), and “feelings of positivity” (questions 4,8,12,16).

RESULTS

Baseline patient characteristics

One hundred and sixty nine patients were studied; 95 male and 74 female. The baseline characteristics of the cohort are reported in Table 1, with further subdivision by exacerbation frequency in Table 2. Patients had a mean \( FEV_1 \) of 1.13 l or 47% predicted. The mean CES-D score for all patients was 14.9 (SD 11.1). 15 patients in the cohort (8.9%) had a clinical diagnosis of depression, 13 of whom were on antidepressants, mean CES-D 18.2 (12.4). The mean CES-D for the two patients not on antidepressants was 34.0 (12.7).
Exacerbation frequency and depression

Sixty one patients were classified as frequent exacerbators, and 106 as infrequent exacerbators. 2 patients did not have their exacerbation frequency calculated due to insufficient diary card data. Frequent exacerbators had a significantly higher baseline depression score than infrequent exacerbators (17.7 (12.4) and 13.6 (10.0) respectively); p = 0.03. (Figure 1) When analysing our data using the cut off of clinical depression as a score of 16, we still found exacerbation frequency to be related to CES-D (p = 0.01). 35 % of the infrequent exacerbators scored > 16 at baseline compared to 54% of the frequent exacerbators.

Multiple linear regression analysis confirmed differences observed in CES-D scores between frequent and infrequent exacerbators were not due to confounding factors such as smoking (p = 0.03).

Systemic inflammation and depression

One hundred and forty two patients had CRP measured in the stable state and 155 had plasma IL-6 measured. There was no relationship between baseline CRP or baseline serum IL-6 and depression score; r = - 0.02, p = 0.77 and r = - 0.09, p = 0.25 respectively. However, baseline CRP and serum IL-6 were significantly related; r =0.20, p = 0.02.

SGRQ and Social variables

One hundred and sixty patients completed the SGRQ when stable. There was a significant relationship between worse (higher) Total SGRQ scores and greater CES-D; r = 0.47, p < 0.001. The three domains of the SGRQ were also strongly related to
CES-D; Activity; r = 0.32, p < 0.001, Impact; r = 0.49, p < 0.001 and Symptoms; r = 0.35, p < 0.001 (Figure 2). CES-D also associated strongly with the MRC dyspnoea scores; r = 0.31, p < 0.001. CES-D increased by 1.2 points with a 4 unit measure in Total SGRQ. Multiple linear regression allowing for exacerbation frequency, found SGRQ was independently significantly associated with depression (p<0.001), with a 2.4 unit change in CES-D corresponded to a 4 unit change in SGRQ ($r^2 = 0.3$).

Data on time outdoors was collected on 96 patients at baseline and 45 at an exacerbation visit. Patients who spend less time outdoors were more depressed; r = -0.34, p = 0.001 (Figure 3) and this was related to worse quality of life as measured by the SGRQ; r = -0.22, p = 0.03.

Women were more depressed than men with a mean CES-D of 18.3 (12.6) compared to 12.2 (9.0) for men; p = 0.001. Depression scores were higher in those who lived alone compared to those co-habiting; 18.9 (12.6) and 11.6 (8.6) respectively; p < 0.001. CES-D also related to the number of people indoors, with individuals being less depressed the more people they live with; r = -0.21, p = 0.007, and specifically less depressed if they live with a spouse; p < 0.001. Sex, exacerbation frequency, living alone and MRC dyspnoea score were all independently related to CES-D (p < 0.001, p = 0.009, p = 0.001 and p = 0.005 respectively).

Depression scores were similar in current and ex-smokers; (53 current smokers and 116 ex-smokers) p = 0.3. CES-D was not related to pack years smoked; r = 0.58, p = 0.46.
Exacerbation characteristics
Seventy patients; 39 frequent and 31 infrequent exacerbators completed the CES-D at an exacerbation visit. The baseline characteristics of these patients are in Table 3. The CES-D increased significantly from baseline to exacerbation; mean CES-D 14.6 (11.8) and 20.3 (10.4) respectively; p < 0.001 (Figure 4). In the frequent exacerbators the baseline CES-D score increased on average by 5.0 (9.4) points at exacerbation, and in the infrequent exacerbators the CES-D increased on average by 6.7 (9.4) at exacerbation (p = 0.43). 42% of the cohort scored above 16 on the CES-D at baseline, and 60% at exacerbation.

Exacerbation inflammatory markers and depression
CRP and IL-6 was measured in 35 patients at an exacerbation visit. CRP and IL-6 increased from baseline to exacerbation; p = 0.001 and p = 0.07 respectively. The increase in CRP correlated with the increase in IL-6; r = 0.62; p < 0.001 but not to the change in CES-D; r = 0.12; p = 0.48 and r = 0.25, p = 0.11 respectively. Exacerbation CRP and IL-6 levels were not related to the CES-D exacerbation score; r = - 0.01, p = 0.95 and r = -0.08, p = 0.66 respectively.

The mean duration of exacerbation symptoms was 13.2 days (9.6). There was no relationship between the change in depression score from baseline to exacerbation and the length of the exacerbation, the time taken to present for treatment of the exacerbation, symptom count, or individual symptoms at exacerbation. There was also no relationship between exacerbation depression score and time to the next
exacerbation. Only 2 patients were hospitalised at exacerbation in the cohort and so we were unable to study the effect of hospitalisation and depression.

No baseline factors e.g. FEV$_1$, FVC, age, inflammatory markers, predicted the change in CES-D from baseline to exacerbation. There were no specific symptoms at exacerbation or pattern of symptoms at presentation of exacerbation associated with greater risk of depressive symptoms.

**Principal component analysis groupings**

Scores in all five subgroups of the PCA changed significantly from baseline to exacerbation except for feelings of self-hatred; difference = 0.05, $p = 0.46$. Feelings of “positivity” and “activity” increased at exacerbation; difference of - 0.30, $p = 0.02$ and difference of - 0.41, $p = 0.001$ respectively. “Reflective feelings”, and “depressive feelings” increased; difference of - 0.48, $p = <0.001$, and difference of - 0.25, $p = 0.06$ respectively. The largest change between baseline and exacerbation was seen in reflective feelings (figure 5).

**DISCUSSION**

This is the first study to show a relationship between depression and exacerbation frequency in patients with COPD. The finding that frequent exacerbators are more depressed than infrequent exacerbators is crucial, as exacerbation frequency is an important outcome measure in COPD. Patients prone to frequent exacerbations have faster decline in lung function (10,7) reduced physical activity (4), impaired health
status (5) and faster disease progression. Frequent exacerbators also have increased mortality (22), more frequent hospitalisations and thus increased health care costs.

Depression affects how individuals utilise health care, and comply with and respond to treatment. Therefore, identifying and treating depression may help to maximise patient outcome and quality of life (15). Early presentation to health care professionals can affect the outcome of an exacerbation and reduce hospitalisation (23). Depressed patients may be less likely to present early for treatment, or to report their exacerbations at all.

Although most COPD exacerbations are treated in the community, they are an important cause of hospitalisation and are responsible for around 10% of all acute medical admissions (24). Depression is a strong independent predictor of mortality in COPD patients admitted to hospital for an acute exacerbation (25), and depression may be a risk factor for frequent admissions (26,27) as well as being a frequent exacerbator (28). We were not able to study the effect of depression on hospitalisation in our cohort as so few patients were hospitalised during the study.

We found that depression is related to worse quality of life, higher MRC score, less time spent outdoors, female sex (12), and social isolation (11). Increased MRC dyspnoea score which relates to perceived symptoms of dyspnoea were strongly related to depressive symptoms, and less time spent outdoors. Previous studies have shown that awareness of dyspnoea is higher in those who have symptoms of anxiety and depression (29,30). Higher depression scores may lead more patients to feel breathless, or to perceive changes in their symptoms more readily. As depression was
closely related to MRC breathlessness score, it is likely patients underestimate their abilities and do not go out when they are depressed. Current lack of recognition and treatment of depression may have implications for uptake and completion of pulmonary rehabilitation, self management plans or use of community services. Patients who score MRC 5 have less significant improvement in pulmonary rehabilitation and a higher dropout rate (31,32) and this may be due to unrecognised depression. This data suggests we should be routinely screening and treating frequent exacerbators for depression if appropriate, and addressing psychological aspects prior to rehabilitation. Awareness of social isolation may also partly explain the benefits of pulmonary rehabilitation.

Depression increased acutely at the time of an exacerbation. Factors occurring at exacerbation which raise the CES-D score above 16 are likely to be of clinical relevance. Therefore we believe that increased depression at exacerbation is clinically important. Whether the increase in CES-D at the time of exacerbation was due purely to psychological factors, or to physical limitations imposed by the exacerbation is difficult to ascertain. Nonetheless, the difference between the frequent and infrequent exacerbators indicates the psychological impact of an exacerbation is greater on those who are less depressed, i.e. the infrequent exacerbators. Thus it is essential not to overlook this group, in whom psychological intervention at exacerbation may particularly be of benefit.

Detailed analysis of groups of specific questions in the CES-D showed that the increased depression seen at exacerbation was mostly due to introversion and reflection. Patients were “bothered by things that do not usually bother them”, and
“talk less than usual.” There is often a negative emotional balance associated with COPD; patients feel guilty they did not give up smoking, they feel that there is a stigma attached with the disease and often have feelings of frustration, fear and hopelessness (33). They also have a fear of dying and the increased depression seen at exacerbation may be patients reflecting about death at this time.

There was no relationship between markers of systemic inflammation and depression in COPD patients. Depression has been shown to be linked with systemic inflammation in other diseases such as cancer (34), suggesting that the mechanism driving depression in COPD does not have an inflammatory basis. This is consistent with the observation that depression was not linked to severity of disease as defined by GOLD staging. Systemic inflammation has been shown to be linked to GOLD staging (35), and CRP has also been shown to be related to SGRQ (35). Previous studies have reported depression to be more strongly related to functional status than COPD severity and other studies have shown depression to be more common in severe disease (14).

This study was conducted in a well characterised cohort of COPD patients, with robust data for exacerbation frequency. It is possible our cohort was less depressed than other populations studied as they volunteered to attend frequent outpatient appointments and fill in daily diary cards. However the prospective nature of the study, accurate calculations of exacerbations frequencies over time from completion of daily diary cards and prompt presentation at exacerbations add to the validity, strength and uniqueness of the depression data in this study. This study was not designed to look at clinically meaningful changes in depression, but we estimated that
a change in 1.2 points in the CES-D would be associated with a 4 point change in SGRQ.

This study has shown for the first time that frequent exacerbators are more depressed than infrequent exacerbators. Depression was more common in women, those with little social contact and negatively affected quality of life. The increased depressive symptoms seen at exacerbation reflect patients increased introversion and contemplation. Understanding the nature of depressive symptoms and treating them is important if we are to improve a patient’s quality of life, maximise healthcare utilisation and treatment outcomes.

Acknowledgements: This research was funded by a grant from the National Institute of Health USA; RO1 HL082578-01.
References


Legends to Figures

Figure 1: Baseline depression scores in infrequent and frequent exacerbators.

Figure 1

\[ p = 0.03 \]

Figure 2: Relationship between SGRQ and depression. a) Worse quality of life (higher Total SGRQ scores) is related to depression; \( r = 0.47, p < 0.001 \). All subgroups of the SGRQ; b) impact, c) activity and d) symptom domains are all strongly related to depression; \( r = 0.49, p < 0.001, r = 0.32, p < 0.001, \) and \( r = 0.35, p < 0.001 \) respectively.

Figure 2

(a)
Figure 3: Relationship between depression and time spent outdoors.

Figure 3

$r = -0.34, p = 0.001$
Figure 4: Depression score at baseline and exacerbation.

Figure 4

$p < 0.001$
Table 1 - Baseline Characteristics, SGRQ and depression scores of 169 patients studied.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>70.9</td>
<td>8.6</td>
</tr>
<tr>
<td>Hours outdoors</td>
<td>3.4</td>
<td>2.3</td>
</tr>
<tr>
<td>FEV1 (litre)</td>
<td>1.1</td>
<td>0.5</td>
</tr>
<tr>
<td>FEV1 % predicted</td>
<td>47.0</td>
<td>18.9</td>
</tr>
<tr>
<td>FVC (litre)</td>
<td>2.4</td>
<td>0.9</td>
</tr>
<tr>
<td>BMI (kgm(^2))</td>
<td>26.3</td>
<td>5.5</td>
</tr>
<tr>
<td>Pack years smoking</td>
<td>48.5</td>
<td>33.7</td>
</tr>
<tr>
<td>SGRQ total</td>
<td>51.0</td>
<td>17.6</td>
</tr>
<tr>
<td>activity</td>
<td>67.1</td>
<td>22.1</td>
</tr>
<tr>
<td>impact</td>
<td>38.1</td>
<td>18.7</td>
</tr>
<tr>
<td>symptoms</td>
<td>62.1</td>
<td>20.1</td>
</tr>
<tr>
<td>MRC Dyspnoea score</td>
<td>2.9</td>
<td>1.2</td>
</tr>
<tr>
<td>Depression score</td>
<td>14.9</td>
<td>11.1</td>
</tr>
<tr>
<td></td>
<td>Frequent exacerbators n = 61</td>
<td>Infrequent exacerbators n=106</td>
</tr>
<tr>
<td>--------------------------</td>
<td>------------------------------</td>
<td>-------------------------------</td>
</tr>
<tr>
<td>Age (years)</td>
<td>70.7 (8.5)</td>
<td>71.1 (8.5)</td>
</tr>
<tr>
<td>Hours outdoors</td>
<td>3.4 (1.9)</td>
<td>3.5 (2.5)</td>
</tr>
<tr>
<td>FEV1 (litre)</td>
<td>1.0 (0.4)</td>
<td>1.2 (0.5)</td>
</tr>
<tr>
<td>FEV1 % predicted</td>
<td>41.7 (15.3)</td>
<td>49.7 (20.0)</td>
</tr>
<tr>
<td>FVC (litre)</td>
<td>2.2 (0.8)</td>
<td>2.53 (0.9)</td>
</tr>
<tr>
<td>BMI (kgm(^{-2}))</td>
<td>25.9 (4.7)</td>
<td>26.5 (6.0)</td>
</tr>
<tr>
<td>Pack years smoking</td>
<td>49.2 (28.3)</td>
<td>48.4 (36.1)</td>
</tr>
<tr>
<td>SGRQ total</td>
<td>59.8 (14.5)</td>
<td>46.0 (17.2)</td>
</tr>
<tr>
<td>activity</td>
<td>75.9 (16.4)</td>
<td>62.3 (23.2)</td>
</tr>
<tr>
<td>impact</td>
<td>46.7 (18.0)</td>
<td>33.2 (17.3)</td>
</tr>
<tr>
<td>symptoms</td>
<td>71.9 (15.2)</td>
<td>56.6 (20.4)</td>
</tr>
<tr>
<td>MRC Dyspnoea score</td>
<td>3.2 (0.9)</td>
<td>2.8 (1.2)</td>
</tr>
<tr>
<td>Depression score</td>
<td>17.7 (12.4)</td>
<td>13.6 (10.0)</td>
</tr>
</tbody>
</table>
Table 3 – Baseline characteristics of the 70 patients in the Exacerbation subgroup

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depression score baseline</td>
<td>14.6</td>
<td>11.8</td>
</tr>
<tr>
<td>Depression score exacerbation</td>
<td>20.3</td>
<td>10.4</td>
</tr>
<tr>
<td>Hours outdoors baseline</td>
<td>3.7</td>
<td>2.3</td>
</tr>
<tr>
<td>Hours outdoors exacerbation</td>
<td>2.8</td>
<td>2.4</td>
</tr>
<tr>
<td>FEV1 (litre)</td>
<td>1.0</td>
<td>0.4</td>
</tr>
<tr>
<td>FEV1 % predicted</td>
<td>41.2</td>
<td>15.8</td>
</tr>
<tr>
<td>FVC (litre)</td>
<td>2.2</td>
<td>0.8</td>
</tr>
<tr>
<td>PEF (litre / min)</td>
<td>230</td>
<td>69</td>
</tr>
<tr>
<td>SaO2 (%)</td>
<td>95.0</td>
<td>1.9</td>
</tr>
</tbody>
</table>